

ARSI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF PUBLIC HEALTH



Incidence and Predictors of Tuberculosis among HIV Positive Adults on Antiretroviral Therapy at Adama Hospital Medical College, Southeast Ethiopia: A Retrospective Follow-up Study.

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ABSTRACT

Background: Although antiretroviral treatment (ART) significantly reduces the risk of tuberculosis (TB), the risk remains higher in HIV infected patients than the general population. Consequently, tuberculosis preventive treatment (TPT) is implemented alongside ART to further reduce the incidence of TB in this population. Previous research has not adequately addressed viral load status predictor influences TB incidence among HIV-positive adults.

Objective: To determine the incidence and predictors TB among Adult PLHIV on ART at Adama Hospital Medical College, Ethiopia, 2025.

Methods: A hospital-based retrospective cohort study was conducted at Adama Hospital Medical College with a total of 640 randomly select records of ART enrolled adults from May 01, 2015 to May 30, 2025. Data was collected by kobo toolbox, exported to an Excel sheet, and then imported to STATA version 17 for analysis. Bivariate and multivariable Cox proportional hazards model was used to identify the predictors of tuberculosis incidence. Adjusted Hazard Ratio with 95% confidence intervals was determined the strength and p-value < 0.05 was declared statistical significance.

Results: In this study, a total of 640 participants included in the study, 119(18.59%) of which were developed tuberculosis, and the incidence rate was 4.18 per 100 person- years with a (95% CI: 3.49–4.99). The mean time to develop tuberculosis of HIV positive adults was 8.3 years. Being WHO clinical stage III (AHR: 2.25; 95% CI 1.11-4.57) and WHO clinical stage IV (AHR = 3.50; 95% CI: 1.72–7.12), not received TPT (AHR: 1.80; 95% CI 1.23-2.64), poor ART adherence (AHR: 1.98; 95% CI 1.18-3.30) and viral load test >1000 copies/ml (AHR: 1.80; 95% CI 1.17-2.76) were predictors of incidence of tuberculosis among HIV positive adults.

Conclusion: The study found that the overall incidence of tuberculosis among adult HIV infected was high. Adults who had WHO clinical stage III and IV, poor adherence, not received TPT and high viral load test were statistically significant with incidence. Therefore, health care provider shall strength the implement regular viral load monitoring and ensure that ART adherence support programs to improve treatment outcomes.

Keywords: Antiretroviral treatment, HIV-positive Adults, Incidence, Predictors, Ethiopia

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ACRONYMS AND ABBREVIATIONS

ART	Antiretroviral Therapy
CDC	Centers for Diseases Control and Prevention
FMOH	Federal Ministry of Health
HIV	Human Immune Virus
6H	6 months of daily isoniazid monotherapy
3HP	Three Months of Weekly Isoniazid Plus Rifapentine
3HR	Three Months of Daily Isoniazid Plus Rifampicin
IPT	Isoniazid Preventive Therapy
MDR-TB	multidrug-resistant tuberculosis
LTBI	Latent TB Infection
ORHB	Oromia Regional Health Bureau
OPDs	Outpatient Departments
PLHIV	People Living with Human Immune Virus
RCT	Randomized Controlled Trial
SSA	Sub-Sahara African
TB	Tuberculosis
TPT	Tuberculosis Preventive Therapy
UNAIDS	Joint United Nations Program on HIV/AIDS
WHO	World Health Organization

1.INTRODUCTION

1.1. Background

Tuberculosis (TB) is a major world health problem which affect one fourth of the world's population is estimated to have been infected and public health concern in general and in people lives with Human Immune virus (PLHIV). There were an estimated 36 million people living with HIV globally in 2017, with approximately one third of these people being co-infected with TB(1).

People living with HIV (PLHIV) are at a significantly higher risk of developing tuberculosis (TB) because HIV weakens the immune system, making it less effective at fighting off the Mycobacterium tuberculosis bacteria that cause TB. This makes it harder for the immune system to prevent either a new infection from becoming active or an existing latent infection from reactivating and becoming active TB(2).

In 2023, an estimated 8% of all incident TB cases globally occurred in PLHIV, but this proportion rises to 18–25% in high-HIV-burden countries of sub-Saharan Africa (SSA)(3, 4). Ethiopia ranks among the 30 high TB/HIV burden countries, contributing roughly 9% of global TB/HIV co-infected cases (Federal Ministry of Health(5).

The use of isoniazid preventive therapy as a TB averting strategy was first conceptualized by WHO in 1998, particularly targeting PLHIV who live in areas where there is a high frequency of TB (6). Isoniazid Preventive Therapy (IPT) reduces the threats of an early occasion of TB or its reoccurrence(6).

In parallel with the WHO recommendation, the Ethiopian TB, TB/HIV, medicine-resistant TB (DR-TB), and leprosy guidance guideline encourage the use of IPT. According to the guideline, children ≥ 12 months, adolescents, and adult HIV/AIDS cases should take TB preventive therapeutic (TPT), including IPT (7).

The Ethiopian government, under its National Strategic Plan (NSP) for Tuberculosis and Leprosy (TBL) 2021–2026, continues to focus on integrated TB/HIV service delivery to reduce morbidity and mortality among people living with HIV (PLHIV). Key ongoing and reinforced

strategies include decentralizing care, strengthening referral systems, and expanding tuberculosis preventive treatment (TPT)(8).

1.2.Statement of the problem

About one third of the world population is estimated to be latently infected with Mycobacterium tuberculosis and hence at threat of developing active TB cases(9). The TB epidemic has been enhanced by HIV co-infection; one accelerates the other's impact. HIV and TB are two of humanity's most challenging infectious diseases, placing a considerable burden on healthcare systems worldwide. Both pose significant global public health challenges, contributing substantially to morbidity and mortality worldwide(10).The risk of developing TB is between 20 to 37 times greater in HIV infected individuals when compared to immune competent individuals (11).

According to WHO 2017 report, there are 10.4 million incident cases of Tuberculosis, with out of which an estimated 1.04 million (10%) occurring in HIV positive people. PLHIV are 21 times more likely to acquire active TB than the rest of the world population(12). In 2018, 10 million new cases of tuberculosis reported, with 8.6% of them occurring among HIV positive individual. Thus, PLHIV is 19 times more likely to developing active TB than the general population (13, 14). In 2019, an estimated 1.4 million people worldwide died from TB, including 208,000 PLHIV (15). In 2021, there were 7.5 million newly diagnosed and officially notified TB cases globally, with 0.63 million individuals co-infected with HIV (16). Most of the people who develop TB disease each year are in 30 high TB burden countries(17).

The African and South-East Asia Regions accounted for 82% of the combined total of TB deaths in HIV-negative and HIV-positive people(18)According to WHO, there were an estimated 0.9 million new cases of TB amongst people who were HIV-positive, 72% of whom were living in Africa(19). In SSA, the incidence rate among children and adolescents was 2017 cases per 100,000 patient years (20).while the incidence rate among HIV-infected patients before and after starting combined ART was 10.5 per 100 person-years and 5.4 per 100 person-years, respectively(20).Sub-Saharan Africa represented for 75% of the global HIV/AIDS prevalence(15).

Ethiopia is one of the countries afflicted by both conditions. According to 2021 global TB report, the country has believed 132 cases per 100,000 people. The country is one of the world's high burden countries for both TB and TB/HIV (7, 21). It remains to be among the 30 countries reported with high burden of TB, TB/HIV and DR-TB for 2015 to 2020. Ethiopia is also one of the top 14 nations with triple burdens of tuberculosis, TB/HIV, and MDR-TB(22). The projected incidence of all kinds of TB in Ethiopia, in 2019, was 140/100,000 population, with 111,039 TB cases reported(22).

According to the CDC, the incidence rate of TB in Ethiopia in 2017 was 164 cases per 100,000 people with about 7% of those infected with HIV, TB incidence ranged from 3.1–8.6 cases per 100 persons year. Despite the reported decline trends of HIV incidence rate there is a huge pool of HIV positive population directly drives the TB epidemic in Ethiopia, whereby 8% of TB patients were found to have HIV co-infection(23).

Tuberculosis remains the leading cause of hospital admission and mortality among people living with HIV. The prevalence of HIV among TB patients is 7.34% with significant regional variations from 0.7% in Oromia to 14.5% in Afar(24).

Previous studies identified several predictors that contribute to the TB incidence among HIV positive adults. low CD4 count, advanced WHO stage, low BMI, anemia, poor ART adherence, non-receipt of IPT, being bedridden, lack of formal education, large family size, and substance use were predictors of TB incidence among HIV positive adults(25-29).

The Ethiopia Federal Ministry of Health has implemented several interventions to address the incidence of tuberculosis (TB) among HIV-positive patients. Key initiatives include integrating TB and HIV services to ensure comprehensive care, enhancing early detection through active screening in healthcare facilities, and providing Isoniazid Preventive Therapy (IPT) to eligible individuals. Additionally, the Ministry encourages adherence to antiretroviral therapy (ART) and strengthening surveillance systems and ensuring the availability of diagnostic tools and treatment options are also critical components of their strategy to reduce TB incidence in this vulnerable group (30, 31).

Previous research has not adequately addressed viral load status predictor influences on TB incidence among HIV-positive adults. Therefore, this study was aimed to assess the incidence

and predictors of TB among HIV positive adults at Adama Hospital Medical College, Southeast Ethiopia.

1.3. Significance of the study

Firstly, the study population will be beneficiary from the result of this study and it is helpful for the Adama Hospital and Medical college planner and Health Bureau. The result of this study will also help Adama Administrative city health office department to draft or rearrange their plan regarding the incidence of tuberculosis and TPT supply and administration practice among people live with HIV and on ART of the Adama administrative city clients.

This study will have a positive effect in IPT implementation; inform policy makers and program developers working at different levels of TB controlling measures, and also health care experts working in TB control and prevention measures.

