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Death and Transferred Out as Competing Event for Lost to Follow-up among HIV-positive Adults on ART, in Eastern Ethiopia Governmental Hospitals from January 2015 to December 2021; (Multicenter Competing Risk Regression Analysis)

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Abstract

Background: Lost to follow-up (LTFU) among patients on antiretroviral therapy accounts for the most of all attrition. In Sub-Saharan Africa, there is a concern regarding high rates of LTFU and early mortality in antiretroviral therapy programs. Mortality and transferred out are the potential competing events for LTFU. Ignoring these events may give an invalid estimate by overestimating the probability of the occurrence of LTFU.

Objective: This study aims to assess the incidence and predictors of LTFU among adult HIV (Human Immunodeficiency Virus) patients who started antiretroviral therapy (ART) in Jigjiga Governmental Hospitals' ART clinics between January 2015 and December 2021.

Methods: A multi-center Institution-based retrospective follow-up study has been conducted in Jigjiga Governmental Hospitals. Gray's test was used to compare the cumulative incidence function (CIF) of LTFU across variable categories. A graphical examination of CIF for each category of variables, as well as the Schoenfeld residuals global test, validate the proportional sub-hazard assumption. We fitted both univariable and multivariable competing risk regression models. In the multivariable analysis, variables with p-values of 0.05 were considered statistically significant predictors of LTFU.

Result: A total of 842 clients were included in the study, and the LTFU incidence rate is 5.25 per 100 PYO. The participants' median age ranged from 29 to 43 years. Those not disclosed their HIV status (aSHR=4.22; 95%CI (2.11-8.47)), those were a fair and poor level of recent adherence (aSHR=2.17; 95%CI (1.18-4.23)) and (aSHR=1.48; 95%CI (2.97-5.34)), patients with severe anemia (aSHR 4.58; 95% CI (1.28-16.39)) ambulatory functional status (aSHR 2.38; 95% CI (1.21-4.68)), patients who do not took cotrimoxazole prophylactic therapy (CPT) (aSHR 2.47; 95% CI (2.99-6.15)) were significant predictors of LTFU.

Conclusion: In this study, the incidence of LTFU was decreased with additional years on ART. Patients on ART who did not disclose their HIV status had poor levels of adherence, did not take CPT prophylaxis, on severe anemia and ambulatory functional status were at higher risk of LTFU. As a result, close monitoring and proper tracing mechanisms aimed at this higher-risk group would reduce AIDS (Acquired immunodeficiency syndrome)-related LTFU.

Keywords: Jigjiga-Ethiopia, HIV/AIDS, Antiretroviral therapy, Lost to follow-up, Cumulative incidence function, Competing risks regression

Introduction

In 2021, approximately 38.4 million people worldwide were living with HIV. Since the beginning of the epidemic, 84.2 million people have become infected with HIV, and 40.1 million have died from AIDS-related illnesses [1]. At the end of December 2021, around 28.7 million people were accessing ART, up from 7.8 million in 2010 [2]. According to the World Health Organization (WHO), the African region continues to be the most severely affected, accounting for nearly two-thirds of people living with HIV [3]. In Ethiopia by 2021, nearly 610,000 people were living with HIV/AIDS. The overall ART coverage is 78% of which adult ART coverage accounts for 76% [4].

ART lowers mortality and morbidity rates in HIV patients while improving their quality of life. The benefits also include preventing HIV transmission by suppressing HIV replication in people who already have the virus. Despite a significant reduction in HIV-related deaths as a result of widely available ART treatment, success remains critically dependent on regular patient follow-up in care [3,5,6].

The goals of ART are to lead and effectively suppress viral replication in order to prevent the development of HIV drug resistance, treatment failure, and lost follow-up. Adherence to ART and retention in HIV care program are critical for achieving optimal health outcomes in HIV patients [7,8]. Loss of follow-up from ART service has a pronounced negative impact on ART treatment outcomes. It can reduce the immunological benefits of ART and increase AIDS-related morbidity, mortality, and hospitalization, resulting in serious consequences such as drug toxicity, treatment failure due to poor adherence, and drug resistance [9,10].

A competing risk is an event that either impedes or modifies the occurrence of the primary event of interest. Classical survival analysis assumes non-informative or independent sampling (censoring), which means that subjects who remain in a given study at any given point in time have a similar future risk of event occurrence as those who are no longer being followed, as if subjects lost to follow up were random and thus non-informative [11,12]. Traditional survival analysis becomes unsuitable when the event of interest is neither censored nor observed, and as a result, the cumulative incidence of an event may be overestimated in the presence of competing risks. Because the assumption of non-informative censoring may be violated and event probability estimation is interpreted as occurring in a setting where competing events do not occur [13,14].

According to competing risk regression model results, the cumulative incidence in different countries was 7.9 per 100 person-year, 5.6 per 100 person-year, 11.6 per 100 person-year, and 10.9 per person-year, respectively [9,14-16]. Similar studies conducted in different parts of Ethiopia based on classical survival analysis reported the cumulative incidence ranging from 3.7 per 100 person-year up to 26.6 per 100 person-year [17-24].

