

Loss to Follow Up from Anti-Retroviral Therapy and Factors Associated among HIV/AIDS Patients at Dubti Referral Hospital, Northeast Ethiopia

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Abstract

Background: Sub-Saharan Africa contributed 76% of the total HIV-infected people, 76% of the total new HIV infections, and 75% of the total HIV/AIDS deaths in 2015. Loss to follow up from ART treatment is one of the reasons for ineffectiveness in developing countries. Therefore, this study aimed to assess the incidence and determinant of loss to follow up among adult clients on ART at Dubti teaching and referral hospital.

Methods: Retrospective cohort study design was conducted among 390 adult people living with HIV/AIDS attending ART clinic between September 1, 2013 and September 1, 2018 at Dubti Hospital, Ethiopia. Patients were selected using systematic random sampling after considering all patients medical charts during the 2013 and 2018 to include in this study. Data were collected using medical document review from the baseline to follow-up treatments using structured checklist. Data were analyzed using STATA version 14. Kaplan-Meier curve was used to estimate the time to loss to follow up. Both bivariate and multivariate Cox proportional hazards models were used to identify predictors of loss to follow up. The goodness of fit of the final model was checked by both Sheffield residual statistical test and Harrell's C concordance statistics.

Results: Total person month contributed by the study participant was 8,589 (715.5 person month). The incidence of lost to follow up was 9.7(95% CI 7.6, 12) per 100 person years and median survival time was 10 months. Patient on monthly based ART program were found more likely to loss from follow up than that of on ART patient on spacing type program (AHR: 6.66, 95% CI, 3.32, 13.4). Patient with CD4 \geq 400 were found more likely lost to follow up than those with CD4 between 50 and 200 (AHR: 1.3, 95% CI, 0.35, and 8.48).

Conclusions: This study revealed as incidence of lost from follow up is high in comparable with world health organization strategic plan which called 90-90-90. Shorter Type of ART program or schedule, adherence to ART, and higher CD4 level WHO stage were the factors associated with lost to follow-up. Defaulter tracing mechanism should be operational and strengthen in the health facility.

Keywords: Loss to follow up from ART; HIV patients; Factors associated; Afar region; Ethiopia

Introduction

The human immunodeficiency virus (HIV) pandemic has had a profound impact on the health care system of all countries worldwide, but especially on those in Sub-Saharan Africa. Antiretroviral therapy (ART) defined as a combination of three or more anti-retroviral drugs for treating HIV infection. ART involves lifelong treatment. Its synonyms are combination ART and highly active ART [1].

Lost to follow up (LTFU) is defined as not taking an ART refill for a period of 3 months or longer from the last attendance for refill and not yet classified as 'dead' or 'transferred-out'. The time to LTFU was calculated in months according to the time interval between the dates of ART initiation to drop out, as recorded by the ART registration health information data manager [2].

High rates of loss to follow-up may affect mortality estimates in ART programs. Those patients lost to follow-up have a different prognosis compared to similar patients remaining in care [3-5].

According to global report on HIV/AIDS shows in 2017, there were 36.9 million (31.1 million–43.9 million) people living with HIV, from them 35.1 million (29.6 million–41.7 million) were reported as adult HIV/AIDS cases [6].

The WHO African Region is the most affected region, with 25.7 million people living with HIV in 2017. Sub-Saharan Africa (SSA)

contributed 76% of the total HIV-infected people, 76% of the total new HIV infections, and 75% of the total HIV/AIDS deaths in 2015 [7].

Ending the AIDS epidemic will inspire broader global health and development efforts, demonstrating what can be achieved through global solidarity, evidence-based action and multi sectorial partnerships [8].

Even though world health organization declare 90-90-90(90% of people with HIV should know their status, 90% patient should know their status should start ART, and 90% of patient those start ART should reach optimal CD4 count level) of target plan on December 2014 to reach on 2020 for solving the problem of HIV/AIDS endemic, the current performance is less than 73% at world level and less than fifty percent in developing countries especially in south and eastern

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Africa countries including Ethiopia because of loss to follow up and poor adherence [4, 5].

Even though some studies done on incidence and predictor for loss to follow up among adult on ART at north Ethiopia Gondar, Mekelle and Pawe, south west Ethiopia at MezanTepi and at eastern part of Ethiopia at Jijjiga, their result of incidence was totally differ one from other for example incidence at Karamara Jijjiga is more than two times of Gondar result. Additional to this most of factor associated with loss follow up at one study area were differ from another [9-11].