The finding of this study can be an input for ORHB and Federal ministry of health policy designers to include the TPT program in their future plan and also for other researchers for future further research on the incidence and predictors of tuberculosis among ART patient and related studies. This study will have a positive effect in IPT implementation; inform policy makers and program developers working at different levels of TB controlling measures, and also health care experts working in TB control and prevention measures.

2. LITERATURE REVIEW

2.1 Incidence of Tuberculosis among HIV positive adults

A study conducted in India indicated that the incidence rate of tuberculosis was 4.39 cases (95%CI 3.86-5.00) per 100 person-years (31). A study conducted among people with HIV on antiretroviral therapy in the United Kingdom showed that tuberculosis incidence rate was 0.6 per 1000 person-years (32).

A study conducted among HIV-infected adults after initiation of antiretroviral therapy in Nigeria revealed that TB incidence after ART initiation was 0.57 per 100 person-years (33). A study conducted among HIV Infected Patients in Northern Tanzania indicated that the overall TB incidence rate of 2.08 per 1,000 person-years (34). A study done in Central African Republic showed that the overall incidence of TB was 15.37 per 100 PLHIV-years(35) .

A systematic review and meta-analysis study conducted in Sub-Saharan Africa revealed that the overall pooled incidence rate of tuberculosis in HIV-infected people was 3.49 per 100 person-years (95% CI: 2.88–4.17) (36). A study conducted in Debre Markos referral hospital, Northwest Ethiopia showed that the overall incidence rate of 6.19 cases per 100 PY (95% CI: 4.83–7.95) (25). A study conducted among adult patients with HIV attending HIV care in North-east Ethiopia showed that the overall incidence density of TB was 8.6 per 100 PY of observation (37).

A study conducted in Gurage zone, South Ethiopia showed that overall incidence rate was 4.79/100 person-year (PY) (38). Another study conducted among Adult PLWHA at Public Health Facilities of Hawassa City reported that the overall incidence density of TB was 8.79 per 100 person-year (PY) (27).

A systematic review and meta-analysis study done in Ethiopia revealed that the overall pooled incidence rate of TB per 100-person year observation (PYO) among HIV-infected patients after initiation of ART therapy was 4.8(95% CI 3.69–5.83) (39). A study conducted among HIV-positive individuals in Addis Ababa, Ethiopia revealed that TB incidence density rate was 6.82/100 person-years(40). Other, study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that the incidence rate in

this cohort was found to be 4.84 per 100-person year(28) .Similarly study conducted among adult HIV/AIDS patients on ART at public hospitals in East and Horro Guduru Wollega zones, West Ethiopia showed that the incidence rate of TB reoccurrence was 6.8 (95%CI: 5.6–8.4) per 100 person-years (41).

2.2 Predictors related to TB incidence

2.2.1 Socio-demographic factors

A study conducted in India revealed that being male and urban residence were associated with higher risk of tuberculosis independent of ART regimen(42). A study conducted in Addis Ababa, Ethiopia indicated that large family size, was significantly associated with TB incidence (40). A study conducted in Hawassa, Southern Ethiopia found that not having formal education, was independently predicted tuberculosis occurrence (27).

2.2.2 Clinical related factors

A study conducted in Debre Markos, Northwest Ethiopia showed that base line Hemoglobin < 10 g/dl was associated with increased risk of tuberculosis(25). A study conducted in Northeast Ethiopia revealed that hemoglobin below 11 g/dL, was significant for the incidence of TB(26).

A study conducted in Debre Markos, Northwest Ethiopia showed that ambulatory/bedridden patients at enrolment was associated with increased risk of tuberculosis(25). A study conducted in Northeast Ethiopia revealed that being bedridden was significant for the incidence of TB(37). A study conducted in Hawassa, Southern Ethiopia found that being bed ridden was independently predicted tuberculosis occurrence(27). A study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that being bedridden was independent predictor for the incidence of TB among HIV positive patients (28).

A study conducted in Addis Ababa, Ethiopia indicated that lower baseline CD4 was significantly associated with TB incidence(40). A study conducted in Hawassa, Southern Ethiopia found that CD4 count <50 cell/ul was independently predicted tuberculosis occurrence(27). A study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that CD4 count<200 was independent predictor for the incidence of

TB among HIV positive patients(28). A study conducted in India revealed that CD4+ counts < 350 cells/ was associated with higher risk of tuberculosis independent of ART regimen (42).

A study conducted in Northeast Ethiopia revealed that previous TB disease, was significant for the incidence of TB(37). A study conducted in Hawassa, Southern Ethiopia found that past TB history was independently predicted tuberculosis occurrence (27).

A study conducted in Northeast Ethiopia revealed that being underweight (body mass index (BMI) <18.5 kg/m²), was significant for the incidence of TB (26). A study conducted in Addis Ababa, Ethiopia indicated that baseline body mass index <18.5 kg/m², was significantly associated with TB incidence(40). A study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that underweight was independent predictor for the incidence of TB among HIV positive patients (28).

A study conducted in Northeast Ethiopia revealed that being in WHO clinical stages III and IV was significant for the incidence of TB (26). A study conducted in Hawassa Southern Ethiopia found that base line WHO clinical stage IV was independently predicted tuberculosis occurrence (27).A study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that baseline WHO stage three or four was independent predictor for the incidence of TB among HIV positive patients(28).

2.2.3 Treatment related factors

A study conducted in Debre Markos Northwest Ethiopia showed that taking Isoniazid Preventive Therapy (IPT) were protective factors of TB occurrence (25). A study conducted in Addis Ababa, Ethiopia indicated that taking isoniazid prophylaxis treatment was significantly associated with TB incidence(40). A study conducted in Addis Ababa found that not taking isoniazid prophylaxis therapy was independent predictor for the incidence of TB among HIV positive patients (28). A study conducted in Northeast Ethiopia revealed that taking isoniazid preventive therapy was significant for the incidence of TB(26). A study conducted in Gurage Zone Southern Ethiopia showed that treatment failure was increases the TB incidence (38).

2.2.4 Behavioral related factors

A study conducted in Debre Markos, Northwest Ethiopia showed that having fair or poor ART adherence were associated with increased risk of tuberculosis (25). A study conducted in Addis Ababa among patients enrolled in Anti-Retroviral Therapy after universal test and treat program found that poor adherence was independent predictor for the incidence of TB among HIV positive patients(28). A study conducted in Hawassa, Southern Ethiopia found that substance use was independently predicted tuberculosis occurrence (27).

2.3 Conceptual Framework for TB Incidence

After reviewing different literatures about predictors of TB incidence among HIV positive adults, the following conceptual frame work is adapted and showing the relationship between treatment, behavioral, sociodemographic and clinical related predictors by broken line and association between dependent and independent variables by solid line.

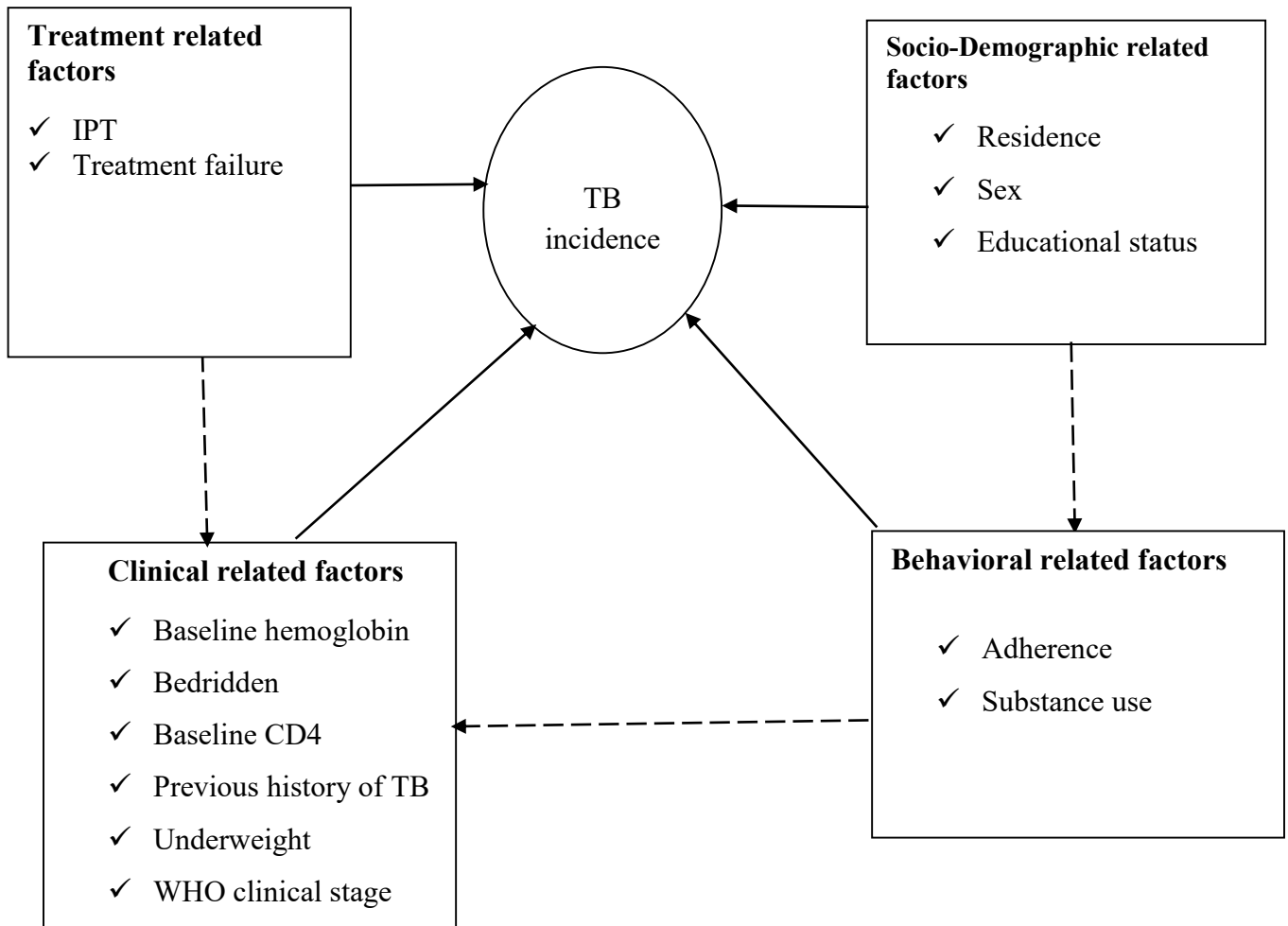


Figure 1: Conceptual framework for TB incidence and predictors among a HIV positive adult on ART(25-29).

