ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

ASSESSMENT OF DETERMINANTS OF SURVIVAL IN ADULT HIV PATIENTS AFTER INITIATION OF ANTIRETROVIRAL THERAPY IN NEKEMTE REFERRAL HOSPITAL, WOLLEGA, WEST ETHIOPIA.

A RETROSPECTIVE COHORT STUDY

BY

MITIKU TESHOME (BSc. in PH)

ADVISOR

Professor Ahmed Ali (PhD)

A THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES,

ADDIS ABABA UNIVERSITY AS PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF PUBLIC HEALTH IN EPIDEMIOLOGY

MAY, 2012

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

ASSESSMENT OF DETERMINANTS OF SURVIVAL IN ADULT HIV PATIENTS AFTER INITIATION OF ART IN NEKEMTE REFERRAL HOSPITAL, WOLLEGA, WEST ETHIOPIA

A RETROSPECTIVE COHORT STUDY

BY

MITIKU TEHOME

School of Public Health, College of Health Sciences

Addis Ababa University

Approved by the Examining Board

Dr Jemal Haider _____ _____

Chairman, SPH signature

Professor Ahmed Ali _____ _____

Advisor Signature

_____ _____

Examiner Signature

ACKNOWLEDGMENT

First of all my heartfelt thanks go to my Advisor Professor Ahmed Ali for his unreserved support, provision of relevant materials and timely comments and guidance throughout my thesis work.

I am very grateful to my Instructor Dr. Alemayehu Worku for the considerable help I got from him in preparing this thesis; his comments and suggestions have been very useful.

My special thanks and appreciation goes to Dr Degu Jerene for his valuable comments and guidance.

I am grateful to the Addis Ababa University, School of Public Health for giving me this opportunity.

My special thanks also go to Nekemte Referral Hospital staff, especially W/o Meseret Etana (Health Officer in Nekemte Referral Hospital ART clinic), for their co-operation during data collection.

I also want to recognize my colleagues Tarekegn Solomon, Yadeta Dessie, and Gezahegn Tesfaye for their valuable comments in the preparation of this report.

Finally, I thank my family for their support, encouragement and prayer during this thesis work.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ACRONYMS (ABBREVIATIONS)

3TC: Lamivudine

AAU: Addis Ababa University

AHR: Adjusted Hazard Ratio

AIDS: Acquired Immune Deficiency Syndrome

ART: Antiretroviral Therapy

AZT: Zidovudine

BMI: Body Mass Index

cART: Combination Antiretroviral therapy

CHR: Crude Hazard Rate

CI: Confidence interval

CPT: Cotrimoxazole prophylaxis therapy

d4t: Stavudine

DOT: Directly Observed Treatment

EFV: Efaviren

EPTB: Extra Pulmonary Tuberculosis

FMOH: Federal Ministry of Health

HAART: Highly Active Antiretroviral Therapy

HAPCO: HIV/AIDS Prevention and Control Office

HIV: Human Immunodeficiency Virus

HR: Hazard Ratio

IQR: Inter-quartile Range

NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor

NRTI: Nucleoside Reverse Transcriptase Inhibitor

NVP: Nevirapine

OR: Odds Ratio

PCP: Pneumocystis Carini Pneumonia

PI: Protease Inhibitor

PIHCT: Provider Initiated HIV Counseling and Testing

PLWH: People Living With HIV

PMTCT: Prevention of Mother to Child Transmission

PTB: Pulmonary Tuberculosis

PYO: Person Years Observation

RNA: Ribonucleic Acid

SD: Standard Deviation

TLC: Total Lymphocyte Count

UNAIDS: United Nations AIDS

UNGASS: United Nations General Assembly Special Session on HIV/AIDS

WHO: World Health Organization

ABSTRACT

Introduction: Studies identified different determinants of survival which includes, viral load, WHO clinical staging, CD4 cell count, body mass index (BMI), total lymphocyte count (TLC), ART adherence and baseline hemoglobin level. Even if these determinants of survival had been identified, there is no single proven model of determinants for predicting mortality of PLHIV and these determinants are dynamic and change over time due to improving quality of care and support and specific interventions like nutritional interventions. Furthermore, the optimal time to start treatment for HIV/AIDS has been a controversial issue since the introduction of HAART.

Objective: To assess determinants of survival in patients living with HIV after starting ART.

Methodology: A retrospective cohort study was conducted in Nekemte Referral Hospital. A total of 416 patients' records enrolled between 2005 to January, 2012 were reviewed consecutively by using patients' ART unique identification number as a reference. Univariate analysis was used to describe patient's baseline characteristics. Life table was used to estimate survival after initiation of ART, and log rank test was used to compare survival curves. Cox proportional-hazard regression was used to calculate the bivariate and adjusted hazard rate and then determined independent determinants of time to death.

Results: Four hundred sixteen adult patients on ART were followed for a median of 47 months. The mean age was 33.6 years (SD=9.04) and the median weight of the study subjects at the initiation of ART was 51 kg (IQR, 45kg-58kg). The estimated mortality was 4%, 5%, 6%, 7%, and 7% at 6, 12, 24, 36 and 48 months respectively. After adjustment, factors such as, age≥40 AHR=3.364(1.211, 9.348, p=0.020), lower baseline hemoglobin level AHR=0.490 (0.300, 0.801, p=.007), and poor ART adherence AHR=132.3(29.9, 585.8, p<0.001) were confirmed as significant independent determinants of less survival after controlling for other factors while, single marital status AHR=0.285(0.1, 0.84, p=0.023) was protective of HIV mortality.

Conclusion: This study has identified the independent significant determinants of less survival in patients living with HIV after initiation of ART which included older age, low baseline hemoglobin level, and poor ART adherence, while single marital status was protective of HIV mortality. These determinants should be taken into account by health care providers to enhance better clinical outcomes.

1. INTRODUCTION

1.1 Background information and statements of the problem

Acquired Immunodeficiency Syndrome (AIDS) continues to be a major global health priority. Although important progress has been achieved in preventing new HIV infections and in lowering the annual number of AIDS-related deaths, the number of people living with HIV continues to increase. AIDS-related illnesses remain one of the leading causes of death globally and are projected to continue as a significant global cause of premature mortality in the coming decades. This continuing rise in the population of people living with HIV reflects the combined effects of continued high rates of new HIV infections and the beneficial impact of antiretroviral therapy (1).

The human immunodeficiency virus (HIV) has created an enormous challenge worldwide. Since its recognition, HIV has infected close to 70 million people, and more than 30 million have died due to acquired immunodeficiency syndrome (AIDS). According to the UNAIDS 2010 report on global AIDS epidemic, 68% of the 33.3 million people living with HIV/AIDS are in sub-Saharan Africa, where AIDS is the leading cause of death (2).

Ethiopia is a low income country in East Africa with rapidly growing population at a rate of 2.7% per year since 2000 and one of the seriously affected countries in sub-Saharan Africa, with large number of PLHIV (approximately 800,000), about 1 million AIDS orphans and an estimated 277,800 people requiring ART treatment (3, 4). Average life expectancy at birth is also relatively low at 48 (47 for males and 49 for females) and is further expected to decline if present HIV infection rates continue (3). According to the Summary and Statistical Report of the 2007 Population and Housing Census, the average life expectancy is 51 years for males and 53 years for females (5).

Only few studies have been conducted to investigate the survival benefit of ART scale-up services in Africa especially in Ethiopia. Based on the recommendations of the United Nations General Assembly Special Session on HIV/AIDS (UNGASS), the Government of Ethiopia launched its fee-based ART initiative in 2003 and free ART initiative in 2005 (3). Health

facilities providing ART reached 551 in 2011(6). The number of AIDS patients ever started on ART has grown to 333,434 in 2011, among which 247,805 were on treatment(6). In the year 2010 alone 91,100 new AIDS patients started ART (7). The country has scaled up its ART program - the service is provided at 551 sites- and has already been decentralized to many health facilities (6). In Ethiopia the adult prevalence of HIV was estimated to be 2.2% in 2008 (8). According to the 2011 EDHS, the adult HIV prevalence was 1.5%; 1.9% for women and1.0 % for men (9).

The total number of People Living with HIV (PLHIV) in the year 2008 was estimated to be 1,037,267 adults and 68,136 children. In addition to that, the number of death due to AIDS for the same period was estimated to be 58,290 for adults and 9,284 among children (8). However, according to Country Progress Report on HIV/AIDS Response 2012, the total number of PLHIV has decreased to approximately 800,000 (4).

1.2. Rationale of the study

Only few studies have been done regarding survival benefits of ART in Ethiopia, especially after decentralization of ART to district hospitals, regional hospitals and health centers. On the other hand, not only the survival benefit of highly active antiretroviral therapy in HIV infection, but also its impact on the incidence of opportunistic infections has been well studied in the developed world. These studies identified different determinants of survival which includes, WHO clinical staging, viral load, age, gender, CD4 cell count, total lymphocyte count, body mass index (BMI), ART adherence and baseline hemoglobin level. Even if these determinants of survival had been identified, there is no single proven model of determinants of survival for predicting mortality of PLHIV and these determinants are dynamic and change over time due to improving quality of care and support and specific interventions like nutritional interventions. In resource-poor settings, where such treatment was started only recently, limited data exist both on treatment results and on how to carry out such interventions and also limited manpower to treat HIV/AIDS. As a result, the existing treatment guidelines and recommendations are based on data from the developed world (10, 11). However, there is geographic variation between and within countries and regions regarding HIV prevalence and epidemiological patterns. The substantial diversity of national epidemics underscores not only the need to tailor prevention strategies to

local needs but also the importance of decentralizing AIDS responses (1). So, all these factors necessitate the urgent need for generating regional data.

This study has investigated determinants of survival at regional referral hospital and provides credible evidence for governmental and non-governmental organizations that work in the area of HIV/AIDS, specifically on ART at national, regional and district levels by providing basic information on factors determining survival of PLHIV who are on ART.

2. LITERATURE REVIEW

2.1 Global HIV /AIDS Burden and Situation of HAART Program in Ethiopian Context

Globally 33.3 million peoples are living with HIV/AIDS. About 2.6 million peoples are newly infected and of these more than 95% of new infections are in developing countries, many of them needing ART (2). In sub- Saharan Africa, 1.8 million people became infected in 2009 (2).
In the industrialized world, the introduction of HAART in 1996 dramatically improved the prognosis for HIV-infected patients (10). Until recently, however, access to treatment has been severely limited in developing countries, where the majority of people with HIV live. In sub-Saharan Africa, only 37% of people eligible for treatment were able to access life-saving medicines in 2009 (2).

In Ethiopia, 47% of the total population is aged 15 to 49 years (12). The highest HIV prevalence occurs in the age group 15-24. HIV infections occurring in adults between 15 to 49 years account for 90 % of all infections (12). According to a single point prevalence estimates by Federal HAPCO, adult prevalence by 2008 was 2.2%, in Male=1.8, Female =2.6. But, according to report on progress towards implementation of the UN Declaration of Commitment on HIV/AIDS March 2010 by Federal HAPCO, adult HIV prevalence in 2009 was estimated to be between 1.4% and 2.8% (7). However, according to the 2011 EDHS, the adult HIV prevalence was 1.5%; 1.9% for women and1.0 % for men (9). In Ethiopia 443,964 PLWH enrolled, 246,347 PLHIV started treatment and 179,183 were envisaged to be on ART (12). The total persons on 1st line ART regimen were 166,444 of whom 156,083 were adults. The total number of persons on 2nd line regimen was 1000 of whom 865 were adults. Among adults on the 1st line regimen 64,605 were on d4t (30)-3TC-NVP, 32,712 on d4t (30) -3TC-EFV, 34,962 on AZT-3TC-NVP and 23,804 AZT-3TC-EFV. The rest 0.6% were on 2nd line regimen, with 132 on ABC-ddI-LPV/R and 733 on TDF-ddI-LPV/R and 11,739 were on others and unspecified regimens (13).

