

Attrition Rate And Predictors Among Adult Patients Receiving Antiretroviral Therapy In Adama Hospital Medical College, Central Ethiopia: A Retrospective Cohort Study Design, 2006 - 2017

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Abstract: Introduction: Efforts are underway in Ethiopia to achieve the 90:90:90 treatment goals set by the UNAIDS. Patient attrition from the treatment is known that a major challenge to ensure long-term retention. Therefore, this study aimed to assess attrition and its predictors among adult patients receiving ART in Adama Hospital Medical College, Ethiopia, from 2006 to 2017. **Methods:** A retrospective cohort study design was used. Adult patients started ART from January 2006 to December 2017 were followed up for 12 years. The statistical analysis was done by using SPSS version 21 statistical software. Descriptive analysis was used present frequencies and mean/median of variables. The Kaplan–Meier survival probability was used to estimate the probability of attrition at different time points. The multivariate Cox-proportional hazard model was used to identify predictors of attrition. **Results:** A total of 7990 patients were followed and observed for 52,934 person-years. At the end of the follow up period, 1016 attrition due to LTFU or death occurred with an annual incidence density [95% CIs] of 19.2% (18.0–20.4). Younger age, male gender, rural resident, not fully recorded patient address in the follow up form, lower CD4 count at baseline and WHO clinical stages III/IV at ART initiation were predictors of time to attrition. **Conclusion:** Considerable incidence of attrition from antiretroviral therapy was observed. Therefore, the hospital management and other concerned staffs should aggressively conduct the lost to follow up tracking measures. Beside that targeted interventions to the above predictors can reduce attrition from care and treatment.

Keywords: Antiretroviral-therapy, Attrition, Ethiopia, predictors

1. Introduction

Acquired Immune Deficiency Syndrome (AIDS) pandemic has remained major health challenges faced by the world. Globally, 36.7 million people are currently living with HIV of whom about 51.8% reside in Eastern and southern Africa [1]. To tackle the problem, access to antiretroviral treatment (ART) has been increasing with time and reach millions of people living with HIV (PLWHIV) [1], [2]. Globally, number of people living with HIV on ART has reached 17.0 million. In the world's most affected region, Eastern and Southern Africa, the number of people on treatment has more than doubled since 2010, reaching nearly 10.3 million people [1]. In Ethiopia currently, HIV prevalence is 0.9% and a total of 610,000 people live with HIV [3], out of which 391,844 people have received ante-retroviral treatment (ART) [4]. Free ART service provision was started in 2005 in Ethiopia. Hence the country has implemented, over the last decade, numerous valuable strategies to scale up antiretroviral therapy (ART) and improve the quality of HIV care [4]–[6]. On the basis of the 2010-2014 strategic plan of the country, ART coverage for adults [age 15+] has reached 79.6% [4]. Despite the expansion of HIV treatment services and improvements in coverage and the need for better management of patients on ART are often encounter multiple barriers that impact retention [4], [7], [8]. Ethiopia has

adopted the test and start recommendation in 2016 from WHO recommendations to achieve the global targets of 90-90-90 in 2020 [4], [5]. Retain at least 90% of HIV positive patients who are put on treatment and achieve viral suppression in 95% of PLWHIV on ART is one of the major target by 2020. However, attrition from ART care or challenge with long term retention on HIV care and treatment was identified as one of the key programmatic gap [5]. Retention in care has been challenging in many regions including of sub-Saharan African ART programs [6], [9–13]. Reduction in long term patient retention and high rates of attrition from treatment programs thus pose a serious challenge to treatment program outcomes [9], [12], [14–17]. A review of 154 general adult patient cohorts comprising 1,554,773 patients from 42 low and middle-income countries revealed that overall, 43% of all patients not retained were known died. Retention at 12, 24 and 36 months after treatment initiation was 78%, 71% and 69% respectively, of which, 65% in Africa, 80% in Asia, and 64% in Latin America and the Caribbean estimation at adult 36 months [14]. Previous studies conducted in Ethiopia reported that patient retention/attrition from the treatment was a major challenge in HIV care and treatment programs [10], [12], [13], [18–20]. Majority identified predictors such as baseline CD4 cells count, WHO clinical stage, functional status,