3. OBJECTIVES

3.1.General Objective

- To assess incidence and predictors of Tuberculosis among HIV Positive Adults on Antiretroviral Therapy at Adama Hospital Medical College, Southeast Ethiopia 2025.

3.2.Specific objectives

- To determine incidence of Tuberculosis among HIV Positive Adults on Antiretroviral Therapy at Adama Hospital Medical College, Southeast Ethiopia 2025.
- To identify predictors of Tuberculosis incidence among HIV Positive Adults on Antiretroviral Therapy at Adama Hospital Medical College, Southeast Ethiopia 2025.

4. METHODS AND MATERIALS

4.1. Study setting

The study was conducted in Adama Hospital Medical College located at Adama city which located at 99 km Southeast of Addis Ababa, the capital city of Ethiopia and is an administrative center for East Shoa Zone in Oromia Regional State. Adama Hospital Medical College was one of the first three hospitals in Oromia that started providing ART services since 2005. The ART case team in the hospital comprised of ART trained physicians; ART trained nurses, pharmacist, laboratory technicians, data clerks, and drug adherence counselors monitoring and evaluation. Since the start of HIV care, the hospital has providing ART service for around 24,027 patients who came from different areas and from this 15355 were adults. Of this, 2961 HIV infected adults were enrolled into ART clinic between May 01, 2015 and May 30, 2025. A total of 7594 HIV infected people currently on ART; of these 7483 HIV infected adults(43). There are 7 outpatient clinics such as 3 refills for adult, 1 refill for pediatric, 1 refill for high viral load, 1 refill for new patient and 2 refills for acute care. These unit provide ART service in the hospital with average visit of 1800 patients to per month. Patient's information's were recorded both in electronic record systems and paper chart.

4.2. Study Design and Period

A retrospective cohort study design was employed among HIV positive adults who were enrolled in the ART clinic at Adama Hospital Medical College from May 30, 2015, and May 30, 2025.

4.3. Source and study population

4.3.1. Source population

All HIV positive adults who were enrolled in the ART clinic at Adama Hospital Medical College were the source population.

4.3.2. Study population

All HIV positive adults who were enrolled ART clinic at Adama Hospital Medical College from May 01, 2015 to May 30, 2025.

Inclusion criteria: All HIV-infected adult patients aged 15 years or older who were on ART follow-up for at least one years were included in the study.

Exclusion criteria: HIV positive adults with incomplete chart recording during the follow-up period, particularly critical information like TB outcome status, date of the event, or censored reporting were excluded from the study.

4.4. Sample size determination and Sampling procedures

4.4.1. Sample size determination

The sample size was determined for Cox proportional regression by using the Schoenfeld formula for survival analysis in STATA statistical package, Version 17 based on considering the following assumptions:

$$E = \frac{(Z\alpha/2 + Z\beta/2)^2}{P1P2(\ln HR)^2}$$

The total sample size is calculated by: $n = \frac{E}{Pr(E)}$

Where E=number of required events,

- ✓ n=sample size,
- ✓ HR is hazard ratio of selected covariates,
- ✓ p1 is proportion of subjects under exposure group,
- ✓ p2 = 1 – p1
- ✓ P (E) is probability of an event from previous study=16.9% (47)
- ✓ Significance level (α) (two-sided)=0.05, $Z\alpha/2 = 1.96$
- ✓ Power = 80%; $\beta = 0.2$, $Z\beta/2 = 0.84$
- ✓ Variability (SD) of 0.5
- ✓ Proportion of withdrawal 0.1

From previous study done in Debre Markos referral hospital, Northwest Ethiopia by taking Hazard Ratio for covariates that predictors of incidence of tuberculosis among HIV-positive adults, the sample size calculation was summarized in the following table by using STATA version 17 (Cox model).

Table 1: Sample size calculations for predictors of incidence of tuberculosis among HIV-positive adults at Adama Medical College Hospital, Southeast Ethiopia 2025.

S/N	Predictor variables	AHR	P-event	Event	Sample size	References
1	Being ambulatory and bedridden	1.8	0.169	91	598	(47)
2	WHO stage III and IV	2.1	0.169	58	375	
3	Poor adherence	2.16	0.137	53	430	(29)
4	Body mass index <18.5 kg/m ²	2.42	0.137	41	327	

The largest sample size, n=598 was selected to address the study's overall objectives out of the sample sizes determined from various predictors. Finally, a sample of 658 patients was included in the study after adding 10% of the nonresponse rate.

4.4.2. Sampling procedures

In Adama Hospital Medical College, a total of 2961 medical records of adult patients who started ART between May 1, 2015 to May 30, 2025, were identified from the ART registration logbooks. The sampling frame was created from these records. A simple random sampling technique was used to select 658 medical records using a computer-generated method. The selected medical records were analyzed retrospectively for the ten-year period from May1, 2015 to May 30, 2025.

4.5. Study variables

4.5.1. Dependent variables

Incidence of tuberculosis (Event/censored).

4.5.2. Independent variables

- ✓ The independent (predictor) variables of this study are baseline CD4, baseline viral load, Hemoglobin level, WHO clinical stage, treatment adherence, ART initiation time, Substance use, age, sex, level of education, body mass index (BMI), and TPT initiation time.

4.6. Operational definition

Incidence of tuberculosis rate: was calculated by dividing the number of HIV-positive adults who develop TB by the total year observation and multiplying it by 100(44).

Event of interest in this study, is defined as any form of TB diagnosed clinically or radiographically and confirmed by laboratory examinations or by patients who empirically started anti-TB treatment after enrolment(45).

Censored: Lost, drop out, transfer out, died of other causes or completed study period before developing tuberculosis(25).

Follow-up time: -Time from the initiation of ART to an event or censor occurs(25).

Survival time: the length of time in years followed starting from initiation of ART to event or censor occurs (25).

4.7. Data collection procedures

Data was collected by kobo toolbox after structured and pretested data-abstraction tool, adapted from ARV-therapy patient intake forms, follow-up charts, registers, and previous studies. The tool was captured socio-demographic, clinical, behavioral and treatment-related factors. The data abstraction tool was prepared in English. Two BSc nurses, who have experience working in the ART unit, were selected for data collection. Additionally, one MPH were assigned as supervisors to oversee the entire data collection process. Data collection was involved reviewing the medical records of adult patients who started ART between May1, 2015 and May 30, 2025. Charts were retrieved using the patient's registration number, which can be located in the electronic database. A data clerk was assisted the data collection team by identifying the corresponding medical charts. If information were missed from the medical records, it was cross-checked using other relevant registration books, such as the ART registration book, and HIV-positive tracking registration book.

4.8. Data quality assurance

Before conducting the actual study, the tool was pretested among 33 (5%) medical records in Dera health center which is located 18 kilometers away from Adama Hospital Medical College to check the consistency of the abstraction tool and the necessary modification were made on the final version of the data abstraction format to ensure the agreement of the data abstraction format

with the need of the study. Data collectors and supervisors was trained for one day on objectives of the study, how to select study participants card, how to keep confidentiality of information, the contents of the tool and on kobo toolbox android application by the principal investigator. The supervisor was conducted a day-to-day follows up during the whole period of data collection. Every day after data collection each checklist were reviewed and checked for completeness by the supervisors and the necessary feedback was given to the data collectors to the next day. The overall activity was supervised by the principal investigator of the study.

Missing data are unavoidable in epidemiological and clinical research, but their potential to undermine the validity of research results has often been overlooked in the medical literature. This data has incomplete records for height (n=20, 3%), viral suppression (n=25, 3.9%), CD4 cell counts (n=221, 34.5%), Hgb (n=285, 44.5%). Since, the missing value for variables CD4 cell counts and Hgb were more than 30%, I excluded them from the analysis due to their potential to undermine the validity of thesis results. However, the missing values for the variables height and viral load were handled by using multiple imputation method.

4.9. Data analysis procedures

Data were collected using Kobo Toolbox, exported to an Excel sheet, and then imported into the Stata version 17 for data cleaning, coding, and analysis. Descriptive statistics of numeric variables were presented in medians with interquartile range (IQR) and categorical variables were presented using frequency and percentages. The Kaplan-Meier survival curve was computed to estimate mean time tuberculosis occurrence and the overall probability of event. The log-rank test was fitted to test survival time for the presence of differences among groups. The Cox proportional hazard regression model was used to analyze the relationship between independent and outcome variables. A bivariable cox-regression analysis was done for all variables and, variables with a p- value <0.25 were transferred to multivariable analysis. Before multivariable analysis, the proportional hazard assumptions were checked using Schoenfeld residual test (global test), which found $P=0.7332$. Also, Cox proportional hazard model fitness to the data was checked using cox Snell residuals, in which the hazard function follows the 45-degree baseline. Adjusted Hazard Ratio (AHR) with 95% Confidence Intervals (CI) was computed to evaluate the strength of the association, and variables having a p-value less than 0.05 was considered statistically significant with the TB incidence.

4.10. Ethical consideration

Ethical approval was obtained from ethical review committee of Arsi University Department of Public Health, College of Health Sciences. An ethical clearance letter was submitted to Adama Hospital Medical College. As the study was conducted through review of medical records, there was no need of taking informed consent from each patient. To keep the confidentiality all collected data was coded and locked in a box. Names and unique ART numbers was not be included in data collection format and the data was not be disclosed to any person other than principal investigator. All information collect from patients' cards was kept strictly confidential and names of patients was not be included in the checklist.

