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Incidence, survival, and risk factors for first-line antiretroviral therapy failure among adults on ART follow-up in health facilities in Southwest Shoa, Oromia, Ethiopia, 2023: a retrospective cohort study

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Abstract

Background The inability of antiretroviral medications to inhibit HIV is known as antiretroviral treatment failure. One of the greatest problems facing HIV patients receiving antiretroviral therapy is treatment failure. Updated data is crucial to assess program realities and effectiveness on ART. In this study, we aimed to determine incidence, survival, and risk factors for first-line ART failure by incorporating clinical, immunological, and virologic criteria, including primary health care.

Methods A retrospective cohort study was conducted among 579 adult patients. These patients were followed between January 1, 2016, and October 2023. Double-stage cluster sampling was used. The data were entered into Epi-Data version 3.1, then cleaned and analyzed via SPSS v.25. The Kaplan–Meier curve was used to estimate the probability of first-line ART failure. The log-rank test was used to compare the time to treatment failure. The Cox proportional hazard model was used to determine predictors of first-line ART failure.

Results The overall incidence rate of first-line ART failure was 2.57/1000 person-months over 24,925.7 person-months of follow-up. The patients' cumulative survival probabilities at 12 and 84 months were 100% and 76.73%, respectively. Predictor variables of first-line ART failure were male sex (AHR = 1.953; 95% CI: 1.11–3.43), disclosure of HIV infection (AHR = 0.53; 95% CI: 0.29–0.95), tuberculosis and HIV coinfections (AHR = 2.79; 95%CI: 1.33–5.87), opportunistic infections (AHR = 2.34; 95% CI: 1.23–4.28), poor/fair adherence (AHR = 3.87; 95% CI: 2.13–7.03), WHO clinical stage III/IV (AHR = 2.54; 95% CI: 1.04–6.20), and provision of CPT (AHR = 0.20; 95% CI: 0.08–0.51).

Conclusions and recommendations The low incidence of first-line ART failure suggests effective ART implementation in the region. However, first-line ART failure was significantly linked to advanced WHO stage, poor adherence, TB/HIV coinfection, male sex, lack of cotrimoxazole prophylaxis, non-disclosure of HIV status,

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and opportunistic infections. These findings showed the need for early monitoring, adherence support, and comprehensive care.

Clinical trial number Not applicable.

Keywords Incidence, Survival, ART, Failure, Adults, Ethiopia

Background

HIV is a global public health issue [1]. Globally, over 85.6 million people have been infected, and 40.4 million have died from AIDS-related illnesses since its inception, and approximately 39 million people still live with the virus [2]. The introduction of antiretroviral therapy marked a pivotal shift in the trajectory of the HIV/AIDS epidemic, converting a once-fatal illness into a treatable, long-term health condition [3]. Researchers found estimated viral suppression rates of 79% after one year of ART, which dropped to 65% after three years [4]. Although nearly 31 million people are on lifesaving ART, 1.3 million adults became infected with HIV in 2023, more than tripling the 2025 target for new infections [5]. Eastern and southern Africa is the hardest-hit region, with the highest HIV prevalence among adults aged 15–49 years (5.9%) in 2022 [2]. In Ethiopia, as reported in HIV estimates in 2023, there was a gradual decline in the number of PLHIV from an estimated 610,350 in 2022 to 603,537 in 2023. Additionally, new HIV infections in Ethiopia declined from 8,257 in 2021 to 7,194 in 2023 [6]. It was 0.8% prevalent in Ethiopia in 2022 [7].

Although effective ART greatly reduces transmission, morbidity, and mortality while improving life expectancy and quality of life, many patients still fail to achieve lasting viral suppression [5, 8–10]. Therefore, ART needs to be regularly monitored to ensure successful treatment [11]. If ART fails to control HIV/AIDS progression in a resource-limited setting, treatment failure is declared based on clinical, immunological, and virologic criteria [12]. Viral load measurement can assess and diagnose treatment failure early [13].

Even if many HIV-positive clients accessed ART, and then the number of AIDS-related deaths declined, first-line treatment failure was a major concern. In sub-Saharan Africa, with targeted and routine viral load assessment, switching to second-line therapy was more likely and occurred sooner after starting ART [14]. In Ethiopia, one in three individuals living with HIV seeks treatment for advanced HIV-related illness. In addition, an increasing number of PLHIV who have interrupted their treatment are now returning to care for advanced disease [11]. Furthermore, studies worldwide have revealed that first-line ART failure and the need for second-line regimens are other concerns [14–20].

In Ethiopia and worldwide, few studies have attempted to demonstrate the incidence of ART failure. Certain studies showed that the incidence of treatment failure varies moderately across cohorts and follow-up periods, ranging from 2.09 to 9.38 per person-year of follow-up [21–23]. Incidence rates of antiretroviral therapy (ART) failure have also been found to vary, ranging from 1.75 to 5.24 per 1,000 person-months of observation [9, 24–26].

Numerous studies conducted globally have highlighted a range of risk factors and predictors associated with antiretroviral therapy (ART) failure. These include regimen changes [27], advanced stages of HIV infection [28, 29], marital dissolution [28], prolonged duration on ART [28], rural dwellers [28], TB/HIV co-infections [29], low CD4 counts [27, 30, 31], nondisclosure of HIV status [30, 32], having multiple sexual partners [31], male gender [22, 31], hemoglobin below 12 mg/dl [33], poor medication adherence [27, 29–32], previous exposure to ART [34], treatment interruptions [27, 31, 32], the occurrence of opportunistic infections during therapy [29, 32], inadequate social support [32], and smoking [32].

Additional studies have also indicated that these factors contribute to a faster progression from the initiation of ART to treatment failure, necessitating an earlier shift to second-line therapy [9, 15, 35].

Although several studies in Ethiopia have examined first-line antiretroviral therapy (ART) failure, most of them have been conducted in referral or teaching hospitals. Many studies report the prevalence of ART failure but rarely examine incidence and survival outcomes, such as time to failure and survival probabilities. Updated data are crucial for assessing program realities and implementing ART strategies in the country.

To our knowledge, a limited study has been conducted in the specific context of Southwest Shoa. This gap is particularly concerning given the unique demographic and health system characteristics of the area. Therefore, this study aims to assess the incidence, survival, and risk factors for first-line ART failure by incorporating clinical, immunological, and virological criteria across a diverse range of health facilities. This study offers a more representative and context-specific understanding of ART outcomes in Southwest Shoa.