provision of co-trimoxazole prophylaxis therapy (CPT) and clinical TB Screening were predictors of attrition from treatment [21]–[24]. Attrition of patients receiving ART can result in serious consequences, such as withdrawal of treatment, drug toxicity, treatment failure due to poor adherence, and drug resistance [25]; this results in an increased risk of death [26] of up to 40% in studies of patients attrition in sub-Saharan Africa [9]. Data on retention is one of the key WHO reportable indicators that should be periodically reported to continuously evaluate the success of ART programs and to ensure successful treatment outcome [2]. However, there is paucity of information in the status and predictors of attrition from care among persons living with HIV and enrolled to antiretroviral treatment. This study aimed to describe attrition and its predictors among adult patients receiving ART in Adama Hospital Medical College of Ethiopia. Examination of these data helps to identify the challenges that must be overcome in ensuring the long-term retention on treatment services and in realizing the 90-90-90 treatment targets.

2. Methods

2.1. Study setting

The study was conducted in Adama Hospital Medical College (AHMC), Adama town, Ethiopia, which is located about 99 kilometers from capital, Addis Ababa. It is one of the largest regional referral hospital established 77 years (1946) ago, serves around 3,000,000 people from surrounding districts and provinces. The hospital runs both inpatient and outpatient treatment activities, with bed capacity of 219 and has about 600 workers of which 321 are health professionals and the remaining are administrative workers. HIV care and treatment clinic is one of the core parts of its activities. Adama Hospital Medical College is also one of the hospitals in the Oromia region with the highest ART patient load. This hospital has started ART service provision in 2005. Hence, 20,282 patients ever enrolled to chronic HIV care, 13,827 ever started ART care. A total of 9851 patients initiated ART between 2006 to 2017, of which 9183 were adult and 668 were children under 15 years age [27].

2.2. Study design and period

A retrospective cohort study design was employed. All adult (aged ≥ 15 years) HIV positive individuals initiated ART in the hospital from January 2006 to December 2017 (covers 12 year of follow up) were considered eligible. Those patients recorded as transferred out to other health facilities and missed data for the outcome variable were excluded from the analysis.

2.3. Data source and variables

We had used secondary data collected routinely in the hospital for clinical monitoring and evaluation purposes and entered to an ART electronic database during the follow up time. A total of 9183 adult patients initiated ART from 2006 to 2017 were eligible for the study. We excluded 781 patients who were transferred out to other health facilities and 412 patients of missed data for the outcome variable [Figure 1].

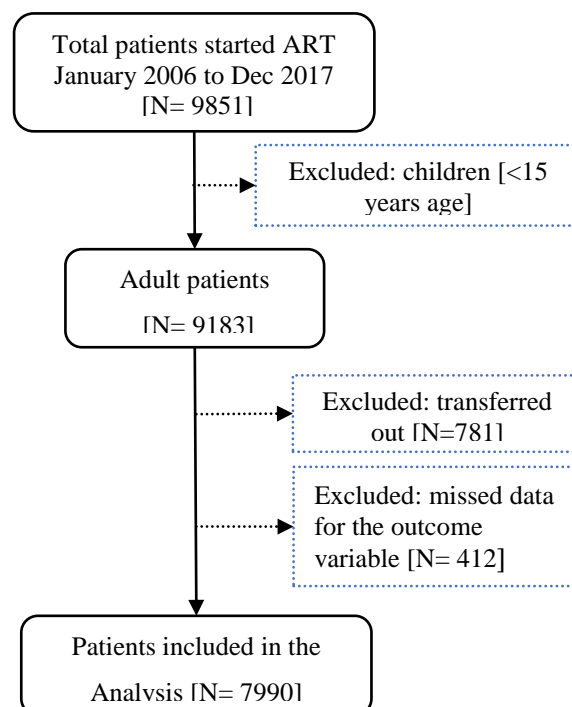


Figure 1: Flow diagram illustrating the eligibility of the cohort patients receiving ART in AHMC, Ethiopia from January 2006 and December 2017