4.11. Dissemination plan

The result of the study will be presented to Arsi University, school of graduate studies for their comment and suggestion. Also, the result will be submitted to the graduate studies of public health in partial fulfillment of the requirement for the degree of the master of public health. In addition, it will be communicated to Adama Hospital Medical College, and respective partners who provide the support on the program in the area.

5. RESULTS

5.1 Socio-demographic characteristics of participants

Among 658 HIV-positive adults' records reviewed, 640 (97.3%) records were included in the final analysis while 18 charts were excluded from the analysis due to incomplete data. The median age of the participants was 35 with IQR (28-45) years. Of the total study participants 182(28.4%) were age range of 25-34 years. About 363(56.6%) of study participants were females. Concerning educational status, 215(33.6%) of participants were attended a primary education. Two hundred Forty-three (38%) were Orthodox and 428(66.9%) were married. About 132(20.6%) of study participants were housewife by occupational status (Table 2).

Table 2: Socio-demographic characteristics of HIV-positive adult receiving Antiretroviral treatment at Adama Hospital Medical College, Southeast Ethiopia 2025.

Variables	Event n (%)	Censored n (%)	Total n (%)
Age			
15-24	27(22.7)	82(15.7)	109(17.3)
25-34	26(21.9)	156(29.9)	182(28.4)
35-44	37(31.1)	140(26.9)	177(27.7)
>=45	29(24.4)	143(27.5)	172(26.9)
Sex			
Male	59(49.6)	219(42)	278(43.4)
Female	60(50.4)	302(58)	362(56.6)
Occupational status			
Housewife	19(16)	113(21.7)	132(20.6)
Daily laborer	18(15.1)	82(15.7)	100(15.6)
Farmer	15(12.6)	65(12.5)	80(12.5)
Merchant	18(15.1)	88(16.9)	106(16.6)
Driver	11(9.2)	33(6.3)	44(6.9)
Civil servant/NGO	12(10.1)	72(13.8)	84(13.1)
Student	26(21.9)	68(13.1)	94(14.7)
Marital status			
Never married	18(15.1)	53(10.2)	71(11.1)
Married	73(61.3)	355(68.1)	428(66.9)
Widowed	11(9.2)	46(8.8)	57(8.9)
Divorced	17(14.3)	67(12.9)	84(13.1)
Religion			
Orthodox	45(37.8)	198(38)	243(38)
Muslim	41(34.5)	181(34.7)	222(34.7)
Protestant	21(17.7)	110(21.1)	131(20.5)
Catholic	12(10.1)	32(6.1)	44(6.9)
Educational status			
No formal education	39(32.8)	122(23.4)	161(25.2)
Primary education	40(33.6)	175(33.6)	215(33.6)
Secondary education	26(21.9)	112(21.5)	138(21.6)
Tertiary education	14(11.8)	112(21.5)	126(19.7)

5.2 Clinical and treatment-related characteristics

Regarding with baseline WHO clinical stage, 502 (78.4%) of the study participants were classified as WHO clinical stage I. About 500 (78.1%) of the study participants were received TPT. Among study participants received TPT, 350 (70%) were received INH types of TPT and 444 (88.8%) were complete TPT provided. Regarding ART adherence status, 550 (85.9%) of study participants had good adherence. Two hundred sixty-seven (41.7%) of study participants had baseline viral load test <50 copies/ml and 464 (72.5%) were <50 copies/ml of recent viral load test. About 241 (37.7%) and 295 (46.1%) of study participants had 200-350 baseline CD4 and >350 recent CD4, respectively. Concerning BMI, 457 (71.4%) of study participants had normal body weight (table 3).

Table 3: Clinical and treatment related characteristics of adult HIV patients on ART in Adama Hospital Medical College, Southeast Ethiopia 2025

Variables	Event n (%)	Censored n (%)	Total n (%)
Baseline WHO clinical stage			
Stage I	85(71.4)	417(80)	502(78.4)
Stage II	16(13.5)	58(11.1)	74(11.6)
Stage III	9(7.6)	28(5.4)	37(5.8)
Stage IV	9(7.6)	18(3.5)	27(4.2)
TPT received			
Yes	72(60.5)	428(82.2)	500(78.1)
No	47(39.5)	93(17.9)	140(21.9)
Types of TPT provided			
INH	61(84.7)	289(67.5)	350(70)
3HP	11(15.3)	139(32.5)	150(30)
TPT complete status TB			
Completed	56(77.8)	388(90.7)	444(88.8)
Incomplete	16(22.2)	40(9.4)	56(11.2)
ART Adherence status			
Good	96(80.7)	454(87.1)	550(85.9)
Fair	5(4.2)	32(6.1)	37(5.8)
Poor	18(15.1)	35(6.7)	53(8.3)
Baseline viral load			
<50	42(35.3)	225(43.2)	267(41.7)
50-1000	30(25.2)	175(33.6)	205(32)
>1000	47(39.5)	121(23.2)	168(26.3)
Recent viral load test			
<50	73(61.3)	391(75.1)	464(72.5)
50-1000	36(30.3)	86(16.5)	122(19.1)
>1000	10(8.4)	44(8.5)	54(8.4)
Baseline CD4			
CD4			
<200	37(31.1)	166(31.90)	203(31.7)
200-350	41(34.45)	200(38.4)	241(37.7)
>350	41(34.5)	155(29.8)	196(30.6)
Recent CD4			
<200	6(5)	54(10.4)	60(9.4)
200-350	56(47.1)	229(44)	285(44.5)
>350	57(47.9)	238(45.6)	295(46.1)
Baseline BMI			
<18.5	27(22.7)	76(14.6)	103(16.1)
18.5-24.9	79(66.4)	378(72.6)	457(71.4)
>=25	13(10.9)	67(12.9)	80(12.5)

5.3 Incidence of tuberculosis

In this study, a total of 640 study participants were followed for 2849 person-years of observation. During the follow-up period, 119 (18.6%) of the study participants experienced TB with an overall incidence rate of TB of 4.18 (95% CI:3.49–4.99) per 100 PY of observation. The mean TB free survival time of the entire follow up was 8.3 years (95% CI: 8.04-8.56 years) (Figure 2).

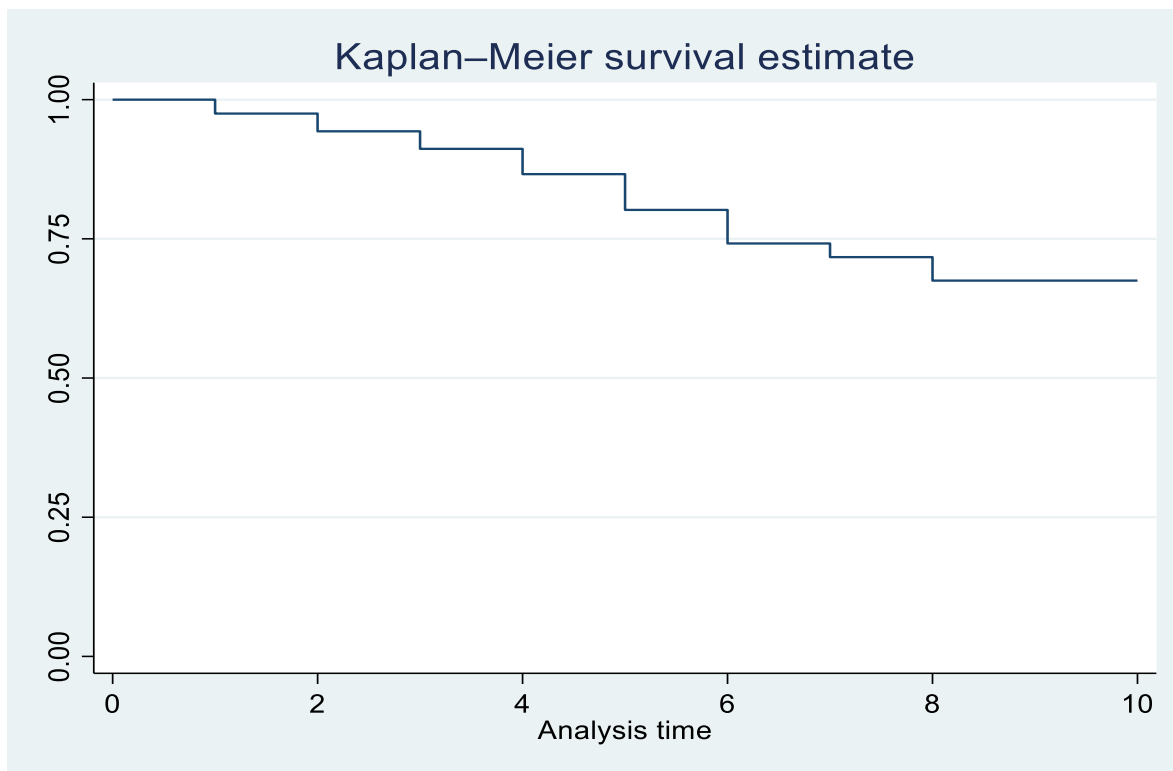


Figure 2: Kaplan Meier survival curve time to TB develop among HIV positive adults on antiretroviral therapy Adama Hospital Medical College, Southeast Ethiopia 2025.

5.4. Survival function for different categorical variables

Kaplan Meier survival curve together with log rank test revealed that there is a significant difference in survival function for different categorical variables. These variables include WHO clinical stage baseline, TPT received, ART adherence and baseline viral load test were statistically significant difference among survival curves of observed groups at p-value <0.05 (figure 3).

This study revealed that study participants who didn't receive TPT have lower survival time as compared to those who received TPT. The survival time difference between the groups was statically significant with P-value=0.0005 (Figure 3).

In this study those study participants who were WHO clinical stage III and IV have lower survival time as compared to those who were WHO clinical stage I. The survival time difference between the groups was showed statically significant with P-value =0084. Similarly, this study also revealed that study participants who had baseline viral load test greater than 1000 have lower survival time as compared to those who had viral load test<50 copy/cell. The survival time difference between the groups was statically significant with P-value=0.0014. Those adults with HIV who had poor ART adherence have lower survival time than that of adults who had a good adherence. The survival time difference between the groups was showed statically significant with P-value=0.016 (Figure 4).

