INCIDENCE AND PREDICTORS OF LOSS TO FOLLOW-UP AMONG HIV INFECTED ADULT PATIENTS ON ART IN HADIYA ZONE PUBLIC HOSPITALS, SOUTHERN ETHIOPIA

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INCIDENCE AND PREDICTORS OF LOSS TO FOLLOW-UP AMONG HIV INFECTED ADULT PATIENTS ON ART IN HADIYA ZONE PUBLIC HOSPITALS, SOUTHERN ETHIOPIA: RETROSPECTIVE COHORT STUDY

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ACRONYMS AND ABBREVIATIONS

ABC	Abacavir
AIDS	Acquired Immunodeficiency Syndrome
AHR	Adjusted Hazard Ratio
ARV	Antiretroviral
ART	Antiretroviral Therapy
AZT	Zidovudine
BMI	Body Mass Index
CD4	Cluster for Differentiation 4
CI	Confidence Interval
CPT	Cotrimoxazole Prophylaxis Therapy
CHR	Crude Hazard Ratio
EFV	Efavirenz
FHAPCO	Federal HIV/AIDS Prevention and Control Office
HO	Health Officer
HIV	Human Immunodeficiency Virus
IHRERC	Institutional Health Research Ethics Committee
IQR	Interquartile Range
INH	Isoniazid
IPT	Isoniazid Prophylaxis Therapy
JUTH	Jimma University Teaching Hospital
LTFU	Loss to Follow Up

LMICs	Low and Middle-Income Countries
3TC	Lamivudine
NVP	Nevirapine
OIs	Opportunistic Infections
SD	Standard Deviation
D4t	Stavudine
TB	Tuberculosis
TDF	Tenofovir
UNAIDS	United Nations Program on HIV/AIDS
VIF	Variance Inflation Factor
WHO	World Health Organization

ABSTRACT

Background: Loss to follow-up from ART-treatment is more common and can result to adverse health impact. In sub-Saharan Africa, including Ethiopia once patients start ART, more than a quarter patients lost within three years. There is limited evidence on the incidence of loss to follow up and its predictors among HIV infected adult patients at antiretroviral therapy in the current study areas.

Objective: To assess incidence and predictors of loss to follow-up among human immunodeficiency virus-infected adult patients after initiation of antiretroviral therapy, at Hadiya zone public hospitals, southern Ethiopia from 2014- 2018. Data were collected from March 1-25/ 2019.

Methods: An institution based retrospective cohort study design was undertaken. Based on ART registration records of HIV infected adult patients were categorized into advanced and not advanced diseases stages. The data were collected from individual folder and database by using data extraction format for 255 exposed and 297 unexposed total study population. Four health workers from the ART clinic collected data. Descriptive statistics were done by using Chi-square test and T-test to compare categorical and continuous variables between the two groups, respectively. Kaplan-Meier failure curves were used to estimate the probability of loss to follow up after ART initiation. The Cox proportional hazard model was used to assess predictors associated with loss to follow up after ART initiation.

Results: The incidence rate of loss to follow up among advanced and not advanced disease of adult HIV infected patients [11.9 per 100 person-years with 95%CI (9.47-14.99)] and [8.6 per 100 person years with 95% CI (6.37-11.67)] respectively. Baseline CD4 cell count < 200cells/mm3[(AHR=3.4, 95%CI: (1.87, 6.18)], advanced disease at ART initiation[(AHR= 0.33, 95%CI: (0.18, 0.58)], not receiving isoniazid preventive therapy [(AHR= 2.5, 95%CI: (1.64, 3.94)], fair or poor adherence to medication [(AHR= 2.8, 95%CI: (1.87, 4.34)] and ambulatory or bedridden functional status [(AHR= 2.4, 95% CI : (1.33, 4.18) were significantly associated with loss to follow up. People with worse status were loss to follow up

Conclusions: The overall incidence rate of loss to follow up among adults was 10.5 per 100 person-years, which was found to be high incidence rate. The loss to follow up among adult HIV infected patients was associated with low CD4 cell count, advanced disease stage, not receiving IPT, fair or poor adherence and ambulatory or bedridden functional status. Therefore, strong interventions is needed to address factors associated with loss to follow up should be implemented for optimal result in patient care.

Keywords: loss to follow up, incidence, adults, antiretroviral therapy, predictors, cox regression

1. INTRODUCTION

1.1. Background

The standard definition of Loss to follow up is when patients failed to take an ART refill for 180 days or more since the last clinic visit and this definition used for program monitoring and evaluation through the globe, it allows comparison of the program, and it minimizes misclassification of patients. Loss to follow up (LTFU) definition depend on a setting, facility type, and level of care, the presence of a program to follow up missed visits, provision of free antiretroviral therapy (ART), availability of food supplementation, and provision of family-centered care. Local, national, or regional definitions of LTFU are appropriate in certain contexts (Chi et al., 2011).

To realize clinical and immunological benefits of ART, retention in care and adherence to treatment is a critical issue to consider in the lifelong treatment follow up. Retention on ART improves quality of life, treatment for HIV prevention, viral load suppression, significantly decrease HIV/AIDS-related morbidity and mortality by accessing care and treatment for everyone living with HIV, reduce ARV drug resistance and less money spent to treat opportunistic infections (WHO, 2013; UNAIDS, 2013; Bain et al., 2017). However, ignoring LTFU undermines immunological and clinical benefits of ART.

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and partners launched the 90–90–90 targets; the aim was to diagnose 90% of all HIV-positive persons, provide antiretroviral therapy (ART) for 90% of those diagnosed, and achieve viral suppression for 90% of those treated by 2020. Demonstrating that are still very far from achieving the 90–90–90 targets. The lowest achievement rates were in low income and middle income countries (LMICs) (Bain et al., 2017). The achievement of second and third targets of the 90–90–90 challenged by experiencing loss to follow up in ART patients.

1.2. Statement of the Problem

Loss to follow up from HIV care is a major public health concern. Loss to follow up increases the risk of drug resistance, drug toxicity, and treatment failure due to poor ART adherence in cases where death is not the reason for LTFU (Berheto et al., 2014). Loss to follow up contributed to poorer health outcomes for patients and constitutes resource wastage (Onoka et al., 2012). Failure to prescribe cotrimoxazole, adherence to ART drug refill appointment < 95 % and very low weight increased risk LTFU (Auld et al., 2014).

Scale up ART brought a remarkable increase in the number of people who access treatment in low-and-middle-income countries 300,000 people were receiving ART in 2002 and increased to 9.7 million in 2012 that represent 65% of the 15 million targets to access ART in 2015. The global scale-up of ART had saved an estimated 4.2 million lives in Low and Middle-Income Countries (LMICs) by the end of 2013. It also contributes significantly to the ongoing drop in annual new HIV infections around the world (WHO, 2013; UNAIDS, 2016).

Antiretroviral therapy is a lifelong treatment that needs retention from its initiation, but patients may drop out in the continued care. Retention of adult patients on antiretroviral therapy according to systematic review and meta-analysis in Low-and Middle-Income Countries at 36 months on treatment averages 65% – 70% (Fox and Rosen, 2015). Loss to follow-up is more common in resource-poor settings. African programs reported higher attrition rates than Latin American and Asian programs due to opportunistic infections occurring in the first three months (Renaud-Théry et al., 2014). In an antiretroviral treatment in lower income countries study, loss to follow-up after 1 year was above 40% in some programs and associated with more advanced clinical disease and lower CD4 cell counts (Schoni-Affolter, 2011).

A systematic review of treatment cohorts in sub-Saharan Africa shows that once patients start ART, about one-quarter of the people temporarily interrupt treatment and another quarter are lost within three years. Among those lost, up to half (46%) may have died (UNAIDS, 2013; WHO, 2013). A systematic review and meta-analysis in 12 sub-Saharan Africa countries show that loss to follow up increases the risk of death (Kathrin Zürcher, 2017).

Although ART coverage for adults has reached 79.6 %, ART implementation status and outcome study for the treatment cohorts conducted in Ethiopia confirms 82.4% of 12 months retention after initiation of ART. Retention in care continues to be a challenge in health facilities (FHAPCO, 2014). In Ethiopia, among HIV-infected adults, 57.7%, and 29.6% of the participants were retained and Loss to follow up respectively and the remaining were dead and transfer out. Over half of those who were LTFU, 57.7%, obtained this status during the first year after ART initiation (Tiruneh et al., 2016). The loss to follow up in the continuum of HIV care ranges over time (Bucciardini et al., 2017). In Southern Nations Nationalities and Peoples Region LTFU or death is a problem that obstacles the success of antiretroviral therapy with 24.6% at 28 months of median follow-up duration (Teshome et al., 2015).

Associated factors of loss to follow up are socio-demographic factors. Clinical characteristics, like CD4 count, advanced WHO clinical stage, functional status and Isoniazid Preventive Therapy (IPT), poor ARV adherence, drug side effects, TB/HIV co-infection, mental illness s, immunological failure, clinical failure, treatment failure, and fear of stigma(Moges et al., 2018; WHO, 2013; Mberi et al., 2015; Gesesew et al., 2017; Kidane and Fisaha, 2014).

As evident from works of literature, the incidence of LTFU and its predictors were investigated among adults in a few previous studies in Ethiopia (Seifu et al., 2018; Moges et al., 2018; Megerso et al., 2016). Loss to follow up rates varied through the country, region, population and health facilities. Loss to follow up still remain questions in health facilities until appropriate intervention strategies designed and implemented to increase ART adherence. As the knowledge of investigator, there is limited evidence on the incidence of loss to follow up and its predictors among adult patients on ART in current study areas. It is an ongoing effort to have a comprehensive understanding of the predictors of LTFU in order to contextualize intervention strategies to retain HIV patients in care. The hypothesis to be tested was loss to follow up is not different among HIV infected adult patients with advanced disease stage when compared with adult patients not in advanced disease stage during ART treatment initiation.

1.3. Significance of the Study

The findings from incidence and predictors of LTFU among adult ART patients will be used as input for local health program planners, health bureaus, and health departments to improve or strengthen strategies related loss to follow up the reduction in ART cohort. In addition, the findings of the study will avail baseline information for researchers interested to do further research on incidence and predictors of loss to follow-up among adult patients after ART initiation. This study will provide insight into the predictors of LTFU among adult patients after ART initiation that will be used by study hospitals to reduce losses from ART care. Moreover, the information obtained from this study will add to the existing knowledge of health care providers to give due attention during follow up time on factors that contribute to LTFU. This study will benefit individuals by improving treatment adherence, which in turn decrease lost from antiretroviral treatment.

1.4 Objectives

1.4.1 General Objective

To assess incidence and predictors of loss to follow-up among HIV infected adult patients on antiretroviral therapy in Hadiya zone public hospitals, southern Ethiopia from 2014- 2018. Data were collected from March 1-25/2019.

1.4.2 Specific Objectives

1. To determine the incidence of loss to follow-up among HIV infected adult patients after initiation of antiretroviral therapy.
2. To determine predictors of loss to follow-up among HIV infected adult patients after initiation of antiretroviral therapy.