Attrition from care is outcome variable and considered as event of interest in this study. Attrition is defined as patients who had discontinued ART or recorded as death or loss to follow up (LTFU). LTFU was defined as patients who missed scheduled visit to the hospital more than three months after the last visit. Retention in care is opposite of attrition defined as being alive and receiving ART after ART initiation which does not include attrition from care. The baseline explanatory variables were sex, age, place of residence, duration from diagnosis to ART started, number of CD4 cells count, WHO clinical stage, body mass index (BMI), functional status, provision of co-trimoxazole prophylaxis therapy (CPT), clinical TB Screening, isoniazid prophylaxis (INH), active TB treatment and full address recorded. Full address record in this study was defined as the patient address recorded at least for the region, zone/sub city/woreda, kebele, house number plus functional phone number. Patient address without functional phone number was considered as not full address recorded.

2.4. Data processing and analysis

The database was recorded in Microsoft Excel, checked for consistencies and completeness, and then cleaned and edited prior to performing analysis in SPSS version 21. Descriptive statistical methods were used in univariate analysis to generate frequencies and measure of central tendencies. The mean, median and inter-quartile ranges (IQR) were calculated for numeric variables and proportions for categorical variables. Bivariate and multivariate analyses were made using Kaplan Meier and Cox regression models respectively. Attrition incidences were calculated per 100 Person-years. Kaplan–Meier techniques were used to estimate the probability of retention in care at different years of follow-up, with the log-rank test being used to test the significance of observed differences between groups. Predictors of attrition were assessed using a multivariable Cox proportional hazards model. Chi-square test was also

used to compare categorized outcomes. Adjusted hazard ratios (AHR), 95% confidence intervals (CI) and P-values were calculated to estimate the association between attrition. P-value less than 0.05 considered as statistically significant. Patients alive on ART were censored on December 31, 2017.

2.5. Ethical approval

Ethical clearance and official letter was obtained from ethical clearance board of Ethiopian Public Health Association. No information obtained from the medical records disclosed to any third person. Patient identification variables such as name were omitted in the extraction. This study does not harm or expose HIV/AIDS patients to unnecessary risk as a result of reviewing their medical records.

3. Results

3.1. Characteristics of study population

A total of 7990 adult patients (aged 15 years and above) initiated ART in Adama hospital between January 2006 and December 2017 were included in the analysis. Of the cohort patients, three fifth, 4707 (58.9%) were female. The mean and standard deviation of age at ART initiation was 39.96 ±10.9 years. About 576 (7.2%) of patients aged 15-24 years and close to one third, 2526(31.6%) were aged ≥45 years. Around nine tenth, 6978(87.3%) were urban residents. Regarding with patient address, only about one third, 2347(29.4%) had full address recorded in patient follow up form. Regarding the base line clinical characteristics, the median (inter-quartile range) CD4 cell count at ART initiation was 424 cells/mm³ (IQR: 276-607) and around a quarter, 2182(27.3%) had CD4 count less than or equal to 277 cells/ mm³. Nine of ten, 7318(91.6%) were classified as WHO stage I or II at the time of ART and other clinical information are presented in Table 1.

