PREDICTORS OF SURVIVAL STATUS AMONG PEOPLE LIVING WITH HIV AFTER ANTIRETROVIRAL THERAPY INITIATION, IN JIJIGA ZONE, SOMALI REGION, EASTERN ETHIOPIA.

BY:- MAHLET YEWONDWESSEN

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BY:-MAHLETYEWONDWESSEN (BSC)

ADVISOR(S):- MR. WONDWOSEN KASSAHUN (PHD)

: - MR. DESALEGN MASSA (BSC, MPH)

ABSTRACT

Back ground: Antiretroviral Therapy ART has shown to delay progression to AIDS, improve survival, and result in a greater and more sustained virologic and immunologic response. In addition it reduces morbidity and mortality, however, the durability of the effectiveness of HAART remains to be delineated because various factors influence its effectiveness.

Objective: To investigate the survival status and identify the potential predictors of mortality after initiation of ART among PLHIV in Jigjiga Karamara hospital, Jigjiga zone, Somali region, Eastern Ethiopia.

Methods: A retrospective follow up study was conducted. Data was collected from February 2014 to March 2014. Secondary data all clients started ART treatment between January 2009 and December 2013 who fulfill inclusion criteria have been included in this study. Both descriptive and inferential statistics methods were done. Hazard ratios were computed for potential covariates after checking the assumption of Cox PH model. All variables significant at $P < 0.25$ level in the bivariate analysis were included in the final multivariable model and independent predictors was identified by making use of AHR, 95%CIs, and p value <0.05 as a cut-off point for statistical significance. All analyses was made using SPSS version 16.0 for windows.

Result: Study participants were 822 adult patients who started ART in Kharamara hospital. They were followed for a median of 22 months. This study demonstrated that simple laboratory and clinical data, prior to ART initiation, can predict patients increased risk of mortality. The identified independent significant predictors of survival status after initiation of ART were being male sex (AHR=2.55, 95%CIs (1.02-2.52)), bedridden functional status (AHR=3.75, 95%CIs (1.33-10.59)), advanced WHO staging III (AHR=3.48, 95%CIs (1.05-11.54)) and IV (AHR=4.13, 95%CIs (1.21-14.10)), low CD4 count < 50cells/µl(AHR=7.57, 95%CIs (3.38-16.9)) and <50-99cells/µl (AHR=5.85, 95%CIs (2.57-13.)), lower BMI<18Kg/m^2 (AHR=6.11, 95%CIs (2.06-18.14))and poor ART adherence(AHR=9.59, 95%CIs (5.03-18.20)).

Conclusion & Recommendation: The study cohort had similarly lower mortality rate when compared to other earlier studies conducted in Ethiopia and other African countries. This emphasizes the importance of ART in reducing morbidity and mortality among PLHIV. However, a lot needs to be done regarding patient retention and adherence.

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ABBREVIATIONS

3TC	Lamuvidine
ABC	Abacavir
AHR	Adjusted Hazard Rate
AIDS	Acquired Immune Deficiency Syndrome
ANC	Ante natal care
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ART	Antiretroviral Therapy
ARV	Anti-Retroviral drug
BMI	Body Mass Index
CI	Confidence Interval
CMV	Cytomegalovirus
CPT	Cotrimoxazole Prophylaxis Therapy
CSA	Central Statistics Agency
d4T	Stavudine
ddI	Didanosine
EDHS	Ethiopian Demographic Health Survey
EFV	Efavirenz
EPTB	Extra Pulmonary Tuberculosis
FMOH	Federal Ministry Of Health
HAART	Highly Active Antiretroviral Therapy
HAPCO	HIV/AIDS Prevention and Control Office
HEP	Health Extension Program
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
HSDP	Health Service Development Plan
IDV/r	Ritonavir Boosted Indinavir
LPV/r	Ritonavir Boosted Lopinavir
LTFU	Lost To Follow Up
MOH	Ministry of Health