2. LITERATURE REVIEW

2.1. Overview of Loss to Follow Up

A Loss to follow up is one outcome status written in an ART clinic for patients while they are interrupted treatment. There are some reasons that contribute to loss to follow up across the world, region, and countries even if the magnitude of distribution for factors is not the same.

2.2. The Incidence of Loss to Follow Up

A retrospective cohort study was done at Anantapur district, India in 2012 showed that the LTFU rate was 7.1 per 100 Person-years. The LTFU were 15.5% with a mean follow-up of 2.17 years (Alvarez-Uria et al., 2013). Once more, Cohort study done both at Australia and Asia among 4689 adults in 2010 reported that the incidence rate of LTFU was 4.4/100 person-years (Guy et al., 2013).

According to a comparative analysis done at Lusaka, Zambia the proportion of LTFU among HIV-infected adults in 2011 was 32.1% and incidence rate per 100 person-years ranged from 8.7 to 13.6 (Li et al., 2013). Likewise, retrospective record review done at KwaZulu-Natal, South Africa showed that the proportion of LTFU 14.7% (Arnesen et al., 2017). Another cohort study done in South Africa showed that the incidence rate of LTFU was 109 per 1000 person-years and the proportion of LTFU was 23.4% (Mberi et al., 2015). On the other hand, retrospective cohort study done in Lilongwe, Malawi showed that LTFU rates among patients in ART were 26 per 100 person-years (Tweya et al., 201 8). LTFU among 31,033 adults' patients who initiated ART in HIV care services in Rwanda at 36 months was 5.5% (Mugisha et al., 2014).

A retrospective cohort study done at Aksum St. Merry hospital, Northern Ethiopia showed that the incidence rate of LTFU from ART caregiving 8.2 per 100 person-years and proportion of LTFU 9.8% (Kidane and Fisaha, 2014). Similarly, a retrospective cohort study was done in Mizan-Aman general hospital, Southern Ethiopia presented that the cumulative incidence of LTFU was 8.8 per 1000 person-months. The proportion of LTFU was 26.7%. The mean age of the cohort was 31.5 years for adults (Berheto et al., 2014). A retrospective cohort study was done at Jigjiga town, eastern Ethiopia in 2015 among adults on antiretroviral treatment indicated that incidence rate of loss to follow up was 26.6% per 100 person months and around 14.8% of patients defined as LTFU (Seifu et al., 2018). A cohort study done at Pawi general hospital in Benshangul-Gumuz region

showed that the proportion of LTFU was 22.6%. The cumulative incidence of LTFU after ART initiation was 11.6 per 100 adult years (Moges et al., 2018).

2.3 Predictors of Loss to Follow up

2.3.1 Socio-Demographic characteristics

Regarding sex effect on loss to follow up from ART, a cohort study done in Nigeria, in Nairobi, Kenya among adult patients, at Aksum St. Merry hospital, and at Karamara general hospital, Eastern Ethiopia showed that male was 1.36, 1.3, 3, and 2 times more likely to be LTFU (develop attrition in case of Kenya) than females (Dalhatu et al., 2016; Mecha et al., 2018; Kidane and Fisaha, 2014; Seifu et al., 2018). Correspondingly, a case-control study done at Oromia region in 2015 showed that male patients were 1.38 times more probable to be LTFU than female patients (Megerso et al., 2016).

A Retrospective cohort study done in Lilongwe, Malawi showed that age 15 – 24 years were1.4 times more likely to be LTFU than age 25 – 34 years (Tweya et al., 2018). Equally, a retrospective cohort study done in Nairobi, Kenya among adult patients showed that age 15 – 19, 20 -24 and 25 – 29 were 1.8, 1.9 and 1.3 times more likely to develop attrition than age 30 – 54 years (Mecha et al., 2018). Correspondingly study done at southern Ethiopia showed that adult ≥20 yrs. were 1.4 times more likely to be lost than child ≤10 yrs. (Berheto et al., 2014) According to a case-control study was done at Oromia region, among adult patients aged 15–24 and 25 – 34 years were 19.8, and 3 times more likely to be LTFU respectively when compared aged > = 55 years (Megerso et al., 2016). However, a retrospective cohort study was done at Pawi general hospital; northwest Ethiopia reported that adults aged above 45 years were 56% lower risk of LTFU compared to aged 15–28 years (Moges et al., 2018).

A retrospective study done in South Africa showed that those who have not committed partner were 2.8 times more likely to be LTFU than having committed partner (Mberi et al., 2015). A retrospective study done at Rwanda among adult clients showed that who were married/ in a union and widowed were 20%, and 40% less likely to be a loss to follow up respectively than single (Mugisha et al., 2014). A retrospective cohort study was done in Nairobi, Kenya among adult patients from 2004–2015 showed that single and divorced were 1.27 and 1.56 times more likely to

develop loss to follow up as compared with married (Mecha et al., 2018). A retrospective cohort study done at South Africa showed that partner status absent for HIV were 2.9 times more likely to be loss to follow up (Mberi et al., 2015).

According to a retrospective cohort study done Lilongwe, Malawi showed that facility location of rural was 2.3 times higher risk to LTFU than urban location (Tweya et al., 2018). Also, a cohort study done in Nairobi, Kenya among adult patients showed living in urban were 1.4 times more likely to be LTFU than rural (Mecha et al., 2018). On the other hand, the case-control study of Oromia region showed that rural residents were 2.37 times more likely to be LTFU compared to the urban dwellers (Megerso et al., 2016).

A mixed method study conducted in Addis Ababa, Ethiopia showed that primary/no education was 1.5 times more likely to be the loss to follow up than secondary/ tertiary education (Tiruneh et al., 2016).

A retrospective cohort study done at South Africa showed that those who were self-employed were 13.9 times more likely to be LTFU (Mberi et al., 2015). Furthermore, a case-control study done at Oromia region showed that day laborers and private/government organization employees were 5.36 and 3.2 times more likely to be LTFU in ART compared to farmer/housewife and others respectively (Megerso et al., 2016).

2.3.2 Clinical, Laboratory and Treatment Predictors

According to retrospective cohort study done at South Africa showed that having known WHO clinical stage III/IV were 2 times more likely to be LTFU than WHO stage I/ II (Mberi et al., 2015). Moreover, a cohort study did at Pawi general hospital among adults who were on WHO clinical stage-IV have 2 times increased the risk of LTFU as compared with stages I and II (Moges et al., 2018). Similarly, a case-control study done at Oromia region showed that patients with WHO stage III and IV were more than 2, and 6 times more likely to be LTFU as compared to WHO stage I (Megerso et al., 2016). According to retrospective cohort Study done at Mizan –Aman general hospital, Ethiopia showed that the risk of LTFU in patients with WHO clinical stage III was 40% less likely to be LTFU than WHO stage I (Berheto et al., 2014). Late WHO clinical stage

is more than 1 times more likely to be lost according to retrospective follow up study was done in southern Ethiopia (Teshome et al., 2015).

A retrospective cohort study done at South Africa, and rural hospital in KwaZulu-Natal, South Africa showed that having a baseline CD4 count < 200 cells/ml were 3.8, and 2.6 times more likely to be LTFU respectively than CD4count > 500 cells/ ml (Mberi et al., 2015, Arnesen et al., 2017). On the hand, retrospective cohort study was done at Mizan –Aman general hospital showed that baseline CD4 cell counts < 200 cells/mm3 were 1.7 times higher risk of LTFU than CD4 counts ≥ 200 cells/mm3 (Berheto et al., 2014).

A retrospective cohort study was done at Mizan –Aman general hospital, a case-control study done at primary public hospital in Wukro, Tigray, Ethiopia, and Oromia region showed that the risk of LTFU in patients who did not take INH prophylaxis was 3.7, 3, and 2.8 times higher than those who did take INH prophylaxis (Berheto et al., 2014; Mehari et al., 2015; Megerso et al., 2016). According to retrospective cohort study done at Pawi general hospital showed that being on IPT lowered hazard ratio for lost follow up by 89%, as compared to those didn't receive IPT (Moges et al., 2018).

According to a retrospective cohort study done at Aksum St. Merry hospital patients diagnosed with TB had a two times higher risk of LTFU than who was TB negative (Kidane and Fisaha, 2014). A retrospective study at JUTH, Southwest Ethiopia among HIV infected adult reported that yes for the history of TB/HIV co-infection was 1.4 times likely to be discontinued than those responded no (Gesesew et al., 2017).

Although study was done at Aksum St. Merry hospital showed that regiment AZT-3TC-NVP have 3.5 times increased risk of loss to follow up than those who were using d4t (30)-3TC-NVP (Kidane and Fisaha, 2014), Patients who were taking a combination of drugs TDF+3TC+EFV were about 1.58 times more likely to be LTFU compared with who was taking AZT+3TC+NVP (Megerso et al., 2016). Likewise, the study done at Mizan –Aman general hospital showed that patients who made regimen substitutions during the follow-up period had 5 times higher risk of developing LTFU (Berheto et al., 2014).

The study done at Oromia region showed that ambulatory or bedridden patients were 2 times more likely to be LTFU when compared to baseline working functional status (Megerso et al., 2016). Similarly, a mixed method study done at Addis Ababa, Ethiopia showed that bedridden patients were 2 times more likely to be LTFU (Tiruneh et al., 2016).

A retrospective cohort study done at South Africa showed that having a last known viral load that was detectable were 3.6 times more likely to be LTFU (Mberi et al., 2015).

According to a case-control study done in a primary public hospital of Wukro, Tigray region, Ethiopia revealed that presence of side effects for ART was 12.34 times more likely to be lost from the care (Mehari et al., 2015). Besides, retrospective cohorts study done at South Africa showed that having a history of an ART-related adverse event was 39% times less likely to be LTFU (Mberi et al., 2015).

A retrospective cohort study from Goma, Democratic Republic of Congo showed Patients not disclosed their HIV status to anyone were 2.28 times more likely to be Lost (Akilimali et al., 2017). A retrospective cohort study was done in Jigjiga town; eastern Ethiopia indicated that not disclosed their HIV status for any one was 2.8 times more likely to be loss to follow up (Seifu et al., 2018). Family relation concern did not show significant association for loss to follow up among adult ART patients from 2009 - 2012 (Mehari et al., 2015).

According to a cohort study done in Lilongwe, Malawi body mass index (BMI) category < 18.5 were 1.2 times more likely to be a loss to follow up than 18.5 – 24.9 (Tweya et al., 2018).

2.3.3. Health Behavior

According to study done Lilonge, Malawi loss to follow up was 4.5 times higher for those no adherence to clinic appointment than adhered to clinic appointment (Tweya et al., 2018). Furthermore, case-control study at Oromia region among HIV infected adult in 2015 indicated that sub-optimal (fair/poor) adherence to ART was 7.4 times more likely to be LTFU than optimal (good) adherence (Megerso et al., 2016). Correspondingly, a cohort study done at JUTH among HIV infected adults showed that fair/poor adherence was 1.6 times more probable to be discontinued than good adherence (Gesesew et al., 2017).

