Survival Pattern and determinants of mortality among Adult HIV positive patients Highly Active Antiretroviral Therapy in Sawla Town public health facilities, SNNPR, Southern Ethiopia

By: Abewa Kebede (BSc)

Thesis submitted to institution of health Faculty of Public Health Department of Epidemiology for the partial fulfillment for the requirement of Master Degree in General Public Health

June, 2019

Jimma, Ethiopia

Survival Pattern and determinants of mortality among Adult HIV positive patients on Highly Active Antiretroviral Therapy in Sawla Town public health facilities, SNNPR, Southern Ethiopia

By: Abewa Kebede (BSc)

Advisors:

1. Fasil Tessema (Associate Professor)
2. Hailu Merga (MPHE)

June, 2019

Jimma, Ethiopia

Abstract

Background: In resource poor countries like Ethiopia the survival of patients treated with antiretroviral therapy depends on factors that might vary greatly with socio demographic, clinical and behavioral risk factors. However, factors affecting survival among adult HIV positive patients in Ethiopia are not fully investigated. Moreover, mortality has been high particularly in the first three to six month of initiating antiretroviral therapy. To avoid such early deaths, the identification of possible risk factors and potential causes of deaths are important.

Methods: A retrospective cohort study was conducted using 455 records of patients who were enrolled on antiretroviral therapy in Sawla General Hospital and Sawla Health center from September 2013 to August 2018. Socio demographic, clinical, immunological, behavioral data and date of antiretroviral treatment initiation including date of follow up status were extracted. Predictor variables were identified by fitting Cox's proportional hazard model using backward stepwise method and statistical significance variables were declared based on p-value < 0.05.

Results: A total of 455 adult HIV/AIDS patients on ART contributed to 867 person year of observation and 299(65.7%) were alive & on treatment, 78(17.1%) were lost follow up, 44(9.7%) were transfer out and 34 (7.5 %) were died. The estimated mortality was 4.4%, 5.3%, 6.1%, 7%, 7.5% and 7.5% at 6, 12, 24, 36, 48 & 60 months of follow up period, respectively. Out of 34 deaths, 20 (58.8 %) were died within the first 6 months of antiretroviral therapy initiation. The overall incidence rate of mortality was 3.92 per 100 person years of observation. In multivariate analysis age 45 and above (AHR: 3.72, 95% CI: 1.21-11.4), bedridden functional status (AHR: 17.4, 95% CI: 6.21-48.79), poor ART drug adherence (AHR: 4.52,95% CI: 2.05-9.96), Tuberculosis co- infection (AHR: 4.1, 95% CI: 1.84-9.13), non-disclosure(AHR: 4.9, 95% CI: 1.82-12.89) & severe anemia (AHR: 5.1, 95% CI: 1.81-14.21) were predictor of survival and statistically significant association with mortality in HIV patients.

Conclusion: This study had identified the independent significant predictors of survival in patients living with HIV/AIDS after initiation of HAART. These factors include Patients with older age, tuberculosis co infection, bedridden functional status and severe anemia (hemoglobin less than 7 mg/dl) should be monitored closely by their clinicians.

Keywords: survival pattern, determinants, HIV/AIDS, HAART

Acknowledgment:

I would like to thank Jimma university faculty of public health department of Epidemiology for selecting and giving me chance to conduct a research on such a crucial public health important topic. My special heartfelt thanks goes to my advisors Mr. Fasil Tessema (Associate professor) and Mr. Hailu Merga (MPHE) for their unreserved support and scarifying precious time to forward constructive comments on this thesis report. I would also like to thank Sawla General Hospital and Sawla Health center for giving necessary information for my thesis work. My appreciation also extends to data clerks for their extensive support in data extraction and my family and friends for their day to day support.

Table of Contents

List of tables

List of figures

List of Acronyms and Abbreviations

AIDS	Acquired immune deficiency syndrome
AHR	Adjusted hazard ratio
ART	Antiretroviral therapy
ARV	Antiretroviral
BTB	Baseline Tuberculosis infection
BM	Body mass index
CD4	Cluster of differentiation 4
CDC	Center for disease control and Prevention
CI	Confidence interval
CPT	Cotrimoxazole preventive therapy
CHR	Crude hazard ratio
HR	Hazard ratio
HAART	Highly active antiretroviral therapy
HBV	Hepatitis B virus
HIV	Human immune virus
HR	Hazard ratio
IQR	Inter quartile range
INH	Isoniazid
KM	Kaplan Meir
LTF	Lost to follow up

MOH	Ministry of health
OI	Opportunistic Infection
PLHIV	People living with human immune virus
SD	Standard deviation
UNAIDS	United Nation Acquired immune deficiency syndrome
WHO	World health organization
PYO	Person years observation

Chapter 1: Introduction

1.1. Background

Survival time for Human immune virus (HIV) infected patients is the survival of HIV patients from date of antiretroviral therapy initiation to till one of the following events registered; death, lost to follow up, transferred out to other health institution or alive under follow up. To increase the longevity of HIV/AIDS patient's world health organization launched test and treat for all HIV confirmed cases(1).

Globally there were total of 36.9 million (31.1 million-43.9 million) people living with HIV at the end of 2017. Almost 20 million people in the world have access to antiretroviral therapy with an impressive achievement. The provision of ART significantly improved the survival of HIV patients and changed HIV infection from a fatal illness to a manageable chronic disease. Because of these benefits, there were high efforts globally to increase ART coverage. As a result, access to ART was improved in resource constrained countries (2,3).

In developing countries especially in sub-Saharan Africa, through further decentralization, treatment coverage can hopefully continue to improve patients in care. However, high early mortality remains high, in particular among individuals presenting to care with advanced disease. Co infection with TB is common and complicates treatment, and constitutes the most common cause of death among people living with HIV in sub-Saharan Africa (2,4).

Recently, Ethiopia adopted test-and-treat offering ART to all PLHIV regardless of CD4 count. This move forward will enable more PLHIV to have access to ART which can further reduce HIV-associated morbidity and mortality, and reduce the number of new HIV-infections (4).

The specific nature of disease demographics in poor resource setting especially high prevalence of TB, HBV, malnutrition and other bacterial infection would affect the nature of disease response to treatment and ultimately changes survival pattern. Currently there is decentralizing of HIV care and treatment services to selected health centers to decrease morbidity and mortality related to HIV disease. Decentralization increases access by taking services closer to more people, reducing transport and related costs for patients and families, resulting in improved adherence and enrolment in care. In view of the non-affordability of ART by most HIV infected patients in Ethiopia, the Ministry of Health launched the free ART rollout program in January 2005 (5).

Even-though access to ARV treatment has shown significant clinical improvement by meeting the goal of therapy, still a number of early deaths occurred that could be avoided by appropriate interventions on certain factors such as socio demographic, behavioral risk and health factors (6–8).

1.2. Statement of the problem

Over 30 years after the first case was reported, human immunodeficiency virus (HIV) remains significant public health problem. Globally there are total of 36.9 people living with HIV. Of these 35.1 million of people living with HIV are adults. More than 39 million people have died of acquired immunodeficiency syndrome (AIDS). The annual numbers of global deaths from AIDS-related illness among people living with HIV were 940,000 at the end of 2017. Of these, 830,000 AIDS related deaths were adult (3).

Eastern and southern Africa remains the region most affected by the HIV epidemic, accounting for 45% of the world's HIV infections and 53% of people living with HIV. An estimated 300,000 men in sub-Saharan Africa died of AIDS-related illness compared to 270,000 women. This reveals good treatment coverage among women. However, huge challenges remain in which gender inequalities and gender-based violence, combined with physiological factors, place women and girls in eastern and southern Africa at huge risk of HIV infection (3,9).

Many factors can affect how quickly HIV infection progresses to AIDS. Factors such as age, co-infections, illiteracy, gender inequality, geographic location, preventive prophylaxis, nutrition, healthcare provider's experience in treating HIV patients and whether or not the patient smokes or uses recreational drugs can affect the rate at which an HIV patient develops AIDS (10).

Study in India revealed that 16.10% were died, 12.13% were lost to follow up, 31.14%) were transferred out to other facilities and 40.63%) were alive from 1689 study participants at the end of two years follow up. Majority of 251 (92%) of deaths were occurred in the first six months of therapy. Determinant factors related to mortality were, Age >30 year, male, poor functional status, hemoglobin level <11 g/dl, body weight <45 kg and CD4 count <100/µl at baseline had significantly higher relative hazard of death. Most LFU also occurred in the first six months and these patients had significantly low CD4 count, weight, hemoglobin level and higher number of patients in Stages III and IV as compared to those who survived (11).

In developing countries baseline characteristics strongly affect mortality on ART, and men initiating ART have more advanced HIV disease than females. In addition, loss to follow-up, education, occupation and marital status as major determinants factors of mortality or survival outcome, and men are more likely to become LTF than females in many settings (12).

Early mortality rates in sub-Saharan Africa are very high; between 8% and 26% of patients die in the first year of ART, with most deaths occurring in the first few months' antiretroviral initiation. Mortality rates are likely to depend not only on the care delivered by ART programs, but more fundamentally on how advanced disease is at program enrollment and the quality of preceding health-care (13).

The factors that cause increased rate of mortality in the early stages of ART initiation were explored in study conducted in Ghana. About 44.4% of the deaths were occurred before the first month of ART initiation. WHO clinical stage, very low CD4 count, and hemoglobin level were indicators of the progression of the disease (14).

In Ethiopia an estimated 610,000 people are living with HIV (all age). Of these 350,000 People living with HIV are (women, 15+) and 200,000 People living with HIV are (men, 15+). The annual number of deaths from AIDS-related illness among people living with HIV (all ages) were 15, 000 (9,100-26,000) in 2017. Of these 11,800 AIDS related deaths were adults (3,15).

Study conducted in Dilla Hospital showed, the median follow-up period was 25 months (survival time for death was 12 months and for alive 26 months). Out of 1391 cohorts of adults on ART, 1081 (77.7%) were alive and continued their treatment in the hospital, 128 (9.2%) were reported dead, 111 (8%) were transfer out, and 71 (5.1%) were lost follow up. HIV patients who developed TB had shorter survival time than not developed TB. Death occurred 33 (26%) and 66 (52%) in the first 3 and 12 months of ART initiation respectively (16).

Finding from previous studies on HIV-infected person's mortality shows that baseline hemoglobin level, gender, and adherence to ART were important influencing factors for HIV survival. High rate of lost follow up, poor CD4 recovery and poor body weight improvement after 6 months of follow-up was one of determinant problems related to adherence and possible treatment failure (17,18).

Even-though access to ARV treatment has shown significant clinical improvement by meeting the goal of therapy, still a number of early deaths occurred that could be avoided by appropriate

interventions on certain factors such as socio demographic, behavioral risk and health factors. Moreover, mortality has been high particularly in the first 3 to 6 month of initiating ART.

Therefore, the aim of this study was to identify determinants of mortality among adult HIV positives patients starting ART in public health facilities in sawla town.