Methods and materials

Study setting, population, and design

An institution-based retrospective cohort study was conducted in Southwest Shoa health facilities, using data collected from January 1, 2016, to December 31, 2022,

with a data extraction period from October 1, 2023, to November 2023. The zone is located in the Oromia region, southwest of Addis Ababa. It has 12 woredas and one town administration. Currently, the zone provides ART in 19 public health facilities (5 hospitals and 14 health centers (HC)) and one private hospital. A total of 1646 active users were receiving HIV care at a non-government hospital called Saint Luke Catholic Hospital, whereas 2370 clients were actively receiving chronic HIV care at a governmental institution until August 2023.

Source population

Medical records of all HIV-positive adult patients (aged ≥ 15 years) in Southwest Shoa.

Study population

Medical records of all HIV-positive adult patients who initiated ART and were followed at SWS, recruited from January 1, 2016, to December 31, 2022. The study units were selected from adult HIV-positive clients' medical records who were on ART for at least six months, who had a baseline CD4 lymphocyte count, and who had WHO HIV clinical stage details available.

Sample size determination and sampling technique

The sample size was calculated using a double-population formula with Epi Info version 7.2.5.0 STATCALC statistical software. The calculation used the most common predictors of FLART failure identified in previous literature, assuming a power of 80%, a significance level (α) of 0.05, and a ratio of 2. WHO HIV clinical stage was used as a predictor variable, with stage I/II as the unexposed group and stage III/IV as the exposed group [25]. This approach resulted in a final sample size of 579, after replacing incomplete documents. Seven of the 20 health facilities providing ART in SWS were selected randomly. The selected health facilities were St. Luke Catholic Hospital (SLCH), Tulu Bolo General Hospital (TBGH), Leman HC, Woliso HC-1 (WHC-1), Busa HC, Citu HC, and Awash-Malka HC. The sample was proportionally allocated across ART sites based on the total number of clients enrolled during the follow-up period (N = 1908; Fig. 1). Double-stage cluster sampling was used to choose ART sites and to select study subjects at each ART site.

Data collection procedures

The data extraction tool was prepared from the ART entry and follow-up forms developed by the Federal

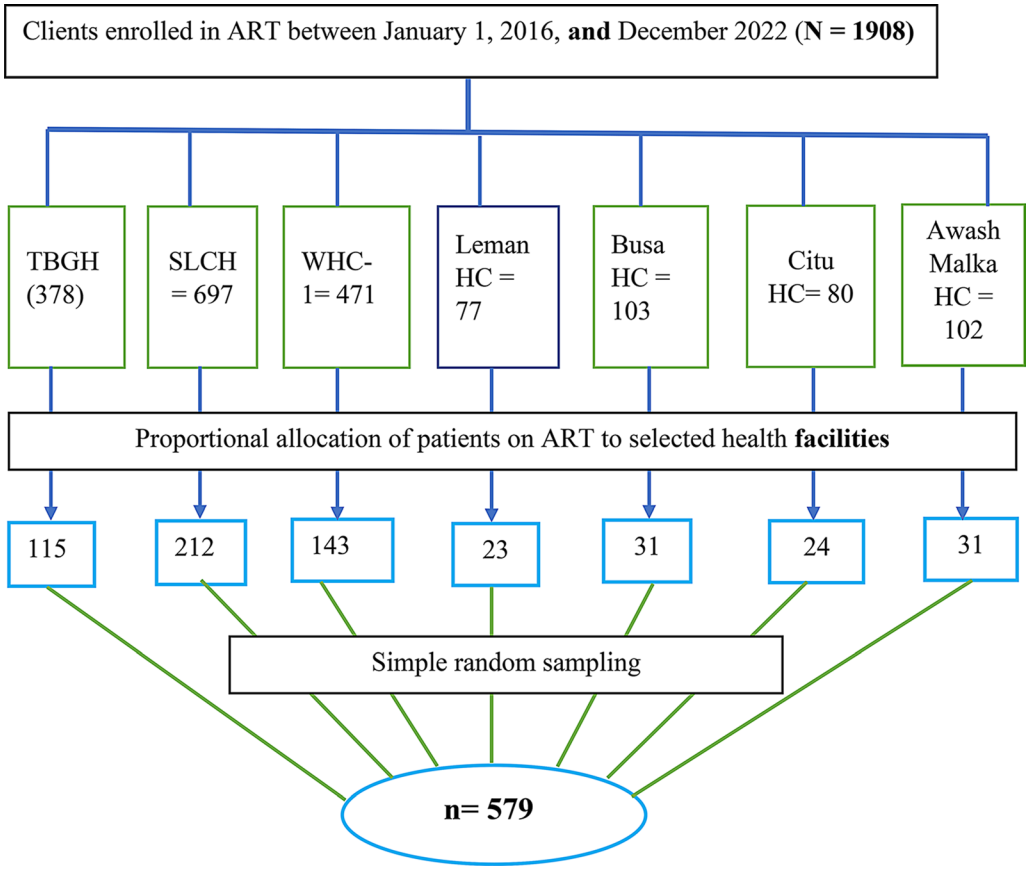


Fig. 1 Schematic presentation of the sampling technique for incidence, survival, and risk factors for FLART failure in health facilities in SWS, Oromia region, Ethiopia, in 2023

Ministry of Health (FMOH). The data extraction checklist included sociodemographic information (age, sex, educational status, marital status, and religion); baseline clinical information (BMI, CD4 count, and WHO stage); comorbidities (OI and TB/HIV coinfections); ART medication-related information (CPT, initial regimen, and regimen substitution); disclosure of HIV status; and ART adherence of the patients. Data were collected from the patient's medical records and the ART electronic data.

Study variables

Dependent variable

First-line ART failure: Censored/Event.

Independent variables included age, sex, marital status, level of education, religion, BMI, baseline hemoglobin, baseline CD4 count, initial drug regimen, drug substitution, cotrimoxazole preventive prophylaxis (CPT) status, TB/HIV coinfections, other opportunistic infections, disclosure status, and ART adherence.

Operational and term definition

ART treatment failure: When an antiretroviral regimen is unable to control HIV infection. ART treatment failure is defined as follows and is diagnosed if one of the following criteria is met:

a) Clinical failure: New or recurrent clinical events indicating severe immunodeficiency (WHO clinical stage 4 condition and certain WHO clinical stage 3 conditions) may indicate treatment failure after 6 months of effective treatment [11].
b) Immunologic failure: CD4 count at or below 250 cells/mm^3 following clinical failure or persistent CD4 levels below 100 cells/mm^3 [11].
c) Virologic failure: Viral load above 1000 copies/ml based on two consecutive viral load measurements in 3 months for individuals taking ART for at least 6 months [11].