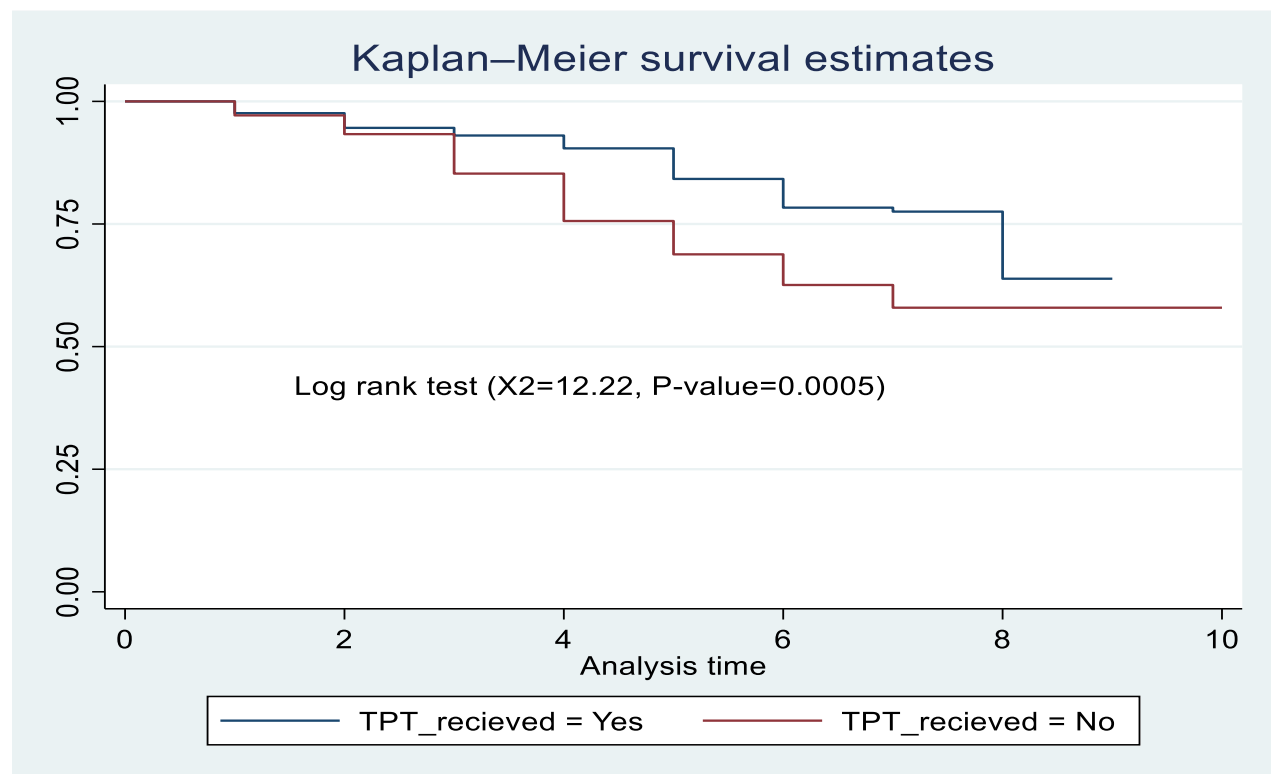


Figure 3: Estimates of survival curves of TPT received among HIV positive adults on antiretroviral therapy at Adama Hospital Medical College, Southeast Ethiopia 2025.

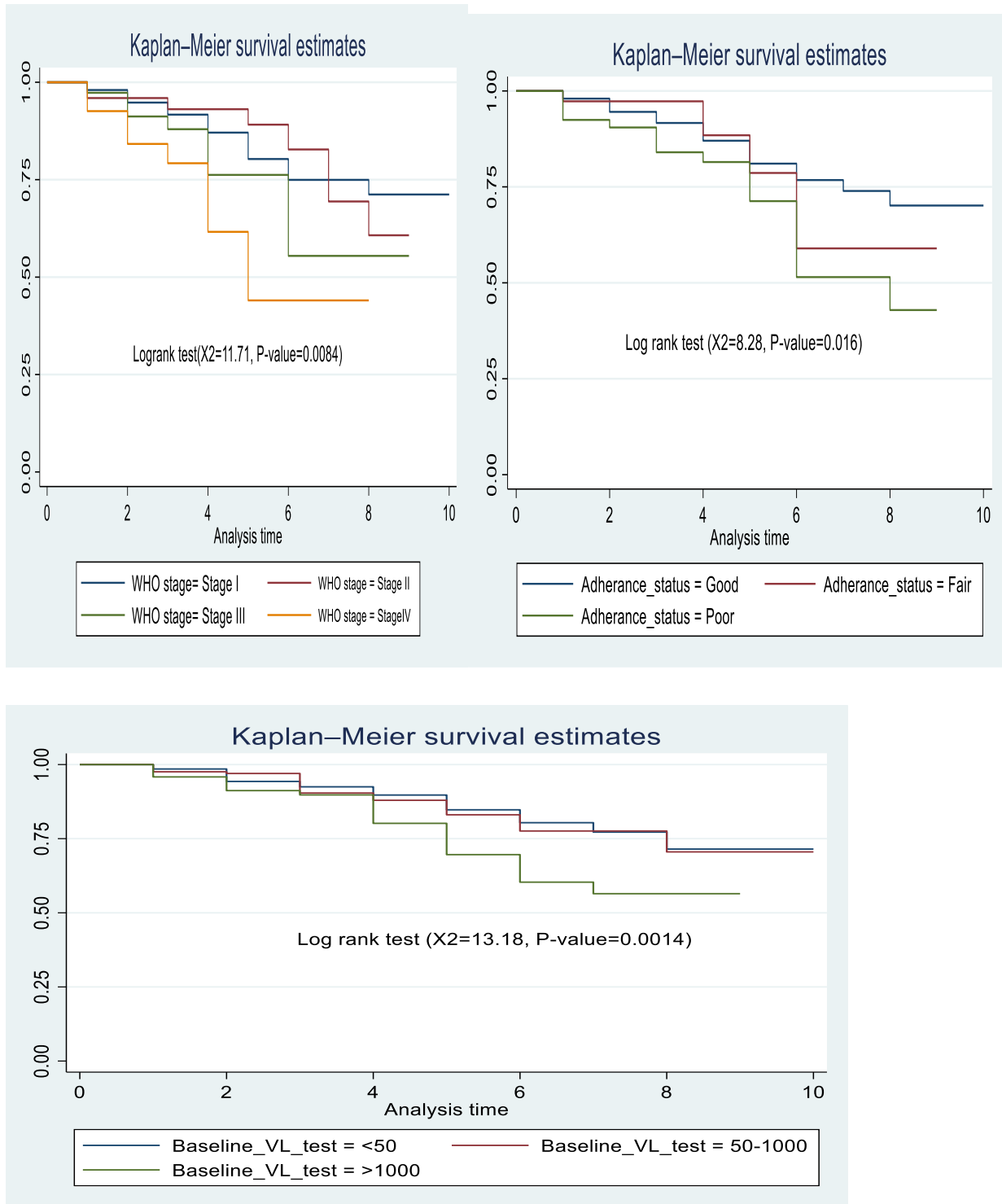


Figure 4: non-parametric estimates of survival curves across categories of WHO clinical stage, adherence and baseline viral load test among HIV positive adults on antiretroviral therapy at Adama Hospital Medical College, Southeast Ethiopia 2025.

5.5 Predictors of Tuberculosis incidence

In the bivariate Cox proportional hazard model, age, educational status, baseline clinical WHO stage, history of TPT received, ART adherence status, baseline viral load test and baseline BMI had a P-value less than 0.25 and entered into multivariate cox proportional hazard. In the multivariate Cox proportional hazard model, WHO clinical stages III and IV, no TPT received, baseline viral load test and having poor adherence levels were significant predictors of tuberculosis incidence among HIV-infected adults.

The assumption of Cox proportional hazard model was checked using the Schoenfeld residual global test and the assumption has been met (P-value = 0.7332). The goodness of fit for the fitted model was performed using the Cox Snell residual test and showed that the model was adequate because the Cox-Snell Residual Graph for the goodness of model fitness indicated the hazard function follows the 45° closed to the baseline (figure 4).