Different studies showed that LTFU is associated with baseline sociodemographic factors like male sex [8,25-31] those whose age is younger 15-24 years [7,14,16,27,28,32,33] and those not having a committed partner [34], patients with no education [27,35,36], and unmarried [27,36], and clinical and treatment-related factors like CD4 count below 200 cells [8,19,37,38], BMI<18.5 kg/m^2 [8,25,32], WHO stage I or II [8,14,15,38-41], anemia [42], fair/poor level of adherence and WHO stage III or IV [17,18,24,28,35], don't take INH prophylaxis [16,17,22], BMI<18.5 kg/m^2 [21,35], no CPT prophylaxis [16,43], ambulatory functional status [16,17,19,44] were significant predictors for LTFU.

Although many studies have been conducted on LTFU and its determinants, valid estimates of incidence and predictors of LFTU can be obtained if death and transfer out are considered as competing events (rather than counting those as censored), especially in poor clinical settings where death is common and alters the probability of the occurrence of LTFU. However, in most of these studies, death and transfer out, which are competing risks of LTFU, are frequently ignored, which can lead to misleading results. As a result, the purpose of this study was to estimate the incidence rate and identify the predictors of LTFU in Jigjiga city Governmental Hospitals ART Clinics, Eastern Ethiopia, by considering death and transfer out as competing events.

Methods

Study design and Setting

An institution-based retrospective follow-up study was conducted in Jigjiga city public hospitals in eastern Ethiopia between January 1, 2015, and December 31, 2021. Jigjiga is the capital city of the Ethio-Somali region, which is located 630 kilometers from Addis Ababa, Ethiopia's capital city. The study was conducted in three governmental hospitals in the city; these hospitals housed the city's only ART Centers. All of these hospitals offer HIV/AIDS interventions, such as free diagnosis, treatment, and patient follow-up. The research was carried out between July 1 and July 30, 2022. During the study period, there were a total of 2016 ART-attending patients in these hospitals, with 1816 of them being adults over the age of 15.

Population

All adult HIV-infected patients (Age ≥ 15years) who initiated ART at Jigjiga public hospitals (Karamara General Hospital, Sheik Hassen Yeberre Referral Hospital, and Ablelle Primary Hospital) from January 01, 2015, to December 31, 2021, were

our study population. Adult HIV-positive patients who had at least one follow-up visit after starting ART were included in the study. HIV patients who transferred in with incomplete baseline data, whose medical charts were unavailable during the data collection period, and those with unknown ART initiation dates were excluded from the study.

Sample size determination and sampling method

The minimum required sample size (842) was calculated using Stata 14 software's survival analysis formula power cox command. The study participants' records were first filtered from the ART database based on their entry time to the follow-up, age, and inclusion criteria, and then we used stratified proportionate random sampling (among health facilities). Finally, we used SPSS Software to select the final sample size using a simple random sampling technique (computer-generated Random Sampling) (**Figure 1**).

Variables definition

The primary outcome variable was time to LTFU, with death and transferred out considered as competing events. The predictor variables assessed were baseline socio-demographic factors like (sex, age, marital status, educational status, occupation, residence), baseline clinical and treatment-related factors like (BMI status at baseline, History of Tuberculosis (TB), Opportunistic infections, Hemoglobin level, Baseline CD4, Viral load, WHO clinical stage, Partner HIV status, Functional status, Co-morbidities) and ART adverse event, Regimen type at the start, Regimen substitution, Year of ART initiation, Registered phone number, OI prophylaxis (INH, CPT), Distance from the Hospitals), Disclosure status, Partner HIV status, Caregiver, Adherence level) were included.

Operational definitions

This study intended to determine the incidence of LTFU using seven-year data retrieved from medical record charts. LTFU is defined as not taking an ART refill for 3 consecutive months or longer after the last scheduled visit (from the last attendance for refill) not yet categorized as dead or transferred out [19]. The competing events were death and transferred out which is defined as patients recorded as dead on the patient's exit form or whose outcome is recorded as death on the follow-up chart and patients formally transferred to another health facility respectively. A patient was classified as censored if he/she had still on follow-up at these hospitals at the end of the study period. Operationally the functional status was defined based on the ART guideline; Working FS: able to perform usual work inside or outside the home, Ambulatory FS: able to perform an activity of daily living, and bedridden FS: not able to perform an activity of daily living [45]. ART medication adherence is defined as the percentage of ART drug dosage calculated from a monthly total dose, and classified as good, fair, or poor. Therefore, good adherence was reported if equal to or greater than 95% or ≤ 3 doses missing per month, fair if 85–94% or 4–8 doses missing per month, or poor if less than 85% or ≥ 9 doses missing per month [46]. Disclosure in this study is defined as disclosure of the status that is being HIV positive to at least one individual. The caregiver is also defined as anyone who can support or assist an individual with HIV.