Good adherence: if a client used greater than or equal to 95% adherence, that is, missing only 3 from the 60 doses.

Fair adherence: if a client had 85–94% adherence, meaning missing 2–4 doses out of 30 or 4 to 9 doses out of 60.

Poor adherence: if a client had less than 85% adherence, that is, missing ≥ 5 doses out of 30 doses or ≥ 10 doses out of 60 doses.

Censored: defined as when the study participants were lost, transferred out, died, or were free from events during the follow-up time or end of the follow-up study.

Event: defined as adults who developed first-line ART failure during the follow-up time.

Time-to-event: defined as the time interval between the date when ART follow-up started and the occurrence of first-line ART failure.

The last date of follow-up: the date at which the adult developed first-line ART failure, if there was any, or the last date of the viral load test measurement done.

Survival time: defined as the time in a month from the start of first-line ART treatment to the development of first-line ART failure.

Data processing and analysis

The data were coded and entered into EPI-data v3.1. Consequently, the data were checked for inconsistencies, missing values, and outliers by running summary statistics, and analysis was performed via SPSS v25. Descriptive statistics were computed to describe the sociodemographic, baseline clinical, comorbidity, adherence status, and medication-related characteristics of the patients. Bivariable and multivariable Cox regression were used after checking the proportional hazard assumption, and model fitness was checked for each covariate. Independent variables that were significant in the bivariable regression with a P-value ≤ 0.25 were included in the multivariable Cox regression analysis. A P-value < 0.05 was used to identify independent predictors of first-line ART failure. The Cox proportional hazards regression model was used to identify factors for the variation in time to develop FLART failure. The Kaplan–Meier (KM) survival curve was used to describe the cumulative incidence rates of first-line ART failure and ART failure-free survival time over the follow-up period.

Data quality

The data collectors included four BSc nurses and two health officers, all of whom received one day of training on the study's objectives and methods. The principal investigator and two supervisors closely supervised the data collection process on-site. Additionally, supervisors performed daily random checks of the collected data from each site to ensure completeness and consistency.

Results

Baseline sociodemographic characteristics

From January 1st, 2016, to the end of October 2023, a follow-up study in which medical records were reviewed was conducted in the southwest Shoa health facilities. Table 1 show that this study included 579 ART clients' medical charts. The median age at the start of ART in the

Table 1 Baseline sociodemographic characteristics of HIV-infected adult patients enrolled in ART in southwest Shoa health facilities, from January 2016 to October 2023

Variables	Frequency *n* = 579	First-line ART Failure	
		Events (64)	Censored (515)
Sex			
Male	225 (38.7%)	29	196
Female	354 (61.1%)	35	319
Age			
15–24	43 (7.4%)	6	37
25–34	126 (21.8%)	7	119
35–44	212 (36.6%)	19	193
45–64	184 (31.8%)	29	155
>= 65	14 (2.4%)	3	11
Marital Status			
Never Married	62 (10.7%)	7	55
Married	324 (56.0%)	29	295
Divorced	132 (22.8%)	14	118
Widowed	61 (10.5%)	14	47
Religion			
Orthodox	342 (59.1%)	39	303
Muslim	49 (8.5%)	6	43
Protestant	176 (30.4%)	19	157
Catholic	3 (0.5%)		3
Other*	9 (1.6%)		9
Educational Status			
No Education	173 (29.9%)	23	150
Primary	230 (39.7%)	22	208
Secondary	124 (21.4%)	14	110
Tertiary	52 (9.0%)	5	47

* Others—Wakefata, Jehovah's Witnesses

Table 2 Study participants by status at the last visit in ART in SWS health facilities from January 2016 to October 2023 (*n* = 579)

Status	Frequency	Percent (%)
Dead	36	6.2
Lost	43	7.4
Transferred Out	38	6.6
On ART	462	79.8
Total	579	100

present study was 39 years (SD ± 11.08). Thirty-six (3.6%) patients died during follow-up (Table 2).

Baseline clinical and antiretroviral medication-related characteristics

At ART initiation, the median CD4 + cell count was 395cells/mm^3, and the mean was 416.7 cells/mm^3, with a minimum of 11cells/mm^3 and a maximum of 1226 cells/mm^3. Approximately two-thirds (67.2%) of the participants disclosed their HIV status. The most frequently used initial first-line ART regimens were EFV-based (52.2%) and DTG-based (46.1%). Greater than one-third (40.9%) of the total had baseline regimen substitutions during their follow-up period (Table 3).

Table 3 Baseline clinical and antiretroviral-related characteristics of HIV-infected patients enrolled in ART in SWS health facilities from January 2016 to October 2023 (*n* = 579)

Variables	Category	Percent (%)	First-line ART Failure	
			Events (64)	Censored (515)
Disclosure	Yes	389 (67.2%)	23	366
	No	190 (32.8%)	41	149
WHO Clinical Stage	I	354 (61.1%)	19	335
	II	92 (15.9%)	9	83
	III	118 (20.4%)	28	90
	IV	15 (2.6%)	8	7
TB/HIV Co-infection	Yes	98 (16.9%)	28	70
	No	481 (83.1%)	36	445
OI other than Tb	Yes	132 (22.8%)	34	98
	No	447 (77.2%)	30	417
Adherence	Good	411 (71.0%)	21	390
	Fair	104 (18.0%)	20	84
	Poor	64 (11.1%)	23	41
Baseline CD4 count	<= 200	158 (27.3%)	20	138
	201–349	85 (14.7%)	3	82
	350–499	126 (21.8%)	22	104
	>=500	210 (36.3%)	19	191
Received CPT	Yes	254 (43.9%)	19	235
	No	325 (56.1%)	45	280
Baseline BMI	<=18.49	232 (40.1%)	38	194
	18.5–24.99	320 (55.3%)	26	294
	>=25	27 (4.7%)	0	27
Baseline Regimen	NVP-Based	10 (1.7%)	1	9
	EFV-Based	302 (52.2%)	42	260
	DTG-Based	267 (46.1%)	21	246
Regimen Substitution	Yes	237 (40.9%)	31	206
	No	342 (59.1%)	33	309

The incidence of first-line ART failure

The study revealed an overall incidence rate of first-line ART failure of 2.568 per 1000 person-months of observations within a total follow-up period of 24,925.7 person-months (Fig. 2). The first patient developed treatment failure at 15 months of observation, whereas the last patient developed treatment failure at 86.20 months of observation. The mean and median follow-up periods were 43.05 and 38.00 months, respectively. Among the 579 patients followed retrospectively, 64 developed first-line ART failure during the follow-up period. The study included 64 persons who experienced treatment failure, 41 (65.1%) of whom were confirmed to experience treatment failure based on virologic criteria (virologic failure). The incidence of immunologic failure was 6.25%, that of clinical failure was 3.1%, and that of both clinical and immunological failure was 26.6%.