2.2. Survival estimates of PLHIV

In a study conducted in Cameroon in 2009, total mortality rate over the study period was 20.2 per 100 person-years, the median survival time was 58 months and the survival probability at 1 year was 77% (95% CI: 75–80) and at 5 years 47% (95% CI: 40–55) (14). According to Degu Jerene, mortality rate in ART+ group was 15.4/100PYO and most of the death occurred during

the first three months (15). In a study conducted in Tanzania, 95 patients (29.7%) died during the follow-up period, among whom 59 died within 3 months of starting ART (10). Estimated mortality was 19.2%, 24.5%, 29.0%, 35.2% and 40.7% at 3, 6, 12, 24 and 36 months, respectively. Mortality was found to be high, with the majority of death occurring within three month of starting ART (16).

According to Lawn et al, early mortality rates in sub-Saharan Africa are very high; between 8 and 26% of patients die in the first year of antiretroviral treatment, with most deaths occurring in the first few months (17). The CD4 counts gradually decline over several years, with a more accelerated decline 1.5 to 2 years before an AIDS defining diagnosis. HIV RNA concentrations in plasma show an initial "burst" during acute infection and then decline to a "set point" as a result of seroconversion and development of immune response (3). The viral load correlates with the rate of CD4 decline (4% decline/year/log10/copies/ml). With continued infection, HIV RNA levels gradually increase. In untreated patients, the median survival after the CD4 count falls to <200cells/mm3 is 3.7 years (3). The median survival after an AIDS defining complication is 1.3 years (3).

In a study conducted at Zewditu Hospital in Ethiopia, the estimated mortality rate after starting ART was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively. After adjustment, the independent significant predictors of not surviving in patients living with HIV/AIDS after initiation of ART remain poor ART adherence (AHR=3.92[95%CI=3.13, 4.90]), advanced WHO staging (AHR=2.47[95%CI= (1.58, 3.81]), being unemployed(AHR=1.87[95%CI= 1.49, 2.34]), moderate anemia (AHR=1.86[95%CI=1.35, 2.56), and Low CD4count (AHR=1.85[95%CI=1.35, 2.52] (18).

On average, six life-years will be saved per person treated, if individuals primarily enter ART programs when symptomatic (19). If individuals are recruited to programs while still healthy and are frequently monitored, and CD4+ cell counts are used to help decide when to initiate ART, three times as many are expected to be treated, and average life-years saved among those treated increases to 15 years (19). Initiating ART at higher CD4+ cell counts than WHO recommends leads to more life-years saved, but disproportionately more years spent on ART. The overall

impact of ART programs will be limited if rates of diagnosis are low and individuals enter care too late. Frequently monitoring individuals at all stages of HIV infection and using CD4 cell count information to determine when to start treatment can maximize the impact of ART and improve survival (19).

2.3. Factors affecting survival of PLHIV

Study conducted in Adama and Shashmane hospitals revealed that in the multivariate analysis, hemoglobin ≤10 g/ dL, clinical stage IV, and non-CPT (Cotrimoxazole prophylaxis therapy) initiation at or before the start of the treatment, were significant predictors of mortality (20).

According to Ojikutu B et al (11), the strongest predictors of mortality were CD4 cell count <50/µl (hazard ratio (HR) 3.70, 95% confidence interval (CI) 1.96 - 7.14), a hemoglobin concentration ≤8 g/dl (HR 1.23, 95% CI 1.08 - 1.40), a history of oral candidiasis (HR 3.17, 95% CI 1.70 - 5.87) and history of cryptococcal meningitis (HR 2.76, 95% CI 1.80 - 19.2). A CD4 cell count <50/µl (HR 3.08, 95% CI 1.54 - 5.88) and history of oral candidiasis (HR 2.58, 95% CI 1.37 - 4.88) remained significant in multivariate analysis (11).

Patients with a baseline CD4 count ≤50 cells ⁄mm3 presented a mortality risk twice as high as those with >50 cells ⁄mm3 (HR 1.85) (21). A 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 (HR = 1.57). This risk rose to 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 and II. Men were at nearly twice the risk of death as women (HR = 1.7). Patients with hemoglobin ≤8.5 g ⁄ dl had two times more risk of death than those with a hemoglobin rate >8.5 g ⁄ dl (14). Patients starting treatment at CD4 50-199 and <50 cells/µl have net health benefits of 7.6 and 7.3 life years. Without treatment, HIV patients with CD4 counts 200-350; 50- 199 and < 50 cells/µl can expect to live 4.8; 2.0 and 0.7 life years respectively (21).

Significant risk factors associated with mortality in the first 3 months included WHO stage IV disease, a CD4 cell count under 50 cells/ml and increasing grades of malnutrition (22). These were similar for mortality within the first 6 months. The results for mortality within the first 6 months included, WHO stage IV, OR, 2.1 (95% CI, 1.4–3.0; P<0.001); CD4 cell count <50 cells/ml, OR, 2.2 (95% CI, 1.3–3.7; P<0.01); BMI=17.0–18.4 kg/m2, OR, 1.8 (95% CI, 1.1–3.0;

P=0.02); BMI=16.0–16.9 kg/m2, OR, 2.4 (95% CI, 1.3–4.3; P<0.01); and BMI≤15.9 kg/m2, OR, 5.8 (95% CI, 3.7–9.1; P<0.001) (22).

A study in Tanzania rural hospital revealed that the significant independent predictors of mortality were moderate and severe anemia (log rank test, $P < 0.001$), thrombocytopenia, and severe malnutrition (log rank test, $P < 0.001$) (10). Study conducted in Durban, however revealed that factors predicting higher mortality rates among PLWH were oral thrush, TLC<1200/ml, BMI less than18.5 kg/m2, anemia, WHO clinical stages III or IV and presence of prolonged diarrhea at baseline (11). However, only low TLC and low BMI were associated with increased mortality both in the pre-HAART (BMI, P = 0.016; TLC, P= 0.009) and in the HAART groups (BMI, P = 0.017; TLC, P = 0.039) while anemia was not associated with increased mortality in either group (pre-HAART, log-rank = 2.2, P = 0.14; HAART, Log-rank = 2.1, P = 0.14) (11).

WHO stage IV disease, however, was found to be a strong predictor of mortality in most studies reporting on mortality (23). In three studies comparing patients with WHO stage IV disease at baseline with those with WHO stages I–III, WHO stage IV was associated with more than double in the hazard of death (23).

In fact, low adherence and retention are two critical reasons for poor treatment outcomes among people receiving antiretroviral therapy. Besides directly affecting personal well-being, poor adherence and retention rates may compromise programmatic and economic efficiency, as many people receiving first-line regimens would fail to respond to treatment at an unnecessarily early stage and would therefore need to switch to more expensive, and often unavailable, second-line regimens. Low retention can also negatively affect public health by increasing drug resistance (24). Stock-outs of antiretroviral drugs may lead to interrupted treatment, increasing the risk of treatment failure or the emergence of drug-resistant HIV variants (24). Drug stock-outs continue to be an issue of concern in low- and middle-income countries. Of the 90 countries that provided information on the experience of stock-outs of required antiretroviral drugs in 2008, 31 (34%) reported that their health facilities dispensing antiretroviral drugs had experienced at least one stock-out during the year, similar to 2007, when 25 (38%) of 66 reporting countries had experienced at least one episode of stock-out of antiretroviral drugs. A higher proportion of

countries in sub-Saharan Africa and the Americas experienced stock-out in 2008 compared to other regions (24).

Combination antiretroviral therapy (cART) has revolutionized the course of HIV disease, transforming HIV infection from a life-threatening infection to a manageable chronic condition, particularly in developed countries. However, a key challenge is the high level of adherence to cART that is required for viral suppression, immunological response and reduced morbidity and mortality in individuals with HIV/AIDS (25). Studies have demonstrated a requirement for adherence levels of at least 95% in order to achieve adequate viral suppression for regimens including unboosted protease inhibitor (PI) therapy. While a lower level of adherence has been shown to lead to viral suppression when using non-nucleoside reverse transcriptase inhibitor (NNRTI) regimens, the development of treatment-resistant mutations has been shown to peak at approximately 70% adherence and there is an ongoing decline in the rate of developing treatment resistant mutations towards 100% adherence, providing a further imperative for achieving near-perfect adherence to cART (25).

The percentage of treatment failure was 3.2% in patients receiving Stavudine, lamivudine and Nevirapine, 7.7% in those receiving Stavudine, lamivudine and Efavirenz, 4.2% in those given Zidovudine, lamivudine and Nevirapine, and 15.8% in those given Zidovudine, lamivudine and Efavirenz (26). Thus, compared to other regimens, the percentage of treatment failure was significantly greater ($P<0.05$) in the regimens that included Efavirenz, which were mostly given to patients receiving rifampicin as part of their treatment for concomitant tuberculosis. There was a significant increase in mortality among the patients who had treatment failure compared with other patients ($P<0.001$). The percentage of mortality among the patients who experienced treatment failure was 26.1%, compared with 3.6% among patients in whom treatment did not fail (26).

The optimal time to start treatment for HIV/AIDS has been a contentious issue since the introduction of Highly Active Antiretroviral Treatment (HAART) (21). Initially a “hit hard and early” strategy was promoted (21). Because of concerns about long term toxicity and fear of developing drug resistant viruses, delayed treatment starts were later recommended in clinical

guidelines (27). The delayed treatment policy implied that, in the absence of particular disease manifestations, treatment should not be started before CD4 counts dropped below 200cells/µl. However, recent evidence indicates that this policy reduces survival compared to earlier treatment start (28). The World Health Organization (WHO) revised the ART guidelines for resource constrained settings accordingly and re-introduced a “hit hard and early” strategy. In the revised 2009 guidelines, it is recommended that HAART is initiated on all HIV patients with CD4 counts below 350cells/µl, regardless of symptoms (28). Despite this change of recommendations, few low income countries have revised the national ART guidelines and many still recommend that initiation of HAART in asymptomatic HIV-infected persons are delayed until the CD4 count drops below 200 cells/µl (29).

3. OBJECTIVE

3.1 GENERAL OBJECTIVE

To assess determinants of survival in adult patients living with HIV after ART initiation.

3.2 SPECIFIC OBJECTIVES

1. To determine independent determinants of survival in PLHIV after initiation of ART.
2. To estimate the time to death of PLHIV who are on ART.

4. METHODOLOGY

4.1 Study area and period

The study was conducted at Nekemte Referral Hospital, East Wollega from December 1, 2011 to January 1, 2012. The hospital is purposely selected for this study to get adequate number of sample and optimal follow up period. Nekemte Referral Hospital is a governmental referral hospital which gives different specialized clinical services for more than 1.5 million inhabitants from the western part of the country. East Wollega is one of the 18 Zones of Oromia Regional State. Nekemte is the administrative capital of East Wollega Zone and is 331km West of Addis Ababa. In Nekemte Town, there is one hospital and one health center. The Hospital gives preventive, curative and rehabilitative services for a catchment population more than 1.5 million. Also the Hospital provides patient care and treatment for HIV/AIDS related opportunistic infections; provider initiated HIV counseling and testing (PIHCT), for TB; follows complicated cases of TB patients and transfers to health center for DOTs. In addition, the Hospital initiates ART and provides prophylaxis (cotrimoxazole and INH). The ART program of Nekemte Hospital was started in 2005. The ART clinic gives services for HIV patients; a total of 6056 patients have been enrolled, 3200 ever started on ART and 1711 were on ART at the time of the study.