1.3. Significance of the study

Identifying survival pattern and determinants mortality among adult HIV positive patients will fill the information gap and provide empirical evidence for program planner, decision makers and ART program implementer at the different level by enabling them to access a base line data on determinants of survival along with other research findings. Moreover it will be a paramount important to curb the horizon of the disease. In addition, the study will enhance the body of knowledge of health care providers regarding ART to be able to reduce the upward trend in mortality of patients on ART in the Sawla town Public health facility. Recommendations from this study will be applied in Sawla town public health facility and in similar setting in the country, which could benefit a number of individuals receiving ART.

Chapter 2 Literature Review

Study conducted in Eastern Uttar Pradesh shows, from a total of 1689 adult HIV positive patients enrolled in care, 272 deaths occurred within the 2-year follow up period and most of deaths occurred within six months of ART initiation. The probability of survival at 3, 6, 12, & 24 months were 87.5%, 84.1%, 82.7% and 82.3% respectively. Age >30 year, male gender, poor functional status, hemoglobin level <11 g/dl, body weight <45 kg and CD4 count <100/µl at baseline were significant predictors of mortality (11).

In Kenya a cross-sectional study conducted on 2453 participants' shows that factors that contributed significantly to the differences in mortality were levels of education, occupation, lost to follow up and marital status of persons under study. More men than women were more likely to be marked as lost to follow (12).

Study which was conducted in India shows that, a total of 956 patients were under HAART during the study period followed. Of which 204 (21.33 %) were died and 75 (36.8%) were lost to follow up. Majority of 180(88.24%) deaths were occurred in the first six months of antiretroviral imitation in patients who had associated tuberculosis or some other AIDs related complications. An important risk factor associated with mortality were male sex, TB related infection, drug adherence and low CD4 count (19).

In Nigeria 5-year retrospective cohort study were conducted on 1256 HIV-infected patients. Baseline CD4 count, year of enrolment, and drug combination were significant predictors of LTFU. Patients enrolled earlier (2008/2009) were twice as likely to be LTFU compared with those enrolled later (2010–2013). Gender and age did not significantly predict LTFU (20).

In Khartoum State, a total of 547 people living with HIV on antiretroviral therapy were included in the study. The most predictors of mortality were, the functional status at start of ART, alcohol use, WHO clinical stage, literacy level & adherence to CTX were had negative impact on survival and increased risks for mortality (21).

Study conducted in south Africa demonstrates that independent predictors of mortality were a CD4 cell count <50/µl, a hemoglobin concentration ≤8 g/dl, a history of oral candidacies and a history of Cryptococcus meningitis (22).

Study conducted in the far north province of Cameroon shows that Patients with a baseline CD4 count <50 cells/mm3 presented a mortality risk twice as high as those with >50 cells/mm3. Body Mass Index (BMI) between 15 and 18.5 kg/m2 was related to a 1.5 times higher risk of death than a BMI >18.5 kg/m2 & three times more for those with a BMI <15 kg/m2. Patients in stage III and IV were two to four times more likely to die than patients in stage I & II. Men were at nearly twice the risk of death as women. Patients with hemoglobin <8.5 g/dl had two times more risk of death than those with a hemoglobin rate >8.5 g/dl (23).

Study demonstrated in Kenya shows a total of 2011 HIV positive adult (> 14 years) patients were studied and the outcome of the cohort showed 147 (7%) died as a result of AIDS related complications, 2% lost to follow-up, 2% stopped treatment by a clinical person due to various reasons, 9% transferred out and 79% were alive. The median duration of patients on ART was 22 months (IQR 10-44) before dying or being censored. The predictor variables for mortality were patients on Stavudine-based regimen, CD4 count <50 cells/µl, WHO Stage IV at ART initiation and bedridden patients (24).

In Ethiopia Systematic reviews were conducted on 17 articles to highlight mortality and its predictors. The result shows 5–40.8% of the patients died during the follow-up period. 50–68.8% of the deaths occurred within 6 months of initiation of ART. Advanced WHO clinical stage disease (stage III and stage IV), functional status (bedridden and ambulatory), low baseline CD4count, low baseline hemoglobin level, TB confection, lower baseline weight, and poor treatment adherence were commonly identified as predictors of death in HIV patients (25).

Studies conducted in Jimma University Specialized Hospital shows, a total of 456 HIV patients were included in the study, of these (312, 68.4%) were female, with a median age of 30 years. The main factors associated with mortality were: baseline age (>35 years old), weight, WHO stage IV , and low adherence to ART treatment (26).

Study conducted in Hawassa University Referral Hospital on Pattern and predictors of (CD4) cell count recovery among cohorts of HIV infected patients on ART shows, low baseline CD4 cell counts were predictive of non-response and initiation of antiretroviral therapy (ART) at a CD4 cell count greater than 500cells/µl is associated with better immune recovery (27).

A study on 272 HIV/AIDS patients on ART in Shashmene and Asela Hospitals, southern Ethiopia; employed Kaplan Meier method to construct survival curves and the Cox proportional

hazards model to determine predictors of mortality. The findings of the study shows WHO clinical stage IV, low hemoglobin , and cotrimoxazole prophylaxis therapy (CPT) initiation as the independent determinants of mortality (28).

Study conducted in Harar town and Goba Hospital shows baseline WHO clinical stage III, IV and lower CD4 count were predictors of mortality among adult HIV/AIDS patients (29).

Study conducted in Aksum hospital shows, (CD4 cell count, 50/ml), (hemoglobin level, 11 mg/dl), (weight =40 kg), gender, illiterate and primary level of education were found to be the independent predictors of mortality among patients enrolled on ART. Patients who were anemic at baseline were two-fold higher risk of mortality. Majority (58.7%) of deaths occurred in the first year of ART initiation and the highest 16(59%) mortality had happened in the first three months of the first year of ART initiation (30).

Study conducted in Armed Forces General Teaching Hospital, 734 patients on ART were followed for a median of 38.5 months. The study shows a high mortality of the cohort in the earlier months of treatment. For instance, nearly 32.6%, 50% and 70.9% deaths occurred within three months, six months and 12 months of ART initiation, respectively. The study revealed that advanced WHO clinical stages (III & IV), lower CD4 cell count (<50 cells/mm3), TB co-infection, being employed, history of OIs, being bedridden and ambulatory patients were strongly related to mortality (31).

A retrospective cohort study was conducted among 416 ART patients in Nekemte Referral Hospital and log rank test was used to compare the survival curves and Cox proportional hazard regression was applied to determine the independent determinants of time to death. The estimated mortality was 4%, 5%, 6%, 7%, and 7% at 6, 12, 24, 36 and 48 months respectively with mortality incidence density of 1.89 deaths per 100 person years. Forty years and above, low baseline hemoglobin level and poor ART adherence were found to be an independent determinant of mortality (32).

A 4-year retrospective cohort study of 654 HIV/AIDS patients in south wollo shows that, about 87% were right-censored (dropout, transferred, loss and alive till the study period) and the remaining 13% Died. The mean survival time of HIV patients were 41.81 months and Living rural, order baseline age, not working due to illness, smaller CD4 count, weight, and lymphocyte count, HIV-TB co-infection developing and being in WHO clinical Stage IV were identified as a

documented risk factors for shortened the survival experience of the HIV-patients who are in care of ART(33).

A study among 350 study participants on ART in Jinka Hospital shows that 315 (90.0%) were censored and 35 (10.0%) were died. 22(62.9%) of the deaths occurred during the first year of treatment. The significant predictors of mortality included non-disclosure of HIV status, a history of tuberculosis, and ambulatory or bedridden functional status, WHO clinical stage IV illness, and substance abusers (34).

Study conducted in Dilla Hospital shows that the presence of lower baseline body mass index (BMI <18.5 kg/m2), CD4 count less than 50 cells/mm3, anemia, WHO clinical stage III and IV, drug addiction and presence of active TB infection were predictor of survival and statistically significant association with mortality in HIV patients under ART follow up (16).

Study conducted in Kembata and Hadiya zones between 2007 to 2011 on 670 HIV-positive adults, used Kaplan-Meier analysis for survival and Cox proportional hazards model to identify determinants for mortality. The median survival time was 25 months with IQR. The study found that baseline (WHO clinical stage IV, CD4 counts of 201 cell/mm3 and , poor regimen adherence, hemoglobin level of 10gm/dl and above and functional status of bedridden were associated with five year survival of HIV patients on ART (35).

2.1 Conceptual framework

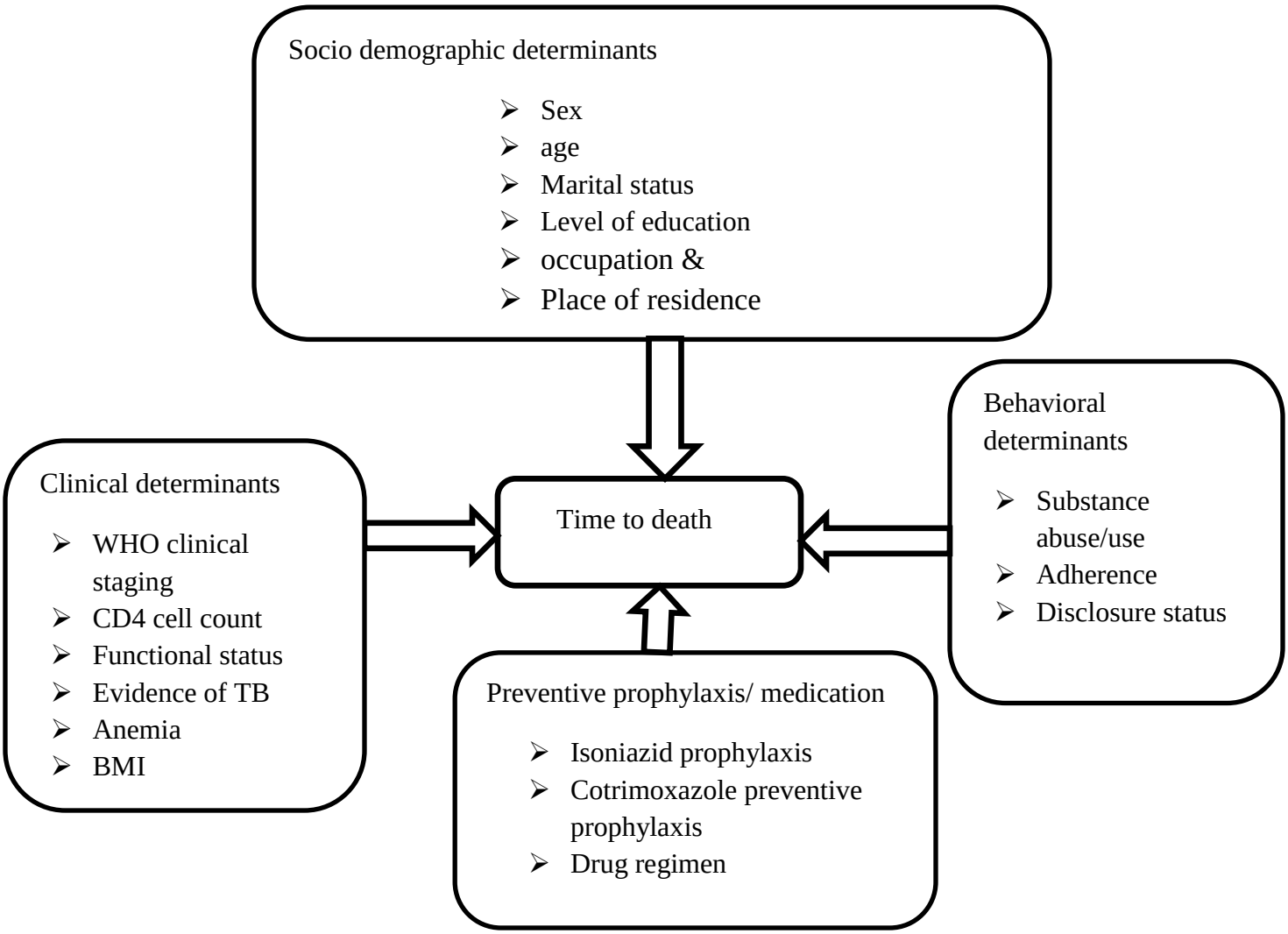

Figure 1: Conceptual framework of determinants of mortality among adult HIV positive patients starting HAART in Sawla Town public health facilities SNNPR, Southern Ethiopia, 2019 adapted from Mosley and Chen analytical framework used for child survival in developing countries formulated in 1984 (36).