2.4. Conceptual Framework

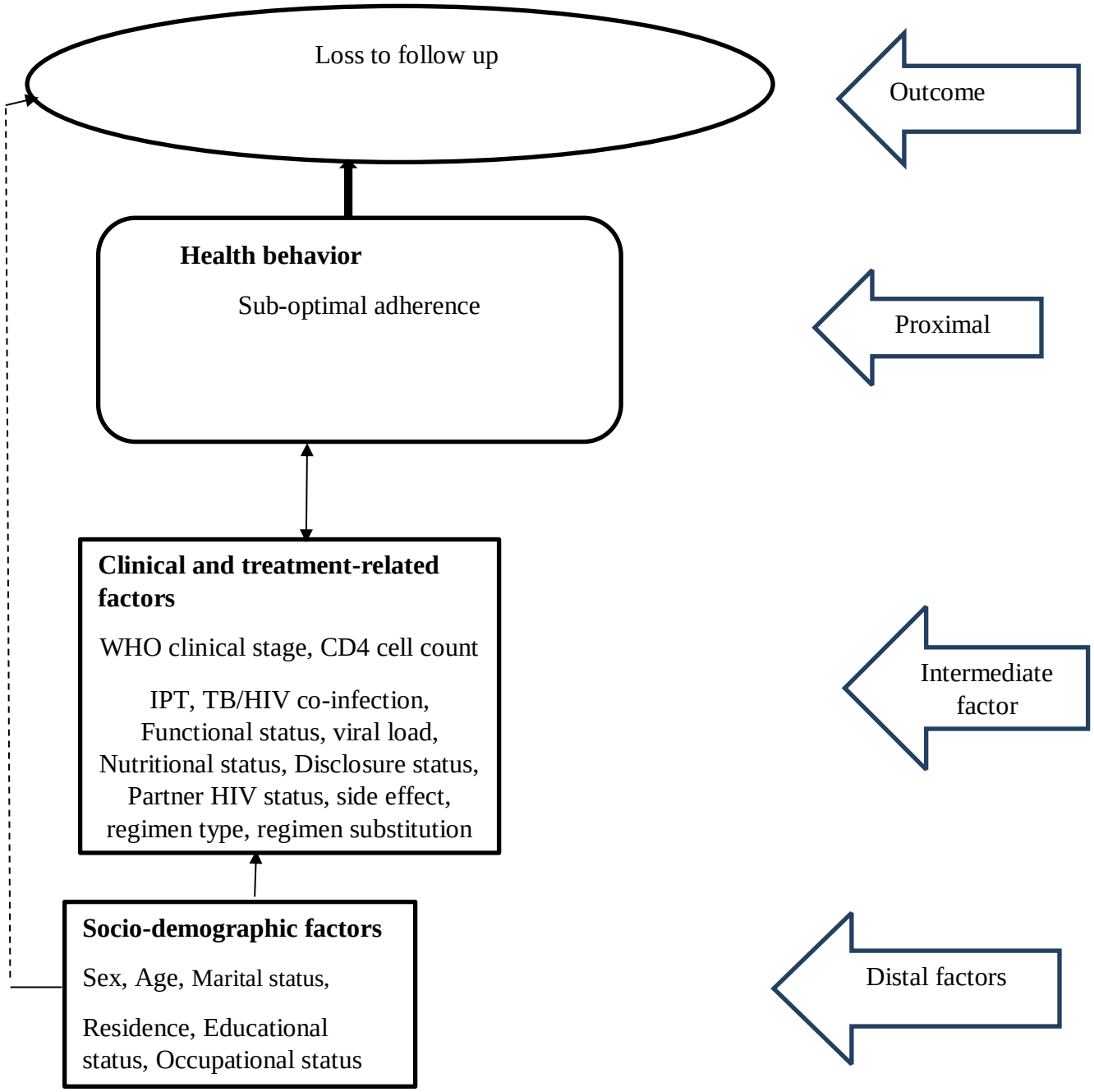

Figure 1. A conceptual framework describing predictors of loss to follow among adults on antiretroviral therapy (ART) at Hadiya zone public hospitals, southern Ethiopia in 2018/9 (adapted from (Rachlis, 2013)).

3. METHODS AND MATERIALS

3.1. Study Area and Study Period

The study was carried out at Hadiya zone public hospitals. Hadiya one of the major zones in Southern Nations, Nationalities and Peoples Region (SNNPR), Hadiya Zone is located in the northern part of the Southern region of Ethiopia. Its capital, Hosanna, is 232 kilometers south of Addis Ababa and situated 196 Km from Hawassa, which is the capital city of SNNPRS. Hadiya Zone is divided into 10 districts and 2 towns administrative. Hadiya zone has three public hospitals namely: Wachemo University hospital, Shone primary hospital, and Homacho primary hospital. The total population of Hadiya zone is 1.5 million from these 750,320 (50.74%) females and 728,560 (49.26%) males, 1,324,185 (89.54%) rural population and 154,695 (10.46%) urban population according to 2017 population projection. Hadiya zone has 336 kebeles, 331 health posts, and 62 health centers (Hadiya zone HMIS report. 2018). Wachemo University Nigist Elleni Mohammed memorial general hospital was built in 1984 GC and it is serving people from Hosanna town and its perspective districts. The public hospitals provide services in various outpatient and inpatient departments. Hospitals have been providing chronic HIV care and support to both pre-ART and ART adult clients since the establishment. Total adult clients enrolled to receive ART service in public hospitals of Hadiya zone was 2,227. The study period was from March 01 – 25, 2019.

3.2. Study Design

An institution based retrospective cohort study design was undertaken.

3.3. Source Population

The source population for this study was all adult people living with HIV/AIDS who are on antiretroviral therapy at Hadiya zone public hospitals.

3.4. Study Population: All adults with advanced WHO clinical stages at ART enrollment from 1 January 2014 - 31 December 2018 at Hadiya zone public hospitals as exposed groups.

All adults without advanced WHO clinical stages at ART enrollment from 1 January 2014 – 31 December 2018 at Hadiya zone public hospitals unexposed groups.

3.5. Inclusion and Exclusion Criteria

3.5.1. Inclusion Criteria

- HIV-infected adults who were 15 years of age or older at the time of registration for HIV care in the ART clinic during a retrospective study period were included.
- Adults' record that had at least two follow-up visit including ART initiation visit was eligible to be included.
- Adults registered from 2014 - 2018 and have maximum follow up for 62 months and minimum follow up of two months.

3.5.2. Exclusion Criteria

- Participants' registration that had unknown initiation date, undefined outcome, and transferred in with incomplete baseline data minimizing important factors were excluded.

3.6. Sample Size Determination

Objective one: The required sample size for objective one was determined by using the following assumptions: The significance level of 5 %, 80% power, the hazard ratio (HR) 0.5, and $\pi 1$ and $\pi 2$ are the proportions to be equally allocated to group 1 and group 2 respectively. The incidence rate(IR) = 8.8 per 1000 person month that converted to five years gives 0.528 person-year in a study conducted southwest Ethiopia (Berhetoetal.,2014).

Event (lost) = $4(z\alpha/2+z\beta)^2 / (\log HR)^2)) = 66$ (Collett, 2014), log HR = 0.69

Where $Z\alpha/2$ and $Z\beta$ are standard normal percentiles which give 1.96 (95%CI) and 0.84 (80%)

n =Lost/Pr (lost), where Pr is the probability of loss and it is calculated by

Pr{Lost} = $1 - (\pi 1 S1 (T) + \pi 2 S 2 (T)) = 1 - 1/2 (S1 (T) + S 2 (T)$ where $S(T)= \exp (- \lambda t)$, $IR=\lambda t$ and $S1(t5)=\exp (-0.528)= 0.5898$ and $S2(t5)=\text{Exp} (-0.528*HR)=0.77$, S(T) is survival function

Pr {Lost} =1–1/2(S1 (T) +S2 (T) =1-1/2(0.5898+0.77) = 0.32

n =Lost/Pr (lost) = 66/0.32 = 206 (adding 10% for incomplete data) = 229

Objective two: Sample size for the specific objective two was performed by using Stata command of stpower cox by considering the following parameters: significance level (α) of 5%, Power (1-β) of 80%, the hazard ratio of 0.6 for WHO clinical stage III versus I (Berheto et al., 2014). Withdrawal of 10% for incomplete data during follow up period and in adjusting for censoring 0.27 of the probability of event taken and allocation ratio 1:1 and 0.5 of standard deviation. By having all the above parameters the Stata command estimated sample sizes for survivor functions of the second specific objective was 516. From this 258 is exposed groups and 258 is unexposed groups. From both objectives sample size calculations, the specific objective sample size calculation for WHO clinical stages give the largest sample size that was 516.

3.7. Sampling Procedure

From ART cohort registration a list of the study population was identified according to the initiation date. Next study population record was selected using age and eligibility criteria then start and end medical record number for five years historic cohort of the study was identified and all records included for data review. Profiles of all adult patients receiving antiretroviral therapy between 1 March 2014 and 28 February 2019 was involved for event loss to follow up review. All exposed and unexposed adult patients' record were retrospectively followed for the event. Total study population at public hospitals of the Hadiya zone was 573; all were included for this study. Patients in the exclusion list were excluded. Data about time to LTFU was collected from patients' charts and database. The total adult population of the study hospitals was 641. From these 68 was excluded due to unknown outcome status, undefined date of ART initiation and transferred in with incomplete baseline data. About 21 records was excluded from analysis since incomplete for baseline exposure variable, final 255 exposed and 297 unexposed was included final analysis.

3. 8. Data Collection Methods

3. 8 .1. Data Collection Instrument

The data were collected using a standard data extraction format, which adapted from National ART baseline, follows up registration, and used as a tool for this study. The form was developed by using the nationally standardized ART intake and follow up chart that used by ART clinic. The extraction format including information about Socio-demographic characteristics like sex, age,

residence, educational status, occupational status and. Clinical, treatment and laboratory characteristics addressed by reviewing records about functional status, WHO clinical stages, CD4 cell count, INH prophylaxis, cotrimoxazole preventive therapy, TB/HIV co-infection, regimen types, functional status, adherence to ART, viral load determination, adverse drug event, nutritional status, have opportunistic infection and Family care or support related factors includes, marital status, disclosure status and partners HIV status will be extracted from ART chart. Whenever relevant information was missed, the ART electronic database was consulted.

3. 8 .2. Data Collectors

Four experienced nurses from ART clinic who were trained on comprehensive HIV care and involved in-patient follow up recruited as data collectors. Before extracting information from the ART registration charts or database two days intensive training was given on how to review records of the patients. Along with data collectors, two supervisors (MSc/MPH) were involved during data collection time to supervise the overall data collection process.

3.8.3. Data Collection Procedure

The data for this study were collected by using secondary data collected routinely in Hadiya zone public hospitals for clinical monitoring and evaluation purposes. The data entered in an ART electronic database/chart and updated during the follow-up time were used. A data retrieval format was used for extracting information from ART registration chart, or electronic database. Patients who missed their clinical appointment are usually registered in the defaulter tracing register and outcome status labeled as lost. This lost was used as an event during the data collection period. During data collection time if there was no baseline data for WHO clinical stages, considered as incomplete data.