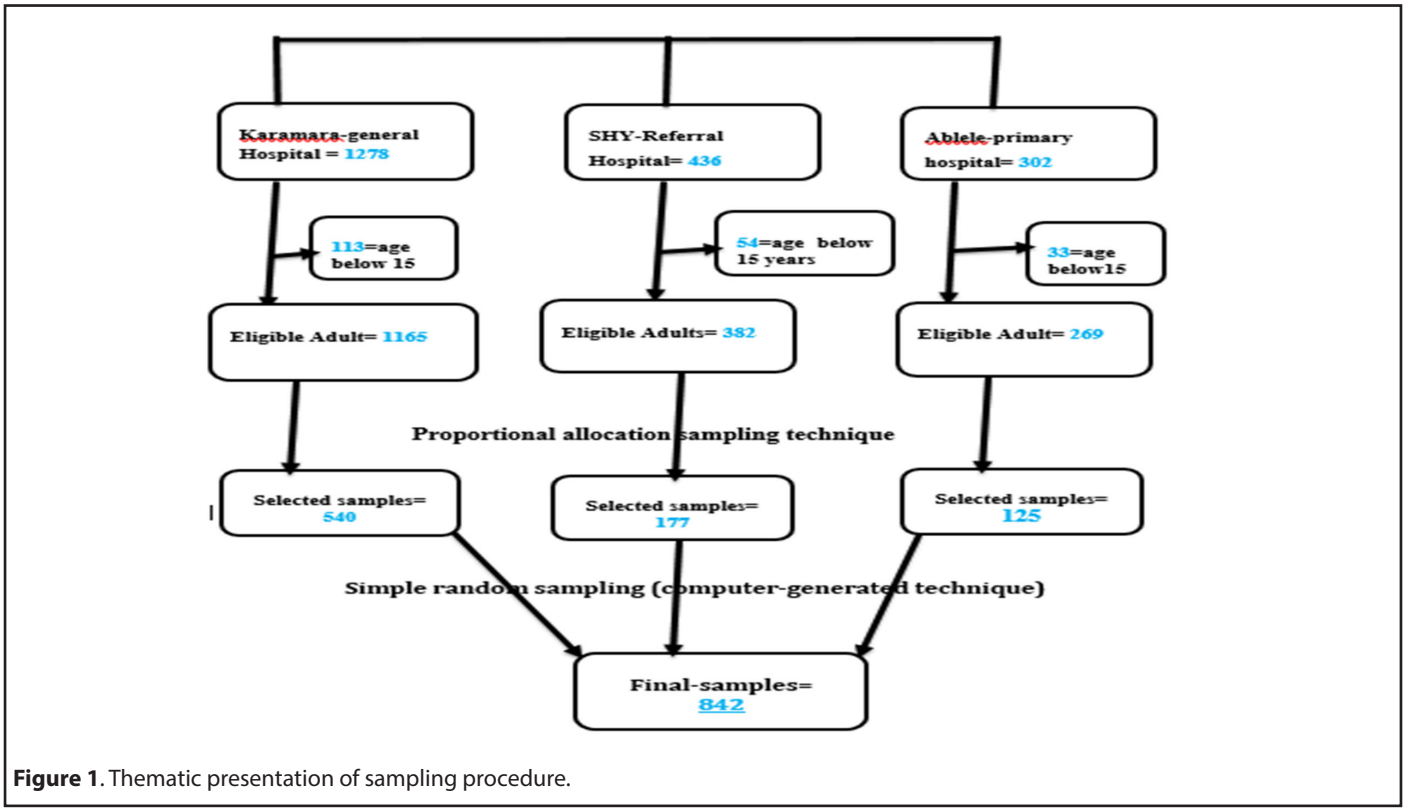

Figure 1. Thematic presentation of sampling procedure.

Data collection tool and procedure

ART patient data is stored in smart care as both a hard copy (chart) and a database. The ART follow-up forms served as the foundation for the data extraction checklist. The data extraction tool was carefully prepared from ART intake follow-up forms to ensure data quality. By randomly selecting and completing 42 sample chart reviews, we demonstrated consistency between data recording systems and the prepared checklist, resulting in minor modification to the data extraction checklist. Seven clinical nurses and health officers were recruited, as well as a data collector and three supervisors for each of the three hospitals.

Data processing and analysis

The Data was entered using Epi-data version 3.1 and then exported to Stata 14 software for analysis. Descriptive statistics including proportions, tables, and charts were done to describe the characteristics of the study participants. Non-parametric estimation of CIF was performed both graphically and using Gray's test. After fitting the model, the proportional sub-distribution hazard assumption was also verified by using the plot of log (- log (1-CIF)) versus the log of time to failure for each covariate, by interacting each covariate with time (tvc) and using Schoenfeld residual test. Univariable competing risk regression analysis was fitted to identify factors associated with LTFU. Variables with a p-value of ≤ 0.2 in the univariable analysis were fit to the multivariable competing risk regression analysis once more. To express the strength of the association, the crude and adjusted sub-distribution hazard ratios were calculated, along with the corresponding 95% CI. Variables with a P-value of ≤ 0.05 were considered statistically significant in multivariable-analysis.