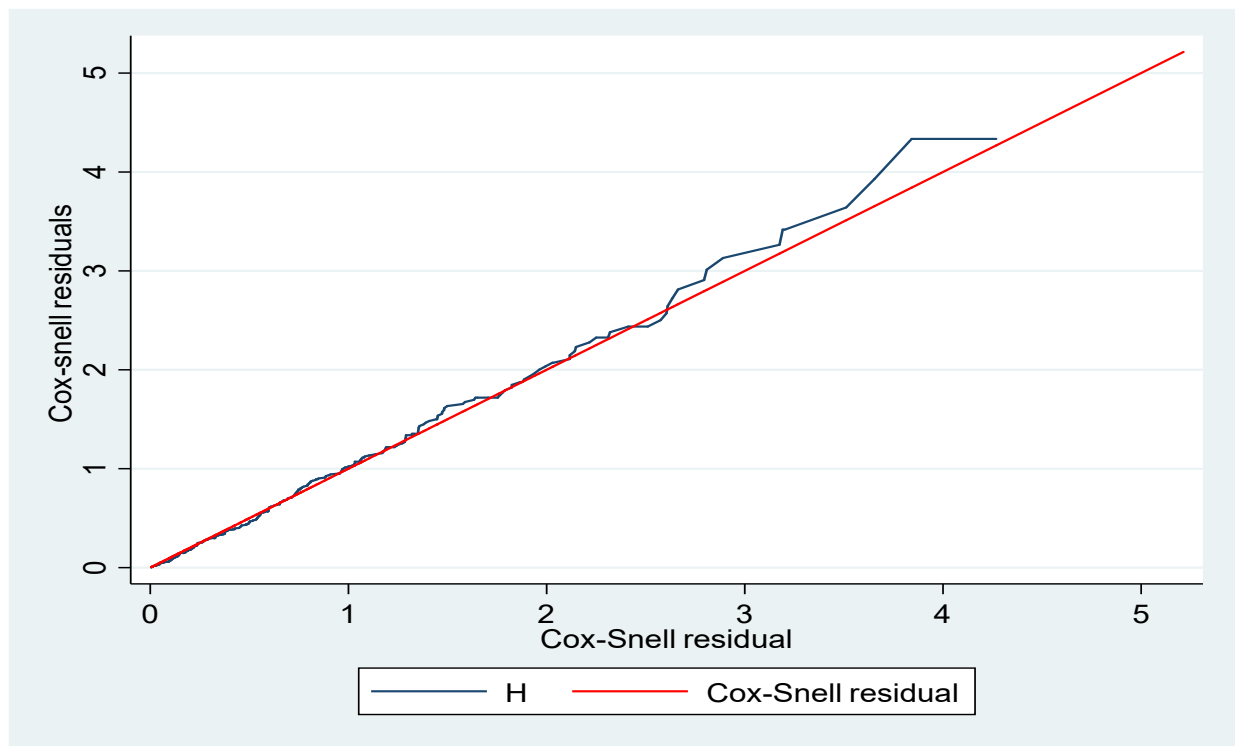


Figure 5: Cox-Snell Residual Graph for the goodness of model fitness incidence to tuberculosis among HIV-infected adults receiving ART at Adama hospital Medical College, Southeast Ethiopia 2025.

The risk of acquiring TB infections among HIV positive adults with WHO clinical stage III had 2.25 times (AHR: 2.25; 95% CI 1.11-4.57) higher than those WHO clinical stage I. Furthermore, HIV positive adults with WHO clinical stage IV were 3.5 times (AHR = 3.50; 95% CI: 1.72–7.12) more likely to developing tuberculosis as compared to those having WHO clinical stage I. The risk of developing TB among HIV positive adults who were not received TPT was 1.80 times (AHR: 1.80; 95% CI 1.23-2.64) higher compared with those who received TPT. The hazard of TB among HIV positive adults with poor ART adherence was 1.98 times (AHR: 1.98; 95% CI 1.18-3.30) higher when compared with that good ART adherence. Furthermore, HIV positive adults with baseline viral load test >1000 copies/ml had 1.80 times (AHR: 1.80; 95% CI 1.17-2.76) increased risk of developing TB compared with those viral load test <50 copies/ml (table 4).

Table 4: Bivariable and Multivariate analysis for predictors of TB incidence among HIV positive adults on ART at Adama Hospital Medical College, Southeast Ethiopia 2025.

Variables (n=640)	Outcome status		CHR (95% CI)	AHR (95% CI)
	Event	Censored		
Age				
15-24	27	82	1.45(0.86-2.46)	1.18(0.68-2.03)
25-34	26	156	0.76(0.45-1.30)	0.73(0.42-1.27)
35-44	37	140	1.11(0.68-1.80)	1.04(0.63-1.72)
45 and above	29	143	1	1
Educational status				
No formal education	39	122	1.79(0.97-3.31)	1.52(0.81-2.85)
Primary education	40	175	1.47(0.80-2.71)	1.56(0.83-2.92)
Secondary education	26	112	1.44(0.75-2.77)	1.43(0.74-2.78)
Tertiary and above	14	112	1	1
Baseline clinical WHO stage				
Stage I	85	417	1	1
Stage II	16	58	0.99(0.58-1.70)	1.08(0.62-1.88)
Stage III	9	28	1.74(0.87-3.45)	2.25(1.11-4.57) *
Stage IV	9	18	2.78(1.40-5.55)	3.50(1.72-7.12) *
TPT received				
Yes	72	428	1	1
No	47	93	1.89(1.30-2.74)	1.80(1.23-2.64) *
Adherence status				
Good	96	454	1	1
Fair	5	32	1.25(0.51-3.09)	1.02(0.40-2.58)
Poor	18	35	2.02(1.22-3.35)	1.98(1.18-3.30) *
Baseline viral load test				
<50	42	225	1	1
50-1000	30	175	1.06(0.67-1.71)	0.97(0.60-1.57)
>1000	47	121	1.97(1.30-2.99)	1.80(1.17-2.76) *
Baseline BMI				
<18.5	27	76	1.57(0.81-3.05)	1.71(0.86-3.38)
18.5-24.9	79	378	1.03(0.57-1.84)	1.01(0.55-1.88)
>=25	13	67	1	1

*Statistically significant at $p<0.05$; 1 = used as reference category, AHR: Adjusted Hazard Ratio, CHR: Crude Hazard Ratio, CI: Confidence Interval; TPT: Tuberculosis Preventive Therapy; WHO: World Health Organization; TB: Tuberculosis; BMI: Body Mass Index. Global test=0.7332

6. DISCUSSIONS

This retrospective cohort study assessed the incidence and predictors of TB among HIV-positive adults at Adama Hospital Medical College. The incidence of TB was found to be 4.18 (95% CI:3.49–4.99) per 100 PY of observation. This finding is in line with studies conducted in the India (4.39 per 100 PY) (33), Sub-Sahara Africa (3.49 per 100 PY) (38), Ethiopia (4.8 per 100 PY) (41), Addis Ababa (4.84 cases per 100 PY) (29) and Gurage Zone (4.79 per 100 PY) (39).

However, it is higher than the studies from United Kingdom, Nigeria and Northern Tanzania which reported the incidence of TB to be (0.6 cases per 1000 PY), (0.57 cases per 1000 PY) and (2.08 cases per 100 PY), respectively (34–36). This might be due to the differences in socio-demographic characteristics of study participants, low healthcare coverage, and high burden of HIV in the study setting. Besides, this study was conducted at specialized hospitals providing tertiary level services for patients referred from health centers or general hospitals. Hence, patients in these hospitals might have advanced disease stage which would increase the risk of developing TB. Furthermore, this discrepancy could be due to poverty, overcrowding, having a large family, and living in poor conditions may all contribute to an increased tuberculosis incidence rate in Ethiopia.

On the other hand, the incidence was lower than the studies conducted in Central Africa Republic (15.37 cases per 100 PY) (37), Northeast Ethiopia (8.6 cases per 100 PY) (27), Debre Markos, Northwest Ethiopia (6.19 cases per 100 PY) (26), Hawassa city (8.79 cases per 100 PY) (40), Addis Ababa (6.8 cases per 100 PY) (42) and Horo Guduru Wollega zone (6.8 cases per 100 PY) (43). This variation could be explained by the difference in the study period. This may be due to variation in strong follow up, and proper implementation in TB/HIV care service. Moreover, creation of better awareness regarding the prevention of TB/HIV co-infection might also contribute to the low incidence.

This study found that the hazards of tuberculosis infection in adult HIV positive with WHO clinical stages III and IV were higher than those in adults with WHO clinical stages I. This finding is supported by studies conducted in Northeast Ethiopia (27), Hawassa, Southern Ethiopia (28) and Addis Ababa (29). This might be due to individuals in stages III and IV typically experience advanced immunosuppression, which severely compromises their immune

response. This weakened immune system makes it more difficult for these individuals to control latent TB infections, increasing the likelihood of reactivation and progression to active TB disease. The severity of immunosuppression correlates directly with the risk of opportunistic infections, including TB, as the body's ability to mount an effective immune response is greatly diminished.

According to this study, the hazard of TB among HIV positive adults with poor ART adherence was higher when compared with that good ART adherence. These findings are supported by research conducted in Debre Markos, Northwest Ethiopia (45) and Addis Ababa (29). This may be due to poor adherence ART offers a favorable environment for viral replication and may hasten the development of ART resistance, which can lead to an increase in viral load, a loss in immune function, and the spread of opportunistic infections including TB.

In the present study, participants who didn't take IPT prophylaxis had increased hazard of having TB. This result is in line with studies conducted in Debre Markos, Northwest Ethiopia (45), Addis Ababa (29) and Northeast Ethiopia (27). This could be explained, the absence of TPT leaves HIV-positive individuals at a higher risk of both progressing from latent TB to active TB and acquiring new TB infections. Latent TB can remain asymptomatic for years; however, without preventive therapy, the risk of it becoming active increases, particularly as HIV progresses. Additionally, HIV-positive patients who do not receive Tuberculosis Preventive Therapy (TPT) face several factors that increase their likelihood of developing TB infections.

Primarily, HIV significantly weakens the immune system and diminishing the body's ability to combat latent TB infections. As the immune response is compromised, individuals become more susceptible to opportunistic infections, including the reactivation of dormant TB bacteria.

HIV-positive adults with a baseline viral load test greater than 1000 copies/ml increased risk of developing tuberculosis (TB) compared to those with a viral load below 50 copies/ml. This may due to Elevated viral loads indicate active viral replication and a compromised immune response, which reduces the body's ability to control latent TB infections. This immunosuppression makes it easier for dormant TB bacteria to reactivate, leading to a higher incidence of active TB disease.

7. CONCLUSION AND RECOMMENDATION

7. 1 Conclusion

In this study, the incidence rate of tuberculosis in HIV-infected adults was found to be high. The risk of TB incidence rate in HIV/AIDS- infected adults was associated with the WHO clinic stages III and IV, being not received TPT, high viral load test greater than 1000 copies/ml and poor adherence levels to ART.

7. 2 Recommendations

Hospital

Hospitals shall implement routine TPT eligibility screening and immediate initiation for all PLHIV, especially those with high viral loads and advanced clinical stages. Additionally, the hospital shall strength the implement regular viral load monitoring and ensure that ART adherence support programs to improve treatment outcomes.

Health care providers

Healthcare professionals shall actively educate HIV-positive patients about the risks associated with high viral loads and the importance of adherence to ART to reduce the incidence of TB. Regular counseling sessions should be implemented to reinforce the necessity of TPT.