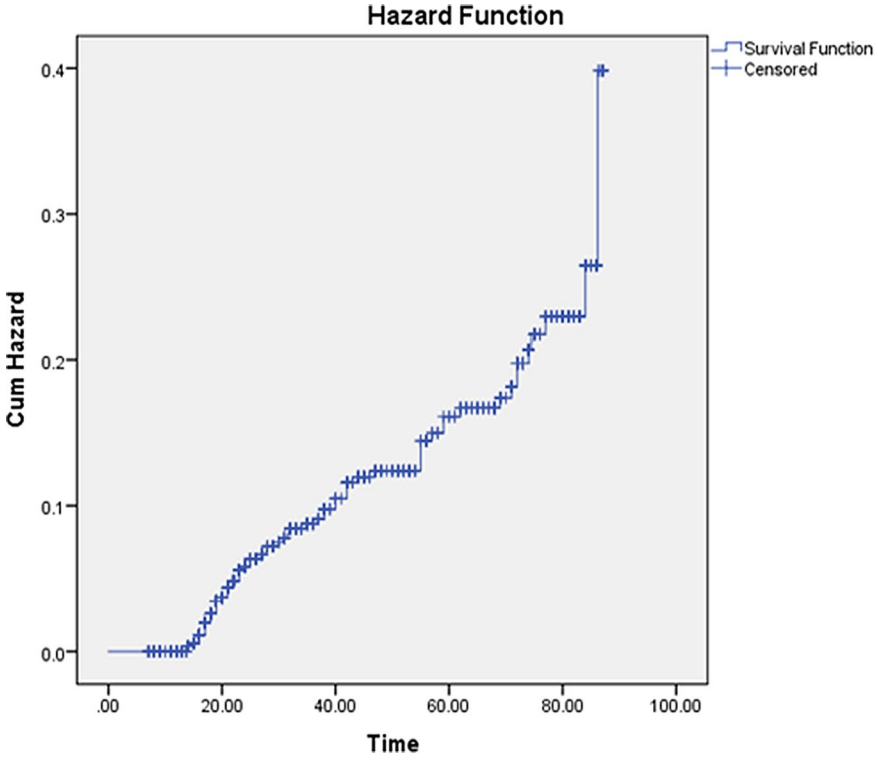


Fig. 2 Cumulative incidence of FLART failure in SWS health facilities from January 2016 to October 2023

Survival time of patients with first-line ART failure

Up to 12, 24, 36, 48, 60, 72, 84, and 87.16 months of observation, the cumulative survival probabilities of first-line ART failure were 100%, 94.32%, 91.64%, 88.33%, 85.11%, 82.07%, 76.73%, and 67.14%, respectively. The Kaplan–Meier survival analysis revealed that the mean survival time was 78.21 months (95% CI: 76.183–80.238). As more months of follow-up are added, the Kaplan–Meier curve in Fig. 3 illustrates a decrease in the likelihood of survival. Individuals who were coinfected with HIV and TB during the follow-up period had a lower chance of survival than those who were not coinfected (Fig. 4).

Predictors of first-line ART failure

This study used multivariable Cox proportional hazard regression analysis to examine the factors that could cause first-line ART to fail. These factors included being male, age (15–24 years and 35–44 years), disclosing an HIV infection, WHO clinical stages III and IV, TB/HIV co-infection, an opportunistic infection other than tuberculosis, receiving cotrimoxazole preventive therapy (CPT), and fair or poor adherence. The study revealed that male patients had a two-fold higher hazard of FLART failure than females (AHR = 1.953, 95% CI: 1.113–3.425). According to the study, patients who disclosed that they had HIV had a 47% lower hazard of FLART failure than those who did not disclose (AHR = 0.530, 95% CI: 0.295–0.954).

The hazard of first-line ART failure was 2.5 times higher in WHO stages III or IV than for WHO stages I or II (AHR = 2.544, 95% CI: 1.043–6.02) (Fig. 5). The hazard of FLART failure was increased by 2.8 times among patients who had TB/HIV coinfections compared to their counterparts (AHR = 2.794, 95% CI: 1.330–5.869). Moreover, those who had OI other than TB had a 2.3-fold greater hazard of first-line ART failure than those who did not have OI (AHR = 2.339, 95% CI: 1.279–4.277) (Fig. 6). The hazard of first-line treatment failure in patients who received CPT was 80% lower than that in their counterparts (AHR = 0.200, 95% CI: 0.078–0.511) (Fig. 7). Compared to patients with good treatment adherence, those with fair or poor adherence had a roughly four times higher hazard of FLART failure (AHR = 3.872, 95% CI: 2.132–7.032) (Fig. 8).

Discussion

ART failure occurs when the medications used to treat HIV/AIDS are ineffective at suppressing the virus. This remains a significant challenge for many individuals living with HIV who are receiving antiretroviral therapy. The study identified overall incidence, event-free time, and risk factors for FLART failure.

This study found that the overall incidence rate of first-line ART failure was 2.57/1000 person-months. This