3.9. Variables

3.9.1. Dependent Variable

Time to loss to follow up in months

3.9.2. Independent Variables

Socio-demographic variables like sex, age, marital status, residence, educational status, occupational status.

Clinical, laboratory and treatment factors/variables like WHO clinical stage, CD4 cell count, INH prophylaxis, cotrimoxazole preventive therapy, TB/HIV co-infection, initial regimen type, current ART regimen, regimen substitution, functional status, viral load, ART side effect, and Nutritional status (BMI category), disclosure status, spouse HIV status

3.10. Operational Definitions

Loss to follow up defined as patients not take ART refill for more than one month and yet not classified as transfer out or death but alive confirmed by post tracing defaulter by home visit or phone call (Chi et al., 2010; Mekuria et al., 2015). Those who are not present for more than one month since the last appointment date for ART medication refill identified as an event. In this study, patients were classified into LTFU (event) and censored.

Time to event (loss to follow up) last appointment date plus 31 or more days late for an appointment for included patients' record reviews (Teshome et al., 2015).

Incidence rate: Number of LTFU among patients enrolled on ART per person at risk per time observations. Numerator = number of LTFU during the entire follow up period. Denominator = Time each person observed totaled for all persons (total person-month observations).

Retention in care: patients who were alive and receiving ART at the public hospitals after ART initiation (this does not include patients who were lost to follow-up (LTFU), who were deceased or who transferred out) (Bucciardini et al., 2017).

Drop from ART defined as a patient had missed his or her planned clinic or pharmacy refill appointment for more than three consecutive months (Mekuria et al., 2015).

Death: defined as a known client death from any cause, confirmed by health care worker or post-loss tracking (Teklu and Yirdaw, 2017).

Transfer out: when a patient is referred from the health facility where he/she started ART to another health facility to continue HAART medication (Teklu and Yirdaw, 2017).

Adherence to ART: is the degree to which a person taking medication, following a diet – corresponds with agreed recommendations from a health worker (WHO, 2016).

Level of adherence

Status	Percentage of prescribed ART intake	No of missing doses out of 30	No of missing doses out of 60	
Good	≥ 95%	≤ 2	≤2	(MOH, 2017)
Fair	85% – 94%	3 – 5	3 – 9	
Poor	<85	> 5	> 9	

Working: Capable of going out of the home and do routine activities including the daily work in or outside the home, including school work, office work, housework, taking care of children, and harvest (WHO, 2006; MOH, 2017).

Ambulatory: Capable of self-care and going to the toilet unsupported but unable to work in or outside the home (WHO, 2006; MOH, 2017).

Bedridden: Cannot go even to the toilet unsupported or patients remained in bed most of the time (WHO, 2006).

Advanced WHO clinical disease at ART initiation: WHO clinical stage III/IV within six months of diagnosis. (Wright et al., 2015).

Detectable Viral load: viral load above 1000 copies /ml (WHO, 2016).

Undetectable Viral load: viral load below 1000 copies/ml (WHO, 2016).

Nutritional status: BMI for adults less than 16 kg/m² show severe malnutrition, BMI from 16-18.49 kg/m² is moderate malnutrition, BMI from 18.5 -24.99 is normal weight, and (MOH, 2017). MUAC (mid upper arm circumference) for pregnant and bedridden patients: not malnourished (> 22cm), moderate mal-nutrition (19-22 cm), (< 19 cm for pregnant), < 18 cm for bedridden patients.

Censored: Patients who have not experienced the event of interest (LTFU) during the specified study follow up period (alive and on treatment, transfer out and death).

3.11. Data Quality Control

The data extraction form was developed in English from the national ART entry and follow up registration. The review was conducted using a data retrieval form. Two days of intensive training to data collectors and supervisors about the purpose, study tool, and an overall data collection procedure to be eminently maintained by them during data collection time, was given. The supervisors checked the completeness and consistency of the filled data retrieval form immediately before submission. In addition, double data entry were done by two data clerk and checked for validation by the principal investigator of the research. Data were cleaned for outliers, incompleteness, and inconsistency. The principal investigator supervised the overall quality of the data collection.

3.12. Methods of Data Analysis

Following the accomplishment of data collection activities, the data were entered to Epi Data version 4.1, and export to statistical packages Stata version 14.0 for data processing and analysis. Descriptive statistics were done by using Chi-square test and T-test to compare categorical and continuous variables between the two groups, respectively. Incidence of LTFU was determined from the start of ART until the last follow-up visit or known date of death. Life table was used to estimate the probability of loss to follow up every twelve months. Kaplan-Meier failure curves were used to estimate the cumulative probability of loss to follow up after ART initiation. The log-rank test was used to test the significance of observed differences between comparison groups and was considered statistically significant at a p-value less than 0.05. Bivariate analysis was carried out to identify candidate variables for the multivariable Cox regression model. Variables with P – value < 0.25 was entered into the multivariable Cox regression model to determine the predictors of time to LTFU. Moreover, Schoenfeld residual global test p- value 0.134 was used to check the overall model fitness. Proportional hazard assumption was checked graphically. Finally, the decision was made using the adjusted hazard ratio (AHR), 95% confidence interval and P-value < 0.05 to declare the statistical significance of variables. Multicollinearity was checked by using variance inflation factor greater than ten. Data were censored at the last follow up clinic visit, if dead at date of death and transfer out at date of transfer out.

13. Ethical Considerations

Ethical clearance letter was obtained from Haramaya University, college of health and medical sciences institutional health research ethics review committee (HU-IHRERC). A permission letter obtained from the school of graduate studies was submitted to Hadiya zone health department to grant official permission. After discussion and explanation about the purpose, method and anticipated benefit of the study by principal investigator written and signed informed consents was obtained from hospitals heads to ensure confidentiality, prior to the actual data collection. The heads had the right to ask any question and refuse the study at any time during data collection. As the study was conducted through a review of clinical records, the individual patients were subjected to minimal harm as long as the confidentiality was kept. To keep the confidentiality, ART clinic nurses of Hadiya zone public hospitals extracted the data from the medical records. In addition to that name, personal identifications or medical record number and other specific

addresses were not be reviewed. The recorded data were not accessed by a third person, except the principal investigator, and was kept confidentially. Privacy and confidentiality of the information provided by each record review were kept properly.

3.14. Information Dissemination

The findings of this study will be presented to the scientific community of Haramaya University College of health and medical science, school of graduate studies. In addition, it will also disseminate to Hadiya zone public hospitals. Besides, the study findings will be considered to be published and present on local or international conferences and peer-reviewed journal.

4. RESULTS

4.1. Socio-Demographic Characteristics

A total of 552 HIV infected adult patients were included in the analysis that makes a 96% response rate of the study. In the current study, both cohorts were not significantly different for most of the socio-demographic characteristics. The median age of study participants were 31 (IQR (27-38)), 30 (IQR (26-37)) for advanced disease stage and not in advanced disease stage at ART initiation respectively. The mean age of participants for advanced and not advanced disease stage were 32±8.6, 32.14±8.8 respectively; difference observed for ages of comparison groups (p = < 0.001).

Females account for the majority of study participants; 130 (41%) and 187 (59%) on advanced and not advanced disease stage respectively. Study participants sex showed significant difference for comparison groups (p-value = 0.004). Majority of participants were married; 165(43.4%) and 215(56.6%) on advanced disease stage and not advanced disease stage respectively (Table 1).

Majority of study respondents were residing in a rural area; 197(50.4%) and 194(49.6%) on advanced disease stage and not advanced disease stage respectively. There was a significant difference for residence on advanced and not advanced disease stage (p-value = 0.002). When the educational status of the respondents compared about 84 (45.16%) and 102 (54.84%) were on primary education for advanced disease stage and not advanced disease stage respectively. More than one-fourth of study participants in a cohort was homemaker, from these 48(37.2%) were on advanced disease stage; 81(62.8%) in not advanced disease stage (Table 1).

Table 1: Baseline socio-demographic characteristics of HIV infected adult patients on ART at Hadiya zone public hospitals, southern Ethiopia from 1 Jan 2014 – Dec 31, 2018

Variables	AIDS-defining illness		
	Advanced disease (n=255) n (%)	Not advanced disease (n= 297) n (%)	P –Value
Sex (n=551)			0.004*
Male	125 (53.4%)	109 (46.6%)	
Female	130 (41%)	187 (59%)	

Marital status(n=551)			0.117
Married	165(43.4%)	215(46.6%)	
Never married	53(47.7%)	58(52.3%)	
Divorced/separated	17(60.7%)	11(39.3%)	
Widowed/er	19(59.4%)	13(40.6%)	
Educational status(n=537)			0.618
No formal education	67(46.2%)	78 (53.8%)	
Primary education	84 (45%)	102(55%)	
Secondary education	58(43.3%)	76 (56.7%)	
Tertiary education	38 (52.7%)	34 (47.3%)	
Occupational status (n=527)			0.134
Gov't employee	34 (53%)	30(47%)	
Farmer	51(54.8%)	42 (45.2%)	
Merchant	41(50.6%)	40 (49.4%)	
Daily laborer	29 (51%)	28 (49%)	
Driver	9 (53%)	8 (47%)	
Housewife	48(37.2%)	81 (62.8%)	
Student	29 (40.3%)	43 (59.7%)	
Others	8 (57%)	6 (43%)	
Residence (n=551)			0.002*
Rural	197 (50.4%)	194 (49.6%)	
Urban	57 (35.6%)	103 (64.4%)	

* Significant at α=0.05

4.2 Clinical, Laboratory, and Treatment-Related Characteristics

When study participants were compared to the AIDS-defining illness, there was a statistical difference in both advanced and not advanced disease stage in the current retrospective cohort study. Regarding nutritional status higher proportion of patients had normal weight; advance 212 (43.26%) and not advanced disease stage 278 (56.74%) with p-value < 0.001. Among the study cohort more than one-third 208(37.68%) had an opportunistic infection; 177(85.1%) and 31(14.9%) on advanced disease stage and not advanced disease stage cohorts respectively. Opportunistic infection showed a significant difference for baseline advanced disease stage of the cohort (p < 001) (table 2).

Majority of study participants were able to perform their usual work (on working); 122(31.12%) and 270(68.88%) in on advanced disease and not advanced disease cohorts respectively and significant difference observed for functional status (p < 0.001). Around three fourth 383 (72.53%) of the participants have baseline CD4 cell count of greater than or equal to 200 cells/mm3. The result showed difference for comparison group of advanced disease stage 122 (31.85%) and not advanced disease stage 261 (68.15%) (p= < 0.001). Study participants in on advanced disease stage cohort had median CD4 cell count of 235.5cells/mm3 and IQR 146-369.5cells/mm3 and not-advanced disease stage with a median of 540.5cells/mm3 and IQR 373-665cells/mm3 (table 2).

There was a significant difference in comparison groups for IPT provision at baseline (p-value < 0.001). About three fourth 400 (72.5%) received IPT in both advanced disease stages and not advanced disease stages 153 (37.4%), 256(62.6%) respectively. In this study disclosure status at ART initiation was not different for advanced disease stage and Not advanced disease stage (p=0.072). Both groups showed a significant difference in Initial regimen prescription (p < 0.001). Most of the respondents were treated at enrollment with Tenofovir + lamivudine + Efavirenz (TDF–3TC–EFV) in on advanced 173(43.25%) and not advanced disease stages 227(56.75%) (table2).