Table 1: Socio demographic and clinical characteristics of adult patients receiving ART in AHMC, Ethiopia, from January 2006 to December 2017 (N= 7990)

Baseline Variable	Total (%)
Age (years)	
15-24	576(7.2)
25-34	1831(22.9)
35-44	3057(38.3)
≥45	2526(31.6)
Sex	
Male	3283(41.1)
Female	4707(58.9)
Residence	
Rural	1012(12.7)
Urban	6978(87.3)
Full address record	
Yes	2347(29.4)
No	5643(70.6)
Baseline CD4 count (cell/mm ³)	
≤277	2182(27.3)
278-427	1655(20.7)
428-611	2059(25.8)
≥612	2094(26.2)
Baseline WHO Stages	

I/II	7318(91.6)
III/IV	672(8.4)
Baseline body mass index	
Under weight	2020(25.3)
Normal	4381(54.8)
Over weight	1589(19.9)
TB screening	
Yes	7275(91.1)
No	715(8.9)
INH prophylaxis	
Yes	618(7.7)
No	7372(92.3)
CPT received	
Yes	4728(59.2)
No	3262(40.8)
Active TB treatment	
Yes	834(10.4)
No	7156(89.6)

N=Number, CD4= Cluster of Differentiation 4, WHO= World Health Organization, TB = Tuberculosis, INH= Isoniazid prophylaxis, CPT =Co-trimoxazole prophylaxis

3.2. Attrition rate

Of the 7990 adults initiated ART, 1016 (12.7%) were attrition due to death or LTFU and 6,974 (87.3%) were in active follow up during the median (IQR) follow-up of 7.17(3.78-9.69) years. Kaplan–Meier estimates of retention in care (95% CIs) were 95% (94–96%), 92% (91-93%), 90% (89-91%) and 78% (77-79%) at 1st, 2nd, 4th, and 12th years after initiation of treatment respectively (Figure 2).

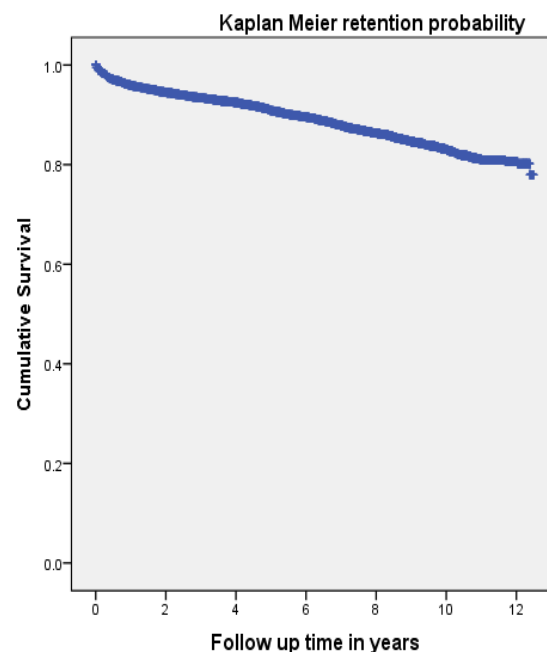


Figure 2: Kaplan Meier survival estimates for attrition among adult patients receiving ART in AHMC, Ethiopia, from January 2006 to December 2017 (N= 7990)

At the end of the follow up period, 1016 attrition (LTFU or death) occurred over 52,934 person-years at risk, with an

annual incidence density (95% CIs) of 19.2% (18.0–20.4). In comparison of the groups, cumulative incidences of attrition (death or LTF) among male was 20.9% while 18.8% in female. It was observed that 36%, 40.6%, 14.9% and 11.5% cumulative incidences of attrition among age 15-24, 25-34, 35-44 and ≥ 45 years respectively. Cumulative incidences among patients from rural were 52.0% whereas 17.8% observed among urban patients. In comparison of patient address, patients who had no full address had 20.8% cumulative incidences while patients who had full address had 15.2% cumulative incidences (Figure 3).