CHAPTER 3: Objective

3.1. General objective

To assess survival pattern and determinants of mortality among adult HIV positive patients on highly active antiretroviral therapy in Sawla Town public health facilities, SNNRP, Southern Ethiopia, 2019.

3.1.1. Specific objectives

1. To determine survival patterns among adult HIV positive patients following initiation of HAART in Sawla town public health facilities, 2019.
2. To identify determinants of mortality among adult HIV positive patients after initiation of HAART in sawla town public health facilities, 2019.

Chapter 4: Methods

4.1. Study Area and Period

This study was conducted in two public health facilities found in Sawla town public health facilities; Sawla General Hospital and Sawla Health Center located in Goffa Zone, Southern Nation Nationalities People Regional State. The town is located 285 km from Hawassa and 515 km from Addis Ababa capital city of Ethiopia in Southern direction. These two health facilities serve for more than 1 million populations from the surrounding.

The hospital started comprehensive HIV care, prevention, treatment, and support services in 2002 and the health center in 1998. Since then the hospital had total of 920 patients ever started on ART and till September 2011, 394 are on treatment. Similarly in the Health center of 1094 patients ever started on ART, 519 are on treatment. The study was conducted from March 1/2019 to April 10/2019 in Sawla town public health facilities for patients who were started ART from September 2013 to August 2018.

4.2. Study design

Retrospective cohort study design was employed

4.3. Population

4.3.1. Source population

Person living with HIV/AIDS, age15years and above and started ART treatment.

4.3.2. Study population

The study population consisted of all adult HIV positive individuals (15 years of age and above) who started HAART between September 2013 and august 2018 in Sawla General Hospital and Sawla health center.

4.3.3. Study unit

Individual records

4.4.Eligibility Criteria

Inclusion criteria

Adults aged 15 and above who started ART with complete baseline data and intake form.

Exclusion criteria

HIV positive adults aged 15 and above who were transfer in for HIV care

4.5. Sample size determination and sampling technique

4.5.1. Sample size determination

The sample size was calculated by using Sample Size Estimation for Longitudinal Studies with 95% confidence level, 80% power, 1:1 allocation ratio and event of interest in exposed (WHO clinical stage III & IV) and non-exposed group (WHO clinical stage I & II).

$$n = \frac{[Z\alpha/2(2p^{-}q^{-})\,1/2+Z\beta(p1q1+p2q2)1/2]2}{(p1-p2)2} \quad (37)$$

Zα/2 = 1.96 at 95 confidence interval, Power =80%, Zβ= 0.84

p_1 = response in non-exposed (q1 = 1−p1), 5.38% (34)

p_2 = response in exposed (q2 = 1−p2), 12.72% (34)

P^{-}= (P1+P2)/2, 9.05%, $^{-}$q =1-P^{-}, 90.95%

n= 1.288/0.0061**n= 424**

Table 2: Sample size determination for determinants of mortality among adult HIV positive patients starting highly active antiretroviral therapy in Sawla Town public health facilities, Southern Ethiopia, 2019(34).

S/No	Determinant factors (exposed vs. non exposed)	% of death among exposed	% of death among non-exposed	Exposed sample	Non-exposed sample	Total sample
1	CD4(≤200 vs.>200)cells/mm3	17.13	7.5	202	202	404
2	WHO stage III & IV vs. I& II	12.72	5.38	212	212	424
3	Substance use(yes vs. no)	16.8	3.6	96	96	192

The sample size calculated for baseline WHO clinical staging was larger than the sample sizes calculated for other determinants of survival. Therefore, the final sample size after adding 10% contingency for incomplete records, the total sample size was **467**.

4.5.2. *Sampling technique*

First 467 samples were proportionally allocated for both health facilities; 211 for Sawla General Hospital and 256 for Sawla Health center. Simple random sampling technique was used by using Excel commands to select those proportionally allocated samples. Patient's ART unique identification numbers were used as sampling frame to select individual records. Profiles of all patients on ART between September 2013 and August 2018 were evaluated. Then patients Started ART since August 2018 or with incomplete electronic data were excluded.

4.6. Study variable

4.6.1. dependent variables

The primary outcome variable was time to death in months. HAART-initiated patients were followed until the date of death, loss to follow-up, transferring out, or the end of the study period. Individuals who were on HAART, lost to follow-up, or had transferred out at the end of the study period were censored; that is, they were considered to be alive for the time period that they had been under follow-up. The survival time was calculated in months using the time between the dates of treatment initiation and the date of the event (death) or date of censoring.

4.3.2. Independent variable

The predictor variables for survival time were related to independent variables of the socio-demographic (Gender, age, marital status, Level of education, Present occupation & Place of residence), baseline clinical determinants (presence of TB before ART initiation , functional status, WHO clinical stage, CD4 count, anemia), nutritional status body mass index (BMI), preventive prophylaxis (cotrimoxazole preventive therapy(CPT) & Isoniazid prophylaxis (INH)), drug regimen and behavioral characteristics (substance abuse and ART adherence) and disclosure status of the patient.

4.7. Operational definition

Time to death: Survival times of HIV patients from date of antiretroviral therapy initiation to death.

Survival time is defined as the survival of HIV patients from date of starting antiretroviral therapy till one of the following events registered; death, lost to follow up, , transferred out to other health institution or still under follow up .

Survival pattern: is a pattern covering a major proportion of observations that experience an event during the study period.

Baseline: the measurement taken nearest to the date of ART initiation

Censored: includes lost to follow up, transfer out and alive beyond the study time.

Poor Adherence: if the percentage of missed dose is between <85 %(> 6 doses of 30 doses or >9 dose of 60 dose) as documented by ART physician.

Fair Adherence: if the percentage of missed dose is between 85-94% (3-5 doses of 30 doses or 3-9 dose of 60 dose) as documented by ART physician.

Good Adherence: if the percentage of missed dose is between >95 %(< 2 doses of 30 doses or <3 dose of 60 dose) as documented by ART physician.

Transfer out: A patient is referred to another health facility for care.

Lost follow up; if a patient discontinued ART for at one to three month as recorded by ART physician or Advanced ART nurse.

Antiretroviral therapy: refers to the use of a combination of three or more antiretroviral drugs to achieve viral suppression.

4.8. Data extraction procedures (Instrument, personnel, data extraction technique)

4.8.1. Data extraction tools

The electronic database format which was developed by center of disease prevention and control was used to as data extraction tool. All variables based on conceptual framework were incorporated.

4.8.2. Data extractors (personnel)

Two ART data clerk who were trained on ART data management were recruited from Sawla General Hospital and Sawla Health center for data extraction.

4.8.3. Data collection in the facility

A secondary data routinely collected for clinical monitoring and evaluation purpose in the health facilities were used. Data were extracted from all eligible electronic records of adult HIV/AIDS patients on ART from ART database form. First the profiles of all patients who started ART between September 2013 and August 2018 were evaluated and for patients who started ART since august 2018 were excluded. Then information about study participants, such as socio-demographic characteristics, clinical and immunological characteristics, behavioral characteristics, medication and prophylaxis and survey endpoints were retrieved from the clinical records in electronic database of HIV/ AIDS patients by trained ART data clerks.

4.9. Data quality management

Prior to data extraction a one day intensive training was given for data extractors about objective and techniques of data extraction. After one day training data extraction was started and different documents for the same patients were cross checked in case of odd values, non logical data or missed data. Finally the Excel data were reshaped and merged and exported to SPSS version 21 for cleaning and analysis. Then exploratory data analysis was carried out to check the levels of missing values, extreme values and presence of outliers.

4.10. Data processing and analysis

After data cleaning by SPSS version 21, descriptive statistics for socio demographic, baseline clinical, laboratory and behavioral characteristics were done. Median and interquartile range (IQR) were calculated for baseline hemoglobin and CD4 count. Total Person years of observation were calculated for HIV positive patients during the study period. The Kaplan Meier (KM) model was used to estimate the survival function. Cox proportional hazards model was used to identify independent factors associated with time to death. Factors associated with time to death at p- value less than 25% significant level in the bivariate Cox proportional hazard model analysis were included in the final Multivariable Cox proportional hazards analysis. Then significant predictor variables were identified by fitting Cox's proportional hazard model using

backward stepwise method. The results of the final model were expressed in terms of Hazard Ratio (HR) and 95% confidence intervals (CI) and statistical significance were declared based on p-value less than 0.05. The proportional hazards assumption has been checked using the log-log plot and plots of partial residuals against rank time.

4.11. Ethical consideration

Ethical clearance was obtained from Jimma university ethical review board and Permission was obtained from Sawla General Hospital and Sawla Health Center.

4.12. Dissemination plan

The findings of this study will be submitted to Faculty of Public Health, Jimma University, to Sawla General Hospital and Sawla Health Center. Attempt will be made to publish in peer review journal.

Chapter 5: Result

5.1. Socio demographic Characteristics of the Study Subjects

A total of 467 HIV-positive individual records were reviewed. Of these 455(97.4%) had complete socio demographic, baseline clinical and immunological data (figure 2).