Table 2: baseline clinical, laboratory and treatment-related characteristics of HIV infected adult patients on ART at Hadiya zone public hospitals, southern Ethiopia from 1 Jan 2014–Dec 31, 2018

Variables	AIDS defining illness		P – Value
	Advanced disease stage (n= 255) n(%)	Not-advanced disease stage (n= 297) n(%)	
Disclosure status at ART initiation(n=551)			0.233
Yes disclosed	211(47.5%)	233 (52.5%)	
Not disclosed	44 (41%)	63 (59%)	
Partner/spouse serostatus (n=550)			0.428
Positive	112 (49%)	116 (51%)	
Negative	66 (43.7%)	85 (56.3%)	
Not tested	28 (39.4%)	43 (60.6%)	
No spouse or partner	49 (49%)	51 (51%)	
Baseline nutritional status (n=547)			< 0.001*
Normal	212(43.3%)	278 (56.7%)	
Moderate malnutrition	12(57%)	9 (43%)	
Severe malnutrition	28 (78%)	8 (22%)	
Baseline functional status (n=551)			< 0.001*
Working	122 (31%)	270 (69%)	
Ambulatory	119(84.4%)	22 (15.6%)	
Bedridden	13 (72%)	5 (28%)	
Baseline CD4 count (528)			< 0.001*
< 200	132 (91%)	13(9%)	
200 and above	122(31.9%)	261(68.1%)	
Screened for TB. (n=552)			< 0.001*
Yes positive	69 (90.8%)	7 (9.2%)	
Yes negative	186(39%)	290(61%)	
Cotrimoxazole prophylaxis(n=542)			< 0.001*

Yes received	220(55.8%)	174 (44.2%)	
Not received	15(18%)	68 (82%)	
Others	10(18.2%)	45 (81.8%)	
Isoniazid preventive therapy (n=552)			< 0.001*
Yes received	153(37.4%)	256 (62.6%)	
Not received	92 (77.3%)	27 (22.7%)	
Taken but not complete	10 (41.7%)	14 (58.3%)	
Opportunistic infections (n=552)			< 0.001*
Have OI	177(85.1%)	31 (14.9%)	
Not have OI	78 (22.7%)	266 (77.3%)	
Initial regimen (n=552)			< 0.001*
1c(AZT/3TC/NVP)	44 (72%)	17 (28%)	
1d(AZT/3TC/EFV)	27 (39.7%)	41(60.3%)	
1e(TDF/3TC/EFV)	173(43.3%)	227 (56.7%)	
1f(TDF/3TC/NVP)	11(47.8%)	12 (52.2%)	

* Significant at α=0.05

Regarding adherence of patients to the medication in their last visit 181(43.5%), 235(56.5%) were found in good medication adherence for advanced and not advanced disease stages respectively. There was a significant difference in adherence of medication for both advanced and not advanced disease stages (p = 0.009). When we see follow up characteristics of study participants in both advanced and not advanced disease stage; drug side effect at follow up time showed the difference for comparison groups (p = 0.018). Drug side effect in advanced disease stage and on not advanced disease stage was 15(71.43%), 6(28.57%) with respectively. Majority of participants between comparison groups were not reported regimen substitution; 238(45%), 290 (55%) on in advanced and not advanced disease stage respectively (p-value 0.009). Furthermore, 28(75.68%) have TB/HIV co-infection in on advanced disease and 9(24.32%) on not advanced disease stage (p-value = 0.009) (Table 3).

From a total of 552 study participants followed about 73(63.5%), 42(36.5%) was lost from advanced and not advanced disease stages respectively. Death was reported in 19(76%) on advanced and not advanced disease stages 6(24%) respectively. Nearly three fourth, 403(73%) of patients were alive and on treatment; 158(39%), 245(61%) alive and on treatment on advanced and not advanced disease stage respectively. Transfer out was reported in 5(55.6%) of advanced disease stage and 4(44.4%) of not advanced disease stage. There was significant difference observed in follow up status for both comparison groups (p – value = < 0.001).

Table 3: Clinical, laboratory and treatment-related characteristics of HIV infected adult patients while on ART at Hadiya zone public hospitals, southern Ethiopia from 1 Jan 2014 – Dec 31, 2018

Variable	AIDS-defining illness		P-value
	Advanced disease (n= 255) n(%)	Not advanced (n = 297) n(%)	
Current regimen(n=535)			<0.001*
1c(AZT/3TC/NVP)	43(70.5%)	18 (29.5%)	
1d(AZT/3TC/EFV)	27(39.7%)	41 (60.3%)	
1e (TDF/3TC/EFV)	162 (42%)	223 (58%)	
1f(TDF/3TC/NVP/Second line	14(48.3%)	15(51.7%)	
Adherence of the patient (n=535)			0.009*
Good adherence	181(43.5%)	235(56.5%)	
Fair/poor adherence	68(57%)	51 (43%)	
Drug side effect (n=548)			0.018*
Yes	15 (71.4%)	6 (28.6%)	
No	238(45.3%)	288 (54.7%)	
Regimen substitution(n=549)			0.009*
Yes	15 (75%)	5 (25%)	
No	238 (45%)	290 (55%)	
Treatment stage (n=514)			<0.001*
T – stage one	54 (33.5%)	107 (66.5%)	
T – stage two	75 (40%)	112 (60%)	
T – stage three	92 (69.7%)	40 (30.3%)	
T – stage four	28 (82.4%)	6 (17.6%)	
Recent nutritional status(n=515)			<0.001*
Normal	195(44.5%)	243 (55.5%)	
Moderate	31(81.6%)	7 (18.4%)	
Severe	24 (61.5%)	15 (38.5%)	

Continued

Table 3(continued)

Recent functional status (n=515)			<0.001*
Working	170(42.4%)	231(57.6%)	
Ambulatory/ bedridden	81(71%)	33 (29%)	
Tb/HIV co-infection (n=515)			0.001*
Yes	28 (75.7%)	9 (24.3%)	
No	222(46.4%)	256 (53.6%)	
Recent viral load (n=512)			0.913
Detected	6 (54.5%)	5 (45.5%)	
Not detected	183(48.2%)	197 (51.8%)	
Not done	59 (48.8%)	62 (51.2%)	

* Significant at α=0.05

4.3. Incidence Rate of Loss to Follow Up

All study, participants (552) had contributed a total of 13190.5 person-months observation; 7348.68person months in on advance disease cohort and 5841.56 person months in not advance disease cohort respectively. In advanced cohort about 73 HIV-infected adult patients lost during ART treatment; 42 from not advanced disease cohort. The incidence rate of LTFU was 11.9 per 100 person-years with 95% CI (9.47-14.99) for advanced disease stage and 8.6 per 100 person-years with 95% CI (6.37-11.67) for not advanced disease stage. The overall incidence of LTFU in both groups were 10.5 per 100 person years with 95% CI (8.71, 12.56).There was variation in LTFU among advanced and not advanced disease stage; 73(13.2%, 95% CI (10.51-16.34)), 42(7.6%, 95% CI (5.54 - 10.15)) respectively. The cumulative incidence of loss to follow up 115(20.8%, 95% CI (17.52, 24.47)).

The median time to have LTFU during ART treatment has shown a variation between the two groups. The median time to develop LTFU was 13 months and 12months in on advanced disease cohort and not-advanced disease cohort respectively. In both cohorts nearly half (47%) of LTFU occur in the first year of ART initiation and decrease in later follow up period. Based on the life table analysis the probability of having LTFU at 12 months and 24 months in on advanced cohort were 14% and 35% respectively. The corresponding values in not advanced disease cohort were 8.9% and 18% respectively (Table 4). About 106 patients were traced and in 79 of them reason of LTFU was identified; 9(8.5%) lost due death, 29 (27.4%) self-transfer out, 16 (15%) extra-medication, 25(23.6%) holy water use.

Table 4: life table analysis of LTFU among HIV infected adult patients on ART in Hadiya zone public hospitals, Southern Ethiopia from 1 Jan 2014 – December 31, 2018

Interval	Beginning total	Cumulative failure	95% CI
On advanced disease			
0-12	255	0.14	0.098, 0.186
13-24	198	0.35	0.288, 0.413
25-36	126	0.40	0.341, 0.474
37-48	92	0.43	0.362, 0.499
49-60	58	0.44	0.373, 0.520
61-72	12	0.44	0.373, 0.520
On not advanced disease			
0-12	297	0.089	0.060,0.132
13-24	192	0.18	0.133,0.241
25-36	95	0.24	0.176,0.316
37-48	43	0.35	0.257,0.484
49-60	15	0.35	0.257,0.484
61-72	3	0.35	0.257,0.484

Kaplan Meier failure curves with CI shows probability of loss to follow up at 20, 40, and 60 months follow up period that indicates increasing over time (figure 2)

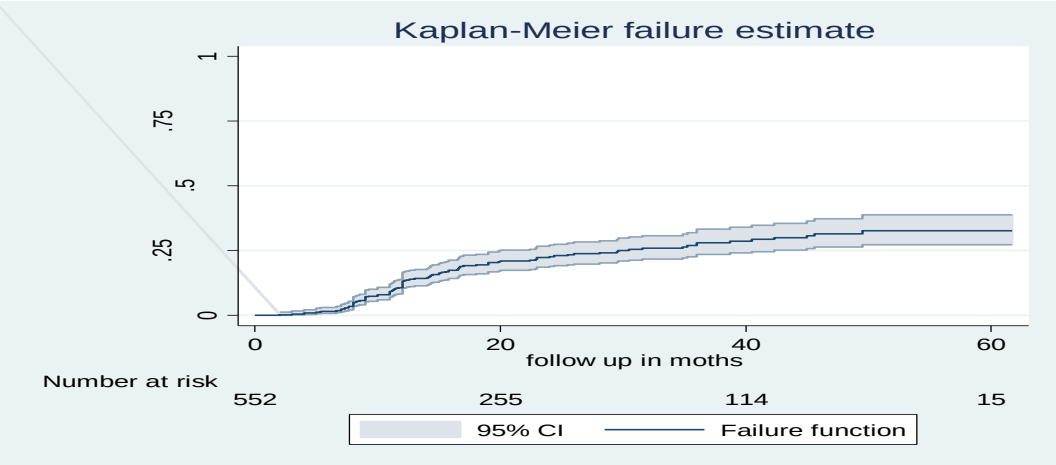

Figure 2: Overall probability of loss to follow up for retrospective cohort study done in Hadiya zone public hospitals, southern Ethiopia from 2014 - 2018.

The Kaplan-Meier failure analysis and the log-rank test used to compare the survival probabilities of the two groups. The overall probability of LTFU in on advance disease cohort was significantly different from not advance disease cohort, i.e. the risk of losing is higher in advance disease cohort (log rank, P=0.02) (Figure 3).