4.2 Study design

An institutional based historical cohort study was conducted in Nekemte Referral Hospital.

4.3 Population

4.3.1 Source population

All HIV positive patients registered for treatment and started antiretroviral therapy in Nekemte referral hospital.

4.3.2 Study population

All adult PLHIV older than age fourteen years and started on ART at Nekemte Referral Hospital, particularly, patients who had started treatment between 2005 and January 1, 2009.

4.3.3 Study subjects

All selected adult HIV infected patients, registered on log book for chronic care and antiretroviral treatment at Nekemte Referral Hospital during the study period.

Inclusion criteria:

- HIV positive adults aged 14 years or older who have been on ART since 2005.
- HIV patients with complete documents and register, intake form and follow up form.

Exclusion criteria:

- HIV patients whose diagnoses were made outside of the health institution (transfer in).
- Transfer out.
- Competing cause of death (cause of death other than HIV).
- Loss to follow up (drop, lost).
- Women who were pregnant at the time of ART initiation and lactating mother (PMTCT).
- Lactating mothers in WHO stage I or II who started ART exclusively to prevent vertical transmission.
- Immunocompromizing Chronic diseases like diabetes, thyroid disease, or any malignancies other than Kaposi sarcoma.

4.4 Sample size determination and sampling technique

4.4.1 Sample size determination

The sample size was calculated using two sample proportion formulas in Epi-Info version 3.5.3 for windows.

$$\text{Let } P=\frac{p1+rp2}{1+r} \text{ and } r = n_2/n_{1=2}$$

$$n_1 = \frac{\left[[Z\alpha/2\sqrt{\left(1+\frac{1}{r}\right)p(1-p)}+Z\beta\sqrt{\left(p1(1-p1)+p2\left(\frac{1-p2}{r}\right)\right)}\right]2}{(p1-p2)2}$$

Where;

P1=mortality rate among non-exposed.

P2=mortality rate among exposed.

$n_{1=}$ stages I-II, HIV infected patients on ART (non-exposed).

$n_{2=}$ stages III-IV, HIV infected patients on ART (exposed).

r=the ratio of exposed to non-exposed HIV infected patients=2

α=level of significance, Zα/2=1.96 at 95%CI

Power=80%=1-β, Zβ=1.28

To determine the sample size, a cohort study conducted at Arbaminch Zonal Hospital, South Ethiopia was used. In that study, categorization was made based on WHO disease stage as WHO Stage III-IV versus Stage I-II. Based on this from their analysis, the mortality rate was 20% (P1=0.20) in stages I-II and 37% (P2=0.37) in stages III-IV (30). Moreover, among the most significant predictors of mortality in most literatures, WHO Staging is the one which gives the maximum sample and strong predictor of mortality among HIV patients (23). In the same way, we assumed that the WHO clinical stage, categorized as Stage III-IV versus Stage I-II, would be the main predictor of mortality in treated patients. Therefore, the sample size was calculated using those mortality rates in unexposed (stages I-II) and exposed (stages III-IV). Taking number of unexposed to number of exposed 1:2 allocation ratio with 80% power and 5% type I error, the resulting sample size was 277. (92, stages I-II HIV infected patients on ART and 185, stages III-IV HIV infected patients on ART). This sample was further multiplied by 1.5 design effect. The final sample size was then calculated as unexposed (stages I-II) (n_1) =138 and exposed (stages III-IV) (n_2) =278 resulting total sample size of **416.**

4.4.2 Sampling technique

Study subjects were selected consecutively based on the inclusion criteria. Profiles of all patients on ART between, 2005 and January 1, 2012 were evaluated and exposure status first identified as stages I-II versus stages III-IV. Then after loss to follow up, drop out, PMTCT, deaths with competing causes, and transfer out or patients started on ART since January 2009 or with incomplete data were excluded. Finally based on the unique ART number, subjects were selected starting from 2005. Then 416 samples from both groups (138 from stages I-II and 278 from stages III-IV) were selected consecutively.

4.5 Data collection procedure

4.5.1 Variables

4.5.2 Independent variables

- Socio-demographic characteristics(age, sex, religion, marital status, employment, educational status and dependent children at home)
- Base line clinical, laboratory and ART information(opportunistic illness, WHO clinical staging, TB test and treatment, ART treatment, chemoprophylaxis, drug allergies, Hemoglobin, T-cell lymphocyte count,CD4count, side effects)
- ART treatment

4.5.3 Dependent variables

The main outcome measure is cumulative survival rates from the initiation of ART to January, 2012.

4.5.4 Data collection tool

The questionnaire consisted of the following parts:

- Socio demographic data
- Baseline clinical, laboratory and ART data
- ART treatment
- Follow up data

4.6 Data collection and quality control

A data collection tool was developed from ART entry and follow up forms being used in the ART clinic of the Hospital. The data were collected by reviewing pre-ART register, lab request, monthly cohort and follow up form, ART intake form, patients' card and death certificate complemented by registration by home visitors and phone calls done by drug adherence supporters to confirm death when patients were absent from their appointment. The most recent laboratory results before starting ART were used as a baseline value. When there was no pre-treatment laboratory test, result obtained within one month of ART initiation was used. A total of three day training was given for one supervisor and two data collectors. The overall data collection process was controlled by the principal investigator of the study. Data quality was ensured by designing proper data collection materials and through checking the collected data on daily bases for completeness and through continuous supervision. All completed data collection

forms were examined once again for completeness and consistency during data management, storage and analysis. The data were entered and cleaned by the principal investigator.

4.7 Data entry, processing and analysis

Data were entered into Epi-Info 3.5.3 for windows and analyzed using SPSS version 16.0 for windows.

The data were edited and cleaned before analysis. Data exploration were undertaken to see if there were items that were not logical and then subsequent editing was made. We described the patient cohort characteristics in terms of mean/median value for continuous data and percentage for categorical data. The end point in this study was death from all AIDS related causes which was confirmed by reviewing medical registration in the Hospital or registration by ART adherence supporters by calling using the registered phone number, individuals alive and on ART at the end of the study period were censored. At the end, the outcome of each subject was dichotomized in to censored or death.

Finally, survival analysis was used to measure the association of patient's characteristics with time from ART initiation to death. Univariate analysis was used to describe patient's baseline characteristics. Life table was used to estimate survival after initiation of ART, and log rank test was used to compare survival curves. Cox proportional-hazard regression was used to calculate the bivariate and adjusted hazard rate to determine independent determinants of time to death.

4.8 Ethical Considerations

Ethical approval was obtained from Research Ethics Committee of the School of Public Health at Addis Ababa University, College of Health Sciences for approval. Following the approval, Official letter of co-operation was written to concerned bodies; Nekemte Referral Hospital and East Wollega Zone Health Bureau by the School of Public Health AAU. As the study was conducted through review of medical records, the individual patients were not subjected to any harm as long as the confidentiality is kept. To keep the confidentiality, ART clinic health officer and nurse of Nekemte Referral Hospital extracted the data from the medical records. In addition to that, no name or personal identifications were used on data collection form. The recorded data were not accessed by a third person, except the principal investigator, and was kept confidentially.

4.9 Dissemination of Study Results

Findings of the study will be communicated to Nekemte Hospital where the study was conducted and to School of Public Health, AAU through hard copy and presentation. The findings will finally be presented on different seminars and published to access others outside.

4.10 Operational Definitions

Immunodeficiency: breakdown in immuno-competence to resist or fight off infections.

Lost: a patient who discontinued ART for at least one to three month as recorded by ART physician or health officer or trained ART nurse.

Opportunistic infections:illnesses caused by various organisms, some of which usually do not cause disease in persons with competent immune systems

Adherence level:

Score	**%**	**of 30 doses**	**of 60 doses**
G(good)	>95%	≤ 2 doses	< 3 doses
F(fair)	85-94%	3-5 doses	3-9 doses
P(poor)	<85%	≥6 doses	>9 doses

Survival: lack of experience of death

Wasting: profound involuntary weight loss of greater than 10% of baseline body weight plus either chronic diarrhea or chronic weakness as documented by physician.

Viral Load: the quantity of HIV RNA in the blood.

Employment status of patients:

- Working: if the patient is full time employee or works on part time base
- Not working: if the patient couldn't work due to HIV related problems
- Unemployed: if the patient doesn't work, not due to HIV related problems but other factors

Drop out: lost to follow up for > 3 months

Transfer out: moving by taking the full medical record from Nekemte Hospital to other health institutions for care and treatment.

Transfer in: if diagnosis was made outside Nekemte Referral Hospital

5. RESULTS

5.1 Socio-demographic characteristics of the study participants.

This study was conducted between November 2011 and January 2012, on 3200 HIV patients ever started on ART. A total of 416 HIV infected patients' records were reviewed for initial and repeated measurements; but repeated values are excluded from the analysis due to the incompleteness of records. Four hundred sixteen (386 alive and 30 death) adult patients were included in the study. Baseline and follow up determinants of survival among HIV patients who started ART were assessed. Patients on ART were followed for a median of 47 months.

Among the study subjects, 174 (41.8%) were males, 58.2% were females, and the mean age was 33.6 (SD=9.04). Three hundred thirty (79.3%) were age<40years, 68.5% were Oromo, 25.2% Amhara, 4.1% Tigire, 2.2% Gurage in ethnicity (Table 1).

Two hundred twenty eight (54.8%) were followers of Orthodox, 35.8% Protestant, 8.4% Muslim, 0.5% Adventist, and 0.5% Catholic religion. One hundred twelve (26.9%) were daily laborers, 25% jobless, 17.5% government employees, 14.2% farmers, 9.9% merchants, 2.6% NGO employee, 2.4% drivers, and 1.4% students in occupation(Table 1).

One hundred thirty five (32.5%) had primary education, 39.4% were not educated, 19.2% had secondary and 8.9% tertiary & above educational level. Three hundred nine (74.3%) had dependent children at home, while 25.7% didn't have any child. Forty (9.6%) of the study subjects were never married (single), 268(64.4%) married, 0.7% separated, 7% divorced, and 18.3% widowed. Two hundred seventy (64.9%) of the study participants were working, 31% not working due to ill health and 2.2% were unemployed (Table 1).

Table 1: Baseline socio-demographic characteristics of HIV patients upon initiation of antiretroviral therapy in Nekemte Referral Hospital, 2012.

Baseline variables	Frequency (n=416)	Percentage
Gender		
Male	174	41.8
Female	242	58.2
Age		
Age 14-40	330	79.3
Age≥40	86	20.7
Ethnicity		
Oromo	285	68.5
Amhara	105	25.2
Tigire	17	4.1
Gurage	9	2.2
Religion		
Protestant	149	35.8
Orthodox	228	54.8
Adventist	2	0.5
Catholic	2	0.5
Muslim	35	8.4
Occupation		
Farmer	59	14.2
Merchant	41	9.9
Government employee	73	17.5
NGO employee	11	2.6
Daily laborer	112	26.9
Jobless	104	25
Driver	10	2.4
Student	6	1.4
Educational status		
No education	164	39.4
Primary	135	32.5
Secondary	80	19.2
Tertiary & above	37	8.9
Dependent children		
Yes	309	74.3
No	107	25.7

Marital status		
Never married	40	9.6
Married	268	64.4
Separated	3	0.7
Divorced	29	7.0
Widowed	76	18.3
Employment status		
working	278	66.8
Unemployed	9	2.2
Not working due to ill health	129	31.0

5.2 Baseline clinical and laboratory information of the study Cohort.

The median weight of the study subjects at the initiation of ART was 51 kg (inter-quartile range (IQR, 45kg-58kg)) (Table 2). The mean hemoglobin level was 12.99 g/dl (IQR, 12.4-13.6). The median CD4 count was 141cells/μl (IQR, 73-199). Among the study subjects, 414 (99.5%) were given Cotrimoxzazole Prophylaxis (CPT) at the time of ART initiation, and 41 (9.9%) had TB co-infection.