Thus, specific study is required for this area to achieve significant and sustainable reductions in the number of antiretroviral therapy (ART) patients lost to follow-up (LTFU), cost-effective, high-impact interventions which will address the underlying causes of LTFU for this specific study area.

As a result, interventions to address this problem have focus on tracking patients who are LTFU and bringing them back into care, which can be labor-intensive and costly, instead of preventing LTFU, which may result in labor and cost savings. In order to inform interventions and programmatic decisions that will achieve significant reductions in patient LTFU, local studies are needed.

Method and Materials

Study setting

This study was conducted in Dubti referral hospital, Dubti, Afar, Ethiopia. Dubti referral hospital is located in Dubti district, which is 8km apart from Samara, the region administrative city of Afar, region, Ethiopia. It is the only referral hospital in the region. The referral hospital has ART clinic with large number of patient visit from all corner of the regional hospitals. The study was conducted from September 1 to October 31, 2019.

Study design and study population

A retrospective follow up study was conducted among adult patient on ART those started treatment at Dubti referral hospital of Afar region. A total of 390 medical charts of adult people living with HIV/AIDS attending ART clinic at Dubti referral Hospital between September 01, 2013 and September 01, 2018 were considered in this study. Systematic random sampling was used to select study participants from the total 1,312 ART adult patient charts which has complete main variables in this study.

Data collection

Data were extracted from patients' ART card by trained three nurses working in the ART Clinic using uniform data abstraction tool. Whenever relevant information was missing, the ART electronic database was consulted. The supervisors checked each completed checklist and principal investigator monitored the overall quality of the data collection.

Measurement

The outcome variable of this study was lost to follow up with time variable. Age, sex, occupational status, marital status, educational status, place of residence, body mass index, WHO stage, CD4 count, functional status, TB status, nutritional status, opportunistic infection, anemia, regimen type, regimes change, and are the independent variables.

Loss to follow up: was defined as not taking an ART refill for a period of 3 months or longer from the last attendance for refill and not

yet classified as 'dead' or 'transferred-out'.

Functional status of participants(12): was measured by considering literatures. Categorized as Working: if patients able to perform usual work inside or outside home. Categorized as Ambulatory: if patients able to perform activity of daily living (ADL), Not able to work. Categorized as Bedridden: if patients not able to perform activity of daily living.

Censored: was measured if patients who died while on treatment, transferred out, or who are not lost from follow up till the end of the study period.

Adherence status (13) was measured by considering literatures. Categorized as Good adherence: if patients taking $\geq 95\%$ of drug prescribed by doctor or nurse (clinician). Categorized as Fair adherence: if patients taking 90 to 95% of drug prescribed by doctor or nurse (clinician). Categorized as Poor adherence: if patients taking $\leq 90\%$ of drug prescribed by doctor or nurse (clinician).

Data analysis

After collection data were cleansed, coded and entered into EPI-DATA version 4.2. Then it was exported to STATA14 for further analysis. Person-year of follow up was calculated by using the time interval between the date of ART initiation and the date of LTFU or date of censoring. The Kaplan–Meier method was used to estimate rates of LTFU at specific time after ART initiation and Nelson–Aalen method was used to generate a cumulative hazard function. In the bivariable analysis with Cox proportional hazards regression model we selected independent predictors for multivariable Cox proportional hazards regression at “P” value less than 0.25. Schoenfeld residual and Cox Snell residual plot for the overall model fitness tests was used to check the model assumption. We used a stepwise backward selection procedure to identify socio-demographic and clinical independent predictors for LTFU at $P < 0.05$ adjusted hazard ratios (AHR) with 95% confidence interval was used as the measure of association. Assumption to cox proportional hazard were checked covariate variable PH assumption test no covariate violate the proportional hazard assumption. Over all VIP was 2.22 and no independent variable with VIP greater than five this indicate that as there was no multicollinearity among variables. In addition, interaction was also checked and indicated there was no interaction among independent variables. The goodness of in this study model was checked by both scoenfeld residual statistical test and Harrell's C concordance statistic. The result of both (global test for shoenfield $/p/=0.38$ and Harrels C $/P/=0.85$) test show as the model is fit to measure survival difference among covariate

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of college of health science and medicine, Mekelle University. Permission letter was obtained from Dubti referral Hospital administration and ART coordinator. The names of patients are not used and confidentiality of information was kept by collecting data only by nurses who are working in the ART clinic.