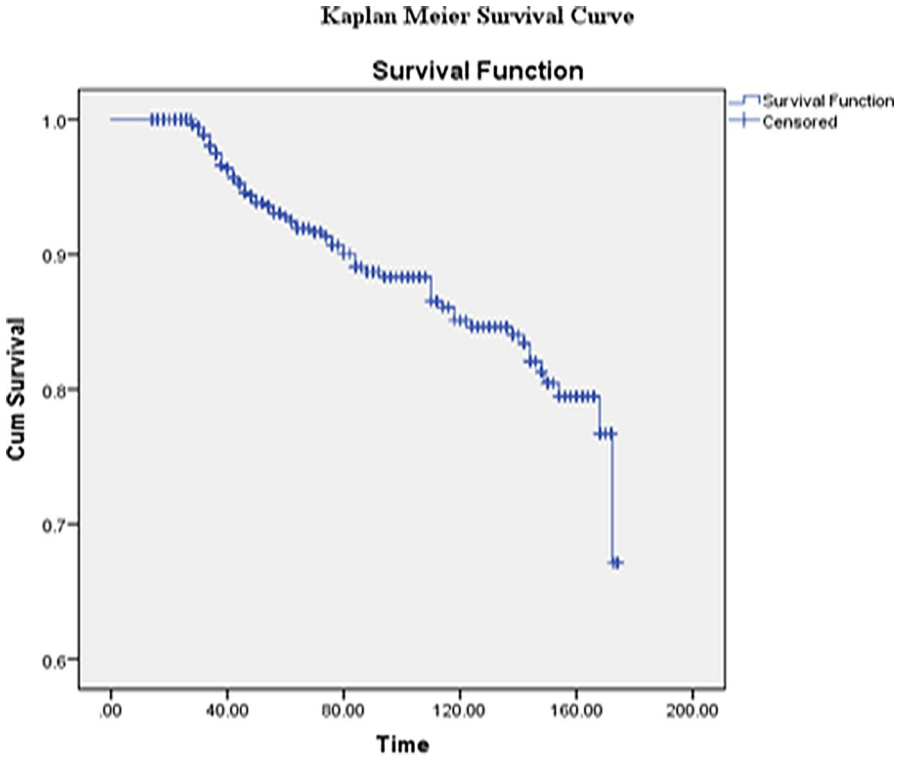


Fig. 3 KM curve showing the cumulative survival probability of first-line ART failure in SWS health facilities from January 2016 to October 2023

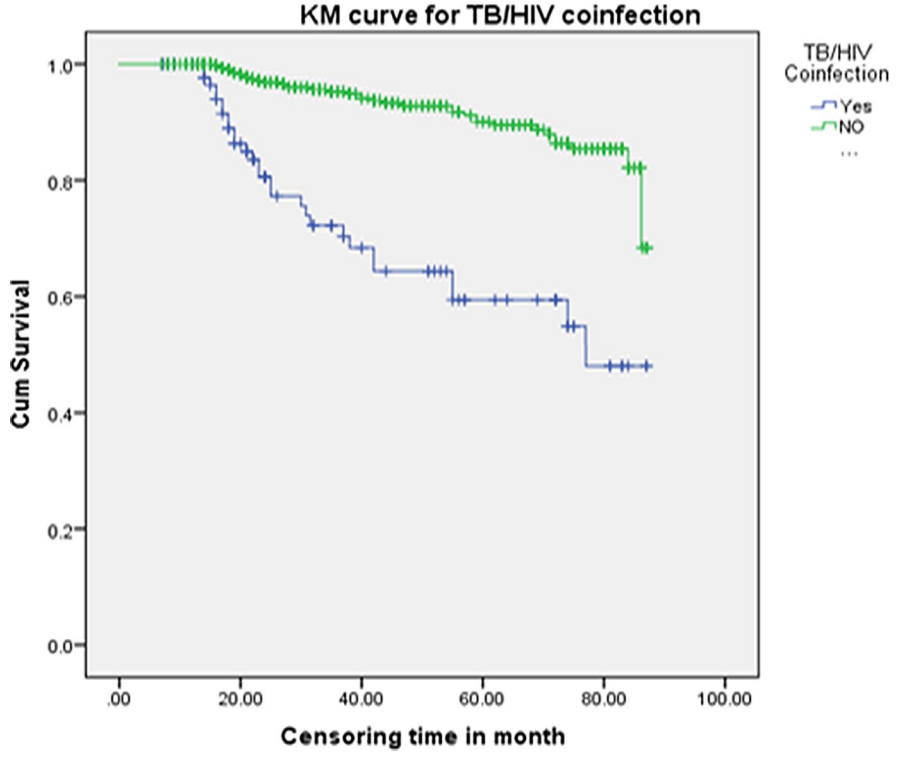


Fig. 4 KM curve comparing the survival probability of FLART failure by TB and HIV coinfections among ART patients in SWS health facilities from January 2016 to October 2023

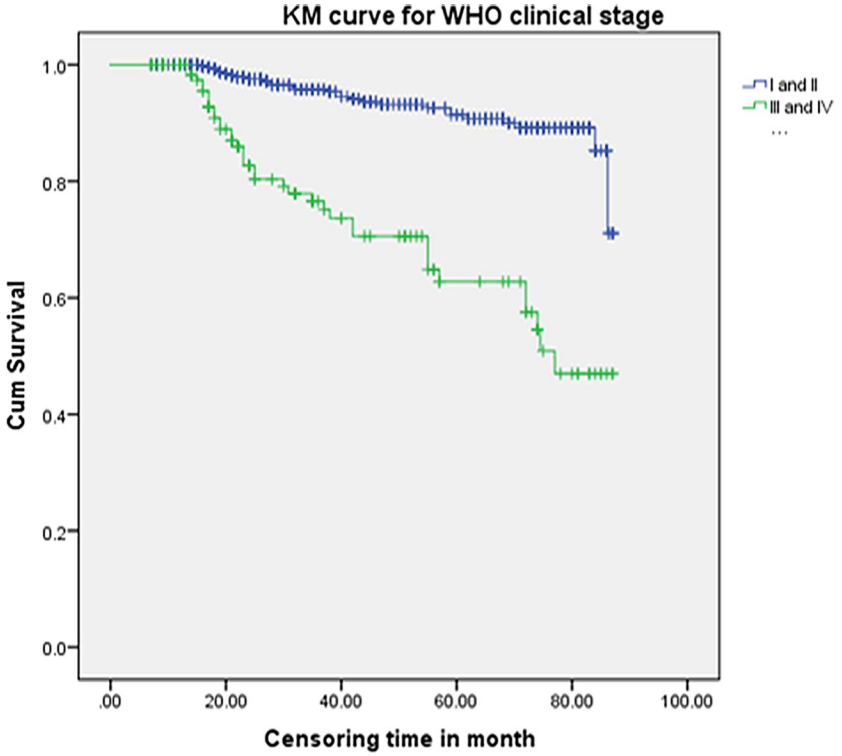


Fig. 5 KM curve showing the cumulative survival probability of FLART failure by WHO clinical stage in SWS health facilities from January 2016 to October 2023