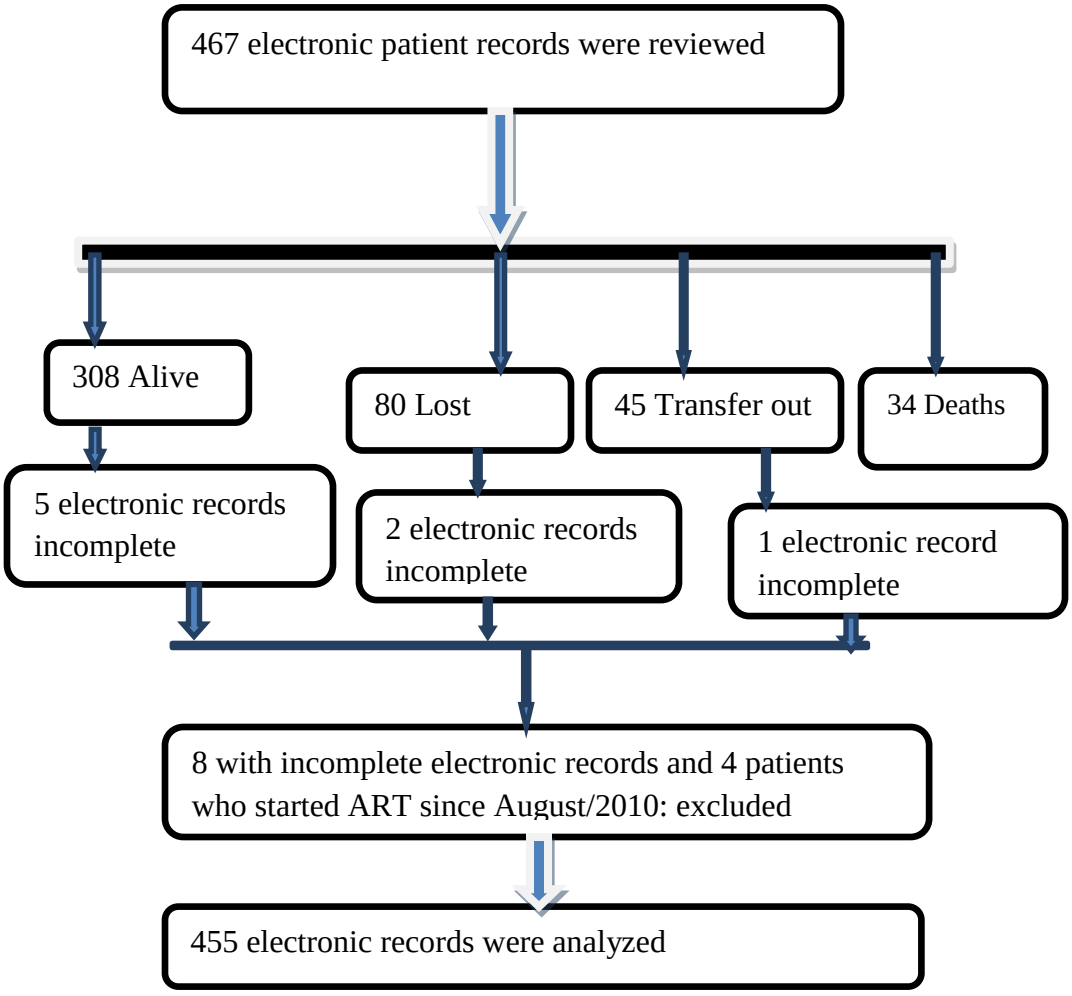

Figure 2: shows inclusion and exclusion of the study cohort for determinants of mortality among adult HIV positive patients (age>15 years) who started ART from September 2013 to August 2019 in Sawla General Hospital and Sawla health center, 2019.

Out of 455 patients on HAART, 265 (58.3%) were females and the mean age was 31.5 (SD=9.4) years. More than half of 275(60.4%) of the patients lived in urban areas, nearly half, 228 (49.7%) were Orthodox Christian by religion, 65.6% were married and 38.7% had primary education (Table 2).

Table 3: Shows Socio demographic Characteristics of the Study Subjects in sawla town public health facilities, 2011.

Variables	Value	Follow up status				Total n(%)
		Active n (%)	Lost n (%)	Transfer out n(%)	Dead n (%)	
Sex	Male	104(22.8)	41(9)	24(5.3)	21(4.6)	190(41.7)
	Female	195(42.8)	37(8.1)	20(4.4)	13(2.8)	265(58.3)
Age	15-24	69(15.2)	21(4.6)	15(3.3)	7(1.52)	112(25.1)
	25-34	133(29.2)	32(7.1)	13(2.8)	10(2.1)	188(41.3)
	35-44	68(14.9)	15(3.3)	12(2.6)	5(1.1)	100(22)
	>=45	29(6.3)	10(2.1)	4(0.9)	12(1.8)	55(12.1)
Residence	Urban	182(40)	44(9.7)	30(6.6)	19(4.2)	275(60.4)
	Rural	117(25.7)	34(7.5)	14(3.1)	15(3.3)	180(39.6)
Educational level	Illiterate	95(20.9)	28(6.2)	7(1.6)	12(2.6)	142(31.3)
	Primary	115(25.3)	35(7.7)	16(3.5)	10(2.2)	176(38.7)
	Secondary	62(13.6)	9(2)	19(4.2)	4(0.9)	93(20.5)
	Tertiary	27(6)	6(1.3)	2(0.4)	8(1.8)	43(9.5)
Occupation	Labor	64(14.1)	25(5.5)	6(1.3)	4(0.9)	99(21.8)
	G. employee	60(13.2)	9(2)	9(2)	6(1.3)	84(18.46)
	Merchant	61(13.4)	12(2.6)	9(2)	5(1.1)	87(19.1)
	NGO	3(0.7)	1(0.2)	6(1.3)	0	10(2.2)
	Farmer	47(10.3)	16(3.5)	8(1.5)	7(1.5)	87(19.1)
	Driver	44(9.7)	12(2.6)	2(0.4)	5(1.1)	63(13.8)
	Others	20(4.4)	3(0.7)	4(0.9)	7(1.5)	34(7.5)

5.2. Baseline Clinical and Laboratory Characteristics of the Study Subjects

The median weight at ART initiation was 53.09 kg (interquartile range (IQR, 46kg–59kg)). The median hemoglobin level and CD4 count at ART initiation were11.6 mg/dL (IQR, 9.6–13.1) and 309 cells/mm3 (interquartile range IQR, 192-484) respectively. Concerning preventive prophylaxis, 361 (78.7 %) patients were given cotrimoxazole preventive therapy (CPT) and 356 (77.6%) patients were given Isoniazid prophylaxis at the time of ART initiation. Out of 455 patients 67(14.7) patients had tuberculosis co infection at the time of ART initiation. Concerning clinical stage, out of 455 (41.1 %) of HIV patients were in WHO stage I, 19.8% were in WHO stage II, 31 % were in WHO stage III, and 8.1 % were in WHO stage IV at the time of ART initiation. Majority of them (84.4 %) had good ART adherence, while 15.6 % poorly adhered. Most of the patients 334(73.4 %) initiated ART at CD4 >=200cells/μL, 71(15.6%) at CD4 101-200 cells/μLand 50 (11 %) were initiated ART at CD4 <100cells/μL (Table 3).

5.3. Survival pattern of the cohorts

Out of 455 cohorts of adults ART patients, 299(65.7%) were alive and continued their treatment in the health facilities, 78(17.1%) were lost follow up, 44(9.7%) were transfer out and 34 (7.5 %) were died. Out of 34 deaths, 20 (58.8%) were died within the first 6 months. The estimated mortality rate was 4.4%, 5.3%, 6.1%, 7%, 7.5% and 7.5 % at 6, 12, 24, 36, 48 and 60 months follow up period, respectively. The overall incidence rate of mortality during ART treatment was 3.92 per 100 person year observations (PYO).

5.4. Bivariate Cox Regression Analysis.

Candidate variables that were associated with time to death at p- value less than 0.25 significant level in the bivariate Cox regression analysis were sex, age, level of education, baseline weight, baseline BMI, baseline CD4 count, baseline hemoglobin, baseline WHO clinical staging, baseline functional status, baseline evidence of TB, tobacco smoking, alcohol drink, Khat chewing, disclosure status, ART adherence, CPT and INH prophylaxis (Table 4, 5 and 6).

Table 4 shows baseline Clinical and Laboratory determinants of mortality among adult HIV positive patients starting HAART in sawla town public health facilities, 2019.

Variables	Category of variables	Follow up status				Total n (%)
		Active n (%)	Lost for FU n (%)	Transfer out n (%)	Dead n (%)	
Weight	=<40	26(5.7)	8(1.8)	6(1.3)	4(1.1)	44(9.7)
	40.1-50	107(23.5)	14(3.2)	12(2.6)	14(3.1)	147(32.3)
	50.1-60	104(22.8)	32(7)	16(3.5)	14(3.1)	166(36.5)
	>60	62(13.6)	24(5.3)	10(2.2)	2(0.4)	98(21.5)
CD4 count	<=100	23(5.1)	8(1.7)	9(2)	10(2.2)	50(11.1)
	101-200	43(9.4)	11(2.4)	12(2.6)	5(1.1)	71(15.6)
	>200	233(51.2)	59(13)	23(5.1)	19(4.2)	334(73.4)
Anemia	No anemia	159(34.9)	27(5.9)	13(2.8)	13(2.9)	212(46.6)
	Mild	76(16.7)	21(4.6)	16(3.5)	6(1.3)	119(26.2)
	Moderate	55(12.1)	25(5.5)	15(3.3)	5(1.1)	100(22)
	Sever	9(2)	5(1.1)	0	10(2.2)	29(6.4)
BMI	>=18.5	219(48.1)	56(12.3)	20(4.4)	17(3.7)	312(68.6)
	16-18.4	54(11.9)	18(4)	14(3.1)	11(2.4)	97(21.3)
	<16	26(5.7)	4(0.9)	10(2.2)	6(1.3)	46(10.1)
INH Prophylaxis	Yes	256(56.3)	59(13)	26(5.7)	17(3.7)	358(78.7)
	No	43(9.5)	19(4.2)	18(4)	17(3.7)	97(21.3)
CPT	Yes	235(51.6)	59(13)	40(8.8)	30(6.6)	364(80)
	No	64(14.1)	19(4.2)	4(0.9)	4(0.9)	91 (20)
WHO clinical staging	I	142(31.2)	31(6.8)	13(2.8)	4(0.9)	190(41.7)
	II	60(13.2)	19(4.2)	7(1.5)	7(1.5)	93(20.4)
	III	82(18)	25(5.5)	18(4)	13(2.9)	138(30.5)
	IV	15(3.3)	3(0.7)	6(1.3)	10(2.2)	34(7)
Adherence	Good	268(58.9)	40(8.8)	41(9.1)	19(4.2)	368(80.9)
	Fair	16(3.5)	6(1.3)	0	0	22(4.8)
	Poor	15(3.3)	32(7)	3(0.7)	15(3.3)	65(14.3)
Functional status	Working	217(47.7)	56(12.3)	27(5.9)	10(2.2)	310(68.1)
	Ambulatory	76(16.7)	18(3.9)	11(2.4)	12(2.6)	117(25.7)
	Bedridden	6(1.3)	4(0.9)	6(1.3)	12(2.2)	28(6.2)
Substance use	Yes	43(9.4)	17(3.73)	15(3.29)	12(2.63)	87(19.1)
	No	256(56.2)	61(13.4)	29(6.4)	22(4.8)	368(80.9)
Evidence of TB	Yes	32(7.1)	7(1.5)	8(1.5)	21(4.6)	67(14.7)
	No	267(58.7)	71(15.6)	37(8.1)	13(5.1)	388(85.3)

Table 5 Shows Bivariate Cox regression analysis of socio demographic and behavioral determinants of mortality among adult HIV positive patients starting HAART in sawla town public health facilities, SNNPR, Southern Ethiopia, from 2013 to 2018.