Result

In this study, 390 adult patients on ART between January 2013 and August 2018 were included Out of the 390 study participants in this study, 243 (62.2%) were males. By the time of enrollment into HIV/AIDS care, around half, 171 (43.1%) of the study subjects were between 20 and 29 years of age while 37 (9.4%) were the age group of less than 20 years of age with a mean (\pm SD) age of 29.69(± 8.21) years.

Of the total study population, 272 (69.7%) were married. With regard to educational status of study participants, 212 (54.4%) of patients can't read and write, followed by 79 (20.3%) patients complete primary education. Around two over three, 250 (64.1) of study participants were Muslim by their religion. More than half (55.4%) of the patients were daily laborer in their occupation at the time of initiation of ART and 56.4 % of the patients were enrolled from other out the city (Table 1).

Clinical character of the patient

Nearly half 208(53.3%) of the study participants have TB infection history. Twenty one percent and 83.3% of adult ART patient have BMI less than 18 and good status drug adherence respectively. Two hundred forty five (62.8) of the client are on monthly based type of treatment. Only 119(30.5) of patient had CD4 greater than or equal to 400.Two hundred nine (53.9%) had at least one OI at entry.

Incidence of loss to follow up

Over all lost to follow up obtained was 9.7(95% CI 7.6, 12) per 100 person years. The incidence loss to follow up in interval period of 0 to 12 month, 12to 24 month, 24 to 36 month, 36 to 48 month and greater than 48 were 11.4 per 100 person years, 8.4 per 100 person years 8.8 per 100 person years,7.08 per 100 person years, and 9.3 per 100 person

years respectively. The incidence of loss to follow up from ART clinic among person on monthly based ART program was 15 per 100 person years and that of spacing (every six month) was 2.4 per 100 person year.

Time to loss to follow up

The participant was followed for a total 8589 month (716.5 year) observation. The median follow-up time was 10 (7, 16) months. The cumulative probability of survival between 0 to 12 and 36 to 48 are 0.68 and 0.13 respectively (Figure 1).

According to the Kaplan Meier plots of hemoglobin and program categorical variable which we had plotted below there was survival difference in among hemoglobin categorical variable and program type (Figure 2).

Factors affecting lost to follow up from ART care

ART patient those on Monthly based program were found more likely to loss from follow up than that of on ART patient on spacing (six month based) of type program (AHR: 6.66, 95% CI, 3.32, 13.4). Patient with CD4 greater than or equal to 400 were found more likely to lost to follow up than that of CD4 between 50 and 200 (AHR: 1.3,95% CI, 0.35, 8.48).It is also found that as anemic patient were more likely loss

Table 1: Socio-demographic characteristics of study participants on ART at Dubti teaching and referral hospital, Afar region, Ethiopia, 2019.

Variable	Category	Frequency	Percent
Sex	Male	243	62.3
	Female	147	37.7
Marital status	Married	272	69.7
	Single	43	11
	Divorced	49	12.6
	Widowed	26	6.7
Resident by Zone	zone one	188	48.2
	zone two	94	24.1
	zone three	67	17.2
	zone four	25	6.4
Religion	Muslim	250	64.1
	Orthodox	104	26.7
	Protestant	34	8.7
	Other	1	0.3
Referral site	within city	170	43.6
	From other city	220	56.4
	<20	37	9.4
Age of patient	20 to 29	171	43.8
	30 to 39	52	13.3
	40 to 49	86	22
	50 to 59	44	11.2
Educational level	Can't read and write	212	54.4
	primary education	79	20.3
	secondary education	63	16.2
	college and above	36	9.2
Occupation of patient	daily labor	216	55.4
	Merchant	91	23.3
	Employee	54	13.8
	Student	18	4.6
	house wife	11	2.8
Ethnicity	Afar	164	42.1
	Amara	131	33.6
	Tigre	65	16.7
	Other	28	7.7