Ethical consideration

We obtained ethical consent from the Institutional Review Board of the University of Gondar, Institute of Public Health. Since the study used an analysis of secondary data from patient charts; we received a waiver for informed consent. To keep privacy, names and other personal identifiers were not included in the data collection tool.

Result

Baseline socio-demographic characteristics

A total of 842 clients enrolled in ART care were included in the final analysis. Nearly half, 466 (53.34%) of the study participants were males. The median age of the participants was 35 (IQR=29-43) years. Of the total, 428 (50.83%) were married, and 270 (32.07%) participants had a primary level of education. The majority of subjects 759 (90.25%) had a caregiver and 673 (80.02%) study participants disclosed their HIV status (**Table 1**).

Table 1. Socio-demographic characteristics for adult HIV patients on ART in Jigjiga city Governmental Hospital ART clinics between January 1, 2015, and December 31, 2021.

Variables	Category	Frequency	Percentage (%)
Sex	Female	466	55.34
	Male	376	44.66
Age	15-24	90	10.69
	25-34	265	31.47
	35-44	298	35.39
	≥45	189	22.45
Marital status	Single	121	14.37
	Married	428	50.83
	Divorced	190	22.57
	Others*	103	12.23
Residence	Urban	552	65.56
	Rural	290	34.44
Distance from HF	Below 5 km	369	43.82
	Above 5 km	473	56.18
Educational status	No education	214	25.42
	Primary	270	32.07
	Secondary	245	29.10
	College & university	113	13.42

Occupation	Unemployed	196	23.28
	Daily laborers	101	12.00
	Housewife	126	14.96
	Government employee	189	22.45
	Self-employee	176	20.90
	Others **	54	6.41
Religions	Orthodox	280	33.25
	Muslim	404	47.98
	Others ***	158	18.76
Year of ART Initiation	Before COVID-19	554	65.8
	After COVID-19	288	34.2
Disclosure status	Disclosed	673	80.02
	Not disclosed	168	19.98
Caregiver	Yes	759	90.25
	No	82	9.75
Others*: Separated, widowed; others**: Farmer, student; others***: Catholic, Protestant.			

Clinical and treatment-related characteristics

About 240 (42.93%) participants were linked to care with a baseline CD4 count between 201-350 cells/ml. The median CD4 count was 292 (IQR=161-421 cells/ml), and 369 (43.82%) of the participants were WHO stage II, followed by WHO stage III & IV 244 (28.98%). Around 89.96% have been started with CPT prophylaxis and the majority (98.8%) of patients were screened for TB, of which 18.67% were positive (**Table 2**).

Table 2. Clinical and treatment-related characteristics of adult HIV patients on ART in Jigjiga city Governmental Hospital ART clinics between January 1, 2015, and December 31, 2021.

Variables	Categories	Frequency	Percentage (%)
Baseline CD4 count	Below 200 cells	275	33.45
	201-350 cells	255	31.02
	Above 350 cells	292	35.52
Baseline WHO stage	Stage I	229	27.20
	Stage II	369	43.82
	Stage III or IV	244	28.98
Last known WHO stage	Stage I	190	22.57
	Stage II	469	55.70
	Stage III or IV	183	21.73
CPT prophylaxis (n=641)	Yes	576	89.86
	No	65	10.14
INH prophylaxis (n=579)	Yes	487	84.11
	No	92	15.89
OI at enrollment	Yes	244	29.72
	No	577	70.28
TB screening status at baseline	Positive	144	18.67
	Negative	667	81.33
Current TB status/last known/	Positive	99	11.76
	Negative	743	88.24

Functional status (baseline)	working Ambulatory Bed-ridden	529 283 30	62.83 33.61 3.56
BMI	<18.5 kg/m2 18.5-24.9 kg/m2 ≥ 25 kg/m2	206 510 126	24.47 60.57 14.96
Baseline adherence	Good Fair poor	485 207 150	57.60 24.58 17.81
last known adherence	Good Fair poor	541 210 90	64.33 24.97 10.70

Incidence of LTFU

Study subjects were followed for different periods of time with a median time of 28.7 months (IQR: 13.9-50.43) months. The minimum and maximum follow-up time was one month and 85.06 months respectively with a total observation time to be 2324.3 person-year. Among the 842 patients enrolled, 91 (10.81%) were dead, 122 (14.49%) had been LTFU, 114 (13.54%) were transferred out, furthermore 515 (61.16%) on treatment until December31, 2021 (**Figure 2**). The overall incidence of LTFU was 5.25 per 100 person-year (95% CI: 2.1–7.2). LTFU was highest in the second 12 months of ART follow-up, 7.4 per 100 person-year (95% CI: 5.4, 10.05).