Variable		Frequency		Bivariate	P value
		Censored n (%)	Death n (%)	CHR(95% CI)	
Age	15-24	105(24.2)	7(1.5)	1	0.10
	25-34	178(39.12)	10(2.2)	0.8(0.30-2.12)	0.66
	35-44	95(20.9)	5(1.1)	0.73(0.23-2.32)	0.60
	>=45	43(9.5)	12(2.6)	4.53(1.77-11.58)	0.01
Sex	Female	252(55.4)	13(2.8)	1	
	Male	169(37.1)	21(4.6)	2.6(1.3,5.21)	0.01
Education level	Not educated	130(28.6)	12(2.63)	0.47(0.191.17)	0.10
	Primary	166(36.5)	10(2.2)	0.32(0.13,0.83)	0.01
	Secondary	90(19.8)	4(0.9)	0.24(0.07,0.8)	0.02
	Tertiary	35(7.7)	8(1.8)	1	0.05
Substance use	Yes	75(16.5)	12(2.6)	2.43(1.2-4.92)	0.01
	No	346(76)	22(4.9)	1	
Tobacco smoking	Yes	66(14.5)	11(2.41)	2.54(1.24-5.23)	0.01
	No	355(78)	23(5.1)	1	
Drinking alcohol	Yes	64(14.1)	9(2)	1.8(0.84-3.87)	0.12
	No	357(78.5)	25(5.5)	1	
Chewing Khat	Yes	61(13.4)	9(2)	1.91(0.89-4.10)	0.09
	No	360(79.1)	25(5.5)	1	
Disclosure status	Disclosed	349(76.7)	7(1.5)	1	
	Not disclosed	72(15.8)	27(5.9)	12.81(5.57-29.43)	0.00
ART drug Adherence	Good	371(81.5)	13(2.9)	1	
	Poor	50(11)	21(4.6)	13.73(6.82-27.61)	0.00

Table 5 Shows Bivariate Cox-regression analysis of clinical determinants of mortality among adult HIV positive patients starting HAART in sawla town public health facilities, SNNPR, Southern Ethiopia, from 2013 to 2018.

Variable with its category		Frequency		Bivariate	P-value
		Censored n(%)	Death n (%)	CHR(95% CI)	
BMI	Not malnourished	295(64.8)	17(3.73)	1	
	Moderate malnourished	86(18.9)	11(2.4)	2.09(0.98,4.47)	0.06
	Sever malnourished	40(8.8)	6(1.3)	2.85(1.11,7.19)	0.02
Anemia	No anemia	199(43.7)	13(2.9)	1	
	Mild anemia	113(24.8)	6(1.3)	0.97(0.37-2.57)	0.96
	Moderate	95(20.87)	5(1.1)	1.03(0.36-2.9)	0.94
	Severe anemia	14(3.1)	10(2.2)	13.79(5.86-32.47)	0.01
Baseline CD4 count in cell/mm3	CD4<=100	40(8.8)	10(2.2)	4.73(2.19-10.24)	0.002
	CD4 101-200	66(14.5)	5(1.1)	1.33(0.49,3.57)	0.56
	CD4 > 200	315(69.2)	19(4.2)	1	0.00
Baseline WHO clinical stage	Stage I	186(40.8)	4(0.9)	1	0.00
	Stage II	86(18.9)	7(1.5)	2.73(0.79,9.35)	0.11
	Stage III	125(27.5)	13(2.9)	4.13(1.34,12.72)	0.01
	Stage IV	24(5.3)	10(2.2)	18.17(5.68,58.13)	0.00
Baseline functional status	Working	300(65.9)	10(2.2)	1	0.00
	Ambulatory	105(23.1)	12(2.6)	3.24(1.40-7.51)	0.01
	Bedridden	16(3.5)	12(2.6)	29.8(12.54-71.13)	0.00
Baseline TB	Yes	46(10.1)	21(4.6)	11.05(5.52-22.09)	0.00
	No	375(82.4)	13(2.9)	1	

Table 6 Shows Bivariate Cox-regression analysis of preventive determinants of mortality among adult HIV positive patients starting HAART in sawla town public health facilities, SNNPR, Southern Ethiopia, from 2013 to 2018.

Variable	Response	Frequency			
		Censored n(%)	Death n(%)	Bivariate CHR(95% CI)	P- value
Cotrimoxazole preventive therapy	Yes	334(73.4)	30(6.6)	1	
	No	87(19.1)	4(0.9)	0.5(0.17,1.42)	0.19
Isoniazid therapy	Yes	341(75)	17(3.7)	1	
	No	80(17.6)	17(3.7)	3.77(1.92,7.4)	0.00

NB: CHR; Crude hazard rate

CI; Confidence interval

5.5. Multivariate Analysis Using Cox-Proportional Hazard Model.

Candidate variables that were associated with time to death at 25% significant level in the bivariate Cox regression analysis were entered into multivariate Cox regression analysis. Predictor variables in multivariate Cox regression analysis were bedridden functional status, presence of tuberculosis co infection at baseline, non disclosure status, age 45 and above, severe anemia and poor ART drug adherence were statistically significant for death in HIV patients at P <0.05 (Table 7).

Table 7 Multivariable Cox-regression analysis of determinants of mortality among adult HIV positive patients starting HAART in sawla town public health facilities, SNNPR, Southern Ethiopia, from 2013 to 2018.

Variables		Frequency		Bivariate	Multivariate
		Censored n (%)	Death n (%)	CHR(CI)	AHR(CI)
Age	15-24	105(24.2)	7(1.5)	1	1
	25-34	178(39.12)	10(2.2)	0.8(0.30-2.12)	0.98(0.32-3.01)*
	35-44	95(20.9)	5(1.1)	0.73(0.23-2.32)	0.45(0.13-1.57)
	>=45	43(9.5)	12(2.6)	4.53(1.77-11.58)	3.72(1.21-11.4)
Functional status	Working	300(65.9)	10(2.2)	1	1
	Ambulatory	105(23.1)	12(2.6)	3.24(1.40-7.51)	1.11(0.44-2.80)
	Bedridden	16(3.5)	12(2.6)	29.8(12.54-71.1)	17.4(6.21-48.79)*
Anemia	No anemia	199(43.7)	13(2.9)	1	1
	Mild anemia	113(24.8)	6(1.3)	0.97(0.37-2.57)	0.72(0.23-2.23)
	Moderate anemia	95(20.87)	5(1.1)	1.03(0.36-2.9)	2.48(0.76-8.07)
	Severe anemia	14(3.1)	10(2.2)	13.79(5.86-32.47)	5.07(1.81-14.21)*
Tuberculosis confection	Yes	46(10.1)	21(4.6)	11.05(5.52-22.09)	4.10(1.84-9.13)
	No	375(82.4)	13(2.9)	1	1
Adherence status	Good	371(81.5)	13(2.9)	1	1
	Poor	50(11)	21(4.6)	13.73((6.82-27.61)	4.52(2.05-9.96)*
Disclosure status	Disclosed	349(76.7)	7(1.5)	1	1
	Not disclosed	72(15.8)	27(5.9)	12.81(5.57-29.43)	4.9(1.82-12.89)*

Note: CHR Crude hazard ratio
AHR Adjusted hazard ratio
CI Confidence interval
1 reference category
(*) p – value less than 0.05

5.6. Comparison of survivorship functions for different predictor variables by using KM plot

HIV infected individuals with working functional status had higher survival rate when compared with bedridden functional status especially in the later time of treatment (figure 3).

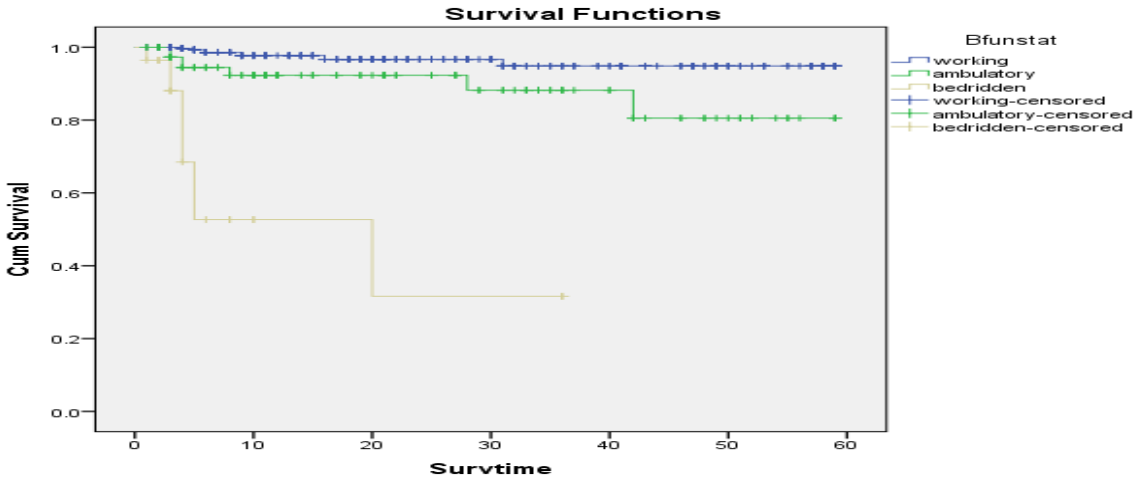

Figure 3: Shows Plots of Kaplan-Meier survivor functions based on functional status of HIV patients under ART in Sawla public health facilities SNNPR, southern Ethiopia, 2011.

HIV infected individuals with no tuberculosis co infection were higher survival rate when compared with HIV infected individuals with tuberculosis co infection (figure 4).

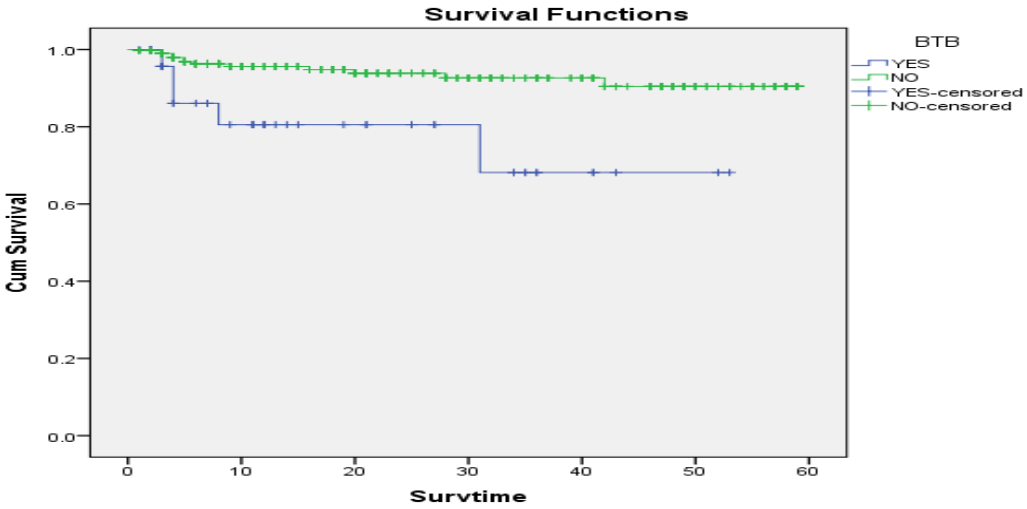

Figure 4: shows Plots of KM survival functions based on TB co infection of HIV patients under ART in Sawla public health facilities, southern Ethiopia, 2019.