Initial ART regimen was d4t (30)-3TC-NVP for 242 patients (58.2%), d4t (30)-3TC-EFV for 82 patients (19.7%), AZT-3TC-EFV for 44 patients (10.6%), AZT-3TC-NVP for 37 patients (8.9%), d4t (40)-3TC NVP for 8 patients(1.9%); d4t (40)-3TC-EFV for 3 patients(0.7%). At ART initiation, 255(61.3%) adults were in WHO stage III, 118(28.4%) were in WHO stage II, 23 (5.5%) were in WHO stage IV and, 20(4.8%) in WHO stage I. Regarding the functional status, 62.7% were working, 34.6% ambulatory and 2.6% were bedridden at ART initiation, 95.9% had good ART adherence, while 4.1% poorly adhered (Table 2).

Adverse side effects to ART were reported in 169 (42.1%) patients including 155 (38.7%) cases of fat change, 1(0.25%) dizzy/ anxiety/ nightmare, 9(2.2%) numbness/tingling, 2 (0.5%) cases of rash and 2 (0.5%) cases of abdominal pain. Regimen change was reported in 169 (42.1%) patients, from those 144 (35.9%) cases due to side effects/toxicity, 3(0.75%) due to pregnancy, 1(0.25%) due to new TB infection, 2(0.5%) due to clinical failure, 7(1.7%) due to immunological failure, and 12(3%) due to other factors, like dizziness, anxiety, and night mere (Table 2).

Table 2: Baseline clinical and laboratory information of HIV patients upon initiation of antiretroviral therapy in Nekemte Referral Hospital, 2012.

Base line Clinical and laboratory information	**Frequency(n=416)**
Weight at presentation (median (25th - 75th quartiles)) (kg)	51 kg (IQR, 45kg-58kg)
Hemoglobin(mean (g/dl))	12.99 (IQR, 12.4-13.6)
CD4 count (median (25^{th} -75th quartiles)) (cells/µl)	141cells/µl (IQR, 73-199)
Cotrimoxazole prophylaxis	
User	414(99.5 %)
Non-user	2(0.5%)
Regimen at baseline	
d4t (30)-3TC-NVP	242(58.2%)
d4t (40)-3TC-NVP	8(1.9%)
d4t (30)-3TC-EFV	82(19.7%)
d4t (40)-3TC-EFV	3(0.7%)
AZT-3TC-NVP	37(8.9%)
AZT-3TC-EFV	44(10.6%)
WHO clinical stage at baseline	
Stage I and II	138(33.2%)
Stage III and IV	278(66.8%)
Functional status	
Working	261 (62.7%)
Ambulatory	144(34.6%)
Bedridden	11(2.6%)
ART adherence	
Poor	17(4.1%)
Good	399(95.9%)
Side effects (**n=401**)	
no side effects	232(57.9%)
fat change	155(38.7%)
dizziness, anxiety, nightmare	1(0.25%)
numbness/tingling	9(2.2%)
rash	2(0.5%)
abdominal pain	2(0.5%)

Status and reason for regimen change (**n=401**)	
not changed	232(57.9%)
toxicity/side effects	144(35.9%)
pregnancy	3(0.75%)
due to new TB	1(0.25%)
clinical failure	2(0.5%)
immunological failure	7(1.7%)
others	12(3%)

As shown in the bar graph below, majority of the patients were in the WHO clinical stage III from which 64.4% were males and 59.1% were females, while 31.4% females and 24.1% males were in stage II, 8.6% males and 3.3% females in stage IV, 6.2% females and 2.9% males in stage I(figure 1).

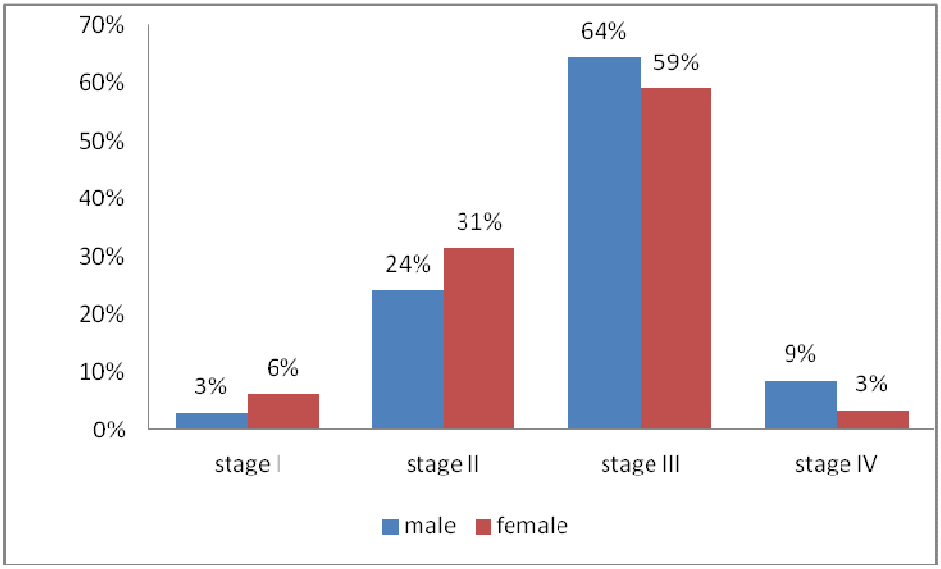

Figure 1: WHO clinical staging at baseline stratified by sex of study participants (n=416) in Nekemte Referral Hospital from February 2005 to January 2012.

As shown in the pie chart below, majority of the patients (83.7%) were initiated ART at CD4<200 cells/ μ L which indicates most of them were in severe immune depression at baseline, while only small portion (5%) of the patients started ART at WHO stage IV (figure 2).

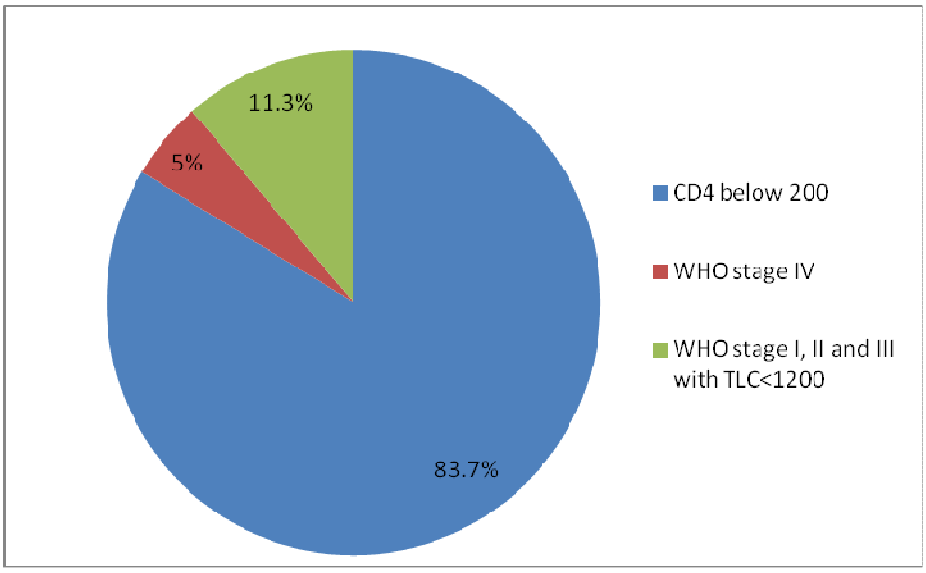

Figure 2: ARV eligibility criteria used to initiate ART at baseline of study participants (n=416) in Nekemte Referral Hospital from February 2005 to January 2012.

5.3 Survival Analysis

A total of 416 patients were followed for a median of 47 months. The minimum follow up time was 14 days and the maximum was 97 months**.** Thirty (7.2%) subjects died; of these 18 (60%) died within 6 months and the rest 92.8% were alive up to the end of last censored date (January 1, 2012). The estimated mortality was 4%, 5%, 6%, 7%, and 7% at 6, 12, 24, 36 and 48 months respectively.

Table 3: Actuarial Table estimates of the cumulative progression to death for 416 study subjects Starting ART between 2005- 2012 in Nekemte referral Hospital.

Life-table

Interval Start Time in months	Number Entering Interval	Number of deaths	Cumulative Proportion of Survival at the end of interval	Hazard Rate
0	416	18	**0.96**	.01
6	395	0	**0.96**	.00
12	395	4	**0.95**	.00
18	391	2	**0.94**	.00
24	388	0	**0.94**	.00
30	388	1	**0.94**	.00
36	386	2	**0.93**	.00
42	306	1	**0.93**	.00
48	205	1	**0.93**	.00
54	154	0	**0.93**	.00
60	148	0	**0.93**	.00
66	138	1	**0.92**	.00
72	66	0	**0.92**	.00
78	10	0	**0.92**	.00
84	4	0	**0.92**	.00
90	2	0	**0.92**	.00

As shown on the life-table analysis above, the Cumulative Proportion of Survival was decreasing at the end of interval as follow up time goes on; while the number of death was very high 18 (60%) in the first 6 months of starting on ART, at the same time mortality rate increases as follow up time increases (Table3).

Kaplan-meier curve showed that patients with BMI ≥18.5kg/m2 were at lower risk of death, while especially patients with BMI <15kg/m2 were at high risk of death compared to others (log rank test, p<0.001) (figure 4).

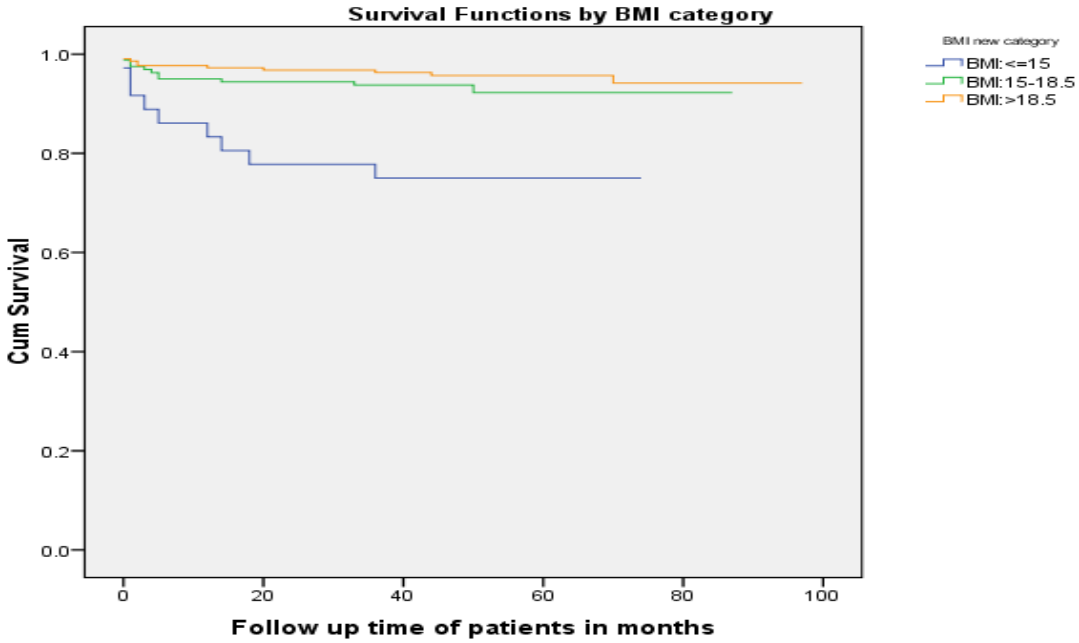

Figure 3: Survival functions of HIV patients by BMI category upon initiation of antiretroviral therapy between 2005- 2012 in Nekemte Referral Hospital.