3.3. Predictors of time to attrition

Cox regression analysis was conducted to determine predictors of attrition (Table 2). At multivariate Cox regression analysis level, age, gender, residence, full patient address, base line BMI, TB screening, base line CD4 count (cells/mm³), base line WHO Stages, co-trimoxazole prophylactic therapy (CPT), base line functional Status and adherence to the treatment were predictors significantly associated with patient attrition from ART care and treatment ($P < 0.05$). The risk of attrition was higher among patients age at entry from 15-24 years ((AHR =1.79, 95%CI (1.41-2.27)) and 25-34 years (AHR) =2.10, 95%CI (1.10-3.05)) as compared to those age equal or greater than 45 years. The risk was also higher among male (AHR =1.17, 95%CI (1.03-1.33)), rural resident (AHR) =3.15, 95%CI (2.45-4.05)) and not had full address recorded in follow up form (AHR) =1.46, 95%CI (1.23-1.74)). The patient with baseline BMI classified underweight had higher risk of attrition (AHR =2.17, 95%CI (1.82-2.58)) as compared to those had baseline BMI classified normal. The risk was lower among patients who had screened for TB (AHR =0.38, 95%CI (0.31-0.48)) and who had provided CPT (AHR =0.46, 95%CI (0.41-0.53)) at enrollment. The risk of attrition was higher in patients with baseline CD4 cell counts ≤ 277 cells/mm³ (AHR =3.29, 95%CI (2.71-4.01)) and base line CD4 cell counts from 278-427 cells/ mm³ ((AHR =1.56, 95%CI (1.25-1.96)) as compared to base line CD4 cell counts ≥ 612 cells/mm³. The risk of attrition in patients with WHO clinical stage one/two at entry (AHR =0.42, 95%CI (0.35-0.50)) were lower compared to clinical stage three/four. The risk was lower in patients with baseline working functional status (AHR =0.45, 95%CI (0.35-0.58)) and ambulatory status (AHR) =0.53, 95%CI (0.41-0.69)) as compared to patients with bedridden status (Table 2).

4. Discussion

This study has attempted to disclose the incidence of attrition from care and factors predicting this. The incidence of attrition (95% CIs) was 19.2 (18.0–20.4) per 100 person years. This finding was slightly higher than study conducted across East African countries, data analysis of 77,362 patients from 29 facilities revealed that incidence of LTFU 16.7 per 100 person-years in the post-ART periods [28]. A study conducted in French hospitals databases of HIV infected patients, the incidence rate of LTFU was estimated to be 3.5 per 100 person-years, a much lower estimate than this study. Even, it was higher than previous study conducted elsewhere in Ethiopia which revealed attrition incidence of 8.2 per 100 person-years [20]. The higher result might be due to the fact that we had conducted long term retention followed up for 12 years back initiated ART in 2006. However, it suggests that attrition remains a major challenge for ART program in our setting. In this study, the proportion of attrition in the first year was 28%. Finding within the first year is consistent with the range of 15 to 40% of LTFU among sub-Saharan Africa countries [7]. It is also similarly to study conducted on outcomes of the ART program in Ethiopia which revealed that out of 7,451 patients who were in the 24-months cohort, 24% were lost to follow-up and 8% died [22]. Collectively, these findings therefore suggest that attrition still remains a major challenge for ART programs in Ethiopia. The main reasons in rising incidence of attrition have been ascribed to poor patient tracing in the low-income setting [29]. In our study, 70.6% of cohort patient had poor recorded address without phone number in their clinical follow up form. Once clients diagnosed HIV, they may not tell us correct address due to fear of social stigma. This might affect loss patient tracking process. Simultaneously, we detected that poor recorded patient address was found predictor of attrition in this study which might need further investigation. Both younger and early adult had higher risk of attrition as compared to the older. This finding was concordant with study from Kenya. Participants aged 15-24 years were more than two-fold more likely to undergo attrition, compared to those aged ≥ 45 years [13]. Similar result reported from other studies [10], [15], [17], [21]. Younger ART patients are more suffering from social stigma and discrimination and lack of disclosure [30]. Evidence elsewhere showed that early HIV