NFV	Nelfinavir
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
OI	Opportunistic Infection
PGL	Persistent generalized lymphadenopathy
PH	Proportional Hazard
PI	Protease Inhibitor
PLHIV	People Living With HIV
PML	Progressive Multifocal Leukoencephalopathy
PYO	Person Year of Observation
RNA	Ribonucleic Acid
SQV/r	Ritonavir Boosted Saquinavir
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
TB	Tuberculosis
TDF	Tenofovir
TLC	Total Lymphocyte Count
UNAIDS	United Nations Joint Program on HIV/AIDS
VCT	Voluntary counseling Testing
WHO	World Health Organization
ZDV	Zidovudine

1. INTRODUCTION

1.1 Background

The emergence of the Human Immunodeficiency Virus epidemic is one of the biggest public health challenges the world has ever seen in recent history. In the last three decades HIV has spread rapidly and affected all sectors of society- young people and adults, men and women, and the rich and the poor. Sub-Saharan Africa is at the epicenter of the epidemic and continues to carry the full brunt of its health and socioeconomic impact [1].

HIV is transmitted from one person to another through sexual contact, invasive contact with potentially infective body fluids, or prenatally. Worldwide, 75% to 85% of HIV infections are transmitted through unprotected sex. There is a risk of transmitting HIV when body fluids come in contact with a part of the body that lets them enter the bloodstream. This can include the vaginal mucosa, anal mucosa, and wounds or sores on the skin [2].

On average, there is a period of 8 to 10 years from initial infection to clinical AIDS in adults, though AIDS may be manifested in less than 2 years or be delayed in onset beyond 10 years. HIV infection does not follow the pattern of more traditional viral diseases in which the risk of serious illness or death decreases with time. There has been no study to date that shows a failure of HIV-infected persons to evolve to clinical AIDS over time, though the speed at which this evolution occurs may vary, and a small number of HIV-infected persons will not progress to AIDS for many years [3].

Long-term sustainable treatment is one choice for people living with HIV. Not only can medications slow the progression of the infection, but can also markedly suppress the virus, thereby restoring the body's immune function and permitting many HIV-infected individuals to lead a normal life. People living with HIV take a number of medications like cotrimoxazole, fluconazole, INH and other medications depending on the type of the opportunistic illness they have. Even though AIDS drugs have become cheaper and more available because of a variety government and private programs, millions of others still do not have access to the drugs. WHO recommends that in resource-limited settings HIV infected adolescents and adults should start ART when the following conditions are met:

WHO stage 4 regardless of CD4 count, stage 3 disease with consideration of CD4 count below 350/mm in assisting decision making, stages 1 or 2 diseases with CD4 cell count below 200/mm. In a setting where CD4 count is not available, the total lymphocyte count (TLC) can be used, and treatment is recommended for WHO stages 3 or 4 (clinical AIDS) irrespective of the TLC and stage 2 with TLC not exceeding 1200/mm [4].

Antiretroviral treatment is the main type of treatment for HIV / AIDS. It is not a cure, but it can stop people from becoming ill for many years. The treatment consists of drugs that have to be taken every day for the rest of someone's life. ART for HIV infection consists of drugs, which work against the virus by slowing down the replication of HIV in the body. For antiretroviral treatment to be effective for a long time, from different category should be taken more than one antiretroviral drug. This is what known as Combination Therapy. Alternatively, modern HIV treatment also called HAART [5].

Taking two or more antiretroviral drugs at the same time vastly reduces the rate at which resistance develop to the drug. It prolonged and improved the lives of hundreds of thousands people in the world. Its benefits are now finally starting to extend to resource constrained settings where 90% of people with HIV/AIDS are living [6].

The discovery of antiretroviral therapy has been one of the" greatest successes" in the history of medicine. Combination antiretroviral therapy (ART), or highly active antiretroviral therapy (HAART), is the cornerstone of management of patients with HIV infection (clinical AIDS) irrespective of the TLC and stage II with TLC not exceeding 1200/mm [4].

The benefits of highly active antiretroviral therapy (HAART) in the treatment of HIV infection have been well described including viral suppression, CD4 lymphocyte repletion, and durable reductions in AIDS related opportunistic diseases and death. However, the durability of the effectiveness of HAART remains to be delineated [7]. Although AIDS-related mortality is declining, it is still unacceptably high. Large numbers of people do not yet know that they are living with HIV, and many of them are eligible for ART [8].