Kaplan-meier curve showed that functional status of patients who were working at ART initiation were at lower risk of death, while those who are bedridden were at high risk of death compared to others (log rank test, p<0.001)(figure 4).

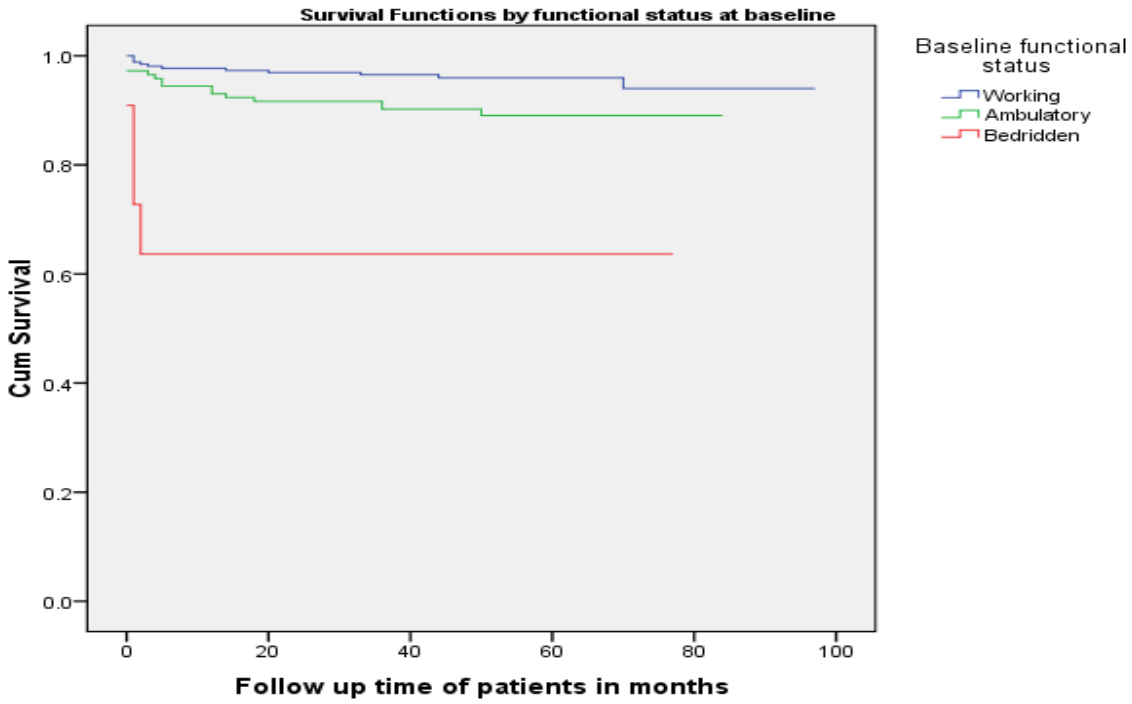

Figure 4: Survival functions of HIV patients by baseline functional status upon initiation of antiretroviral therapy between 2005- 2012 in Nekemte Referral Hospital.

Kaplan-meier curve showed that patients in WHO clinical stage III and IV at ART initiation were slightly at higher risk of death, while those who were in WHO clinical stage I and II at lower risk of death, but the risk is not statistically significant (log rank test, p=0.126)(figure 5). Mortality rate in stage I and II was 1.4%, while it was 6% in advanced disease stage III and IV.

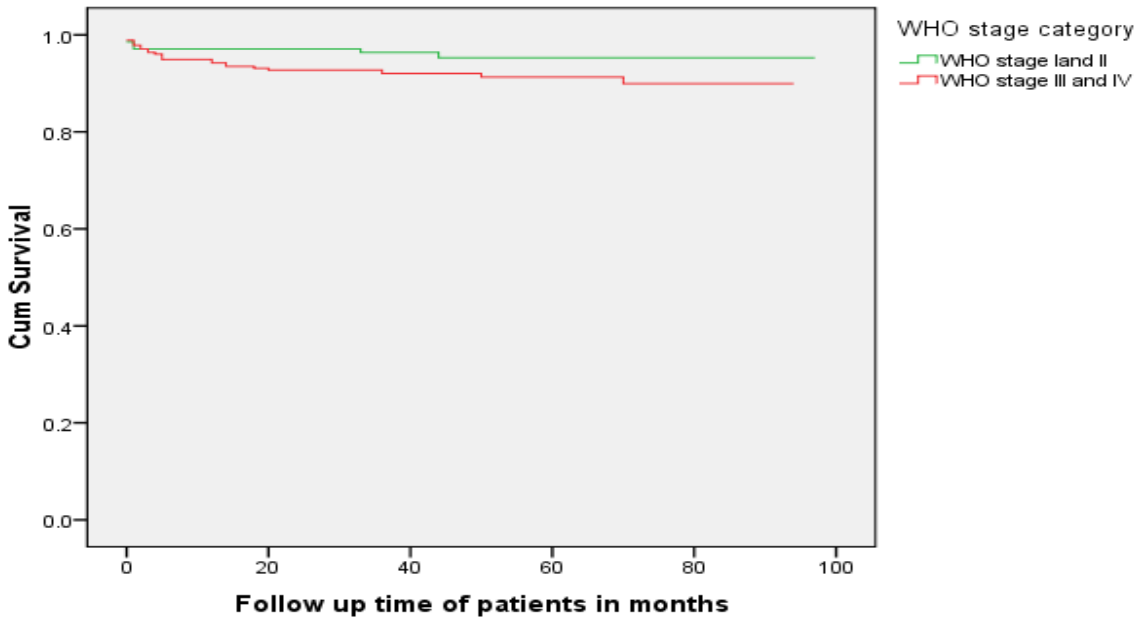

Figure 5: Survival functions of HIV patients (n=416) by WHO clinical stage category upon initiation of antiretroviral therapy between 2005- 2012 in Nekemte Referral Hospital.

As shown in the graph below, overall survivals curve of the cohort starting ART between 2005-2012 in Nekemte Referral Hospital, shows rapid decline of survival in the first 6 months of ART intake (figure 6).

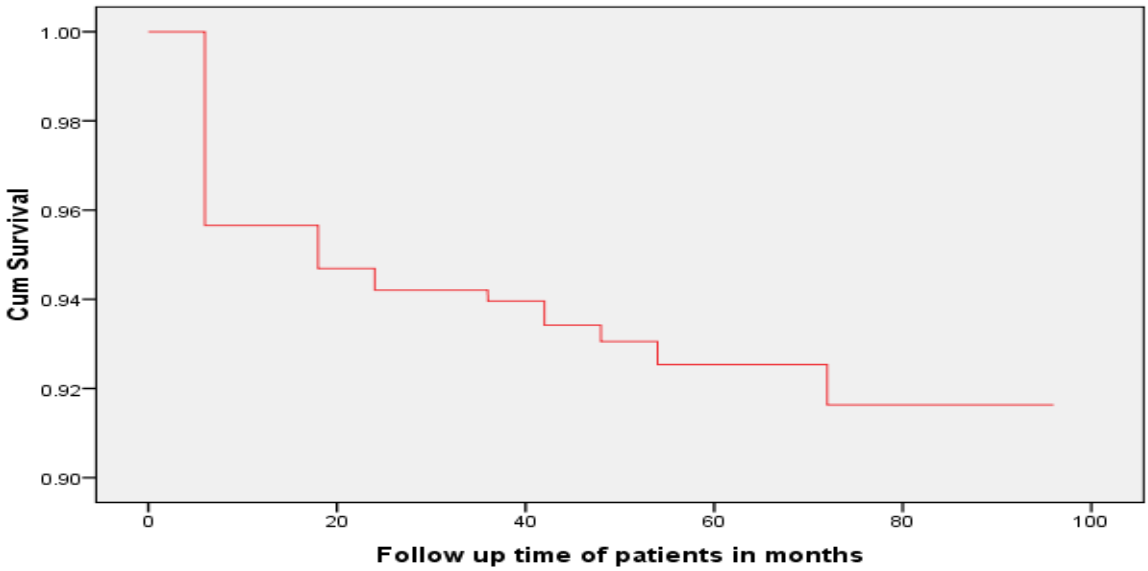

Figure 6: Overall survival curve of the cohort (n=416) starting ART between 2005-2012 in Nekemte Referral Hospital.

Bivariate Cox regression analysis

In bivariate Cox regression analysis, age, sex, educational status, occupation and WHO clinical staging were not associated with survival (table 4). Nevertheless, functional status, dependent children at home, marital status, baseline hemoglobin, CD4 count, TLC (total lymphocyte count) BMI (body mass index), and ART adherence were all associated with survival (as shown in table 4).

Table 4: Bivariate Cox-regression analysis of the cohort studied (N = 416) between 2005-2012 in Nekemte Referral Hospital, Ethiopia.

Determinants	Crude HR(95%CI)
Gender	
Male	1.233(.602, 2.527)
Female	1
Age	
14-40	1
≥40	1.977 (0.925, 4.224)
Educational Status	
Primary and below	1
Secondary and above	2.047 (.784 , 5.349)
Occupation	
Farmer	1
Merchant	2.924(.535, 15.965)
Government employ	1.964(.381, 10.123)
Daily laborer	1.884(.391, 9.071)
Jobless	2.865(.628, 13.075)
Other*	2.053 (0.289, 14.587)
Functional status at baseline	
Working	1
Ambulatory	2.460(1.129, 5.360)#
Bedridden	10.634(3.373, 33.520)#
Dependent children at home	
No	4.013 (1.948, 8.266)#
Yes	1
Marital status	
Married	2.114(.839, 5.329)
Never married	0.243(.094, 0.629)#
Separated	3.207(.405, 25.364)
Divorced	0.886 (0.24, 3.273)
Widowed	1
Baseline Hemoglobin	0.556(.427, .724)#
WHO clinical stage at baseline	
WHO stage I and II	1
WHO stage III and IV	1.982(.810, 4.851)
CD4 count category at baseline	
CD4count:>150	6.287(2.318, 17.051)#
CD4count:100-149	4.340(1.542, 12.217)#
CD4count:50-99	1.499(0.423, 5.314)
CD4count:<50	1
Baseline TLC category	
TLC:>1200	8.183(1.831, 36.576)#
TLC:600-1200	4.655(1.397, 15.518)#
TLC <600	1

BMI category	
BMI:>18.5	6.426(2.599, 15.890)#
BMI:15-18.5	1.553(.659, 3.658)
BMI:<=15	1
ART adherence	
Poor	52.672(24.393, 113.735)#
Good	1

Note: # means statistically significant at 5% level of significance.
*other includes NGO employ, driver and student.