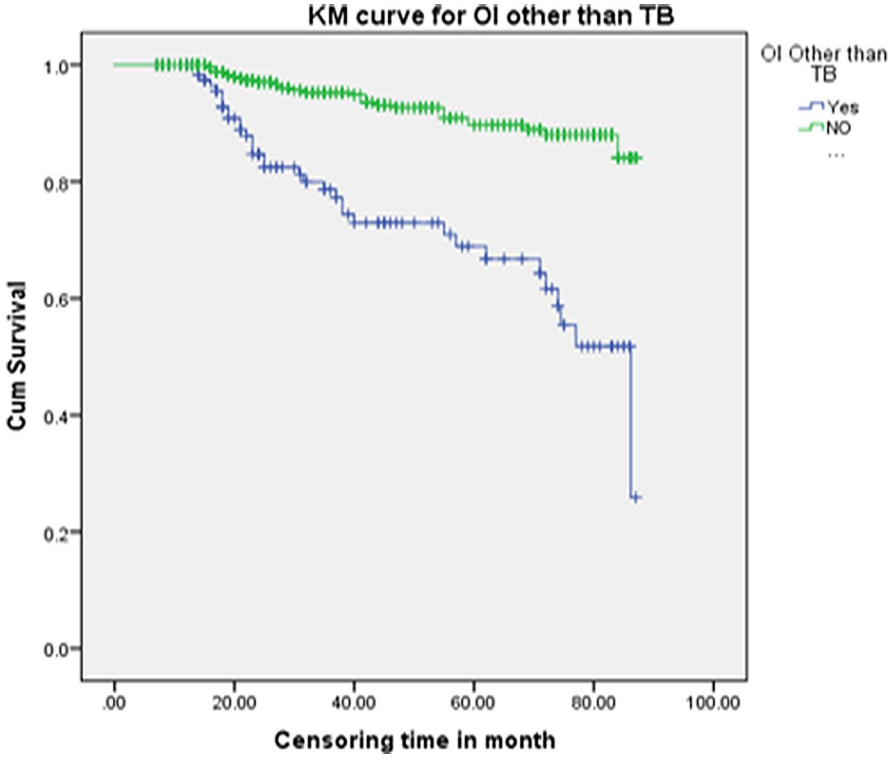


Fig. 6 KM curve comparing the survival probability of FLART failure by opportunistic infections among ART patients in SWS health facilities from January 2016 to October 2023

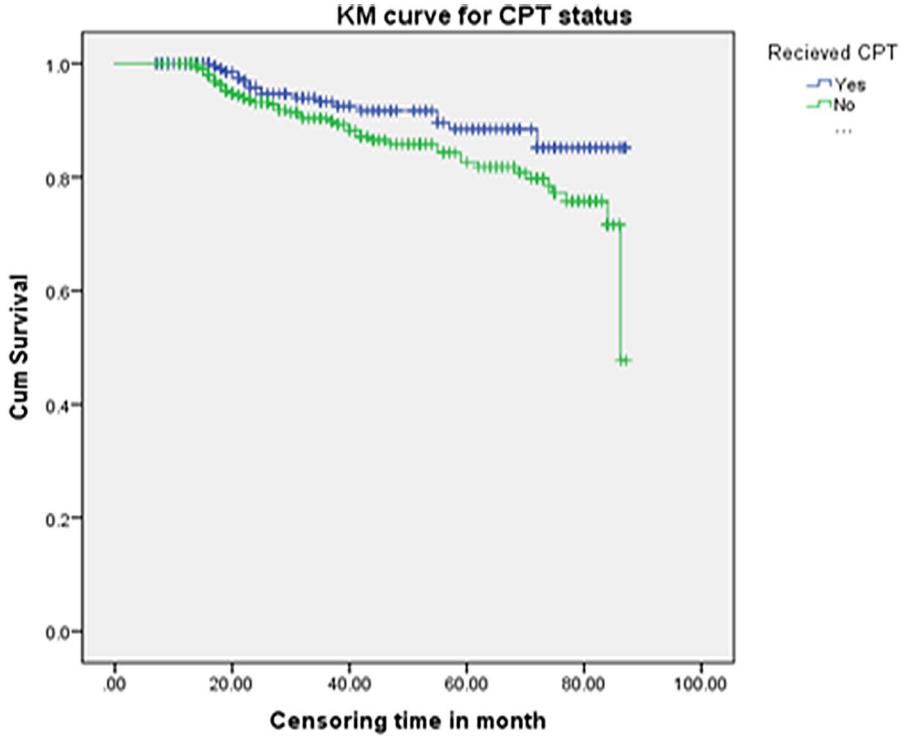


Fig. 7 KM curve comparing the survival probability of FLART failure by CPT status among ART patients in SWS health facilities from January 2016 to October 2023

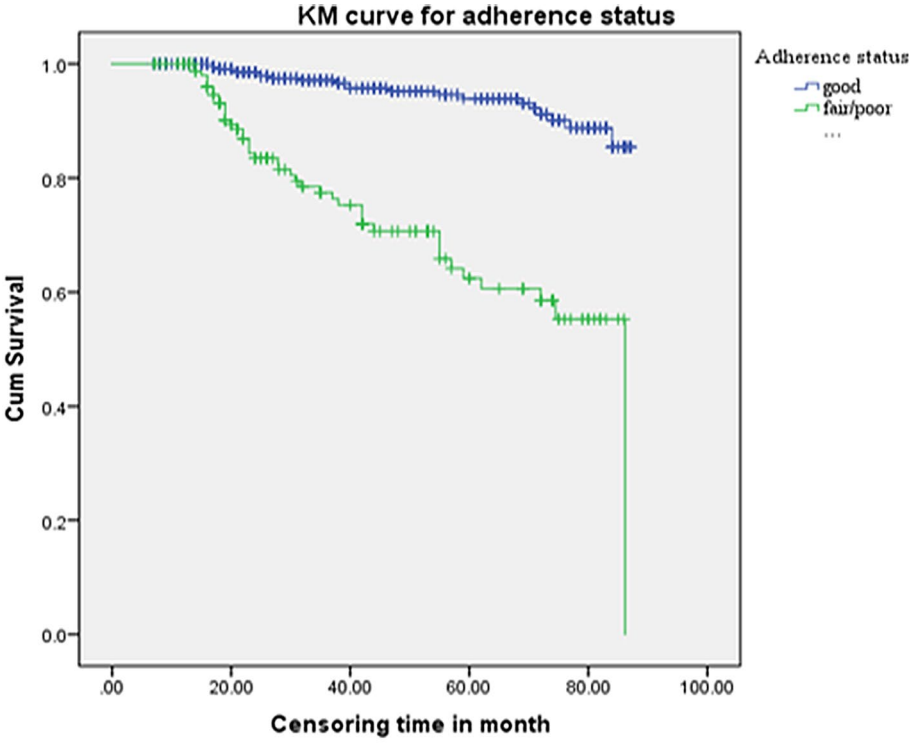


Fig. 8 KM survival curve showing the cumulative survival probability of FLART failure by adherence status of patients on ART in SWS health facilities from January 2016 to October 2023

finding was consistent with studies that were conducted in northwest Ethiopia [25], SPHMMC [9], and Myanmar [23]. At the same time, it was inconsistent with studies that were conducted at Zewditu Memorial Hospital [36], Addis Ababa [37], and Amhara regional referral hospitals [24]. This discrepancy may be due to variations in the study periods and the increase in medical care for ART patients, which included improved adherence counseling and support. Furthermore, the majority of patients at Addis Ababa's private medical facilities had baseline CD4 + counts less than 200 cells/mm^3, which was linked to a higher chance of treatment failure [31].