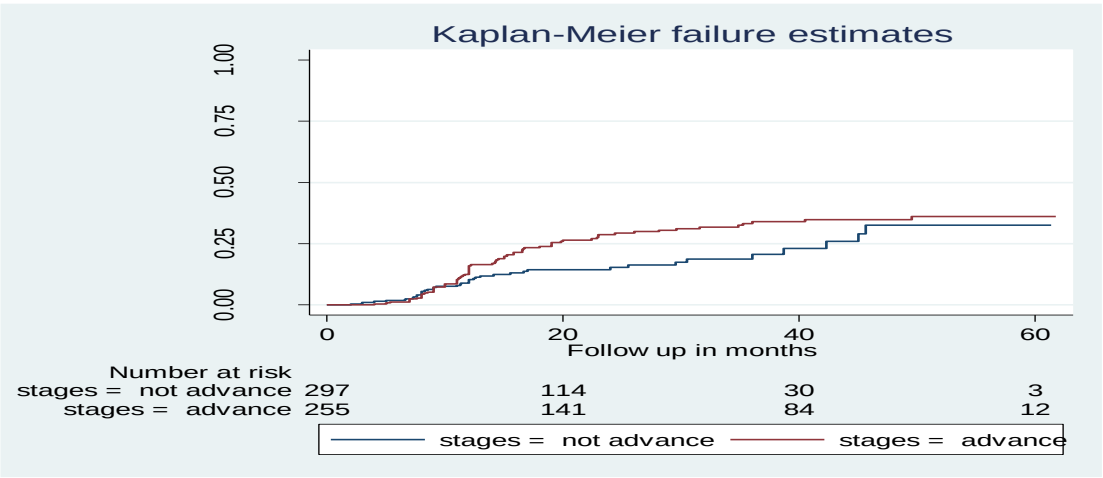

Figure 3: Kaplan-Meier failure estimate of LTFU among HIV infected adult patients on ART with and without advanced disease stage in Hadiya zone public hospitals, Southern Ethiopia, from 2014 – 2018.

4.4. Predictors of the Time to LTFU after ART Initiation

In a bivariable Cox regression analysis sex, widowed marital status, baseline ambulatory or bedridden functional status, baseline CD4 cell count < 200 cells/mm3, baseline advanced disease stage, opportunistic infections, Isoniazid prophylaxis, fair or poor adherence status, and TB/HIV co-infection were associated with an increased risk of LTFU. These factors significantly associated with LTFU before adjusting for potential confounders.

The risk of LTFU was higher in male than female (crude hazard ratio (CHR) 2.5 with (95% CIs (1.73, 3.73)). The risk of LTFU was higher in widowed/er patients than married (CHR 2.9 with 95% CI (1.66, 5.08)). The risk of LTFU was higher in patients with ambulatory/bedridden functional status than working (CHR 5.3 with 95% CI (3.63, 7.93)). The risk of LTFU was higher in patients with baseline CD4 cell counts <200 cells/mm3 (CHR 5.2 with 95% CI (3.55, 7.70)) compared to baseline CD4 counts ≥200 cells/mm3. The hazard of loss to follow up in patients who did have advanced disease stage were 1.5 with 95% CI (1.04,2.23) times higher than those have not advanced disease stage at admission.

The hazard of loss to follow up in patients who did have an opportunistic infection were 2.7 times higher with 95% CI (1.83, 3.95) than those have not an opportunistic infection. The risk of LTFU in patients who did not receive INH prophylaxis were higher than those who received INH prophylaxis (CHR 3.9 with 95% CIs (2.74, 5.74)). The risk of LTFU in patients who did have fair/poor (sub-optimal) adherence to ARV medications were higher than those who did have good (optimal) adherence (CHR 5.7 with 95% CIs (3.95, 8.42)). The risk of LTFU in patients who have TB/HIV co-infection were higher than did not have TB/HIV co-infection (CHR 3.2 with 95% CIs (1.94, 5.54)).

Table 5: Bivariable Cox regression analysis for predictors of LTFU among HIV infected adults patients in Hadiya zone public hospitals, southern Ethiopia from Jan 2014–Dec 2018

Variables	Follow up status		CHR 95% CI	P – value
	Lost n(%)	Censored n(%)		
Age category (n= 552)				
15-24	19(11.3%)	71(88.7%)	1	1
25-34	50 (20%)	195(80%)	1.07(0.63,1.82)	0.27
35-44	35(22%)	123(78%)	1.06(0.61,1.86)	0.81
≥ 45	11(18.6%)	48(81.4%)	0.9(0.44,1.96)	0.85
Sex (n = 551)				
Male	73(31.2%)	161(68.8%)	2.5(1.73,3.73)	0.000*
Female	41(13%)	276(87%)	1	1
Educational status(n= 537)				
No education	32(22%)	113(78%)	1.4(0.73,2.89)	0.28
Primary education	40(21.5%)	146(78.5%)	1.2(0.62,2.37)	0.56
Secondary education	29(21.6%)	105(78.4%)	1.3(0.65,2.61)	0.45
Tertiary education	11(15.3%)	61(84.7%)	1	1
Occupational status (n = 527)				
Gov't employees	10(15.6%)	54(84.4%)	1	1
Farmer	21(22.6%)	72(77.4%)	1.37(0.64,2.91)	0.41
Merchant	17(21%)	64(79%)	1.34(0.61,2.94)	0.45
Daily laborer	12(21%)	45(79%)	1.30.56, 3.02)	0.53
Driver	5(29%)	12(71%)	1.5(0.51, 4.37)	0.46
Housewife	29(22.5%)	100 (77.5%)	1.5(0.73, 3.9)	0.26
Student	15(20.8%)	57(79.2%)	1.2(0.55, 2.0)	0.59
Others	5(36%)	9(64%)	1.8(0.57, 5.0)	0.31
Residence (n= 551)				
Urban	29(18%)	131(82%)	1	1
Rural	86 (22%)	305 (78%)	1.28(0.84,1.95)	0.247
Marital status (n = 551)				

Married	73(19%)	307(81%)	1	1
Never married	18(16%)	93(84%)	0.79(0.47,1.32)	0.374
Divorced/separated	9(32%)	19 (68%)	1.95(0.97,3.91)	0.06
Widowed/er	15 (46.8%)	17(53.2%)	2.9(1.66,5.08)	0.000*
Partner or spouse HIV status(n = 550)				
Positive	46(20%)	182(80%)	1	1
Negative	31(20.5%)	120 (79.5%)	1.08(0.68,1.71)	0.72
Not tested	15(21%)	56 (79%)	1.16(0.65,2.09)	0.6
No partner or spouse	22 (22%)	78 (78%)	1.0(0.61,1.70)	0.91
Disclosure status (n=551)				
Yes	90 (20.3%)	354 (79.7%)	1	1
No	25 (23%)	82 (77%)	1.35(0.86,2.10)	0.18
Baseline nutritional status(n= 522)				
Normal	99 (20%)	391(80%)	1	1
Moderate	6 (28.6%)	15 (71.4%)	1.26(0.55,2.89)	0.57
Severe	8(22%)	28 (78%)	1.08(0.52,2.22)	0.82
Baseline functional status(n = 551)				
Working	38(9.7%)	354(90.3%)	1	1
Ambulatory/bedridden	76(47.8%)	83(52.2%)	5.3(3.63,7.93)	0.000*
Baseline CD4 cell count(n = 503)				
< 200	73(50.3%)	72(50.7%)	5.2(3.55,7.70)	0.000*
200 and above	40 (10.4%)	343 (89.6%)	1	1
Baseline HIV disease stage (n = 552)				
Not advanced disease stage	42 (14%)	255(86%)	1	1
Advanced disease stage	73(28.6%)	182 (71.4%)	1.5(1.04,2.23)	0.031*
Screened for TB.(n= 552)				
Yes positive	18 (23.7%)	58 (76.3%)	1.2(0.76,2.09)	0.36
Yes negative	97 (20.4%)	379 (79.6%)	1	1
Cotrimoxazole preventive therapy (n= 542)				
Received	86 (21.8%)	308 (79.2%)	1	1
Not received	29 (19.6%)	119 (80.4%)	1.18(0.77,1.86)	0.43
Isoniazid preventive therapy (n=527)				

Received	60 (13.8%)	373 (86.2%)	1	1
Not received	55 (46%)	64 (54%)	3.9(2.74,5.74)	0.000*
Opportunistic infections (n= 552)				
Have OIs	75 (36%)	133 (64%)	2.7(1.83,3.95)	0.000*
No OIs	40 (11.6%)	304 (88.4%)	1	1
Initial regimen (n = 552)				
1c(AZT/3TC/NVP)	13 (21%)	48 (79%)	0.9(0.51,1.65)	0.77
1d(AZT/3TC/EFV)	16 (23.5%)	52 (76.5%)	1.06(0.63,1.82)	0.80
1e(TDF/3TC/EFV)	81(20%)	319 (80%)	1	1
1f(TDF/3TC/NVP)	5(21.7%)	18 (78.3%)	1.15(0.47,2.86)	0.75
Adherence of the patients (n=535)				
Good	46(11%)	370 (89%)	1	1
Fair/poor	66 (55.5%)	53 (44.5%)	5.7(3.95,8.42)	0.000 *
Drug side effect (n = 547)				
Yes	6(30%)	14 (70%)	1.5(0.65,3.41)	0.33
No	108(20.5%)	418 (79.5%)	1	1
Regimen substitution (n = 549)				
Yes	5 (25%)	15 (75%)	1.2(0.51,3.07)	0.619
No	109(20.6%)	420 (79.4%)	1	1
Recent functional status (n = 515)				
Working	58 (14.5%)	343 (84.5%)	1	1
Ambulatory /bedridden	49 (43%)	65 (57%)	3.7(2.5,5.39)	0.000 *
TB/HIV co-infection (n = 491)				
Yes	17 (46%)	20 (54%)	3.2(1.94,5.54)	0.000*
No	90 (18.8%)	388 (81.2%)	1	1

Note: * significant in bivariate analysis without controlling for confounder.

In a multivariable Cox regression analysis baseline ambulatory or bedridden functional status, CD4 cell count < 200 cells/mm3, not receiving Isoniazid prophylaxis, fair or poor adherence status were associated with an increased risk of LTFU. Whereas advance disease stage was associated with a decreased risk of LTFU. These predictors remained significantly associated with LTFU after adjusting for potential confounders in the multivariable analysis.

The risk of LTFU in patients who were ambulatory/bedridden was higher than working functional status (adjusted hazard ratio (AHR) 2.4 with (95% CIs (1.33, 4.18)). The risk of LTFU was higher in patients with baseline CD4 cell counts <200 cells/mm3 (AHR 3.4 with 95% CI (1.87, 6. 18)) compared to baseline CD4 counts ≥200 cells/mm3. The hazard of loss to follow up in patients who did have advanced disease stage were 67% times less than those who have not to advanced disease at admission (AHR 0.33; 95% CIs (0.18, 0.58)). The risk of LTFU in patients who did have fair/poor (sub-optimal) adherence to ARV medications were higher than those who did have good (optimal) adherence (AHR 2.8; 95% CIs (1.87, 4.34)). The hazard of LTFU in patients who did not receive INH prophylaxis therapy were higher than those who received INH prophylaxis therapy (AHR 2.5 with 95% CIs (1.64, 3.94)) (Table 6).