Multivariate analysis using Cox proportional hazard model

In multivariate Cox regression analysis, only variables associated with survival were entered in to the final model including, age and sex as they are the most common cofounders regardless of their association with survival. After adjustment using Cox proportional hazard models, never married (single marital status) AHR=0.285(0.097, 0.840, p=0.023) was protective of HIV mortality, while other factors such as, age≥40years AHR=3.364(1.211, 9.348, p=0.020), lower baseline hemoglobin level AHR=0.49 (0.30, 0.8, p=0.007), and poor ART adherence AHR=132.376(29.909, 585.887, p<0.001) were indicated as significant independent determinants of not surviving after controlling for other factors. Of those, patients with poor ART adherence and older age had the highest risk of death with HR of 132.38 (95% CI 29.9-585.88) and 3.36 (95% CI 1.21- 9.35), respectively, while one unit increase in hemoglobin level reduces HIV mortality by 51% HR 0.49 (95% CI 1.21 -9.35), (Table 5).

Table 5: Multivariate cox-regrssion analysis and model fit of the cohort studied (N = 416) between 2005- 2012 in Nekemte Referral Hospital, Ethiopia.

Determinants	**Crude HR(95%CI)**	**Adjusted HR(95%CI)**
Gender		
Male	1.233(.602, 2.527)	1.563(0.627, 3.896)
Female	1	1
Age		
14-40	1	1
≥40	1.977 (0.925, 4.224)	3.364(1.211, 9.348)#
Functional status at baseline		
Working	1	1
Ambulatory	2.460(1.129, 5.360)#	1.614(.640, 4.071)
Bedridden	10.634(3.373, 33.520)#	1.482(.279, 7.860)
Dependent children at home		
No	4.013 (1.948, 8.266)#	1.026 (.326, 3.227)
Yes	1	1
Marital status		
Married	2.114(.839, 5.329)	1.924(.416, 8.892)
Never married	0.243(.094, .629)#	0.285(.097, .840)#
Separated	3.207(.405, 25.364)	0.413(.024, 7.074)
Divorced	0.886 (0.240, 3.273)	1.209(.246, 5.934)
Widowed	1	1
Baseline Hemoglobin level	0.597(.431, .827)#	0.490(.300, .801)#
CD4 count category at baseline		
CD4count:>150	6.287(2.318, 17.051)#	2.940(.829, 10.427)
CD4count:100-149	4.340(1.542, 12.217)#	2.298(.652, 8.092)
CD4count:50-99	1.499(0.423, 5.314)	0.671(.165, 2.726)
CD4count:<50	1	1
Baseline TLC category		
TLC:>1200	8.183(1.831, 36.576)#	1.265(.138, 11.602)
TLC:600-1200	4.655(1.397, 15.518)#	3.942(.894, 17.375)
TLC <600	1	1
BMI category		
BMI:>18.5	6.426(2.599, 15.890)#	1.385(.427, 4.493)
BMI:15-18.5	1.553(.659, 3.658)	1.058(0.379, 2.958)
BMI:≤15	1	1
ART adherence		
Poor	52.672(24.393,113.735)#	132.376(29.909, 585.887)#
Good	1	1

Note: # means statistically significant at 5% level of significance

6. DISCUSSION

In this retrospective cohort study, we found that the independent determinants of not surviving in patients living with HIV after initiation of ART were age≥40years, lower hemoglobin level at baseline and poor ART adherence, while never married (single marital status) was found to be protective of HIV mortality. In contrast to other studies, in which the WHO clinical stage was found to be stronger predictor of mortality (10, 14, 20); it was not found to be associated with survival in our study. Similar to our finding, in a study conducted in Southwestern Uganda**,** significant association was not found between WHO clinical stage and mortality in the corrected analysis (31). The observed result in our study might be due to the fact that majority of the patients (95.9%) have good ARV adherence, large proportion (33.2%) started ART early at WHO stage I and II and very large proportion (91.4%) of patients in WHO stage III and IV were alive up to the last censored date which indicates low number of events in this category. This may also reflects possible misclassification of WHO clinical staging as it is determined by clinical judgment of health care providers which is the common problem in a setting with limited man power and diagnostic capabilities.

In this study, 7.2% of the patients died, most of the deaths (60%) occurring within the first 6 months. The overall mortality rate was comparable with the study done in Assela and Shashemane hospitals (10.3%) in Ethiopia (20). However, it was lower compared to other studies in Africa, in which it was shown that in Tanzania, 29.7% of the patients died during the first 12 months of ART (10). This could be due to the fact that the real-case scenario (only confirmed dead cases were used as events) was considered that may under-estimate mortality. However, Andinet Worku and Miguel San revealed that, there is a similar finding in both assumptions [a real-case assumption (confirmed dead cases were used as events) and a worst-case assumption (lost cases were also considered as events)], which strengthen our results (20). In addition to this, the worst-case scenario is probably over-estimating the true mortality risk, as in AIDS patients not on ART only 25–50% will have died after 1 year in study conducted by Schneider M, Zwahlen M & Egger M in resource-poor setting (Africa, Asia & Latin America) (32) thus why we preferred the real-case assumption from the very beginning. Furthermore, previous studies were conducted during the early advent of HAART, when there were poor adherence counseling and strong stigma and discrimination; so, higher mortality is inevitable.

The high mortality rate in the first few months of therapy was similar to other studies from different African countries, including Ethiopia (10, 14, 15). The reason is probably that most of the patients in Nekemte (84.4%) had advanced disease as evidenced by a baseline CD4<150 cells/mL and advanced WHO clinical stage in which 66.8% of patients were in WHO stage III and IV. Stigmatization and denial surrounding HIV⁄AIDS and limited availability of VCT services in most areas might have played a role in delaying diagnosis. Lack of proper screening of latent OI and limited availability of prophylaxis, diagnostic facilities and man power to treat AIDS and OIs may have also contributed to the early mortality. In addition to this, about half of the patients (47.6%) were malnourished at baseline (BMI<18.5kg/m^2), and a high proportion (15.6 %) of them were in severe immune depression (CD4 count <50 cells⁄mm3).

According to a study conducted in Zewuditu Hospital in Ethiopia, the estimated mortality was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively (18). However, according to a study carried out by Zachariah R et al in Malawi, the probability of being alive on ART at 6, 12 and 18 months was 89.8%, 83.4% and 78.8% respectively (22). Our study showed estimated mortality of 4%, 5%, 6%, 7%, and 7% at 6, 12, 24, 36 and 48 months respectively. This survival difference might be attributed to, large proportion of the patients started ART at WHO stage I and II (33.2%), there is good follow up, default tracers recruited by ICAP-Ethiopia program supported the patients, high drug accessibility, differences in the types of drug regimen and the study is conducted in regional hospital out of Addis Ababa and the study time is different as well.

There was no significant difference in survival rates between the sexes in our study which is in agreement with the study done in Assela and Shashemane Hospitals in Ethiopia (20). In contrast to this, study done in Arba Minch Hospital revealed that men had higher risk of death AOR= 1.78 (CI:1.47–2.16, p<0.001) (33), as majority of the studies showed females have significantly higher survival than males (3, 10, 34). These studies justified this sex difference in survival by more men are lost to follow up and men poorly adhere than females. But in case of our study, loss to follow up were excluded and there was no association between gender and ART adherence, rather majority of the patients (95.9%) have good ART adherence.

Andinet Worku and Miguel San reported that survival was significantly associated with the clinical stage of the disease, baseline hemoglobin, and cotrimoxazole prophylaxis therapy (CPT) at or before ART initiation (20).

According to Johanssen et al, the significant independent predictors of mortality were CD4 count <50/µl at base line, moderate and severe anemia, thrombocytopenia and severe malnutrition (10). Ojikutu et al, on the other hand indicated that the independent factors predicting higher mortality rate were lymphopenia (TLC<600) and low BMI both in ART+ and ART- group, while anemia was not associated with increased mortality in either group (11). But in our study, low BMI was not a significant determinant of survival which may be due to the recent nutritional intervention for severely malnourished patients in this specific hospital.

In addition to this, low CD4 count and low TLC were also not associated with increased mortality which might be attributed to small sample size and the sample in this study was determined by WHO clinical staging based on the fact that WHO clinical staging is the established independent predictor of mortality from previous studies (10, 11, 30) which may not guarantee significance of CD4 count and TLC (total lymphocyte count); and also almost half of the patients in Nekemte Referral Hospital (45.9%) had a baseline CD4<50 cells/mL that might have made the comparison with the higher CD4 unstable.

On the other hand, single marital status (never married), was protective of HIV mortality, AHR=0.285(0.097, 0.840, p=0.023) in this study. Nevertheless, study conducted in Spain had shown a lower mortality among married persons compared to single and widowed persons supporting a number of studies that have shown an association between marital status and mortality, with most of them finding a lower mortality in married as compared to unmarried persons which most likely reflects the beneficial effect of marriage as a source of social support (35). However, in our case as the study is conducted in a developing country, the result may be attributed to the fact that single individuals are usually free of thinking about dependent children at home and economic problems as they have less social responsibility that may prolong their life; but large scale study should be done for further exploration of this factor.

Study conducted in Arba Minch Hospital in Ethiopia indicated that, those patients aged 45 years and above (OR = 2.04, 95%CI 1.48–2.82) were at higher risk of being in advanced clinical stage at presentation which is one reason among others for high mortality (33). In our study, age 40 years and above [AHR=3.364(1.211, 9.348, p=0.020)] were 3 times at higher risk of mortality than those patients aged less than 40 years which is consistent with previous studies (33, 36). Possible causes of higher mortality rates among the older patients could be because these individuals are at a higher risk of complications such as cancer and respond poorly to ART due to combined effect of aging, HIV infection and antiretroviral treatment (36). In summary, it is the well known fact that as age increases, immune status becomes incompetent and risk for many chronic diseases and death.

In our study, patients with poor ART adherence had the highest risk of death with 132 times more likely to die than adherent patients [AHR 132.38 (95% CI 29.9- 585.88)]. Similarly, a study conducted in Kampala, Uganda, non-adherent participants had a mortality of 42.5 deaths per 100 person-years and, after adjusting for age, sex and education level, were two times as likely to die as adherent participants (37). 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. Non-adherence to HAART also leads to failure to prevent further viral destruction of the cellular immune system with consequent reduction in the level of CD4+ cells and development of opportunistic infections (38). Adherence to HAART is critical to the survival of HIV/ AIDS infected people, because low adherence is the main reason for poor treatment outcomes among people receiving antiretroviral therapy (24). In addition to directly affecting personal well-being, poor adherence may compromise programmatic and economic efficiency, as many people receiving first-line regimens would fail to respond to treatment at an unnecessarily early stage and would therefore need to switch to more expensive, and often unavailable, second-line regimens (24). In our study the hazard rate of poor ART adherence is inflated (132 times than adherent patients) and the CI is very wide showing low precision and lower frequency in this category even if it is highly significant which necessitates large scale study.

Finally in our study, the independent significant determinants of less survival were age≥40years, lower hemoglobin level at baseline, and poor ART adherence which is consistent with other previous studies (3, 10, 11, 20, 24), while single marital status was found to be independent significant determinant protective of HIV mortality.

7. STRENGTH AND LIMITATION

7.1 **Strengths**

- Important baseline variables like BMI, CD4 count and TLC were added to address the limitation of previous cohort studies in Ethiopia.
- Cohort study design
- It may serve as a bench mark for further evaluating WHO recommendation on initiation of HAART in resource limited setting.