HIV infected individuals with severe anemia were at lower risk of death when compared with HIV infected individuals with no severe anemia (figure 5).

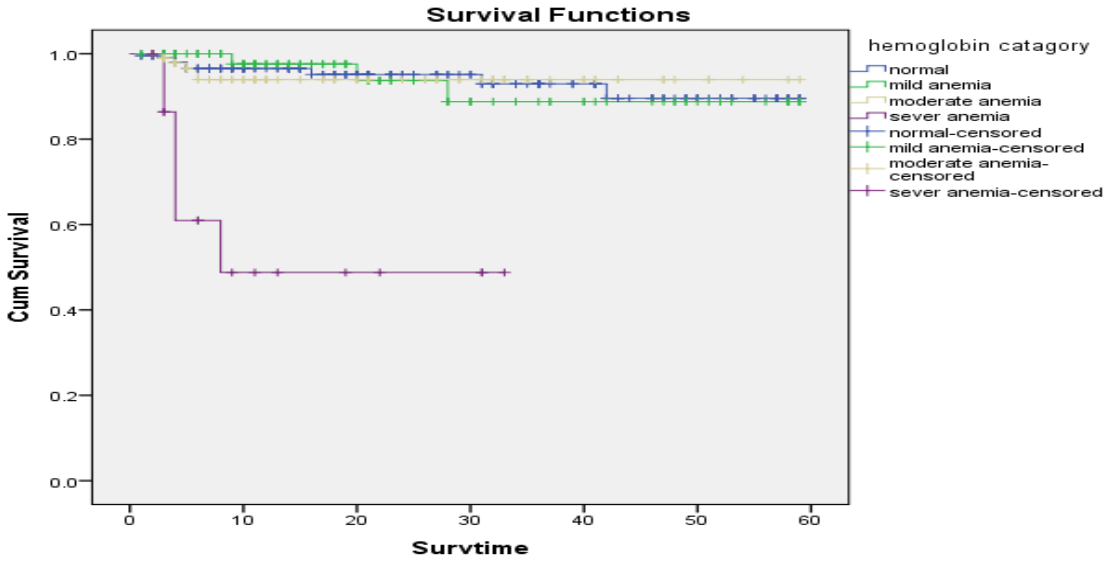

Figure 5: shows Plots of KM survival functions based anemia status of HIV patients under ART in Sawla public health facilities SNNPR, southern Ethiopia, 2019.

HIV infected individuals with non disclosure status were at higher risk of death when compared with HIV infected individuals with disclosure status (figure 6).

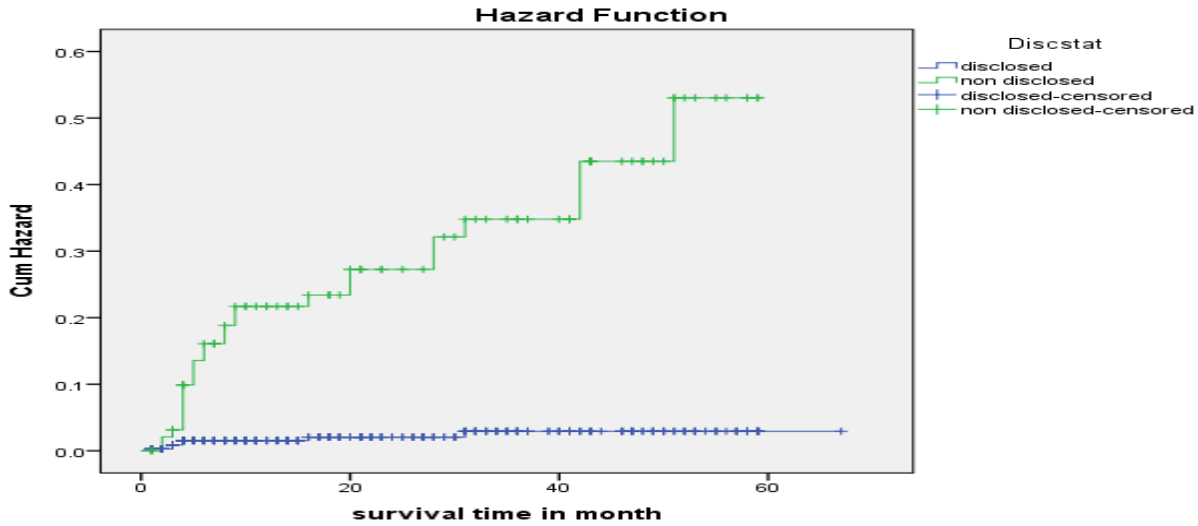

Figure 6: shows Plots of KM hazard functions based disclosure status of HIV patients under ART in Sawla public health facilities SNNPR, southern Ethiopia, 2019.

Chapter 6: Discussion

This retrospective cohort study of HIV/AIDS patients on ART gives an insight into survival and determinants of mortality in Sawla town public health facilities. The findings from the registered cohort, there were 34 (7.5%) deaths, providing an incidence density of mortality during ART treatment 3.92 per 100 person year observations (PYO) which was higher compared to other studies conducted in Ethiopia 1.75 and 3.2per person year observation (31,35) but lower than other studies conducted in Ethiopia (26) and Cameroon (24) 5.3 and 52 per 100 person year observation (PYO) respectively. This indicates that ART is significantly reducing deaths among AIDS patients in Ethiopia and proves that the ART program is functioning well.

Majority of death 20(58.8%) were occurred in the first 6 months of ART initiation which was comparable to previous studies conducted in Ethiopia (28) and other country in sub-Saharan Africa (24). A lot of factors could have contributed to the early mortality in Sawla town public health facilities. These may be due to nearly one third of patients started ART in an advanced stage of the disease which were explained by 29.2% of patients had CD4 count less than 200 cells/mm^3, 28.6% of patients had moderate and severe anemia, 39.1 % of patient were in WHO clinical stage III & IV and 33.2 % patients were ambulatory and bedridden at baseline in which most of patients continue in severe form over time. The reason for early mortality may be due to poor early diagnosis of HIV infection, delay initiation of antiretroviral treatment, and weak HIV care continuum.

The estimated mortality in the study period was 4.4%, 5.3%, 6.1%, 7%, 7.5% and 7.5% at 6, 12, 24, 36, 48 & 60 months of follow up period, respectively. This finding was comparable with study conducted in Nekemte referral hospital (32).

Patients with poor ART adherence had the highest risk of death with 4.5times more likely to die than adherent patients (AHR4.52: 95%CI: 2.05-9.96). Similarly study conducted in Ethiopia, non-adherent participant's had a mortality of 27 times compare to adherent ART patients (32). In addition study conducted in other parts of Ethiopia the risk of death in non- adhered patients is 4 times higher compared to adhered patients (7). This was comparable with current study results which indicate there is strong association between mortality and ART drug adherence. The non-adherence to HAART leads to virologic, immunologic, clinical failure, and failure to suppress viral replication, thus increasing the likelihood of developing HIV mutations that could

lead to the development of drug-resistant viral strains. Adherence to HAART is critical to the survival of HIV/AIDS infected people as poor adherence is the main reason for poor treatment outcomes among people receiving antiretroviral therapy (5,13).

Mortality rate was associated with baseline tuberculosis co infection in this study. It was found that people who start ART with tuberculosis co infection were dying nearly 4 times higher rate than those who had no baseline tuberculosis co infection. These are explained by, from 67 HIV/AIDS patients with tuberculosis confection; 82%were in WHO clinical stage III & IV, 73% were ambulatory and bedridden and 55% had CD4 count less than 100 cells/mm3 at baseline. This is similar in many other studies found tuberculosis co infection was found to be the significant predictor of mortality in Ethiopia (16,25) and India (19). This may be because TB is the leading cause of death worldwide in HIV infection and mycobacterium tuberculosis is a virulent organism that can produce disease in HIV-infected persons at any stage of disease even when the immune suppression is minimal.

Patients who were severe anemia at baseline were 5times higher risk of mortality than those who doesn't have. The same study done in Ethiopia(7,29,31) and across many parts of Africa (23) reported that low level of hemoglobin at baseline is associated with high level of mortality among patients on HAART. Similar comparable finding showed in Ethiopia that anemia could be an indicator of advanced disease or clinical feature of some opportunistic infections which might aggravate the risk of death in ART patients (35).

Previous studies reported that age at baseline was found to be the predictor of mortality, where most of the patients in older age were more likely to die(26,33). Similar scenario had happened in this study, age 45 years and above was nearly 4 times at higher risk of mortality than in which patients aged 15-24 years. This could be due to the fact that individuals are at higher risk of complications and respond poorly to ART as a result of combined effect of aging, HIV infection, and antiretroviral treatment. It is known that as age increases immune status becomes incompetent which is considered to be a risk for many chronic diseases which results in death.

Patients with non disclosure status to his/her family had high risk of death than patients with disclosure status. This finding is comparable with study conducted in other parts of Ethiopia (34). This might be due to disclosed patients psychologically ready and get social support from their partner in adapting the illness and taking the drug correctly. Correspondingly, non-

disclosure has negative health impacts associated with distress, loneliness, and medical non-adherence as a way to hide the presence of disease from others, and these factors may lead to a higher rate of mortality than in those who have disclosed their HIV status.

A patient who initiated ART as bedridden (inability to attain self-care in the daily living) had more likely to die compared to working functional status (able to perform routine activities). Patients with bedridden functional status had 17.4 times higher risk of death compare with working patients. Similarly, study conducted in Jinka hospital, Mizan hospital and Addis Ababa among armed forces members bedridden patients had a high mortality compare to working patients(10,34).

Cross checking of electronic database data with different documents in time of non logical and incomplete data were the strength of this study. Limitation of the study is that mortality might be underestimated due to lost to follow up patients probably includes more individuals dying at home without being reported.

Chapter 7: Conclusion and Recommendation

7.1. Conclusion

This study has shown a high mortality of the cohort in the first 6 months and showing an overall lower mortality compared to other African studies. The study had identified the independent significant predictors of survival in patients living with HIV/AIDS after initiation of HAART. These factors include Patients with older age, tuberculosis co infection, bedridden functional status and severe anemia (hemoglobin less than 7 mg/dl) should be carefully monitored closely by their clinicians.