Non-parametric estimation of CIF of LTFU

CIFs across groups were checked statistically using Gray's test (which is equivalent to the log-rank test of classical survival analysis) and graphically by plotting each predictor variables against failure time (Non parametrical checking).

Based on the result of the modified X^2 test (Gray's test), there was a significant difference in CIF among categories of age, marital status, occupation, education, IPT, CPT, Functional status, disclosure status, baseline WHO stage, caregiver, and type of regiment at start. Graphically, belonging to age 15-24, poor adherence level (baseline), non-disclosure status and

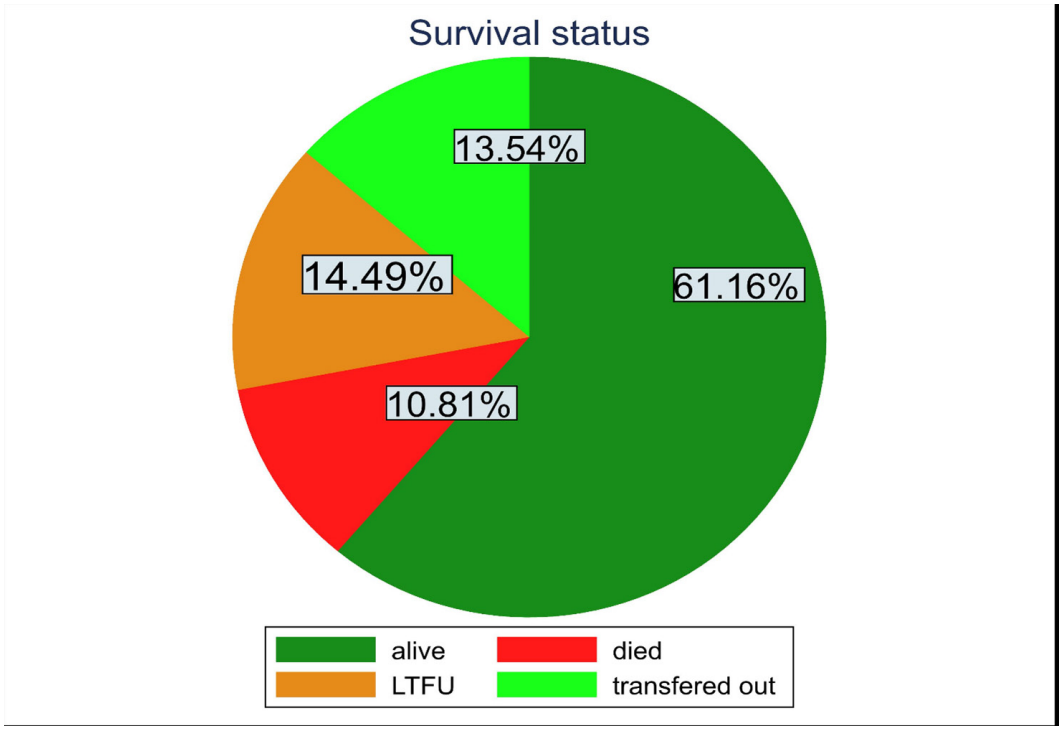

Figure 2. Pie chart proportion of survival status.

WHO stage III &IV, male gender, and bedridden functional status were all risk factors for LTFU (**Figure 3**).

Modeling bivariable & multivariable competing risk regression model

After fitting a bivariable competing risk regression model almost all the predictor variables except educational status, occupation, opportunistic infection & INH prophylaxis, were crudely associated with LTFU at 0.2 level of significance. The Schoenfeld residuals and The Cox-Snell residuals (together with their Nelson-Aalen cumulative incidence function) were done to check the goodness fit test or model fitness (**Figure 4**). The sub-hazard proportionality assumption with the Schoenfeld residual of the global test was 0.3479, indicating no evidence for violation of the proportional sub-hazard assumption. Finally, those variables like: Functional status, disclosure status, hemoglobin, recent adherence level, and CPT prophylaxis, were found to be significant predictors for LTFU at 5% level of significance.