Researchers

Future studies shall evaluate the impact of universal TPT scale-up on TB incidence.

8. STRENGTHS AND LIMITATIONS

The limitations of this study were, since it was conducted through record review some of the variables missing values were inevitable such as recent hemoglobin, and CD4 count of the study participants were not analyzed due to the missing value may undermine the result if it is related with incidence. Despite the above potential limitations, the study has the following strengths. The study was conducted for a long follow up (ten years) period which increases period of observation, and enabled to know the long-term impact of chronic HIV care and highly active antiretroviral therapy on TB incidence. As compared to cross-sectional survey, this study has strengths related to the design.

9. REFERENCES

- 1.Morty RE, Morris A. World AIDS Day 2021: highlighting the pulmonary complications of HIV/AIDS. American Physiological Society Rockville, MD; 2021. p. L1069-L71.
- 2.Burman W, Ellis J, Hale G, Hill K. Adequacy of recommendations for adverse event management in national and international treatment guidelines for rifampicin-susceptible tuberculosis: a systematic review. *EClinicalMedicine*. 2025;82.
- 3.Gulumbe BH, Abdulrahim A, Danlami MB. The United Nations' ambitious roadmap against tuberculosis: opportunities, challenges and the imperative of equity. *Future Science OA*. 2024;10(1):2418787.
- 4.UNAIDS Global AIDS Update 2024: The Urgency of Now: AIDS at a Crossroads: Stylus Publishing, LLC; 2024.
- 5.Dan D, Yuan Y. Global, regional, and national burdens of MDR-TB attributable to smoking from 1990 to 2021 with a prediction from 2022 to 2050. *Frontiers in Public Health*. 2025;13:1634772.
- 6.Organization WH. Global tuberculosis report 2021: supplementary material: World Health Organization; 2022.
- 7.Organization WH. WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment: World Health Organization; 2020.
- 8.Olana DE. Socio-cultural perspectives of HIV/AIDS communication amongst the Borana Pastoralist community in Ethiopia: University of South Africa (South Africa); 2024.
- 9.Hareru HE, Ashuro Z, Debela BG, Sisay D, Ashenafi E, Abebe M, et al. Satisfaction with HIV/AIDS treatment and care services and its associated factors among adult people receiving antiretroviral therapy in Ethiopia: a systematic review and meta-analysis. *BMJ open*. 2025;15(2):e085169.
- 10.Gray RT, McManus H, King J, Chacón GP, Rule J, Petoumenos K, et al. Twenty Years of Progress Towards Ending AIDS as a Public Health Threat in Australia: Trends in Epidemiological Metrics between 2004–2023. Available at SSRN 5265901.
- 11.Charles MK, Lindegren ML, Wester CW, Blevins M, Sterling TR, Dung NT, et al. Implementation of tuberculosis intensive case finding, isoniazid preventive therapy, and infection control ("Three I's") and HIV-tuberculosis service integration in lower income countries. *PloS one*. 2016;11(4):e0153243.
- 12.Genet C, Andualem T, Melese A, Mulu W, Mekonnen F, Abera B. Quality of care for tuberculosis patients in public health facilities of Debre Tabor town, Northwest Ethiopia. *PloS one*. 2020;15(6):e0234988.
- 13.Swaminathan S, Padmapriyadarsini C, Narendran G. HIV-associated tuberculosis: clinical update. *Clinical Infectious Diseases*. 2010;50(10):1377-86.
- 14.Rana N, Johnston JC, Schwartzman K, Oxlade O, Suarez PG, Gasana M, et al. Achieving tuberculosis elimination in Canada and the USA: giving equal weight to domestic and international efforts. *BMC Global and Public Health*. 2024;2(1):85.
- 15.Joulaei H, Shooshtarian S, Dianatinasab M. Is UNAIDS 90-90-90 target a Dream or a Reality for Middle East and North Africa Region on Ending the AIDS Epidemic? A Review Study. *AIDS reviews*. 2018;20(2).
- 16.Zhang S-X, Wang J-C, Yang J, Lv S, Duan L, Lu Y, et al. Epidemiological features and temporal trends of the co-infection between HIV and tuberculosis, 1990–2021: findings from the Global Burden of Disease Study 2021. *Infectious diseases of poverty*. 2024;13(04):79-94.

17. Goletti D, Meintjes G, Andrade BB, Zumla A, Lee SS. Insights from the 2024 WHO global tuberculosis report—more comprehensive action, innovation, and investments required for achieving WHO end TB goals. *International Journal of Infectious Diseases*. 2025;150.
18. Organization WH. Tuberculosis in the WHO African Region: 2023 progress update. *Tuberculosis in the WHO African Region: 2023 progress update* 2023.
19. Gilpin C, Korobitsyn A, Migliori GB, Raviglione MC, Weyer K. The World Health Organization standards for tuberculosis care and management. *European Respiratory Society*; 2018.
20. Mandalakas AM, Kay AW, Bacha JM, Devezin T, Golin R, Simon KR, et al. Tuberculosis among children and adolescents at HIV treatment centers in sub-Saharan Africa. *Emerging infectious diseases*. 2020;26(12):2933.
21. Souza AA, Ducker C, Argaw D, King JD, Solomon AW, Biamonte MA, et al. Diagnostics and the neglected tropical diseases roadmap: setting the agenda for 2030. *Transactions of The Royal Society of Tropical Medicine and Hygiene*. 2021;115(2):129-35.
22. Organization WH. WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents: World Health Organization; 2022.
23. Tusho AR. Best Practice Guidelines to Address Barriers to Treatment Completion For Patients With Drug-Resistant Tuberculosis in Ethiopia: University of South Africa (South Africa); 2022.
24. Organization WH. Guidance for national strategic planning for tuberculosis: World Health Organization; 2022.
25. Aemro A, Jember A, Anlay DZ. Incidence and predictors of tuberculosis occurrence among adults on antiretroviral therapy at Debre Markos referral hospital, Northwest Ethiopia: retrospective follow-up study. *BMC infectious diseases*. 2020;20(1):245.
26. Ahmed A, Mekonnen D, Shiferaw AM, Belayneh F, Yenit MK. Incidence and determinants of tuberculosis infection among adult patients with HIV attending HIV care in north-east Ethiopia: a retrospective cohort study. *BMJ open*. 2018;8(2):e016961.
27. Bekele H, Kote M, Yesuf A, Girum T. Incidence and predictors of tuberculosis among adult PLWHA at public health facilities of Hawassa City. *Int J Public Health Sci*. 2017;6(3):266-74.
28. Getu A, Wolde HF, Animut Y, Kibret AA. Incidence and predictors of Tuberculosis among patients enrolled in Anti-Retroviral Therapy after universal test and treat program, Addis Ababa, Ethiopia. A retrospective follow-up study. *Plos one*. 2022;17(8):e0272358.
29. Wondifraw EB, Chanie ES, Gebreeyesus F, Biset G, Tefera BD, Zeleke M. Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. *Heliyon*. 2022;8(12).
30. Biset S, Teferi M, Alamirew H, Birhanu B, Dessie A, Aschale A, et al. Trends of Mycobacterium tuberculosis and Rifampicin resistance in Northwest Ethiopia: Xpert® MTB/RIF assay results from 2015 to 2021. *BMC Infectious Diseases*. 2024;24(1):238.
31. Bayisa L, Keno TS, Ayana GE, Abera T, Akuma AO. Out-of-Catchment area antiretroviral therapy initiation and its factors among HIV positive people on lifelong therapy in Western Ethiopia: implementation of decentralized ART services. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2025;24:23259582241307467.
32. van Halsema CL, Okhai H, Hill T, Sabin CA. Incidence of and risk factors for tuberculosis among people with HIV on antiretroviral therapy in the United Kingdom. *Aids*. 2020;34(12):1813-21.

33. Pathmanathan I, Dokubo EK, Shiraishi RW, Agolory SG, Auld AF, Onotu D, et al. Incidence and predictors of tuberculosis among HIV-infected adults after initiation of antiretroviral therapy in Nigeria, 2004-2012. *PloS one*. 2017;12(3):e0173309.
34. Mollel EW, Maokola W, Todd J, Msuya SE, Mahande MJ. Incidence rates for tuberculosis among HIV infected patients in Northern Tanzania. *Frontiers in public health*. 2019;7:306.
35. Longo JDD, Woromogo SH, Diemer HS-C, Tékpá G, Belec L, Grésengué G. Incidence and risk factors for tuberculosis among people living with HIV in Bangui: A cohort study. *Public Health in Practice*. 2022;4:100302.
36. Wondmeneh TG, Mekonnen AT. The incidence rate of tuberculosis and its associated factors among HIV-positive persons in Sub-Saharan Africa: a systematic review and meta-analysis. *BMC infectious diseases*. 2023;23(1):613.
37. Ausman Ahmed AA, Desalew Mekonnen DM, Shiferaw A, Fanuel Belayneh FB, Yenit M. Incidence and determinants of tuberculosis infection among adult patients with HIV attending HIV care in north-east Ethiopia: a retrospective cohort study. 2018.
38. Girmu T, Yasin F, Dessu S, Zeleke B, Geremew M. “Universal test and treat” program reduced TB incidence by 75% among a cohort of adults taking antiretroviral therapy (ART) in Gurage zone, South Ethiopia. *Tropical diseases, travel medicine and vaccines*. 2020;6(1):12.
39. Azanaw MM, Derseh NM, Yetemegn GS, Angaw DA. Incidence and predictors of tuberculosis among HIV patients after initiation of antiretroviral treatment in Ethiopia: a systematic review and meta-analysis. *Tropical medicine and health*. 2021;49(1):18.
40. Alemu A, Yesuf A, Zerihun B, Getu M, Worku T, Bitew ZW. Incidence and determinants of tuberculosis among HIV-positive individuals in Addis Ababa, Ethiopia: A retrospective cohort study. *International Journal of Infectious Diseases*. 2020;95:59-66.
41. Feyisa JW, Dufera M, Feyisa BR, Debelo S, Dori J, Shama AT. Time to reoccurrence of tuberculosis and its predictors among adult HIV/AIDS patients on ART at public hospitals in East and Horro Guduru Wollega zones, West Ethiopia: a retrospective cohort study. *BMC Public Health*. 2025;25(1):1939.
42. Gupte AN, Kadam D, Sangle S, Rewari BB, Salvi S, Chavan A, et al. Incidence of tuberculosis in HIV-infected adults on first-and second-line antiretroviral therapy in India. *BMC infectious diseases*. 2019;19(1):914.
43. Oljira T, Megerso A, Deksis A, Regea F, Zewdu T. Determinants of loss to follow-up in HIV care among adults on ART at Adama Hospital Medical College, Ethiopia: a case-control study. *BMC Infectious Diseases*. 2025;25(1):1-10.
44. Girma D, Abita Z, Shifera N, Arage MW, Abate BB, Alie MS, et al. Incidence rate of tuberculosis among HIV infected children in Ethiopia: systematic review and meta-analysis. *BMC pediatrics*. 2024;24(1):363.
45. Moore BK, Graham SM, Nandakumar S, Doyle J, Maloney SA. Pediatric tuberculosis: a review of evidence-based best practices for clinicians and health care providers. *Pathogens*. 2024;13(6):467.