7.2. Recommendations

Based on above study finding, the following recommendations can be forwarded;

To hospitals and health centers with ART clinic

- A careful monitoring of patients with bedridden functional status, tuberculosis confection, severe anemia and elder patients are necessary particularly during the first 6 months of ART initiation.
- The high early mortality has to be addressed by increasing the availability of early HIV diagnosis and treatment services.
- Careful follow up for poorly adhered patients and giving them drug counseling is crucial to improve survival
- Develop a way to control the completeness and reliability of base line data being collected especially hemoglobin.
- Preventive efforts should focus on high risk groups.

To Goffa zone health bureau

- Giving in-service training for the health care giver on HIV/AIDS care and support especially on how to recognize and manage patients with high risk patients like older age, bedridden functional status, poor adherence and patients with severe anemia.

Reference

1. Support WHO, Country FOR. PROGRESS REPORT 2016 PREVENT HIV, TEST AND TREAT ALL. 2016;
2. National Department of Health South Africa 2015. National Consolidated Guidelines. 2015;(November):1–78.
3. United Nations Joint Programme on HIV/AIDS (UNAIDS). Unaids Data 2018. 2018; Available from: http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf
4. Reepalu A. Antiretroviral Treatment at Ethiopian Health Centers [Internet]. 2017. 116 p. Available from: http://portal.research.lu.se/ws/files/32283580/Avhandling_Anton_R_web.pdf
5. Federal Minstry of, Health. National Guidelunes for comprehensive HIV Prevention, Care and Treatment. 2017;1.226.
6. Damtew B, Mengistie B, Alemayehu T. Survival and determinants of mortality in adult HIV/Aids patients initiating antiretroviral therapy in Somali Region, Eastern Ethiopia. Pan Afr Med J. 2015;22(October).
7. Abose G. Survival Status among Patient Living With HIV AIDS who Are on Art Treatment In Durame And Hossana Hospitals. 2015;(May):1–106.
8. Bhatta L. Survival Pattern and Determinants of Survival in Adult Hiv-Infected Patients on Antiretroviral Treatment in Far-Western Development Region , Nepal . 2012;
9. WHO. HIV/AIDS surveillance in Europe 2017 Surveillance report, 2016 data. 2017.
10. Kebebew K. Determining factors that affect the survival rate of HIV-infected patients on ART ;The Case of Armed Forces General Teaching Hospital, Addis Ababa, Ethiopia. 2011;
11. Chakravarty J, Tiwary NK, Prasad SR, Shukla S, Tiwari A, Mishra RN, et al. Determinants of survival in adult HIV patients on antiretroviral therapy in eastern Uttar Pradesh: A prospective study. Indian J Med Res. 2014;140(October):491–500.
12. Tallam KK. Survival of Persons Starting HAART in HIV / AIDS care Facility in Nairobi, Kenya by University of Nairobi Institute of Tropical and infectious Diseases College of Health Sciences. 2015;
13. WHO. Consolidated guidelines on the us for the of Antiretroviral drugs for the treating and preventing HIV infection. 2013.
14. Okyere GA, Alalbil PA, Ping-Naah H, Tifere Y. Determinants of survival in adult HIV clients on antiretroviral therapy in lawra and jirapa districts of upper west region, Ghana. J Int Assoc Provid AIDS Care. 2015;14(3):255–60.
15. CSA. Federal Democratic Republic of Ethiopia demographic and health survey 2016 key indicators report [Internet]. Ethiopians Water Sector Development Program. 2016. 1-49 p. Available from: https://www.usaid.gov/sites/default/files/documents/1860/Ethiopia DHS 2016 KIR - Final 10-17-2016.pdf

16. Sapa WB, Negassi NT, Haile A. Survival Pattern and Its Determinants among Adult HIV-Infected Patients after Initiation of HAART in Dilla Hospital Ethiopia. 2016;1(1):1–7.

17. Worku A, Miguel SS. Pattern and determinants of survival in adult HIV patients on antiretroviral therapy , Ethiopia Author : Andinet Worku. 2009;

18. Hailemariam S, Tenkolu G, Tadese H, Kumar Vata P. Determinants of Survival in HIV Patients: A Retrospective Study of Dilla University Hospital HIV Cohort. 2016;3(2):4–9.

19. Roja Y R, Benu P, Himanshu S, Rao B, Ramachandra M V, Simanchal P, et al. Predictors of Mortality among HIV Patients on HAART in an ART Centre – A Retrospective Study. 2016;6(4):175–9. Available from: http://web.a.ebscohost.com/ehost/pdfviewer/pdfviewer?vid=4&sid=157e77ed-849c-4b77-95fb-b25cc1f41373%40sessionmgr4009&hid=4112

20. Eguzo K, Lawal A, Umezurike C, Eseigbe C. Predictors of loss to follow-up among HIV-infected patients in a rural South-Eastern Nigeria Hospital: A 5-year retrospective cohort study. Ann Med Health Sci Res [Internet]. 2015;5(6):373. Available from: http://www.amhsr.org/text.asp?2015/5/6/373/177988

21. Hassan R, Hassan A, Abdelaal AA, Mohammed HA, Elbashir MA, Khalid KB. Survival and Mortality Analysis for HIV Patients in Khartoum State , Sudan 2017. 2018;3(4):118–24.

22. Ojikutu BO, Zheng H, Walensky RP, Lu Z, Losina E, Giddy J, et al. Predictors of mortality in patients initiating antiretroviral therapy in Durban, South Africa. South African Med J. 2008;98(3 PART 1):204–8.

23. Sieleunou I, Souleymanou M, Schönenberger AM, Menten J, Boelaert M. Determinants of survival in AIDS patients on antiretroviral therapy in a rural centre in the Far-North Province, Cameroon. Trop Med Int Heal. 2009;14(1):36–43.

24. Muhula SO, Memiah P, Sibhatu B, Meshack N, Lennie K. Effects of highly active antiretroviral therapy on the survival of HIV-infected adult patients in urban slums of Kenya. Pan Afr Med J. 2015;8688:1–9.

25. Biset Ayalew M. Mortality and Its Predictors among HIV Infected Patients Taking Antiretroviral Treatment in Ethiopia: A Systematic Review. AIDS Res Treat [Internet]. 2017;2017(in 2005):1–10. Available from: https://www.hindawi.com/journals/art/2017/5415298/

26. Seyoum D, Degryse JM, Kifle YG, Taye A, Tadesse M, Birlie B, et al. Risk factors for mortality among adult HIV/AIDS patients following antiretroviral therapy in southwestern ethiopia: An assessment through survival models. Int J Environ Res Public Health. 2017;14(3):1–12.

27. Serawit D, Alemayehu T, Fiker T. Pattern and predictors of cluster of differentiation 4 (CD4) cell count recovery among cohorts of human immunodeficiency virus (HIV)-infected patients on antiretroviral therapy in Hawassa University Referral Hospital. J AIDS HIV Res [Internet]. 2018;10(3):40–8. Available from: http://academicjournals.org/journal/JAHR/article-abstract/CBC376156173

28. Alemu AW, Sebastián MS. Determinants of survival in adult HIV patients on antiretroviral therapy in Oromiyaa, Ethiopia. Glob Health Action [Internet]. 2010;3(1):5398. Available from: https://www.tandfonline.com/doi/full/10.3402/gha.v3i0.5398

29. Digaffe T, Seyoum B, Oljirra L. Survival and Predictors of Mortality among Adults on Antiretroviral Therapy in Selected Public Hospitals in Harar , Eastern Ethiopia. 2014;2(5).

30. Tadesse K, Haile F, Hiruy N. Predictors of mortality among patients enrolled on antiretroviral therapy in Aksum hospital, Northern Ethiopia: A retrospective cohort study. PLoS One. 2014;9(1).

31. Kebebew K, Wencheko E. Survival analysis of HIV-infected patients under antiretroviral treatment at the Armed Forces General Teaching Hospital, Addis Ababa, Ethiopia. Ethiop J Heal Dev. 2012;26(3):186–92.

32. Hambisa MT, Ali A, Dessie Y. Determinants of Mortality among HIV Positives after Initiating Antiretroviral Therapy in Western Ethiopia : A Hospital-Based Retrospective Cohort Study. 2013;2013.

33. Ayalew J, Moges H, Worku A. Identifying Factors Related to the Survival of AIDS Patients under the Follow-up of Antiretroviral Therapy (ART): The Case of South Wollo. 2014;1(2):21–7.

34. Erdaw T, Ameni G. Survival and predictors of mortality among human immunodeficiency virus patients on anti-retroviral treatment at Jinka Hospital , South Omo , Ethiopia : a six years retrospective cohort study. Epidemiol Health. 2016;38(e2016049):1–10.

35. Ayele W, Mulugeta A, Desta A, Rabito FA. Treatment outcomes and their determinants in HIV patients on Anti-retroviral Treatment Program in selected health facilities of Kembata and Hadiya zones , Southern Nations , Nationalities and Peoples Region , Ethiopia. BMC Public Health [Internet]. 2015;1–13. Available from: http://dx.doi.org/10.1186/s12889-015-2176-5

36. Mosley WH, Chen LC. An analytical framework for the study of child survival in developing countries. 1984. Bull World Health Organ. 2003;81(2):140–5.

37. Hedeker D. Sample Size Estimation for Longitudinal Studies Don Hedeker University of Illinois at Chicago www.uic.edu/ ~ hedeker. 1999;70–93.

ANNEXE:

Annex 1 graphical PH assumption

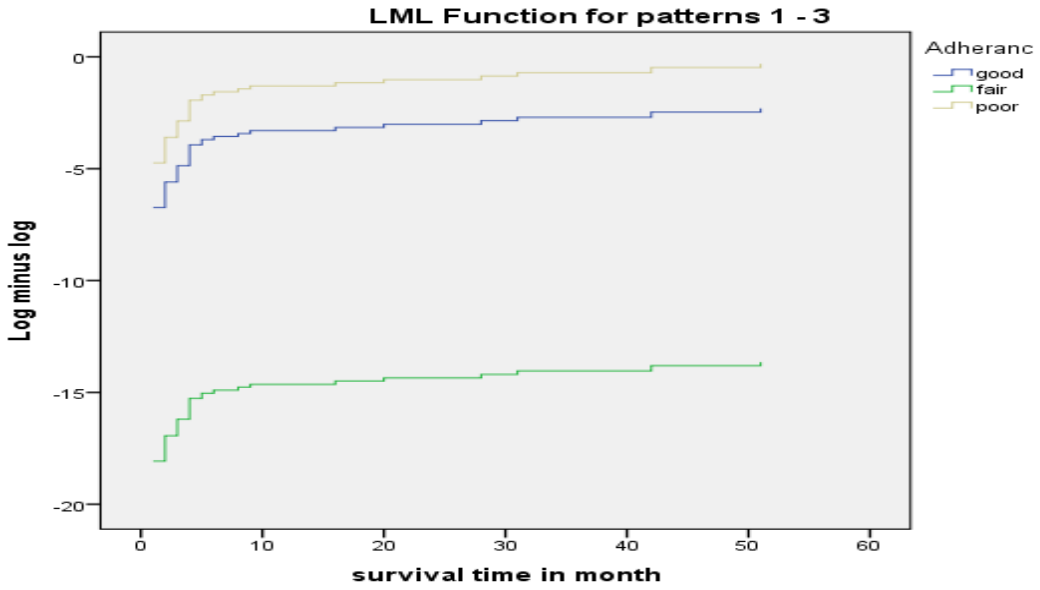

Figure 7: PH assumption checking for baseline functional status for HIV positive patients in sawla town public health facilities, southern Ethiopia, 20111.