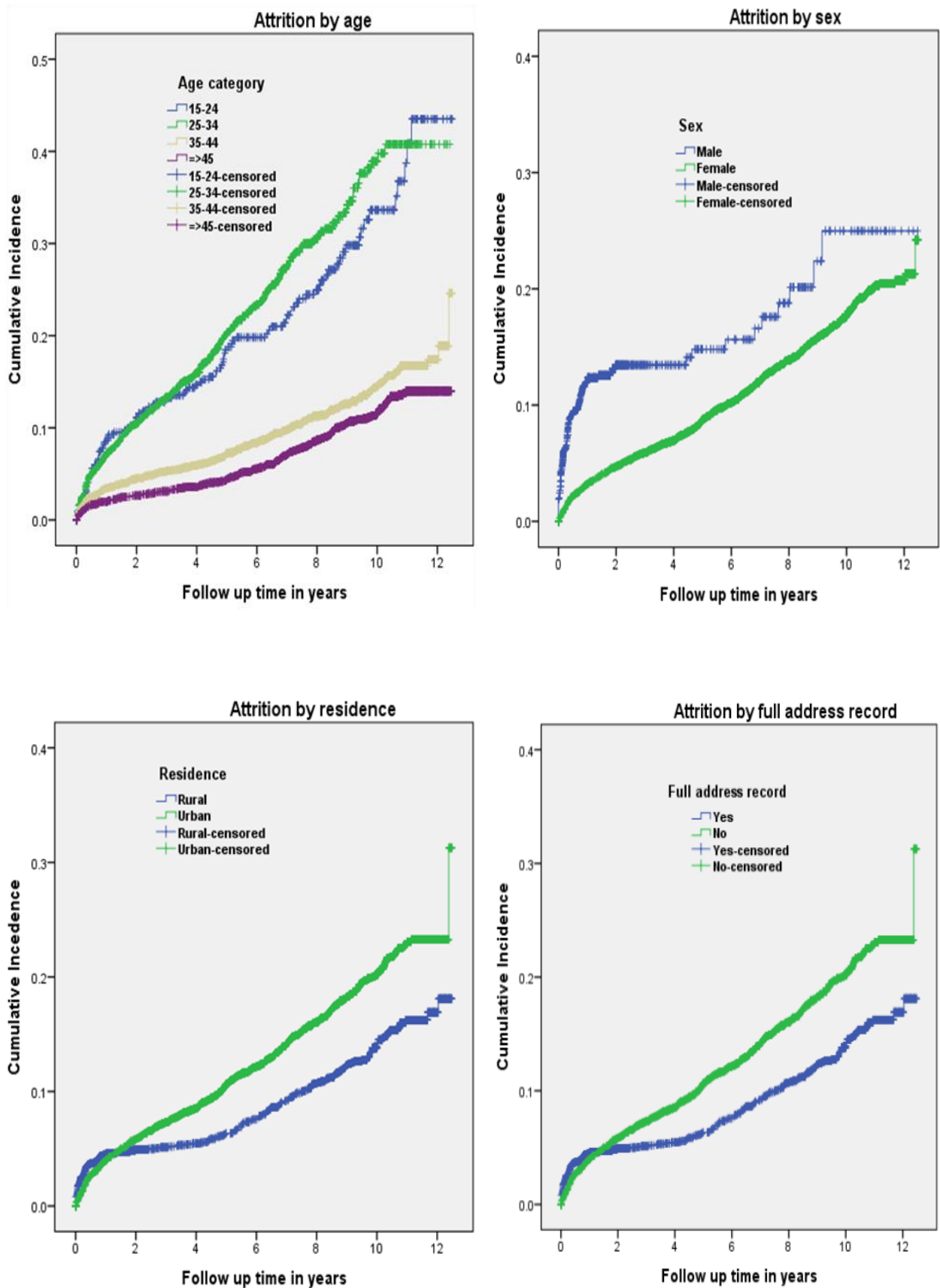


Figure 3: Cumulative incidence of attrition by sex, age, residence and full address among adult patients receiving ART at AHMC, Ethiopia, from January 2006 to December 2017