7.2 **Limitations**

- One of the limitations of this study was the lack of data on viral load during the course of ART, which could have been more suitable to serve as immunological or virological marker.
- Narrow scope of the study setting, study population being only from one hospital set up and population from specific area.
- Missing data prevented us from analyzing the role of past opportunistic infections on survival time, though several studies report this as an important determinant.
- Adverse side effect to ART and reason for regimen change were not fully analyzed due to 15 missing values (only 401 samples were analyzed in these cases).
- Incomplete and inconsistent follow up values makes it difficult to see the clinical and immunological responses of the patients.
- Selection bias is possibly introduced due to the fact that patients with incomplete records of major variables were excluded.
- Low number of events in poor ART adherence category.

8. CONCLUSION AND RECOMMENDATIONS

This study has shown an overall lower mortality rate, but a high mortality of the cohort in the first 6 months of ART initiation and also has identified the independent significant determinants of less survival in patients living with HIV after initiation of ART which included older age, low baseline hemoglobin level, and poor ART adherence, while single marital status was protective of HIV mortality. These determinants should be taken into account by health care providers to enhance better clinical outcomes.

Based on this finding, the following recommendations can be forwarded for the responsible body:

To health facilities providing ART services

- Preventive efforts should focus on high risk groups.
- The high early mortality has to be addressed by increasing the availability of early HIV diagnosis and treatment services, and by strengthening the quality of existing ones.
- A careful monitoring of patients with lower hemoglobin level at baseline is necessary particularly during the first 6 months of ART initiation.
- Early recognition and managements of risk factors or clinical markers of survival in PLHIV.
- Careful follow up of poorly adhered patients and giving them drug counseling is crucial to improve survival.
- Proper nutritional assessment, including anemia evaluation and treatment, has to be part of routine care.

To East Wollega Zone health bureau and NGOs that work in the area of HIV/AIDS specifically on ART:

- Giving in-service training for the health care providers on HIV/AIDS care and support, especially on how to recognize and manage patients with high risk factors like lower hemoglobin level at baseline, poor adherence and older patients.
- Monitoring, evaluating and getting feedback about the quality of service and care given to the patients either through assigning clinical mentoring or supportive supervision is crucial.

9. REFERENCES

1. UNAIDS. AIDS epidemic update, Geneva December 2009.

2. UNAIDS. UNAIDS report on the global AIDS epidemic. Geneva 2010.

3. Federal HIV/AIDS Prevention and Control Office Federal Ministry of Health E. Guide for implementation of the antiretroviral therapy program in Ethiopia Addis Ababa July 2007.

4. FHAPCO. Country Progress Report on HIV/AIDS Response. Addis Ababa April, 2012.

5. Federal Democratic Republic of Ethiopia PCC, Central Statistics Agency. Summary and Statistical Report of the 2007 Population and Housing Census. Addis Ababa 2008.

6. FMOH E. Health and Health related indicator. Addis Abeba 2010/11.

7. Federal HIV/AIDS Prevention and Control Office Federal Ministry of Health E. Report on progress towards implementation of the UN Declaration of Commitment on HIV/AIDS. Addis Ababa March 2010.

8. UNAIDS. AIDS epidemic update Geneva December 2007.

9. Central Statistical Agency Addis Ababa E. Ethiopia Demographic and Health Survey ICF International, Calverton, Maryland, USA: Central Statistical Agency; 2011.

10. Johannessen A, Naman E, Ngowi BJ, Sandvik L, Matee MI, Aglen HE, et al. Predictors of mortality in HIV-infected patients starting antiretroviral therapy in a rural hospital in Tanzania. BMC Infectious Diseases 2008; 8(52).

11. 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. S Afr Med J2008; 98(3):204-8.

12. MOH/FHAPCO. Single point HIV prevalence estimate June 2007.

13. Federal HIV/AIDS Prevention and Control Office Federal Ministry of Health E. Monthly HIV and ART update. Addis Ababa February 2010.

14. Sieleunou I, Souleymanou M, Scho¨nenberger A-M, Menten J, Boelaert M. Determinants of survival in AIDS patients on antiretroviral therapy in a rural centre in the Far-North Province, Cameroon. Tropical Medicine and International Health 2009; (14) 36-43

15. Jerene D, Næss A, Lindtjørn B. Antiretroviral therapy at a district hospital in Ethiopia prevents death and tuberculosis in a cohort of HIV patients. BMC AIDS Research and Therapy 2006; 3:10.

16. M A, Tang, L D. Increasing Risk of 5% or Greater Unintentional Weight Loss in a Cohort of HIV-Infected Patients, 1995 to 2003. J Acquir Immune Defic Syndr 2005; 40.

17. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. Wolters Kluwer Health | Lippincott Williams & Wilkins 2008; 22:1897-908.

18. Bedru A. Assessment of predictors of survival in patients living with HIV/AIDS after the advent of highly active antiretroviral therapy in Addis Ababa Ethiopia. Addis Ababa: Addis Ababa University; 2009.

19. Hallett TB, Gregson S, Dube S, Garnett GP. The Impact of Monitoring HIV Patients Prior to Treatment in Resource-Poor Settings: Insights from Mathematical Modelling. PLoS Medicine2008 volume 5 (3).

20. Worku A, Sebastia´n MS. Determinants of survival in adult HIV patients on antiretroviral therapy in Oromia, Ethiopia. Global health action 2010;3:5398.

21. Johansson KA, Robberstad B, Norheim OF. Further benefits by early start of HIV treatment in low income countries: Survival estimates of early versus deferred antiretroviral therapy. BMC AIDS Research and Therapy 2010; 7:3.

22. Zachariah R, Fitzgerald M, Massaquoi M, Pasulani O, Arnould L, Makombe S, et al. Risk factors for high early mortality in patients on antiretroviral treatment in a rural district of Malawi. Lippincott Williams & Wilkins2006; 20:2355-60.

23. Mbirimtengerenji ND. Is HIV/AIDS epidemic outcome of poverty in sub Saharan Africa? Croate Med J 2007 48:605-17.

24. WHO/UNAIDS/UNICEF. Towards universal access: scaling-up priority HIV/AIDS intervention in the health sector, Progress report.2009.

25. Grierson J, Koelmeyer R, Pitts ASaM. Adherence to antiretroviral therapy: factors independently associated with reported difficulty taking antiretroviral therapy in a national sample of HIV-positive Australians. British HIV Association HIV Medicine 2011.

26. Rajasekaran, Sikhamani, Jeyaseelan, Lakshmanan, Vijila, Sundaraj, et al. Predictors of failure of first line antiretroviral therapy in HIV infected adults: Indian Experience. Lippincott Williams & Wilkins 2007; 21:S47-S53.

27. Yeni P. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA Panel. JAMA 2004; 292:251-65.

28. WHO. Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents. 2009.
29. Raizes E. A Comparison of the Adult National Antiretroviral Therapy (ART) Guidelines of 15 PEPFAR Focus Countries 2008.
30. Jerene D. HIV antiretroviral therapy in Ethiopia: Overcoming implementation challenges. Centre for International Health University of Bergen, Norway 2007.
31. Geng EH, Glidden DV, Emenyonu N, Musinguzi N, Bwana MB, Neilands TB, et al. Tracking a sample of patients lost to follow-up has a major impact on understanding determinants of survival in HIV-infected patients on antiretroviral therapy in Africa. Tropical Medicine and International Health June 2010;15:63-9.
32. Schneider M, Zwahlen M, Egger M. Natural history and mortality in HIV-positive individuals living in resource-poor settings: A literature review. Geneva: UNAIDS 2004.
33. Mulissa Z, Jerene D, Lindtjørn B. Patients Present Earlier and Survival Has Improved, but Pre-ART Attrition Is High in a Six-Year HIV Cohort Data from Ethiopia. PLoS ONE 2010; 5 (10).
34. Chen SC-C, Yu JK-L, Harries AD, Bong C-N, Kolola-Dzimadzi R, Tok T-S, et al. Increased mortality of male adults with AIDS related to poor compliance to antiretroviral therapy in Malawi. Tropical Medicine and International Health 2008; 13:513-9
35. Burgoa M, Regidor E, Rodriguez C, Gutierrez-Fisac JL. Mortality by cause of death and marital status in Spain. European Journal of Public Health 1998; 8:37-42.
36. Grabar S, Weiss L, Costagliola D. HIV infection in older patients in the HAART era. J Antimicrob Chemother 2006; 57:4-7.
37. Abaasa AM, Todd J, Ekoru K, Kalyango JN, Levin J, Odeke E, et al. Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of The AIDS Support Organization (TASO), Kampala, Uganda. BMC Health Services Research 2008; 8:241.
38. Maggiolo F, Airoldi M, Kleinloog HD, Callegaro A, Ravasio V, Arici C, et al. Effect of Adherence to HAART on Virologic Outcome and on the Selection of Resistance-Conferring Mutations in NNRTI- or PI-Treated Patients. HIV Clin Trials 2007; 8(5):282-92.

10. ANNEX-I: PATIENT INFORMATION SHEET (ENGLISH VERSION):

This study is intended to assess determinants of survival in adult HIV patients after initiation of ART in Nekemte Hospital. The study was conducted through reviewing secondary data. The study will give credible evidence and basic information for governmental and non-governmental organizations which work in the area of HIV/AIDS specifically on ART at national, regional and district level by providing basic information on factors affecting survival of PLWH who started ART treatment. Information which is necessary for the study was taken from ART log book. As the study was conducted through review of medical records alone, the individual patients were not subjected to any harm as far as the confidentiality is kept. To preserve the confidentiality, nurses and health officers working in ART clinic in Nekemte Hospital ART clinic extracted the data from the medical records. Moreover, no personal identifiers were used on data collection form.

Date of review

Day---------- month---------- year----------

Name of reviewer---------- Signature----------

Time started---------- Time ended----------

Total number of records reviewed----------

Reviewed patients card number from----------to----------

Result; (A) complete (B) incomplete (C) excluded

Action taken for incomplete data----------

Name of supervisor----------

Signature----------

Principal investigator address: +251913036311

Date----------/month----------/year----------

Name of data collector---------- signature----------

Name of supervisor----------signature----------

11. Annex II: QUESTIONNAIRE

Part I, Study subject's baseline information (to be filled from ART clinic intake form)

SECTION-I: SOCIO DEMOGRAPHIC CHARACTERISTICS.