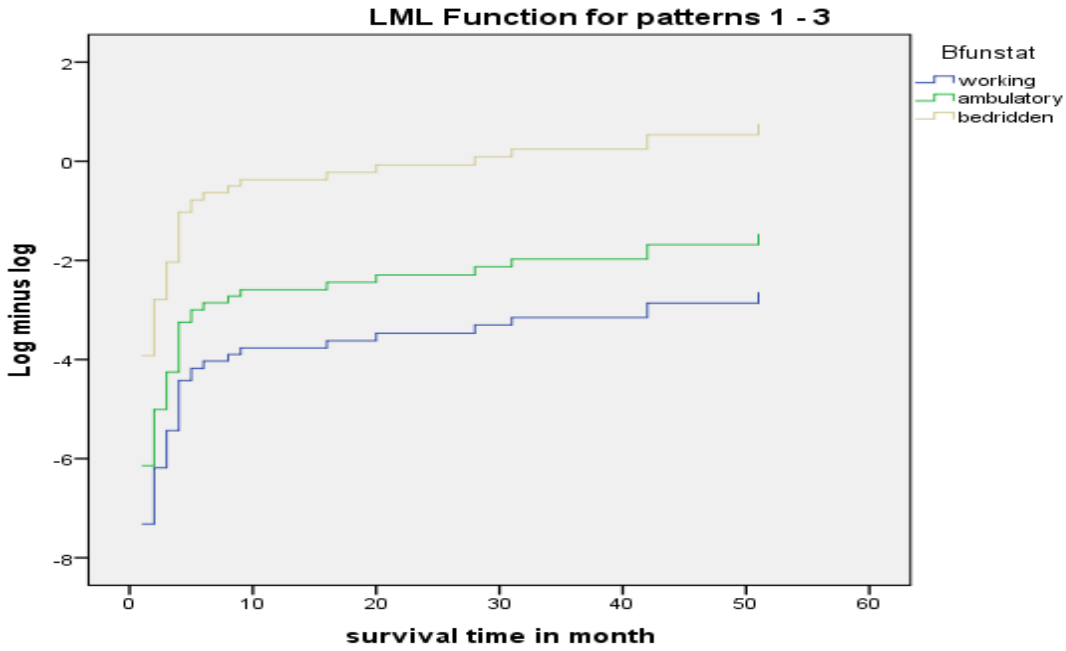

Figure 8: Shows PH assumption checking for baseline functional status for HIV positive patients in sawla town public health facilities, southern Ethiopia, 20111.

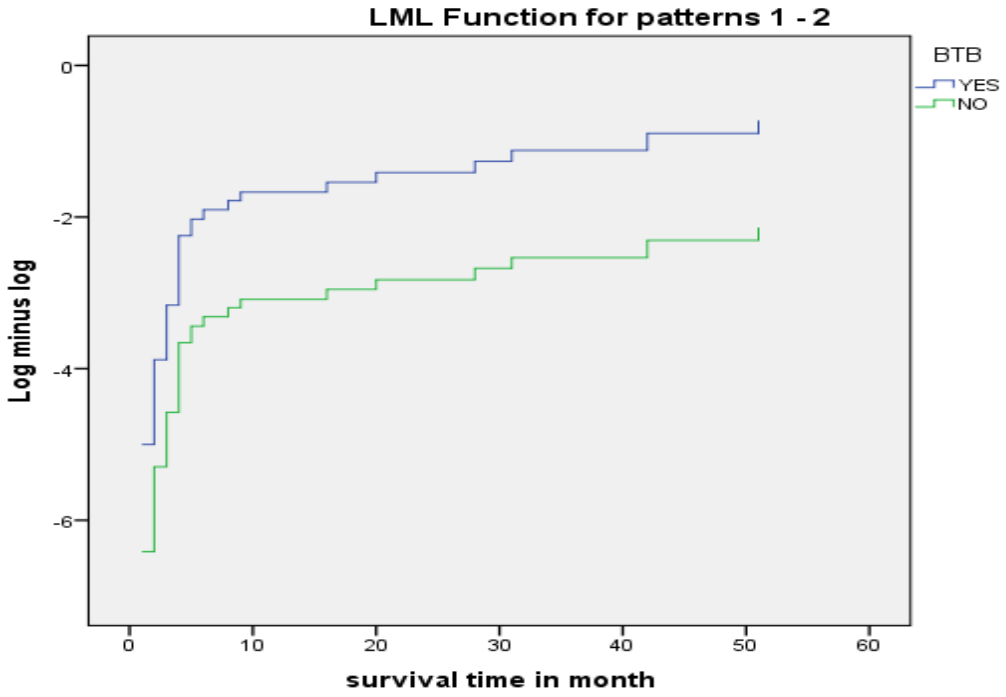

Figure 9: Shows PH assumption checking for baseline tuberculosis co infection for HIV positive patients in sawla town public health facilities, southern Ethiopia, 20111.

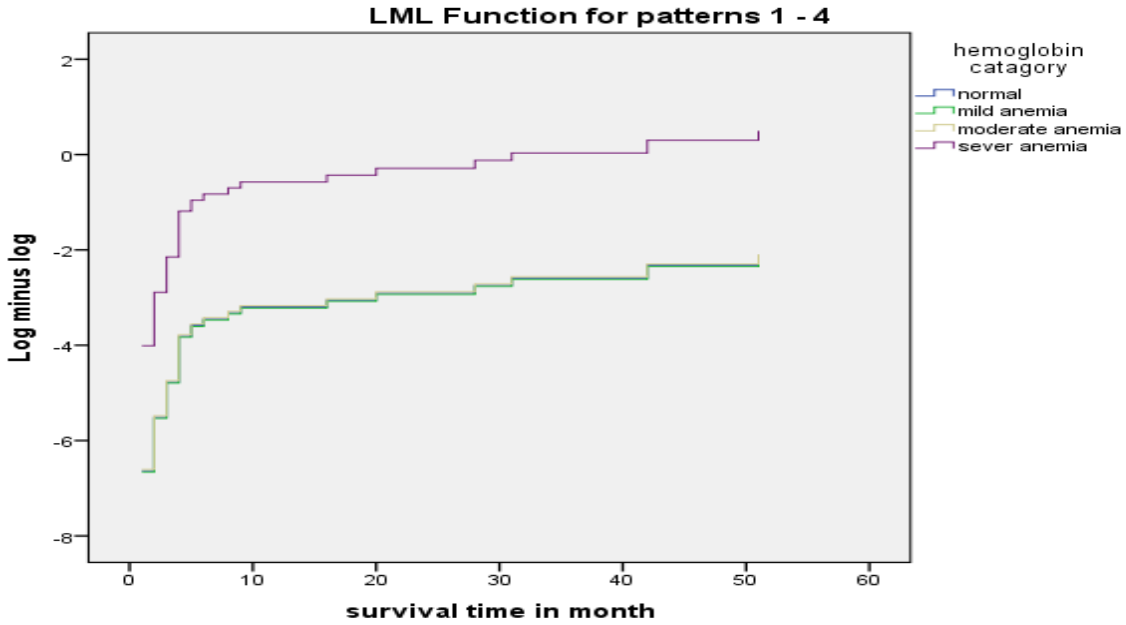

Figure 10: shows PH assumption checking for baseline anemia status for HIV positive patients in sawla town public health facilities, southern Ethiopia, 20111.

Annex 2: Data extraction tool

INTRODUCTION:

This patient information collection sheet is intended to assess survival pattern and its determinants among Adult HIV positive patients on Highly Active Antiretroviral Therapy in Public Health Facilities, Sawla Town, SNNPR, Southern Ethiopia. The study will be conducted through reviewing electronic database records and ART follow up forms. The study is aimed to fill the information gap and provide empirical evidence for program planner, decision makers and ART program implementer at the different level by enabling them to access a base line data on determinants of survival. Moreover it will be a paramount important to curb the horizon of the disease. And it assists in the development of a system for improving the survival of people living with HIV/AIDS.

Date of review -----day-----month-----year

Name and signature of reviewer----------

Time Started_____ Time ended_____

Name and signature of the supervisor……

Date……

Result:

a) Completed ---------- b) Incomplete ----------c) excluded----------

Action taken for the incomplete data_____ (please use additional blank paper if the space is not enough)

ART clinic intake form, enrolled in care

1. Socio-demographic information when enrolled in chronic HIV care			
S/No-	Variables	Coding Categories	Comment
101	ART Unique ID No	/__/__/__/__/__/	
102	Age in completed years	_____	
103	Sex	1. Male 2. Female	
104	Marital status	1. Never married 2. Married 3. Separated 4. Divorced 5. Windowed	
105	Level of education	1. Not educated 2. Primary 3. Secondary 4. Tertiary	
106	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others (specify)_____	

107	Residence	1. Urban 2. Rural	
108	Employment status	1. Working full time 2. Working part time 3. Not working	
109	HIV confirmed date	Date _____	
110	Date of ART started	Date _____	
2. Anthropometry, functional status, and WHO clinical Staging when enrolled in care Please, provide the ART measurement values at start of ART/baseline data/			
201	Height	/__/__/__/cm	
202	Weight	_____ kg	
203	BMI	_____kg/m^2	

204	CD4 cell count	_____cells/mm^3	Report date _____
205	Hemoglobin	_____ mg/dl	Date _____
206	WHO clinical staging	1. I 2. II 3. III 4. IV	
207	Functional status	1. Working 2. Ambulatory 3. Bed ridden	
208	Evidence of TB at start of ART	1. Yes 2. No	
3. Behavioral characteristics			
301	Substance use/abuse	1. Tobacco 2. Alcohol 3. Khat, shisha 4. None 5. Others (specify)_____	
		1. Yes 2. No	

302	Disclosure status		
303	Adherence	1. Good 2. Fair 3. Poor	
4. OI prophylaxis and Drug regimen at baseline			
401	CPT Prophylaxis at base line	1. Yes 2. No	
402	INH prophylaxis	1. Yes 2. No	
403	ART regimen	1. 1st line treatment 2. 2nd line treatment	
5. Follow up status			
501	Follow up status	1. Currently on ART 2. Lost 3. Transfer out 4. Dead	If 2/3/4the exact date _____

			Dd/mm/yy
502	Latest follow up date	_____dd/mm/yy	
502	Duration of follow up in months since initiation of ART	_____ in months	