Table 6. Multivariable Cox regression analysis for predictors of LTFU among HIV infected adults in Hadiya zone public hospitals, southern Ethiopia from Jan 2014 – Dec 2018 (n=492)

Predictors	Follow up status		CHR(95% CI)	(AHR 95% CI)
	Lost	Censored		
Sex				
Male	73	161	2.5(1.74,3.73)	1.4(0 .94, 2.11)
Female	41	276	1	1
Residence				
Urban	29	131	1	1
Rural	86	305	1.28(0.84, 1.95)	0.87(0.53,1.43)
Disclosure status at ART initiation				
Yes	90	354	1	1
No	25	82	1.35(0.86, 2.10)	1.02(0.60, 1.72)
Marital status				
Married	73	307	1	1
Never married	18	93	0.79(0.47,1.33)	1.02(0.59, 1.75)
Divorced/Separated	9	19	1.9(0.97,3.91)	1.57(0.77, 3.19)
Widowed/er	15	17	2.9(1.66,5.08)	1.73(0. 94, 3.16)
Baseline CD4 count				
< 200 cells/mm3	73	72	5.2(3.55,7.70)	3.4(1.87, 6.18) *
≥ 200 cells/mm3	40	343	1	1
Baseline functional status				
Working	38	354	1	1
Ambulatory/Bedridden	76	83	5.3(3.64,7.94)	2.4(1.33, 4.18) *
Baseline WHO disease stage				
Not advance	42	255	1	1
Advance	73	182	1.5(1.03,2.23)	0.33(0.18, 0.58) *

Continued

Table 6 (continued)

INH preventive therapy				
Received	60	373	1	1
Not received	55	64	3.9(2.74,5.73)	2.5(1.64, 3.94) *
Opportunistic infections				
Have OIs	75	133	2.69(1.83,3.95)	0.9(0.50, 1.71)
No OIs	40	304	1	1
Adherence to treatment				
Good	46	370	1	1
Fair/poor	66	53	5.7(3.95, 8.42)	2.8(1.87, 4.34) **
Recent function status				
Working	58	343	1	1
Ambulatory/Bedridden	49	65	3.67.(2.50, 5.39)	1.09(0.67, 1.78)
TB/HIV Co-infection while on HAART				
Yes	17	20	3.28(1.94, 5.54)	1.2(0.69, 2.21)
No	90	388	1	1

Note: * p – value < 0.05 ** p – value < 0.001

5. DISCUSSIONS

The incidence rate of LTFU was 10.5 per 100 person years among 13190 months of adult observation in HIV infected adult patients on ART in the current study. Baseline ambulatory or bedridden functional status, baseline CD4 cell count < 200 cells/mm3, WHO clinical stage III/IV, not receiving isoniazid preventive therapy and fair or poor adherence of patients to medications were identified as independent predictors of the loss to follow up.

The incidence estimated in this study was 10.5/100 person-years. This finding is in line with incidence rate in other African countries Zambia (8.7-13.6/100 person-years), South Africa (109/1000 person-years), Benshangul-Gumuz (11.6/100 person-years) and Mizan-Aman (8.8/1000 person months), (Li et al., 2013; Mberi et al., 2015Moges et al., 2018; Berheto et al., 2014). The possible explanation might be patients receiving the medication that have similar effects. This study finding is lower than the study done in Malawi (26/100 person-years) (Tweya et al., 2018). The possible explanation for this variation might be due to difference in total months of observation. Furthermore, the incidence rate of the current study was higher than studies done in Australia and Asia (4.4/100 person-years), Anantapur district in India (7.1/100 person-years) and studies from Ethiopia in Axum (8.2/100 person-years), and Jigjiga (26.6%/100 person-years) (Guy et al., 2013; Alvarez-Uria et al., 2013; Kidane and Fisaha, 2014; Seifu et al., 2018). The variation might be explained by differences in the study settings, health-seeking behavior, and due to lack of reporting the death events that can be considered as LTFU. The transfer out without prior information to their caregiving health institutions of initial registration necessary for proper recording may be another reason.

The proportion of loss to follow up among HIV infected adult patients in this study was found to be 20.8%. This finding is in line with studies from South Africa which was 23.4% (Mberi et al., 2015) and Benshangul-Gumuz region 22.5% (Moges et al., 2018). This finding was higher than the findings of other previous studies conducted in India, Kwazulu-Natal, Rwanda, Axum, and Jigjiga were 15.5 %, 14.7 %, 5.5%, 9.8% and 14.8% respectively (Alvarez-Uria et al., 2013; Arnesen et al., 2017; Mugisha et al., 2014; Kidane and Fisaha, 2014; Seifu et al., 2018). This difference might be due to the variation in the sample size. Another possible explanation might be of travel costs patients had to cover to reach ART clinics because the study conducted over the

zonal public hospitals and dissimilarity in outcome measurement. This study finding was less than findings from Zambia 32.1% (Li et al., 2013) and Mizan-Aman that was 26.7% (Berheto et al., 2014). This variation might be due to the implementation of retention strategies.

Adult HIV infected patients whose baseline functional status was ambulatory or bedridden were 2.4 times more likely to be loss to follow up than working. This finding is consistent with other studies from Oromia region and Addis Ababa that states LTFU increased for functional status of ambulatory or bedridden (Megerso et al., 2016; Tiruneh et al., 2016). This is because ambulatory or bedridden patients are unable to work in or outside of home and remained in bed most of the time and need close supervision to maintain on ART. They are also immunocompromised likely to develop ART side effects that make them lost during the follow-up periods.

Adult patients whose CD4 cell count < 200cells/mm^3 were show strong association of more likely to be loss to follow up than CD4 cell count ≥ 200cell/mm^3. This finding is consistent with previous studies in Mizan-Aman, South Africa and KwaZulu-Natal, South Africa (Berheto et al., 2014; Mberi et al., 2015; Arnesen et al., 2017). The possible explanation for this might be half of the patients with CD4 cell count < 200cell/mm^3 lost from the treatment. Another possible explanation might be the risk of LTFU increases with low baseline CD4 cell counts on ART.

Adult ART patients with advanced WHO disease stage at enrollment were 67% times less hazard of loss to follow up when compared with not advanced disease stage. This finding is in line with a study from Mizan-Aman that showed advance stages of illness were associated with reduced LTFU (Berheto et al., 2014). The possible explanation for this might be patients with advanced disease stage at ART initiation counseled for good adherence in the lifelong follow-up treatments and patients with advanced diseases stage feel sick enough to accept restrictive medical care. This finding is in contrary with studies of South Africa, Oromia region, Benshangul-Gumuz and Southern Ethiopia (Mberi et al., 2015; Megerso et al., 2016; Moges et al., 2018; Teshome et al., 2015). This variation might be due to increased health-seeking behavior of the adult ART patients and improvements in awareness of the community to support ART patients stay in care.

Adult HIV infected patients who did not take IPT was 2.5 times more likely to be LTFU when compared with those who did take IPT at ART initiation. This finding is in agreement with other studies from Mizan-Aman, Oromia region and Tigray (Berheto et al., 2014; Mehari et al., 2015;

Megerso et al., 2016). This might be explained by the fact that when patients believe that in the advanced stage and immunocompromised, they should strictly follow-up so that they can start prophylaxis. Increase in reinforced counseling to patients taking INH prophylaxis might have contributed to better follow-up.

Poor/fair adherence of the HIV infected adult patients towards medication explained the loss to follow up in current study. Adult HIV infected patients with poor/fair adherence were 2.8 times more likely to be loss to follow up when compared to good (optimal) adherence. This finding is in agreement with Malawi, Oromia region, Jimma University Teaching Hospital (Megerso et al., 2016; Gesesew et al., 2017; Tweya et al., 2018). The possible explanation might be having adequate awareness about good adherence in time of recruitment. The other possible explanation might be fair or poor adherence may result in bedridden or ambulatory functional status, which in turn results in financial dependence of the patients.

In current study sex, residence, disclosure status, marital status, and TB/HIV co-infection did not show significant statistical association with loss to follow up among adult HIV infected patients, but in other similar study, there were significant association with loss to follow up. (Dalhatu et al., 2016; Mecha et al., 2018; Kidane and Fisaha, 2014; Seifu et al., 2018; Tweya et al., 2018; Megerso et al., 2016; Mberi et al., 2015; Mugisha et al., 2014). This difference might be due to difference in study setting and the way study population adhere to prescribed medication as well.

Strength and Limitations of the study

This study includes all functional Hadiya zone public hospitals, which accounts for more than half of the HIV/AIDS patients of the entire zone. The follow-up period in the present study is relatively short and the results may not be applicable to longer follow-up periods. Variables that had incomplete record were not included. Finally, Loss to follow up due to dissatisfaction with care of the healthcare system may not be ruled out. Thus, this finding should be interpreted with this limitation in mind.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1. Conclusions

This study indicated that the incidence rate of loss to follow up among HIV infected adult patients was 10.5/100 person –years which was found to be a high loss to follow up. Loss to follow up occurred among adult HIV infected patients with ambulatory or bedridden functional status, advanced disease stage, low CD4 cell count, not receiving INH preventive therapy, and fair or poor adherence of the patients to the medication were significantly associated predictors.

6.2. Recommendations

To Hadiya zone public hospitals

- Tracing patients as early as possible according to national guideline to reduce LTFU.
- Provision of INH prophylaxis therapy for ART patients at enrollment according to national ART guidelines indications for prophylaxis.
- Adherence supporting should be strengthened in order to reduce fair or poor adherence to the prescribed medication.
- Focused counselling for advanced disease cases, ambulatory or bedridden patients, and those with low CD4 cell count not to be lost from ART service.

To Hadiya zone health department

- Build the capacity of health care providers on managing factors that contribute to LTFU.
- Implement strategies for better tracking services and minimizing LTFU from HIV care at early.

To Researchers

- Further study should be conducted using prospective cohort studies are needed to asses other causes of patients LTFU by using a larger sample size.

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8. ANNEXXES

8.1. Annex I: Information sheet and informed voluntary consent form for heads of hospitals

My name is _____ I am working as a data collector for the study being conducted in this community by Belachew Bikoro who is studying for his master's degree in at Haramaya University, the College of Health and Medical Sciences. I kindly request you to lend me your attention to explain to you about the study and your institution being selected as the study setting.

1. The study/Project Title: Incidence and predictors of loss to follow up among adult patients on antiretroviral therapy at Hadiya zone public hospitals, Southern Ethiopia

2. Purpose of the study: The findings of this study can be of paramount importance for the hospitals to plan an intervention program to prevent loss to follow up in your community; thereby improving ART patients health and patients survival in general. Moreover, the aim of this study is to write a thesis as a partial requirement for the fulfillment of a master's program in Epidemiology for the principal investigator.

3. Procedure and duration: I was reviewing records of the adult's age > = 15 years using a data retrieval form to provide me with pertinent data that is helpful for the study. There are 42 questions to answer where I filled the data retrieval form by reviewing records. The review on each record of adults took about 20 minutes.