1.2 Statement of the problem

Currently there are 34 million people living with HIV and AIDS compared to 26.2 million more than a decade ago in 1999. The global incidence of HIV infection has stabilized and begun to decline in many countries with generalized epidemics. The number of people accessing treatment increased by 63 percent from 2009 to 2011; however 7 million people eligible for treatment is not getting it. Of even more concern is the fact that 72 percent of children worldwide who are eligible for treatments are not accessing it [9].

Ethiopia is one of the few sub-Saharan countries showing a decline of more than 25% in new HIV infections [10]. Data indicate a declining trend of HIV prevalence: a success and cause for optimism. However, with nearly 800,000 people living with HIV, Ethiopia remains a country highly affected by the epidemic [1]. Although the HIV/AIDS prevalence in Ethiopia is lower than many other Sub-Saharan African countries, there are still an estimated 780,254 (revised estimated 2012) people living with HIV, placing substantial demand on the country‘s already strained care and treatment resources as it has the fourth highest burden of PLHIV in East Africa [11].

Results from the 2005 EDHS indicate that 1.4% of Ethiopian adults age 15-49 were infected with HIV. Data for 2011 EDHS show a prevalence of 1.5%. For both men and women HIV prevalence levels rise with age, peaking among women in their early to mid-30s and among men in their late 30s. The age patterns suggest that young women are particularly vulnerable to HIV infection compared with young men [12].

The primary goals of antiretroviral therapy are preventing HIV-related morbidity and improving quality of life, reducing mortality and improving survival, restore and preserve immunologic function, maximally suppress viral load, and ultimately preventing mother to child transmission [6]. ART has clearly shown to be effective in reducing mortality among those who remain in treatment and adhere to therapy. In recent years in developing countries with a high burden of AIDS, ART has become more widely available.

According to estimation by the World Health Organization (WHO), about 6, 650,000 patients were receiving ART in low and middle income countries by the end of 2010, which is a huge improvement from the levels in 2003. In Ethiopia, there were more than 222,000 patients on

antiretroviral treatment at the end of 2010[13]. ART has improved the survival and improved the quality of life of people with HIV/AIDS [14].

Recognizing the benefits, the Ethiopian government has made concerted and sustained effort over the last several years to introduce and scale-up counseling and testing services and use of antiretroviral drugs both for treatment and prophylaxis. A National Guideline on the use of ARV drugs was developed and the Antiretroviral Treatment program was launched in 2003. Subsequently, in 2004, a free ART program was initiated in three government hospitals in Addis Ababa. The efforts have led to marked increase in the number of health facilities and sites providing HIV treatment and care services. While there were 550 facilities providing ART in 2009/10, this reached 743 public and private health facilities in 2010/11 fiscal year. Overall, with the increase and fast expansion of facilities providing ART, coverage has increased over the years. As a result, currently the ART coverage for adult populations is high (86% of estimated eligible) for CD4 cutoff less than 200[1].

Despite this, 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. Patients typically access ART with advanced symptomatic disease, and mortality is strongly associated with baseline CD4 cell count less than 50 cells/ml and WHO stage IV diseases (AIDS). Although data are limited, leading causes of death appear to be tuberculosis, acute sepsis, cryptococcal meningitis, malignancy and wasting syndrome [15]. Factors that limit the success of HAART include poor therapy adherence, regimen complexity, viral resistance, pharmaco -dynamic interactions, drug tolerability and toxicity, therapy costs, and presence of co -morbid conditions such as substance abuse and addiction [13].

ART decreases human immunodeficiency virus (HIV) viral load, increases the CD4 T-cell count, and dramatically improves survival. However, 90 percent of the world's 40 million people with HIV infection or AIDS live in developing countries, where high rates of co-infection with tropical diseases, tuberculosis, and malnutrition, together with limited laboratory monitoring, may decrease the efficacy of antiretroviral therapy. Since treatment has only recently become available in developing countries, data on the effects of antiretroviral therapy in these settings are limited [16].