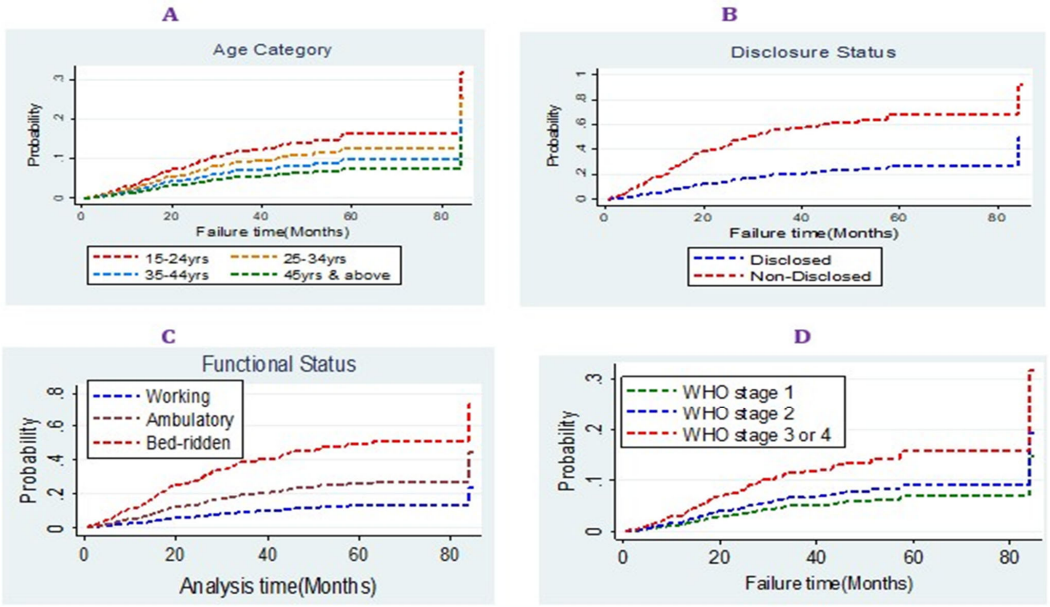

Figure 3. Graphical estimations of CIF among different categorical variables.

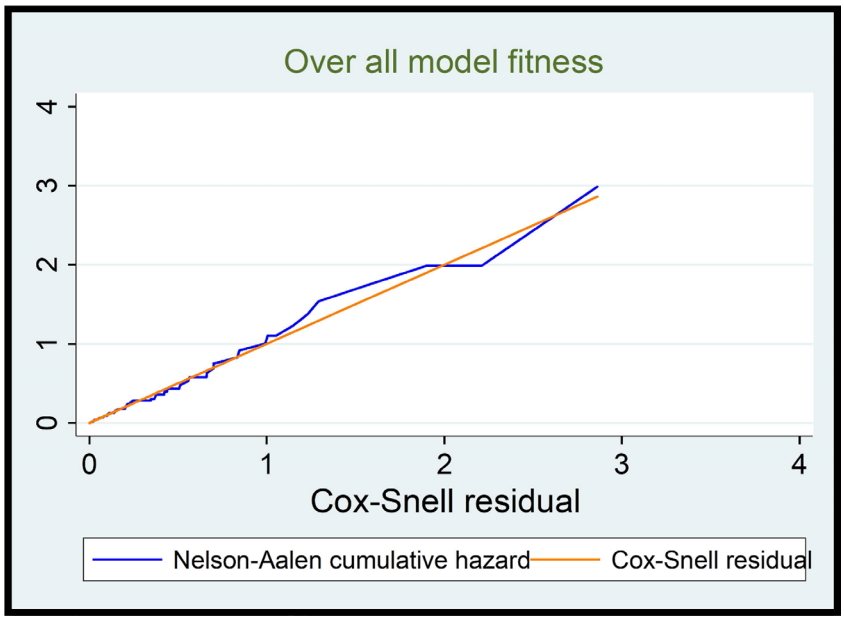

Figure 4. Cox Snell residual plot for model fitness.

In multivariable analysis disclosure status, adherence level (last known), CPT prophylaxis, functional status, hemoglobin level was statically significant for LTFU (p-value<0.05). The patients who did not disclose their HIV status can increase the sub-hazard of LTFU by 4.22 (asHR=4.22; 95%CI (2.11-8.47)) times compared with their counterparts. The sub-hazards of LTFU among the fair and poor level of recent adherence were 2.17(asHR=2.17; 95%CI (1.18-4.23)) and 2.27 (asHR=1.48; 95%CI (2.97-5.34)) times higher than those who have a good level of adherence respectively. The sub-hazard of LTFU is 2.47 higher among patients who do not take CPT prophylaxis 2.47 (asHR=2.47; 95%CI (2.99-6.15) compared with the counterparts. The sub-hazard of LTFU among patients with ambulatory functional status was 2.38 (asHR=2.38; 95%CI (1.21-4.68)) times higher compared with the patients in working functional status. The patient who had moderate and severe anemia increased the sub-hazard of LTFU by 2.22 (HR=2.22; 95%CI (1.09-4.52)) and 4.58 (asHR=4.58; 95% CI (1.28-11.39) times compared with that of those who had no anemia (**Table 3**).

Table 3. Bivariable and multivariable competing risk regression analysis for predictors of LTFU among HIV-positive adults at Jigjiga city Governmental Hospital ART clinics between January 1, 2015, and December 31, 2021.