4. Risks and Benefits: The risk of reviewing in this study is minimal, but only taking a few minutes from patients card/ database and follow up charts being used by hospitals. There would not be any direct payment for reviewing in this study. Nevertheless, the findings from this research may reveal important information for the local health planners.

5. Confidentiality: The information that we were provided will be kept confidential. There were no information that was identify the records in particular. The findings of the study will be general for the study community and will not reflect anything particular of individual persons. The data retrieval form was coded to exclude showing names. No reference was made in oral or written reports that could link participants to the research.

6. Rights: Participation in this study is fully voluntary. Your hospital has the right to declare to review or not in this study. If you decide to review, you have the right to withdraw from the study at any time and

this will not label you for any loss of benefits which you otherwise are entitled. Your hospital does not have to answer any question that you do not want to answer /review.

7. Contact address: If there are any questions or enquires any time about the study or the procedures, please contact:

Name: Belachew Bikoro Institute of health research ethical review committees

Mobile phone: 0931561798 (IHRERC) at the office phone Tel 2512542011

Email address: belechewbf@gmil.com P.O.Box 235, Harar

8. Declaration of informed voluntary consent:

I have read the participant information sheet. I have clearly understood the purpose of the research, the procedure, the risk and benefits, issues of confidentiality, the rights of participating and the contact address for any queries. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that participants/hospital have the right to withdraw from the study at any time or not to answer any question that they do not want. I also informed that the hospital the right to stop this study from being conducted if any misdeeds and unethical procedures are observed during the data collection process in the Hospital's premises. Therefore, I declare my voluntary consent on behalf of hospital management to allow this study to be conducted in the hospital with my initials (signature).

Name and signature of head of hospital: _____

Name and signature of data collector: _____

N.B This is signed face to face in the presence of the data collectors

Please provide a copy of this signed consent to the responsible body.

8.2. Annex II: Data Extraction Format

This patient data extraction format was intended to determine the incidence and predictors of loss to follow up among HIV infected adults after ART initiation at Hadiya zone public hospitals, Southern Ethiopia. The study was conducted by reviewing secondary data. This study was aimed to fill the information gap and provide empirical evidence for program managers, decision makers, and ART program implemented at the different level by enabling them to access a baseline data on predictors of loss to follow up. Moreover, it assists in improving the outcome of ART program.

Data extraction format ID. No _____

Name of the reviewer _____ Signature _____date_____

Name of supervisor._____ Signature _____ date_____

Time started _____/ time ended _____of reviewing this profile

Available data: 1. Complete 2. Incomplete

Action taken for the incomplete data

_____

_____

_____

_____

_____

__

(Please use additional blank paper if space is not enough)

Part I: Baseline Socio-Demographic characteristics

NO	VARIABLES	CODING CATEGORIES	SKIP
101	Age	_____	
102	Sex	1. Male 2. Female	
103	Educational status	1. No formal education 2. Primary 3. Secondary 4. Tertiary 99.missing	
104	Occupational status	1.government employees 2.Farmer 3. merchant 4.Day laborer 5.Driver 6. Housewife 7. Student 8. others specify_____ 99. missing	

105	Residence	1. Hosanna town 2. East badewacho 3. Gibe district 4. Other district in Hadiya zone 5. Other specify_____	

Part II: Family or Support Related Characteristic

201	Ever disclosed	1. Yes 2. No 99. missing	
202	Partner or spouse HIV status	1. positive 2. negative 3. Not tested 4. No spouse/ partner 99. missing	
203	Marital status	1. Married 2. never married 3. Divorced 4. Widowed/widower 5. separated 99. missing	

Part III: Baseline clinical, laboratory and treatment information

301	Enrollment date	_____/_____/_____	
302	Eligible date for ART	_____/_____/_____	
303	ARV eligibility criteria used	1. CD4 count 2. WHO clinical stage 3. Both the WHO clinical stage and CD4 4. Pregnancy	

		5. Test and treat all policy 6. Other specify_____ 99. missing	
304	ART initiation date	_____/_____/____	
305	Baseline nutritional status of the patient	1. Normal 2. Moderate 3. Severe 99. missing	If 3 go to 306
306	Food treatment provided	1. Yes 2. No 99. missing	
307	Baseline functional status	1. Working 2. Ambulatory 3. Bedridden 99. missing	
308	Baseline CD4 count	_____	
309	Baseline WHO staging	1. Stage I 2. Stage II 3. Stage III 4. Stage IV 99. missing	
310	Screened for TB.	1. yes positive 2. yes negative 3. not done 99. missing	

311	INH preventive therapy	1.Yes received 2. Not received 3.Taken, but not completed	
312	Cotrimoxazole prophylaxis	1.Yes received 2.Not received 3. if no specify reason_____	
313	Opportunistic infections	1. have opportunistic infections 2. no opportunistic infections 99. missing	
314	Initial ARV regimen	1. 1c=AZT/3TC/NVP 2. 1d=AZT/3TC/EFV 3. 1e=TDF/3TC/EFV 4. 1f=TDF/3TC/NVP 5. 1g=ABC/3TC/NVP 6. Others specify_____	

Part IV: Characteristics of Patients While on ART Follow Up Period

401	Current ARV regimen	1. 1c 2. 1d 3. 1e 4. 1f 5. 1g 6. 2nd line regimen (2e/2f/2g/2h/2i) 7. Other specify_____ 99. missed	

402	Recent ARV medication adherence of the patient	1.Good 2.Fair 3.Poor	
403	ARV drug side effect	1. Yes 2. No	
404	Regimen substitution	1. Yes 2. No	
405	Recent functional status while on HAART	1. Working 2. Ambulatory 3. Bedridden 99. missing	
406	Recent WHO staging while on HAART	1. T stage one 2. T stage two 3. T stage three 4. T stage four 99. missing	
407	Recent nutritional status while on HAART	1. Normal 2. Moderate 3. Severe	
408	Taking CPT until the last visit	1. Yes taking until the last visit 2. Yes but now stopped 3. No 4. Other specify_____	
409	IPT provision while on HAART	1. Yes 2. No	
410	TB/HIV co-infection while on HAART	1. Yes 2. No	

411	The most recent viral load while on ART	1. Detectable 2. no detectable 3. not done 99. missing	
412	Status of the patient in the record	1. alive and on ART 2. lost/drop out 3. death 4. transfer out	If 2 go to 413
413	Lost date	_____/_____/____	
414	Total number of month(s) from ART enrollment to lost	_____month(s)	
415	Is patient traced back	1. Yes 2. No	If 2 go to 418
416	If yes, what was the final outcome after tracing,	1. Alive 2. Dead 3. Confirmed lost 4. Unknown	
417	If alive, what was the reason for lost/drop	1. self-transfer out 2. having extra medication 3. refill from other institution 4. religious/holy water 5. promised to come back 6. refuse to come 7. other specify_____	
418	The reason why patient did not track back	1. no telephone no was mentioned in the medical record 2. Unreachable with the mentioned phone no	

		3. other specify_____	
419	Date of last visit	_____/_____/_____	
420	Last appointment date(or for death confirmed date of death or for TO date of transfer)	_____/_____/_____	

8.3. Annex III: Curriculum Vitae (CV) of the Principal Investigator

1. Personal details:

Name: Belachew Bikoro

Place of birth: Shashogo, Hadiya zone

Date of birth: 15, May 1991

Sex: Male

Marital status: Single

Nationality: Ethiopian

Contact address: E-mail: belechewbf@gmail.com

Phone: +2519 31561798

2. Educational background:

Elementary: Musagesa Shiro primary school (1-8)

Secondary: Bonosha secondary school (9-10)

Preparatory: Wachemo secondary and Preparatory School (11-12)

Educational qualification - Graduated from Arba Minch University with BSc in Public Health officer

3. Work experience

Institution	Duration	Job position
Moholin health center	November 2013-July 30 2015	Junior HO professional
Shamo Ajacho Health Center	August 2015-August 2016 September 2016-September 2017	Junior HO professional Director of the primary health care unit

4. Language skill	Listening	Speaking	Reading	Writing
Hadiyisa	Excellent	Excellent	Excellent	Excellent
Amharic	Excellent	Excellent	Excellent	Excellent
English	Excellent	Good	Excellent	Excellent
Afi-Somali	Poor	Poor	Good	Good

5. Skills: Basic clinical skills

Basic computer skills

Managing, monitoring and evaluating skills

6. Interests

7. Reading different books

Helping patients

Conducting research and serving the community

7. Awards

Graduated from Arba Minch University with BSc in Public Health officer

Essential newborn care organized by Ethiopian Pediatrics society (EPS) in collaboration with the federal ministry of health, UNICEF

Comprehensive LAFP method and insertion and removal for health workers organized by the Integrated Family Health Program (IFHP)

Comprehensive TBL/TBHIV Organized by Wolaita Soddo University, DC PEPFAR

Adolescent, maternal, infant, and Young Child Nutrition Behavior Change Communication AMIYCN-BCC organized by IFHP.

References: Teshome Bikoro E-mail: tashebk234@gmail.com

Phone: 0916718028

8.4. Annex IV: WHO clinical stages

WHO clinical stage1: Asymptomatic, Persistent generalized lymphadenopathy (MOH, 2017)

WHO clinical stage 2: Moderate unexplained weight loss (5-10% of presumed or measured body weight), recurrent upper respiratory tract infections (sinusitis, tonsillitis, otitis media, and pharyngitis), herpes zoster, angular cheilitis, recurrent oral ulceration, papular pruritic eruption, fungal nail infections, and seborrhoeic dermatitis (MOH, 201 7)

WHO clinical stage 3: Unexplained severe weight loss (>10% of presumed or measured body weight), unexplained chronic diarrhea for longer than 1 month, unexplained persistent fever k(intermittent or constant for longer than 1 month), persistent oral candidiasis, oral hairy leukoplakia, pulmonary tuberculosis, Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia), acute necrotizing ulcerative stomatitis, gingivitis or periodontitis, unexplained anemia (<8 g/dl), neutropenia (<0.5 x 109/l) and/or chronic thrombocytopenia (<50 x 109/L) (MOH, 2017).

WHO clinical stage 4: HIV wasting syndrome, Pneumocystis (jirovecii) pneumonia, Recurrent severe bacterial pneumonia, Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site), esophageal candidiasis (or candidiasis of trachea, bronchi or lungs), extra-pulmonary tuberculosis, Kaposi sarcoma, Cytomegalovirus infection (retinitis or infection of other organs), Central nervous system toxoplasmosis, HIV encephalopathy, extra-pulmonary cryptococcosis, including meningitis, disseminated non-tuberculous mycobacterial infection, Progressive multifocal leukoencephalopathy, chronic cryptosporidiosis, Chronic isosporiasis, Disseminated mycosis (extra-pulmonary histoplasmosis, coccidioidomycosis), Lymphoma (cerebral or B-cell non-Hodgkin), Symptomatic HIV-associated nephropathy or cardiomyopathy, recurrent septicaemia (including Non-typhoidal Salmonella), Invasive cervical carcinoma, atypical disseminated leishmaniasis (MOH, 2017).