Table 2: Cox regression analysis for predictors of attrition among adult patients receiving ART in AHMC, Ethiopia from January 2006 to December 2017 (N= 7990)

Baseline Variables	Attrition, N (N /100 PYO)	CHR (95% CI)	P-Value	AHR (95% CI)	P-Value
Total N	1016 (19.2)				
Age category					
15-24	115(36)	3.06(2.44-3.83)	<0.001	1.79(1.41-2.27) ***	<0.001
25-34	360(40.6)	3.47(2.93-4.11)	<0.001	2.10(1.10-3.05) ***	<0.001
35-44	315(14.9)	1.30(1.09-1.54)	0.003	1.14(0.96-1.37)	0.146
≥ 45	226(11.5)	1.00		1.00	
Sex					
Male	456(20.9)	1.16(1.02-1.31)	0.020	1.17(1.03-1.33)**	0.019
Female	560(18.0)	1.00		1.00	
Residence					
Rural	111(52.0)	2.28(1.86-2.79)	<0.001	3.15(2.45-4.05) ***	<0.001
Urban	905(17.8)	1.00		1.00	
Full address record					
Yes	228(15.2)	1.00		1.00	
No	788(20.8)	1.41(1.22-1.64)	<0.001	1.46(1.23-1.74) ***	<0.001
BMI					
Under weight	524(45.0)	3.44(3.01-3.92)	<0.001	2.17(1.82-2.58) ***	<0.001
Normal	382(12.9)	1.00		1.00	
Over weight	110(9.5)	0.75(0.61-0.93)	0.007	0.83(0.65-1.06)	0.136
TB screening					
Yes	604(12.3)	0.12(0.10-0.13)		0.38(0.31-0.48) ***	<0.001
No	412(10.9)	1.00	<0.001	1.00	
Provided CPT					
Yes	415(12.9)	0.45(0.39-0.51)	<0.001	0.46(0.41-0.53) ***	<0.001
No	601(29.0)	1.00		1.00	
CD4 count (cells/mm ³)					
≤ 277	539(48.2)	5.23(4.34-6.31)	<0.001	3.29(2.71-4.01) ***	<0.001
278 - 427	186(15.9)	1.78(1.43-2.22)	<0.001	1.56(1.25-1.96) ***	<0.001
428 - 611	151(10.3)	1.14(0.90-1.43)	0.275	1.06(0.84-1.34)	0.609
≥ 612	140(9.1)	1.00		1.00	
WHO Stages					
I/II	624(12.4)	0.09 (0.08-0.09)	<0.001	0.42(0.35-0.50) ***	<0.001
III/IV	392(>100)	1.00		1.00	
Functional Status					
Working	741(14.8)	0.07(0.05-0.08)	<0.001	0.45(0.35-0.58) ***	<0.001
Ambulatory	191 (80.1)	0.35(0.27-0.45)	<0.001	0.53(0.41-0.69) ***	<0.001
Bedridden	84(>100)	1.00		1.00	
Active TB treatment					
Yes	423(>100)	9.68(8.53-10.99)	<0.001	0.98(0.77-1.24)	0.867
No	593(12.0)	1.00		1.00	

N=Number, PYO = Person years of observation, BMI = Body Mass Index, CPT =Co-trimoxazole prophylaxis, TB = Tuberculosis, CHR= Crude Hazard Ratio, AHR= Adjusted Hazard Ratio, 1.00= Reference category, **P-value <0.05, ***P-value <0.001,