Variables	Categories	Censored (515)	LTFU (122)	Competing event (205)	cSHR (95% CI)	aSHR (95% CI)
Sex	Female	304	53	109	1	1
	Male	211	69	96	1.56 (1.02-2.33)	1.37 (0.75-0.52)
Age	15-24	53	16	21	1.66 (0.83-3.34)	2.03 (0.65-6.33)
	25-34	152	43	70	1.29 (0.73-2.27)	1.57 (0.77-3.22)
	35-44	187	37	74	0.95 (0.53-1.69)	0.81 (0.36-1.82)
	≥ 45	123	26	40	1	1
Residence	Urban	374	71	107	1	1
	Rural	141	51	98	1.44 (0.95-2.18)	0.91 (0.49-1.66)
Marital status	Single	62	21	38	2.09 (1.17-3.72)	0.98 (0.39-2.46)
	Married	283	45	100	1	1
	Divorced	117	30	43	1.65 (0.97-2.81)	1.25 (0.59-2.63)
	Others	53	26	24	2.37 (1.34-4.19)	1.23 (0.43-3.56)
Functional status	Working	369	46	114	1	1
	Ambulatory	139	70	74	4.34 (2.82-6.67)	2.38 (1.21-4.68)*
	Bedridden	7	6	17	2.31 (0.82-6.49)	2.66 (0.70-10.04)
BMI	Below 18.5	98	28	80	0.95 (0.56-1.61)	0.78 (0.33-1.85)
	18.5-24.9	342	68	100	1	1
	Above 25	75	26	25	1.65 (1.02-2.72)	1.63 (0.84-3.14)
Care giver	Yes	495	97	167	1	1
	No	19	25	38	2.55 (1.53-4.24)	0.59 (0.26-1.32)
Disclosure status	Yes	458	65	150	1	1
	No	56	57	55	4.12 (2.73-6.19)	4.22 (2.11-8.47)**
TB-Screening status	Positive	76	31	50	1.49 (0.93-2.39)	0.56 (0.25-1.25)
	Negative	438	91	155	1	1
CD4 count (baseline)	Below 200 cells	115	53	107	2.14 (1.24-3.69)	0.77 (0.31-1.89)
	201-350 cells	158	43	54	2.46 (1.43- 4.23)	1.05 (0.49-2.22)
	Above 350 cells	226	23	43	1	1
WHO stage (baseline)	Stage one	165	17	47	1	1
	Stage two	246	42	81	1.51 (0.79-2.86)	0.99 (0.39-2.53)
	Stage 3 or 4	104	63	77	3.77 (2.02-7.05)	2.08 (0.58-7.45)

WHO stage (recent)	Stage one Stage two Stage 3 or 4	119 325 71	15 59 48	56 85 64	1 1.52 (0.80-2.87) 3.45 (1.77- 6.73)	1 0.83 (0.34-2.03) 0.49 (0.17-1.40)
Hemoglobin level	Severe anemia Moderate anemia Mild anemia No anemia	26 135 126 226	20 59 21 21	10 71 51 72	7.81 (4.0-15.20) 3.18 (1.83-5.52) 1.64 (0.84-3.22) 1	4.58 (1.28-16.39)* 2.22 (1.09-4.52)* 1.24 (0.54-2.84) 1
Adherence level (baseline)	Good Fair Poor	358 99 58	49 41 32	78 67 60	1 2.39 (1.49-3.83) 2.02 (1.21-3.38)	1 1.74 (0.79-3.86) 1.34 (0.62-2.89)
Adherence level (recent)	Good Fair Poor	387 102 26	49 46 26	105 62 38	1 2.99 (1.89-4.75) 3.63 (2.11-6.25)	1 2.17 (1.11-4.23)* 2.27 (2.97-5.34)*
CPT prophylaxis	Yes No	357 45	67 12	152 8	1 1.43 (0.67-3.09)	1 2.47 (2.99-6.15)*
****= p value<0.01, *= p value<0.05**						

Discussion

In this study, we assessed the incidence and predictors of LTFU among adult HIV/AIDS patients under ART follow-up in Jigjiga Governmental Hospitals. A number of variables were used to explain the variation in the LTFU of HIV/AIDS patients using this competing risk regression model. In our study, we tried to assess socio-demographic, clinical, and treatment-related factors by using secondary data.

The estimated Incidence rate for LTFU was 5.25 per 100-person year observation. It is similar to the finding of a study conducted in different places in Ethiopia [18,21,23] Zimbabwe [14] and Zambia [47]. This might be due to the similarity in the quality of care given according to ART guidelines for HIV/AIDS patients across these different Hospitals since all study areas were in eastern African regions, have almost consistent guidelines prepared by WHO.

However, the current finding is higher than the findings in Debre Markos [24], Kenya [13], Republic of Democratic Congo [48]. This may be due to the study areas being located around the capital city of the region and the majority of the respondents were rural residents, so the flow of the population around the city is somehow low. In addition, the area is located at a small distance from the Ethio-somaliland border, and many of the long-track drivers and emigrants have joined the city most of the time. This also could be due to variations in study design, patient follow-ups, and definitions of LTFU is defined when a patient is lost for at least 90 days since some studies defined LTFU as 180 days [32,40].