The availability of body of research evidences that addresses issues about HIV/AIDS in Ethiopia is very large. But the level of understanding about factors associated with mortality rate of PLHIV as a result of HIV related death is low. Since now little is known about the survival status and predicting factor of early mortality in HIV patients after the initiation of HAART in resource limited settings like our country. Therefore, this study tries to elaborate survival status and its predictors of mortality among HIV patients after the initiation of ART.

2. LITERATURE REVIEW

2.1 Burden of HIV/AIDS and ART

Globally, an estimated 35.3 (32.2–38.8) million people were living with HIV in 2012. There were 2.3 (1.9–2.7) million new HIV infections globally, showing a 33% decline in the number of new infections from 3.4 (3.1–3.7) million in 2001. At the same time the number of AIDS deaths is also declining with 1.6 (1.4–1.9) million AIDS deaths in 2012, down from 2.3 (2.1–2.6) million in 2005. Two - thirds of all people infected with HIV live in Sub-Saharan Africa, although this region contains little more than 12 percent of the world's population [17]. During 2010 alone, an estimated 1.2 million adults and children died as a result of AIDS related illnesses in Sub-Saharan Africa. Since the beginning of the epidemic more than 15 million Africans have died from AIDS related illnesses [18].

The demonstrated benefits of ART in terms of averted deaths and prevented infections exceed many of the expectations. By the end of 2011, 8 million people had started antiretroviral therapy (ART) worldwide. The roll out of ART has added 15 million life years in low and middle-income countries, and it is estimated that it can reduce the HIV incidence by 17-32% [19].

Globally 1.6 million more people were receiving ART in 2012 compared with 2011, the largest increase ever in one year. The extent of ART provision differs considerably between regions. In 2012, ART continued to be rolled out at a remarkable pace in the African Region, which bears a disproportionately large s hare of the global HIV burden [1].

Although access to ART is starting to lessen the toll of HIV/AIDS, fewer than half of African who needs treatment are receiving it [17]. In 2011, an estimated 10.9 million [10.3 – 11.6 million] people in this region needed ART (according to the 2010 WHO treatment guidelines), of whom 6.2 million were receiving it. The number of people on ART increased by one fifth to more than 7.5 million at the end of 2012.

2.2 HAART and Estimates of Survival in PLHIV on ART

HARRT significantly decreases mortality overall, but death rates are also highest in the first three months of ART. These complications are commonest when the people starting ART

already have advanced HIV disease with severe immunodeficiency and existing co -infections and /or co-morbidities, severely low hemoglobin, low body mass index and very low CD4 counts or are severely malnourished [20].

For PLHIV starting ART when symptomatic, an average six potential life years per person treated would be saved. On the other hand, if individuals were recruited to programs while still healthy and are frequently monitored with their CD4+ cell counts used to help decide when to initiate ART, three times as many, would have been expected to be treated, and average life -years saved among those treated increases to 15years [21].

In a study from Malawi, the probability of being alive on ART at 6, 12, and 18months was 89.8%, 83.4%, and 78.8% respectively [22]. In a study from South Nations, Nationalities, and Peoples Region (SNNPR), the cumulative mortality rate was 7.45/100 Person-year of observation (PYO) in which 70.8% (335/473), 15.2% (72/473), 11.0% (52/473) and 2.9%(14/473) deaths occurred in the first 6 months, six to one year, one to two years, and after second year of follow up respectively [23]. In a study in western Ethiopia 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 (95%CI 1.74, 3.62)[24].

Study conducted in Thailand showed that the Survival rates at 1, 2, and 3 years after TB diagnosis were 96.1%, 94.0%, and 87.7% respectively for ART+ group and 44.4%, 19.2%, and 9.3% respectively for ART group (log-rank test, P<0.001). Among patients in ART+ group, the patients who delayed ART>or=6 months after TB diagnosis had a higher mortality rate than those who initiated ART<6 months after TB diagnosis (P 0.018, hazard ratio=2.651, 95% confidence interval=1.152-6.102) [25]. The 5-year risk of AIDS or death (death alone) from the start of HAART ranged from 5.6 to 77% (1.8-65%), depending on age, CD4 cell count, HIV-1-RNA level, clinical stage, and history of injection drug use. From 6 months on the corresponding figures were 4.1 -99% for AIDS or death and 1.3-96% for death alone [26].