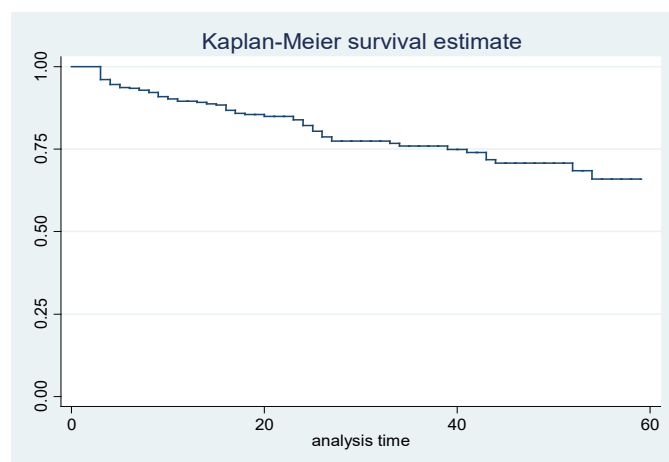


Figure 1: Over all model Kaplan Meier survival curve of adult patients on ART therapy at Dubti teaching and referral hospital, January 2013 to December 2018, Afar region, Ethiopia, 2019.

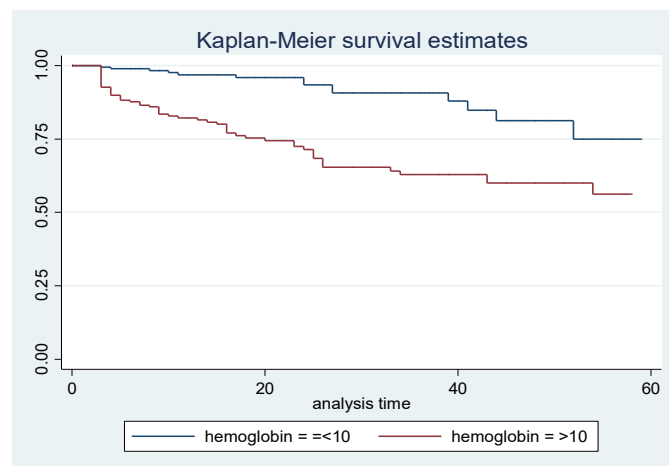


Figure 2: Kaplan Meier of hemoglobin status among adult patients on ART therapy at Dubti teaching and referral hospital, January 2013 to December 2018, Afar region, Ethiopia, 2019.

to follow up from ART program than that of non-anemic ART patient (AHR: 3.4,95% CI 1.8,6.3).Additional to those listed above, ART patient those at WHO stage one were more likely to lost from follow up when compared with WHO stage four patients (AHR:2.6, 95% CI,1.1, 5.8). On the other hand the variable patient contact, educational level, occupation, marital status, functional status, TB treatment status and opportunistic infection status were not found to be significant predictor of time to lost follow up from ART clinics (Table 2).

Discussion

This study revealed that the incidence of lost to follow up from ART program and was 9.7 per 100 person years and median survival time of 10 month. It also found that as ART program type, CD4, WHO stage, anemia and adherence to ART were the associated factors with loss to follow up among adult patient on ART at Dubti referral hospital.

The result of studies done among adult population on treatment at ART clinics in different part of the world France, North America and Thailand shows as the incidence of loss to follow up from the program is from 2.9 to 10.2 per 100 person-year and in the same way, four similar studies done in different part of Ethiopia at Gondar university hospital, pawe general hospital and Kara Mara general hospital shows as that the incidence of loss to follow from 11.6 to 26 per 100 person years which is consistence with our result. This similarity may be explained by the

similarity of HIV/AIDS treatment protocol through the country as well as world [9, 11].

During our follow up we found that as the incidence to lose from follow up from ART program was high during first twelve month and become low during last month of follow up, this result is consistence with study done at north east Ethiopia in karamara hospital among the same population. This may be because of high mortality and morbidity in early period of ART follow up [10,12].

According to this study Median survival time to follow up among adult on ART program is two to three times lower than similar studies done at pawe hospital south Ethiopia, Aksum at St. Marry hospital Tigray, and mezantepi south Ethiopia. This difference may be justified by lower accessibility of health facility in the region which is only seventeen [13,17] health centers, five district hospitals and one referral hospital through the region.

As this study result shows being WHO stage one HIV patient is predictor variable for lost to follow up among adult ART patient from clinic when compared with stage four patients. This result is supported by similar longitudinal studies done in Gondar university referral hospital north Ethiopia and Mizan Tepi University hospital south west Ethiopia. On the other hand it's in contrast with the result of studies done among adult population in Cote d'Ivoire and other

Table 2: Factors associated with LTFU among adult patients on ART therapy at Dubti referral hospital, January 2013 to December 2018, Afar region, Ethiopia, 2019.