The current finding is lower than the findings in Myanmar [37], Guinea-Bisaw [8], South- Africa [34], Cameroon [29], Nigeria [30], Uganda [42], Malawi [33], Ethiopia (mekelle, Jigjiga, Pawi, Gondar) [9,19,20,23]. The difference might be due to variations in study design and the operationalization of terms, as we know that our model is a competing risk regression model, majority of the preceding studies were classical survival analysis, so basically, it makes overestimate the incidence rate. Patients who were not taking CPT were more likely to be lost from ART care and this result is consistent with the study conducted in Myanmar [37], Gondar [16], and Tepi [43]. This might be due to the fact that CPT, given for the prevention of many opportunistic infections such as pneumocystis pneumonia, toxoplasmosis, bacterial infections, and diarrheal diseases [5] results from the patient feels better and intend to attend their schedule of ART follow-up accordingly. In contrast, patients who are not taking CPT, are more vulnerable to many opportunistic infections and finally, they may have such diseases and either they may develop drug toxicity due to drug-drug interaction or they may prefer to go to Traditional healers (Holly water) by discontinuing such burden of drugs and finally end up with LFTU or Death [10,31].

Patients who were in ambulatory functional status increased the risk of LTFU, this finding is in agreement with the study conducted in Indonesia [44], and different studies in Ethiopia [16,17,19,30]. This may be due to ambulatory patients being more likely to be LTFU could be due they become poor performance status at the initiation and due to the social, economic, and financial influences that are caused by their inability to work, this may lead to enabling to staying to the care [17]. The sub-hazard of LFTU was higher among patients with a fair and poor level of adherence, this is in agreement with studies in Gunie-Bisaw [8], Zimbabwe [14], Uganda [41],

Ethiopia [17,18,31], this may be due to that the patients with the poor level of adherence for ART drug become interrupt the treatment schedule which leads to resisting to the virus. This treatment interruption make fail to suppress the viral load and become prone to poor treatment outcome like treatment failure, this leads the patient to lose hope for a good prognosis, and He/she prefers to lost from care after all the outcome turned to death [4,7].

The patients with severe and moderate anemia status were more likely to LFTU compared with their counterparts, this finding is in agreement with studies conducted in Mynamar [37], Togo [40], Mizan-Teferi [22], the possible reasons for this finding might be the azidothymidine (AZT) based regimen have an interruption on bone marrow function and it becomes resolved as time goes and can be treatable as easy, but the patients who develop anemia due to this AZT based regimen lack their trust about the treatment and they hesitate to continue the care [21]. The patient with severe anemia at baseline hope that immediate resolution by ART treatment and if the expectation is not soon, then they try other medication like traditional healer and they become lost from the care. Patients who did not disclose their HIV/AIDS status were 2.27 times more at the risk of lost from the treatment program as compared to their counter parts. This study is similar with studies conducted in South Africa [37], Tepi [43], Oromiya region [28]. This might be due to that patients may remain on treatment much more if they disclose their status and they had someone else to share their ideas and feelings about the treatment and the diseases condition. Since staying on treatment needs intensive support and care from different parts of the community as well [3]. This study has some limitations because of the retrospective nature of the study, which lacks completeness of some potentially important predictors (patient information) like substance use. Since the study uses baseline socio-demographic and clinical-related factors, there may be a change of these variables (change of exposure variable) after a time.

Conclusion

In this study, the incidence of LTFU was one person lost from twenty patients within a one-year follow-up time. For examining the predictor variables of LTFU, competing risk regression analysis was done considering death and transferred out as competing events. After all, patients on ART who disclosed their HIV status, not taking CPT prophylaxis, being ambulatory functional status, those have moderate to severe anemia at baseline, and have a poor level of adherence to ART were at higher risk for LTFU. Therefore, giving more consideration and close follow-up of these high-risk groups could reduce the rate of LTFU.

Competing Interests

All the authors declared that they have no competing interest.

Authors' Contributions

GSA: conception of the research idea, study design, data collection, analysis and interpretation, and manuscript write-up. KAG, AML, FMA, and YMC: analysis and interpretation, manuscript write-up, Writing – review & editing, visualization. All authors have read, validate, and approved the final manuscript.

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Availability of Data and Materials

Please contact the author for further dataset requests.

Abbreviations

AIDS: Acquired Immune Deficiency Syndrome; cART: Combination Antiretroviral Therapy; CD4: Cluster Differentiation Four; PLWH: People Living with HIV; BMI: Body Mass Index; cSHR: Crude Sub Hazard Ratio; aSHR: Adjusted Sub Hazard Ratio; CIFs: Cumulative Incidence Functions; CPT: Cotrimoxazole Preventive Therapy; HIV: Human Immune Deficiency Virus; INH: Isoniazid Preventive Therapy; LTFU: Lost To Follow Up; OIs: Opportunistic Infections; FS: Functional Status; TB: Tuberculosis; WHO: World Health Organization; FMOH: Federal Ministry of Health; HAART: Highly Active Antiretroviral Therapy

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