The KM curve showed that the cumulative probabilities of surviving or being free from the event of interest at the end of 24 and 36 months of observation were 94.32% and 91.64%, respectively. The findings of this study were nearly in line with those of the SPHMMC study, which were 96.30% and 94.49%, respectively [9]. This could be due to the proximity of the study area and socio-cultural similarities. The findings of the current study showed that the mean survival time of virologic failure was 14.8 months. This could be attributed to the drug's adverse effects, which result in poor adherence and ART failure.

The study revealed that male patients had nearly twice the hazard of FLART failure compared to females. This hazard was lower than that found in a previous study conducted at Bale Zone Hospitals [22]. The difference may be attributed to the longer follow-up duration and earlier study period in the Bale Zone research, which covered 2004 to 2014, whereas the current study spanned from 2016 to 2022. These temporal and methodological differences could have influenced the observed outcomes.

Patients who disclosed their HIV status exhibited a 47% lower hazard of FLART failure compared to those who did not disclose. This aligns with reports from other studies in SPHMMC [9], reporting that individuals who disclosed their HIV status were 96.2% less likely to experience virological failure. While both studies affirm the protective effect of disclosure, the magnitude of impact differs, potentially due to variations in outcome definitions, statistical models, or population characteristics. FLART failure encompasses a broader spectrum of clinical and immunological indicators, whereas virologic failure is narrowly focused on viral load suppression.

Patients with fair or poor treatment adherence were 3.9 times more likely to experience FLART failure compared to those with good adherence (Table 4). This finding is consistent with studies conducted at SPHMMC [9] and Bale Zone Hospitals [22], but it shows a higher failure rate than studies from Addis Ababa [37] and Arbaminch town [35]. The study in Addis Ababa private hospitals reported a notably high adherence rate (97.7%), which may be attributed to higher literacy levels and better access to health information. In contrast, the Arbaminch study population had distinct sociodemographic characteristics, particularly in education. Approximately 90% of participants had at least a primary education, compared to 70% in the current study, which may have contributed to the observed differences in adherence and treatment outcomes.

The hazard of FLART failure was 2.8 times greater among patients who had TB/HIV coinfections than among their counterparts (Table 4). This finding aligns with previous studies conducted at SPHMMC [9], Tanzania [26], Bale Zone hospitals [22], and Gondar Hospital [38], suggesting a consistent pattern across similar healthcare settings. The observed similarity may be attributed to shared treatment protocols and resource limitations that impact adherence and drug efficacy. Such consistency reinforces the generalizability of the current study and highlights the need for targeted interventions. In contrast, studies from Myanmar [23] reported a lower hazard, potentially due to larger sample sizes and a higher proportion of patients with advanced disease (45.6%) compared to 23% in the present study, which may have influenced treatment outcomes.

Opportunistic infections (OIs) are also significant predictors of first-line ART failure. Patients with OIs other than TB had a 2.3-fold higher hazard of ART failure compared to those without OIs (Table 4). However, this hazard was lower than that reported in studies conducted at SPHMMC [9] and Bale zone hospitals [22]. This difference may be due to a higher proportion of patients with CD4 counts below 200 cells/mm^3 in those studies—36.5% at SPHMMC and 65.5% in Bale zone hospitals—compared to 27% in the current study. HIV/AIDS patients with low CD4 counts have impaired humoral and cellular immunity, increasing their susceptibility to opportunistic infections and ART failure [34, 39]. Additionally, studies in Bale zone hospitals were conducted before Ethiopia adopted the 'test and treat' strategy, which enrolls all HIV-positive individuals regardless of CD4 count. Consequently, those studies included a higher proportion of patients with advanced disease at ART initiation (67.5%).

Our study found that patients who received CPT had an 80% lower hazard of FLART failure compared to those who did not. This aligns with findings from another study in Addis Ababa [9], which reported that patients on CPT were 86.6% less likely to develop virologic failure (VF). Although the magnitude of effect differs slightly, both studies consistently demonstrate a strong protective association between CPT use and reduced risk of ART failure. CPT is important in maintaining immune stability and preventing complications that can undermine ART effectiveness and contribute to ART failure [40].

WHO clinical stage is another predictor in this study. Compared with WHO stage I/II, being at WHO clinical stage III/IV was associated with a 2.5-fold increased

Table 4 Bivariable and multivariable Cox regression analysis of predictors of first-line ART failure in adult HIV-positive patients in SWS health facilities from January 2016 to October 2023