Variable	Categories	CHR(95%CI)	AHR 95% CI	P value
Patient contact	Present	1	1	
	Absent	1.9(1.2, 3.15)	1.06(0.5, 1.90.)	0.82
Program type	monthly based	5.7(2.9, 11.2)	6.66 (3.3, 13.4)	0.00**
	Spacing	1	1	
Education level	Can't read and write	1	1	
	Primary education	0.8(0 .16, 3.9)	0.77(0 .39, 1.5)	0.46
	Secondary	1.4(0.36, 5.5)	1.04(0.47, 2.27)	0.91
	College and above	0.71(0.08, 5.8)	0.75(0.25, 2.1)	0.6
Occupation	Daily laborer	1	1	
	Merchant	1(0.28, 4.2)	0.89(0.42 , 1.87)	0.76
	Employee	0.5(0.06, 4)	1.06(0.36 , 3.1)	0.9
	Student	4.4(0.90, 220)	1.6(0 .49, 5.87)	0.4
	House wife	1.2(1.17,7.1)	0.74(0.15, 3.6)	0.71
Marital status	Married	1	1	
	Single	2.1(1.9,5.6)	1.4(0 .68, 2.8)	0.34
	Divorced	0.5(0.06, 3.9)	0.72(0.28, 1.8)	0.51
	Widow	1.5(0.2, 12.4)	2(0.99 4.0)	0.51
CD4 Level	less than 50	0.34(0.18,0 .630)	0.43(0.2,0.82)	0.01*
	50 to 200	0.43(0.23,0.82)	0.98(0.43, 2.2)	0.97
	200 to 400	0.34(0.18,0 .63)	0.47(0.16, 1.3)	0.17
	greater than or equal to 400	1		
WHO Stage	stage I	0.8(0.30, 2.46)	2.6(1.1, 5.8)	0.025*
	stage II	0.46(0.16, 1.2)	0.74(0.2, 2.1)	0.58
	stage III	0.86(0.3, 2.4)	1.04(0.35, 3.0)	0.93
	stage IV	1	1	
Anemia	Anemic	4 (2.2, 7.3)	3.4(1.8, 6.3)	0.00**
	not anemic	1	1	
functional status	Working	1	1	
	Ambulatory	0.66(0.3, 1.13)	1.8(0.72, 4.6)	0.19
	Bedridden	0.67(0.2, 1.70)	1.33(0 .21, 8.3)	0.75
opportunistic infection	Yes	1	1	
	No	1.6(0 .9, 2.7)	0.5 (0.24 , 1.0)	0.06
adherence	Poor	5.3(2.8, 9.8)	2.8 (1.4, 5.41)	0.002*
	Fair	2.3(1.24, 4.4)	2 (1.08, 4.0)	0.027*
	Good	1	1	

part of Ethiopia kambata southern Ethiopia, Aksum, north Ethiopia and country wide level prospective study. This may be explained by the variations in the study settings between the studies [14-16].

In this study, ART patient with CD4 greater than or equal to four hundred were more likely to lost to follow up from ART clinic when compared with patient with ART patient with CD4 less than or equal to fifty. The finding supported by difference study in different part the world like Study done in America and Thailand among adult population those start treatment at ART clinics and same way study done in different part of Ethiopia like Kambata southern part of Ethiopia, Jijjiga eastern part of Ethiopia and Gondar northern part of Ethiopia. This may be explained by poor health seeking behavior until we developed complication [10, 14].

According to our study having poor and fair level ART drug adherence is one of positive predictor for lost to follow up from ART clinics. This result is in supported with study done in Amara region hospital. It might be due to; this difference in adherence will have an effect on the level of loss to follow up. Those who have lower adherence might be at higher risk of being loss like death [17].

As limitation, the use of medical data may be limits in terms of the availability of variables included in this study. Data incompleteness especially for follow up variables was also the other limitation which made difficulty to see clinical responses of patients since the data was collected from secondary source.

Conclusion

This study revealed as incidence of lost from follow up is high in comparable with world health organization strategic plan which called 90-90-90. It is also found that as the median survival time of loss to follow up from program is short. Type of ART program, anemia status, adherence to ART, CD4 count level and WHO stage were the predictors of lost to follow up from ART program. The Hospital ART monitoring and follow up department should strengthen and make the clients tracing system so as to increase client retention in the facility.

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