status disclosure in adolescents on ART has been shown to improve retention [31]. Male gender was predictor associated with a higher rate of attrition from care (AHR =1.17, 95% CI (1.03-1.33)). This finding was consistent with many studies conducted in Africa counters [16], [21], [32–37] including in Ethiopia [18], [19]. Report from elsewhere also revealed that men have low probability of being earlier initiation of ART and retain on the care [8], [38]. In high-prevalence settings, men are less likely ever tested for HIV and more likely to start ART at later clinical stages of HIV disease as compared to women. Barriers to men accessing HIV testing include fear, stigma, the perception that health facilities are spaces for women [2]. Patients from rural area was underwent higher attrition. This finding confirms what was described by other study in Ethiopia [12]. However, currently provision of ART services have been decentralized to both urban and rural areas in Ethiopia, there is still fear of social stigma and patients preferred to access service at urban treatment centers. A study from South Africa conducted in patient attitudes towards decentralization showed that many patients experienced less stigma in centralized sites where there is

less proximity to their local community [39]. Besides, they might be suffering from transportation related challenges and forced to miss their appointments or drop from the treatment. The risk of attrition was higher among patients with low baseline CD4 counts at the entry point of ART. This finding is similar to other findings [10], [11], [18], [40]. This higher chance of attrition among patients with lower CD4 count may be due to advance in disease that could have resulted in death. Those who working or ambulatory functional status at the initiation of the treatment had lower risk of attrition as compared to patients with bedridden status. This finding was revealed elsewhere in previous studies conducted in Ethiopia [10], [12]. Patients with advanced WHO clinical stage III/IV also underwent more attrition from the treatment as compared to those stage I/II. Consistent with other findings [12,13], markers of poor immunologic patient health at ART initiation such as low CD4 count and WHO stage III/IV were associated with increased hazard of lost to follow up. Early HIV diagnosis and initiation of treatment could increase survival rates [41]. Our findings confirmed that the importance of initiating treatment immediately after the

diagnoses recommended by the recently published 2016 WHO consolidated HIV guidelines [2].

Strengths and Limitations of the study

This study has tried to use power full data to investigate the attrition from care and predictors of attrition among patients followed for long period in one of the largest hospital within the region. However, there are also several limitations. First, it should be acknowledged that patients who were transferred out to other facilities and patients with missing data of outcome variable were excluded from the analysis. Secondly, since we used routinely collected data from electronic record, it might limit our ability to gather data factors that may influence the risk of attrition. As a result, important socio background factors and patient could not be analyzed. We were not also able to analyze the trends using biological markers after ART initiated. Finally, this analysis did not take into account patients who are lost prior to ART initiation, which might be a period of high attrition in other literatures.

5. Conclusion and recommendations

Overall incidence rate of attrition from ART treatment was substantially high. Younger age, male gender, rural resident, not full patient address, did not provided CPT and screened for TB, bedridden functional status, lower CD4 count [cells/mm³] and WHO clinical stages III/IV at ART initiation were predictors significantly associated with high patient attrition from ART care and treatment. Therefore, the regional health bureau and Adama hospital medical college management and other stakeholders should be put emphasis on tackling of challenges with retention. In first, hospital staff shall conduct aggressive lost to follow up tracking measures to improve patient retention. Having full patient address with phone number to trace loss patient is mandatory at patient level monitoring system. Getting correct address record with phone number could be possible at medical record unit prior to be diagnosed HIV. Structural and behavioral interventions that may reduce social stigma and discrimination among young patients should be focused area. Male patients shall need greater emphasize during on care and treatment by providing them window of service opportunity such as making health service available, accessible and acceptable. To improve retention among patient from rural or out of the catchment, efforts should be needed to strengthen the decentralization of ART service and psychosocial support activities that may encourage the patients to access the service in their vicinities.

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7. Authors' contributions

Tamrat Endebu Gebre: conceived the topic, wrote the proposal, supervised the conduct of the study, analyzed the data and finalized the manuscript

Alemayehu Bekele (PhD): assisted the study design and proposal writing, supervised the conduct of the study, data analysis and reviewed the manuscript.

8. Competing interests

We declare no conflicts of interest.

Consent for publication

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