NO	Variables	Coding categories	Remark
101	Unique ART number		
102	Age of the patient		
103	sex	1. Male 2. Female	
104	Ethnicity	1. Oromo 2. Amhara 3.Tigire 4. Gurage 99.Other(specify)_____	
105	Religion	1. Protestant 2.Orthodox 3. Adventist 4.Catholic 5.Muslim 99. Others specify_____	
106	Educational status	1. No education 2.primary(1-8) 3. Secondary (9-12) 4. Tertiary & above	
107	Occupational status	1. Farmer 2. Merchant 3. Governmental employee 4. NGO employee 5. Daily laborer 6. Jobless 7. Driver 99. Others (specify)____	
108	Marital status	1. Never married 2. Married 3.separated 4. Divorced 5. widower	
109	Dependent children at home	1.yes 2.no	

SECTION 2- BASE LINE CLINICAL, LABORATORY AND ART INFORMATION.			
NO	VARIABLE S	CODING CATAGORIES	Remark

201	Past opportunistic illness (list all mentioned)	0. No 1.candidiasis 2.CMV 3.Crypt.meningitis 4.Kaposi's Sarcoma 5. Cryptosporiodiosisis 6. Diarrehea 7. Diss.atypical.myco. 8.Encephalopathy 9.fever 10.Herpes simplex 11. Minor mucocuan.man. 12.mycosis 13. PGL 14. PCP 15.PML 16. Pneumonia 17.salmonella 18.EPTB 19.Toxoplasmosis 20. Wasting syndrome. 21.other specify_____	
202	Past TB test	1.No 2.Not determined 3.Positive 4.Pos+1 5.Pos+2 6.Pos+3 7.unknown	
203	Past TB treatment	1.No 2.Not determined 3.2SRHZ/6EH 4.2HRZES/1HRZE/5HRE 5.2HRZE/6HE	
204	past CD_4 test	1. Yes, date [_____/_____/_____] 2. No	
205	Past medications (check all)	1. No 2. Cotrimoxazole 3. INH 4. Fluconazole 5. Other medications	
206	Height(cm) at base line	_____	(look, Vital signs part)
207	weight(kg) at base line		
208	Functional status at base line	**W**. working **A**. Ambulatory **B**. bedridden	
209	WHO Clinical stage of HIV disease at base line	1.Stage I 2.Stage II 3.Stage III 4.Stage IV	
210	WHO Clinical stage of HIV disease at base line	1.Stage I or II 3.Stage III or IV	
211	Hemoglobin at base line		

212	CD4 count at base line	_____date[_____/_____/_____]	
213	WBC at base line		
214	TLC at base line		
SECTION 3- Base line Social conditions			
301	Employment	1.working 2.working full time 3. Working part time 4. unemployed 5.not working /staying due to ill health 6.other specify_____	
302	Religious /supportive care	1. No b. Yes	
303	HIV sero-status disclosure	1.wife/husband knew 2.own children 3.parent(s) 4.brother(s)/sister(s) 5.relatives 6.no body knew 7.others specify_____	
304	Spouse information		
	1.condition of the husband/wife	a. health b. chronically ill c .dead d. unknown	
	2.HIV tested	a. not asked b. negative c. positive d. unknown	
	3.Tb tested	a. not asked b. negative c. positive d. unknown	
	4.was/is on Tb treatment	a. yes b. no	
	5. was/is on ART treatment	a. yes b. no	
305	General concern identified	1.financial issue 2.about the children 3.marital relationship 4.family relations 5.beravement/grief 6.HIV status disclosure 7.adherence to treatment 8.dietary problems 9.other specify_____	
SECTION 4. Risk behavior			
401	Had regular sexual partner	1.yes 2.no	
402	Had causal sexual partner	1.yes 2.no	
403	If yes, no of causal partner in last 3 months	A.1 B.2 C.3 D.>3	

404	Condom use	1.NA 2.never 3.rarely 4.sometimes 5.mostly 6.always 7.no response	
405	Barriers to ART adherence	1.stigma (from family and friends) 2.afraid of medications(side effects:"poison") 3.doubt that medications will work 4.depressed/anxious 5.will forget to take medications 6.other specify_____	
406	Impression about mental condition	1. At ease 2.Confused 3.Depressed 4.Anxious 5.Suicidal	
407	Barriers to ART adherence	1.stigma (from family and friends) 2.afraid of medications(side effects:"poison") 3.doubt that medications will work 4.depressed/anxious 5.will forget to take medications 6.other specify_____	
408	**Addictions**		
	A. tobacco	1. NA 2.- 3. + 4. ++ 5. +++	
	B. alcohol	1. NA 2.- 3. + 4. ++ 5. +++	
	C. soft drugs (e.g. Khat, shisha, pills, etc)	1. NA 2.- 3. + 4. ++ 5. +++	
	D. hard drugs(e.g. cocaine, morphine, IV drugs, etc)	1. NA 2.- 3. + 4. ++ 5. +++	
SECTION 5. ART and treatment			
501	ARV eligibility criteria used	1.CD4 below 200 2 .CD4 below 350 3.WHO stage IV 4.WHO stage I,II, and III with TLC<1200	
502	OI prophylaxis at base line	0. Not given 1.cotrimoxazole 2.INH 3.fluconazole 4. Other_____	

503	Regimen Recommended at base line	1)1a (30) =d4t (30)-3TC-NVP 2)1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7)2nd line regimens(2a/2b/2c/2d)	
Part II. Patient's follow up information (to be filled from ART follow up form). Please document the current or the recent results.			
600	**variables**	**Coding categories**	**Remark**
601	Latest follow up date	[_____|_____|_____] E.C	
602	Date confirmed HIV+	[_____|_____|_____] E.C	
603	**Eligible date (ART initiated date)**	[_____|_____|_____] E.C	
604	Duration in months since initiation of ART	_____(wks/month)	
605	recent weight	_____(in kg),date[_____|___|_____]	
606	recent functional status	**W**. working **A**. Ambulatory **B**. bedridden	
607	recent WHO staging	1.Stage I 2.Stage II 3.Stage III 4.Stage IV	
608	TB screened recently	1. No 2. Positive 3. negative	
609	recent Tb prophylaxis	1. No 2. yes	
610	recent Tb treatment	1. No 2. yes	
611	Recent Opportunistic infections	0.No 1.Zoster 2.bacterial pneumonia 3.PulmonaryTB 4.ETB 5.oral(vaginal) thrush 6.mouth/genital ulcer 7.chronic or acute diarrhea 8.PCP 9.CNS toxoplasmosis 10.Cryptococal meningitis	

		11. others specify----------	
612F	Cotrimoxazole	1. not given 2.good 3. Fair 4. poor	
613	Recent ARV adherence	1. Good 2. Fair 3. poor	If 1,skip to 615
614	Reason for fair or poor adherence	1.Toxicity/side effect 2.Share with others 3. Forgot 4. Felt better 5.Too ill 6.alcohol 7.stigma disclosure 8.drug stock out 9.lost/run out of pills 10.inability to pay 11.delivery/travel problems 12.depression 13.other specify_____	
615	Recent Dispense (code/dose)	1)1a (30) =d4t (30)-3TC-NVP 2)1a (40) =d4t (40)-3TC-NVP 3) 1b (30) =d4t (30)-3TC-EFV 4) 1b (40) =d4t (40)-3TC-EFV 5) 1c= AZT-3TC-NVP 6) 1d=AZT-3TC-EFV 7)2nd line regimen (2a/2b/2c/2d)	
616	Side effects	0. No side effects 1. Nausea 2. diarrhea 3. Fatigue 4. Headache 5.numbness/tingling 6.rash 7. anemia 8.abdominal pain 9.jaundice 10.fat change 11.dizzy,anxiety, night more	
617	Reason for regimen change	0. Not changed 1.toxicity/side effects 2.pregnancy 3.Risk of pregnancy 4.due to new TB 5.new drug available	

		6.drug out of stock 7.clinical failure 8.immunological failure 9.virological failure 10.other_____	
618	Reason for stopping regimen	0. Not stopped. 1.toxicity/side effects 2.pregnancy 3.treatment failure 4.poor adherence 5.illness hospitalization 6.drug out of stock 7.patient lack finance 8.other patient decision 9.planned treatment interruption 10.other_____	
619	Recent CD4 count	_____ [_____/_____/_____]	
620	Recent WBC		
621	Recent TLC		
622	Recent Hgb		
623	Recent ALT		
624	Recent AST		
625	**outcome of the patient at the end of follow up**	1. **active**[_____/_____/_____] E.C 2.**dead**[_____/_____/_____]E.C	

ANNEX-III CONSENT FORM (ENGLISH VERSION) (TO BE USED FOR ALIVE PATIENTS IN CASE, IF THEY COME FOR FOLLOW UP)

My name is _____, I am ART clinic nurse/health officer working in Nekemte Hospital ART clinic and now I am collecting data from our patients ART logbook for the research being conducted to assess determinants of survival in adult HIV patients after initiation of ART in Nekemte Hospital by Mitiku Teshome who is the student of Masters in Public Health in Addis Ababa University. You are selected as one of study subject by chance. The investigator employed me (from this ART clinic) for this data collection to maintain your data strictly confidential, We believe that the findings of this study will have some evidence and information for governmental and non -governmental organizations which work in the area of HIV/AIDS specifically on ART at national, regional and district level by providing credible evidence & basic information on factors affecting survival of PLWH and who started ART treatment.

Information which is necessary for the study will be taken from your ART log book. As the study will be conducted through review your medical records alone, it will not cause any harm as far as the confidentiality is kept. The information will be taken when you give permission, participation is totally voluntary. Your willingness for your ART record information to be utilized in this study will help us achieve the stated benefits of the study. Your name and other personal identifiers will not be recorded on data collection form and the information that you give us will be kept confidential and will also be used for this study purpose only. You have full right not to let your information on ART logbook to be used for this study. But the information that would be taken will be quite useful for the study. You will not face any problem if you do not allow the information to be taken from your records and you will not also be denied of getting any medical services from the hospital. If you have any questions about this study you may ask me or the principal investigator Mitiku Teshome Tel: 0913036311

E-mail: mitikkuuf@gmail.com

Are you willing to let your information to be used for this study?

1. Yes 2. No (End the interview)

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study _____

ANNEX IV: INFORMED CONSENT FORM (AFAN OROMO VERSION)

Uunka Hayyamsiisa maamilaa qoraqnnoo keessatti hirmaatanii ibsu.

Maqaan koo _____jedhama. Ogeessa fayyaa hojjetaa hospitaala kanaa yommuun ta'u, qorannoo matadureensaa 'namoota dawwa HIV/AIDS kan umurii dheeressu fudhataniif akka isaan umurii dheeraa jiraataniif wantootni gargaaran maalfa'i' jedhamu; Uunvarsiitii Finfnneetti barataa Fayyaa digirii lammaffaa kan ta'e obbo Mitikkuu Tashoomeen qoratamuuf galmee wal'anamtootaarraa funaanaa jira.Qorataan kun anaan nama galmee kanarra hojjetu kan nafileef akka iccitiin wal'aanamtootaa eegamuuf jedheeti. Jechuun nammootni kiliinika kanaa ala jiran yommuu ragaa kana funaanan maqaa keessaniif ragoolee kan biraas akka hin argineef jecha.

Qorannoon kun bifa Saayinsawaa ta'een raga funaanee dhiyeessuudhaan, sagantaa ittisaaf qorannoo HIV maalirra akka jiru madaaluuf akkasumas namoota vaayirasii nkanaa wajjin jiraataniif eega nnoon addaa akka taasifamuufiif buu'aan isaa guddaadha jedhamee yaadama. Kanaafis ragooleen qrannoo kanaaf barbaaadaman galmee ART keessan irraa funaanama. Qorannoon kun galmeerraa fudhatama waan ta'eef isin irratti miidhaa fidu tokko hin qabu. Ragaa kana yoo nuu eyyamtan kaayyoo qorannoo kanaaf bu'aansaa guddaa dha. Galmee keessan irraa ragaan yommuu sassabamu maqaan keessanin fi waantootni isi ibsan tokkolleee hin fudhataman. Ragaan fudhatamu kun icciitiinsaa guutumaa gutuutti eegamee qorannoo kana qofaaaf oola. Ragaan keessan akka qorannoo kanaaf hin oolle dhorkuuuf mirgaa qabdu; garuu, ragaan kun qorannoo kanaaf yoo oole bu'aansaa guddaaa dha. Ragaa keessan kana yoo qorannaa kanaaf hin kennu jettan tajaajila yaalaa keessan irraatti dhiibbaan isiinirra ga'u tokko hin jiru. Gama biraatiin raga kana waan kennitaniif bu'aa dhuunfaa/addaa argattan hin qabdan. Qorannaa kana ilaalchiisee gaaffii yoo qabaattan ana ykn qorataa olaanaa(PI) gaafachuu ni dandeessu.

Ragaan kun akka qorannaa kanaaf oolu fedha qabduu?

1. Eeyyee 2. Lakkii

Ragaan kana eeyyamaniiru. Maqaa fi mallattoo nama ragaa funaanee_____