Variable	FLART Failure		Bivariable Analysis		Multivariable Analysis	
	Yes	No	*p*-value	CHR (95% CI)	*p*-value	AHR (95% CI)
Gender						
Male	30	196	0.026	1.746 (1.067–2.855)	0.020*	1.953 (1.113–3.425)
Female	34	319		1		
Educational Status						
No Education	23	150	0.274	1.719 (0.651–4.451)		
Primary	22	208	0.956	1.028 (0.388–2.720)		
Secondary	14	110	0.439	1.498 (0.538–4.166)		
Tertiary	5	47		1		
Marital Status						
Never Married	7	55	0.189	0.544 (0.219–1.350)	0.248	0.481 (0.140–1.662)
Married	29	295	0.002	0.370 (0.195–0.701)	0.414	0.720(0.327–1.585)
Divorced	14	118	0.021	0.417 (0.198–0.877)	0.20	0.571 (0.243–1.346)
Widowed	14	47		1		1
Age						
15–24	6	37	0.332	0.503 (0.125–2.021)	0.050	0.297 (0.088–0.999)
25–34	7	119	0.018	0.196 (0.050–0.758)	0.206	0.486 (0.159–1.488)
35–44	19	193	0.081	0.337 (0.099–1.145)	0.049	0.314 (0.099–0.995)
45–64	29	155	0.303	0.533 (0.161–1.763)	0.639	1.449 (0.307–6.829)
>= 65	3	11		1		
Disclosure						
Yes	23	366	0.000	0.335 (0.202–0.554)	0.034*	0.530 (0.295–0.954)
No	41	149		1		1
Baseline WHO stage						
I/II	28	418		1		1
III/IV	36	97	0.000	5.430 (3.311–8.904)	0.040*	2.544 (1.043–6.202)
TB/HIV Coinfection						
Yes	25	70	0.000	4.122(2.492–6.819)	0.007*	2.794 (1.330–5.869)
No	39	445		1		1
OI other than TB						
Yes	31	98	0.000	0.262 (0.161–0.428)	0.006*	2.339 (1.279–4.277)
No	33	417		1		1
Adherence						
Good	21	390		1		1
Fair/poor	43	125	0.000	6.529 (3.863–11.033)	< 0.001*	3.872 (2.132–7.032)
Baseline CD4 count						
< 200 cells/mm^3	20	138	0.194	1.421 (0.836–2.414)	0.555	1.338 (0.508–3.524)
>= 200 cells/mm^3	44	377		1		1
Received CPT						
Yes	19	235	0.037	0.564 (0.330–0.965)	0.001*	0.200 (0.078–0.511)
No	45	280		1		1
Baseline BMI						
<=18.49	38	194		1		1
18.5- 24.99	26	294	0.000	0.389 (0.236–0.642)	0.626	0.854 (0.453–1.6110
>=25	0	27	0.957	0.000 (0.00–5.270)	0.000	0.000 (0.000 -2.912E + 205)
Baseline Regimen						
NVP-Based	1	9	0.539	0.531 (0.071–3.998)		
EFV-Based	42	260	0.698	0.898 (0.521–1.547)		
DTG-Based	21	246		1		
Regimen Substitution						

Table 4 (continued)

Variable	FLART Failure		Bivariable Analysis		Multivariable Analysis	
	Yes	No	*p*-value	CHR (95% CI)	*p*-value	AHR (95% CI)
Yes	237	31	0.013	0.521 (0.310–0.873)	0.119	0.625 (0.346–1.129)
No	342	33		1		1

* Significant at p-value < 0.05 1: Reference category

hazard of FLART failure (Table 4). The findings of this study showed a higher hazard than that reported in the Amhara region referral hospitals [24]. The observed difference might be due to delays in patient enrollment in these study areas, which could have led to the progression of opportunistic infections. Additionally, variations in the knowledge level of health professionals regarding the accurate classification of patients into the appropriate WHO clinical stage may have contributed. Additionally, the poor adherence status in the current study (71% vs. 84.5%) might be another contributing factor, as poor adherence is well known to be associated with ART failure [27].

Despite these findings, this study has several limitations that should be considered. As a retrospective cohort design, it relied solely on data extracted from patient admission forms, follow-up records, registries, and the ART electronic database, which may have been incomplete or inconsistently documented. A substantial number of medical records were excluded due to missing information that could not be validated through chart review. In addition to that, only variables with complete data were included, excluding key factors like anemia levels and functional status that may influence first-line ART failure. Furthermore, death, loss to follow-up, and transfer out were treated as censoring, though such patients can no longer experience ART failure.

Conclusions

The incidence of first-line ART failure was relatively low in the present study setting, suggesting effective implementation of ART services in the region. However, first-line ART treatment failure was significantly associated with advanced WHO clinical stage, poor adherence, TB/HIV coinfection, male sex, lack of cotrimoxazole prophylaxis, non-disclosure of HIV status, and the presence of opportunistic infections. These findings highlight the need for early monitoring, adherence support, and comprehensive care.

Based on these findings, to reduce the incidence of first-line ART failure and improve survival, we recommend that the Ministry of Health and stakeholders strengthen early HIV diagnosis and timely ART initiation through enhanced testing strategies such as PITC. Health facilities must be supported in delivering consistent adherence counseling and ensuring the regular provision of TB and cotrimoxazole prophylaxis. Providers should address adherence barriers through follow-up and promote HIV status disclosure to facilitate home-based care. Furthermore, integrating basic health services such as nutritional support into HIV care may enhance treatment adherence and overall patient outcomes.

Abbreviations

AIDS	Acquired immune deficiency syndrome
AHR	Adjusted hazard ratio
ART	Antiretroviral therapy
BMI	Body mass index
CHR	Crude hazard ratio
CI	Confidence interval
CPT	Cotrimoxazole preventive therapy
DTG	Dolutegravir
EFV	Efavirenz
FLART	First-line antiretroviral therapy
HAART	Highly active antiretroviral therapy
HC	Health Center
HRs	Hazard ratios
HIV	Human immunodeficiency virus
KM	Kaplan–Meier
PITC	Provider initiated testing and counselling
PLHIV	People living with HIV
OI	Opportunistic infections
SD	Standard deviation
SPHMMC	St. Paul's Hospital Millennium Medical College
SWS	Southwest shoa
TB/HIV	Tuberculosis and HIV coinfections
TB	Tuberculosis
UNAIDS	Joint United Nations Programme on HIV and AIDS
WHO	World Health Organization

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Author contributions

SG: Conceptualization, Writing, and Formal Analysis, Investigation, AM and RS: Methods, Supervision, Visualization, DT: Software and data curation, YK: revising or critically reviewing the manuscript. All authors reviewed and edited the manuscript before submission.

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Data availability

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request via (mailto: gurmessa07@gmail.com).

Declarations

Human ethics and consent to participate

This study involved the use of patients' medical records and databases. The research was conducted in compliance with the Declaration of Helsinki and

all relevant national guidelines and regulations [41, 42]. Ethical clearance was granted from the Institutional Review Board of Ambo University with reference number AUWC/PG/11/16. The Ethics Committee of Ambo University, Woliso campus, waived the requirement for informed consent on behalf of patients' medical records and databases. Official support letters were obtained from the Zonal Health Office. Then, an official letter was submitted to the selected health facilities, and signed permission was obtained to access the ART clients' medical records and databases. Written consent was also obtained from the ART providers and data clerks. To maintain confidentiality, patient names and unique ART numbers were not included in the data extraction checklist, and data were not used for any purpose other than the stated study objectives.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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