10. ANNEXES

Annex 8.1. Information Sheet & Informed voluntary Consent Form for study participants

My name is Jemal Amin; I will be conducting a study in this community for my master's degree at Arsi University, College of Health and Medical Sciences. So, I kindly request you to lend me your attention to explain you about the study, study participants and your hospital being selected as the study setting.

Study title: Incidence and Predictors of Tuberculosis among adult people living with HIV (PLWH) and on ART at Adama Hospital and Medical College, Central Ethiopia.

Aim of the Study: The findings of the study help Adama Hospital medical college and Oromia Health Bureau to plan on Incidence and predictors Tuberculosis among people living with HIV (PLWH) patients on ART interventions. Moreover, the aim of this study is to write a thesis as a requirement for the partial fulfillment of master's program in Public Health.

Procedure and duration: I was reviewed secondary data using a questionnaire between may1, 2015 and may30, 2025 to get a relevant data that is helpful for the study.

Risks and benefits: There is a minimal risk that may face them when participating in this study by reviewing secondary data. There was no any direct payment for participating in this study. However, the finding from this research might be reveal important information for the local health planners and implementers.

Confidentiality: The information was held confidential. There was no information that identify participants in particular. The finding of the study will be generalized to the study participants and will not reflect any thing particular of individual person. The questionnaire will be coded to exclude showing names and other specific identity. No reference will be made in oral or written reports that could link participants to the research.

Rights: Participation of the study will be fully voluntary. You have the right to allow this study to be conducted or not. You have also the right to stop the study at any time if you observe any misdeeds and this will not label for any loss of benefits which you otherwise entitled.

Contact Address: If you have any question or inquire at any time please contact with the following principal investigator: Jemal Amin, Email: aminjemal955@gmail.com, Mobile phone: 0915968549/097412416603.

Declaration of informed voluntary consent: I have read the participant information sheet. I have clearly understood the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, the rights of participating and the contact address for any queries. I have been given the opportunity to ask questions for things that have been unclear. I was informed that I have the right to stop this study from being conducted if any misdeeds and unethical procedures are observed during the data collection process in the school premises. Therefore, I declare my voluntary consent to allow on behalf of management with my initials (signature) as indicated below.

Name & Signature of the Medical director of Hospital _____ Date _____

Name & Signature of principal investigator _____ Date _____

Annex 8. 2: English version of Questionnaire

Questionnaire for a study on “Tuberculosis Incidence and Duration of Preventive Treatment Protection among People Living with HIV (PLWH) Patients on ART at Adama Hospital.”

Section-one: Patient's demographic information			
Code	Question	Response options	Remark
Section-one: Basic and socio-demographic information			
101	Patient ART ID	ART No: _____	
102	Age at ART initiation (in years)	_____ year	
103	Sex	0. Female 1. Male	
104	Occupational status	1. Housewife 2. Daily laborer 3. Farmer 4. Merchant 5. Driver 6. Civil servant/NGO 7. Student	
105	Marital status	1. Never married 2. Married 3. Widowed 4. Divorced	
106	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic	
107	Educational status (highest grade completed)	0. No formal education 1. Primary education 2. Secondary education 3. Tertiary education	
Section-two: Patient's clinical information			
201	Date diagnosed for HIV infection	DD/MM/YYYY: _____	
202	Baseline WHO clinical stage	_____	
203	Date initiated on anti-retroviral treatment (ART)	DD/MM/YYYY: _____	
204	What type of ART regimen was initiated?	0. First-line regimens 1. Second-line regimens	
205	Baseline Viral Load at ART initiation	_____ copies/ml	
206	Baseline CD4 cell count at ART initiation	_____ cells/mm ³	
207	History of TB before ART initiation	0. No 1. Yes	If “No,” skip to Q208

208	If 'Yes' to Q206, when was TB diagnosed before ART initiation? If there were multiple episodes, provide the date of the most recent diagnosis (yyyy/mm/dd).	DD/MM/YYYY: _____	
209	Was the patient diagnosed with TB at the time of ART initiation?	0. No 1. Yes	
210	Did the patient develop TB after starting ART during the 10-year (or shorter) follow-up period?	0. No 1. Yes	If “No,” skip to Q2017
211	If 'Yes' to Q209, when was the patient diagnosed with TB?	DD/MM/YYYY: _____	
2012	If ‘Yes’ to Q209, what diagnostic method was used to confirm TB?	0. GeneXpert 1. Smear microscopy (AFB) 2. X-ray & TB signs/symptom complex 3. Other (specify) _____	
2013	If 'Yes' to Q209, what was the site of TB?"	0. Bacteriologically confirmed (BC) pulmonary TB (PTB) 1. Not bacteriologically confirmed (NBC) PTB 2. Extra pulmonary TB (EPTB) 3. Both PTB & EPTB	
2014	If 'Yes' to Q209 and 'EPTB' to Q2011, which type of EPTB was it?	0. TB of lymph nodes (specify) _____ 1. Pleural TB 2. TB meningitis 3. Peritoneal TB 4. Intestinal TB 5. Bone& joint TB [Osteoarticular TB] [Specify] _____ 6. Other (specify): _____	
2015	If 'Yes' to Q209, was the TB categorized as a severe form?	0. No 1. Yes	
2016	If 'Yes' to Q2013, which type of severe TB was it?	1. PTB with extensive disease 2. Miliary TB 3. TB Meningitis 4. TB of spondylitis	

		(Pott's disease) 5. Other (specify)	
2017	If 'Yes' to Q209, was the TB drug-susceptible or drug-resistant?	0. Drug-susceptible TB 1. Drug-resistant TB	
2018	What was the patient's weight at ART initiation (in kilograms)?	_____kg	
2019	What was the patient's height at ART initiation (in meters, rounded to two decimal places)?	_____m	
Section-three: Patient's TB Preventive Treatment Information			
301	Did the patient receive TB preventive treatment (TPT) at any time after ART initiation?	0. No 1. Yes	If "No," skip to Q401
302	If 'Yes' to Q301, when did the patient receive TPT?	DD/MM/YYYY: _____	
303	If 'Yes' to Q301, what type of TPT was provided?	1. INH 2. 3HP 3.	
304	If 'Yes' to Q301, what was the duration of TPT?	0. Completed 1. Incomplete	
Section-four: Follow-up and patient's outcomes			
401	What is the patient's current status?	0. Alive 1. Dead 2. Lost to follow up/Unknown 3. Transferred to another healthcare facility 4. Other	
402	If 'Dead' is selected in Q401, what was the cause of death?	1. TB 2. Other opportunistic infection (specify): _____ 3. Accident 4. Unknown	
403	ART adherence during follow-up period:	1. Good 2. Fair 3. Poor	
404	What was the patient's TB status during the follow-up period (within 10 years post-ART initiation)?	0. TB free throughout the follow-up period 1. Experienced at least one TB episode 2. TB status	

		unknown	
405	What is the patient's most recent viral load (in copies/ml)?	_____copies/ml	
406	When was the most recent viral load test done?	DD/MM/YYYY: _____	
407	What is the patient's most recent CD4 cell count (cells/mm ³)?	_____cells/mm ³	
408	When was the most recent CD4 cell count test done?	DD/MM/YYYY: _____	
409	What is the patient's most recent weight (in kilograms)?	_____kg	
410	When was the patient's most recent weight measured?	DD/MM/YYYY: _____	
411	What is the patient's most recent height in meters? (Round to two decimal places)	_____m	
412	When was the patient's most recent height measured?	DD/MM/YYYY: _____	

DD/MM/YYYY: _____

Declaration of Investigator

I, the undersigned student of General Master of Public Health, declare that this thesis is my original work in partial fulfillment of the requirement for the degree of General Master of public health to my best knowledge.

Name of investigator: Jemal Amin

Signature: _____ Date Dec 2/2025

Declaration of Advisors

We, the undersigned Advisors, declare that this thesis is our original work in partial fulfillment of the requirement for the degree of General Master of public health for the stated student above to our best knowledge. We confirmed that this thesis is ready for defense with our approval as the university advisor(s).

Date of Submission: _____

Name of primary Advisors:

Signatures

Date

1. Abay Burusie Adere



24 November 2025

Name of secondary Advisors:

Signatures

Date

2. Getu Tesfame



Dec-02/2025

Examining Board Approval

We, the undersigned Examining board, approved that this thesis is original work with the basic scientific merits for partial fulfillment of the requirement for the degree of Master of public health for the stated student above to our best knowledge. We confirmed that this research proposal is sufficient for the student's promotion to the higher level.

Name of External Examiner

Signatures

Date

Name of Internal Examiner

Signatures

Date

Name of Department Head

Signatures

Date