Providing HIV care and treatment for co -infected TB patients through HIV testing, with cotrimoxazole preventive therapy and timely ART for those diagnosed with HIV is one of the recognized strategies to reduce the dual burden of disease [17].

2.3 Factors affecting survival

2.3.1 Socio demographic factors

Female patient had significantly lower age, higher prevalence of heterosexual contact and lower prevalence of intravenous drug use as risk factors for HIV infection than male subjects. They were also reported to have higher previous exposure to antiretroviral therapy, higher CD4 cell counts and lower viral loads than male individuals [27]. Study conducted in India showed Mortality was higher in males [14.68 per 100 person years of follow up (95% CI: 11.79, 18.27)], participants in the age group of 35yr and above [19.93 per 100 person years of follow up (95% CI: 15.27, 26.03)] and in those with presence opportunistic infections other than TB [12.60 (95% CI: 7.94, 20.01)] at any study time point [28].

Other studies have shown that females have significantly higher survival rates than males ($P< 0.01$). Further regression analysis showed that males are more likely to die than females (HR 1.63; 95% CI: 1.31-2.03) after controlling for WHO clinical stages, body mass index and age [21].

A higher mortality was observed in people from urban residents when compared to rural (HR 2.05; 95% CI: 1.35-2.15), mortality was higher in singles than married ones ($P<0.001$). Primary education, advanced (old) age, and unemployment are other significant predictors of survival [29]. At Arbaminch Hospital in Ethiopia, higher mortality was associated with advanced clinical stage at start of treatment (HR [95%CI] = 2.4 [1.5, 4]), age over 45 years at presentation (HR [95%CI] = 1.7 [1.2, 2.4]) and men had higher mortality rates than women (HR [95%CI] = 1.4 [1.1, 1.8]) [30].

2.3.2Baseline clinical, laboratory and ART

Baseline CD4 cell count was strongly associated with the probability of progression to AIDS or death: when compared with patients starting HAART < 50 CD4 cells/μL, the hazard rates are: AHR 0.74 (95% CI: 0.62-0.89) for those starting with 50-99 cells/μL, AHR 0.52 (95%CI: 0.44-0.63) for 100-199 cells/μL, AHR 0.24 (95%CI: 0.20-0.30) for 200-349 cells/μL, and AHR0.18 (95%CI: 0.14-0.22) for 350 and above CD4 cells/μL.

Baseline HIV-1 viral load was associated with a higher probability of progression only if 100,000 copies/μL or above [25]. Survival functions differed by level of CD4 cells at

baseline (log-rank test <10_2) and the cumulative probability of dying at 12 months attained 17.9% (95% CI, 11.5 –27.2%), 13.1% (95% CI, 8.9–19.0%) and 5.8% (95% CI, 2.8–11.9%) for less than 50, 50–199 and more than 200 CD4 cells/ml respectively [31].

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[32]. In a study by Tarekegn, 2012, baseline CD4 cell count <50/µl was a significant predictor of mortality (HR 3.70, 95%CI: 1.96-7.14, P<0.0001). A study from Durban, however, revealed that factors predicting higher mortality rates among PLHIV were oral thrush, TLC<1200/µl, BMI less than18.5 kg/m2, anemia, WHO clinical stages III or IV and presence of prolonged diarrhea at baseline. Patients who experienced severe morbidity had higher risks of mortality, virological failure, and immunological failure. Other independent risk factors for mortality and/or severe morbidity were: baseline, high viral load, advanced clinical stage, past history of tuberculosis, low BMI, low hemoglobin, low CD4 cell count, OIs, and drug resistance; during follow-up: low CD4 cell count and persistently detectable viral load[6].

According to a study conducted in Harar and Dire Dawa, 10% weight loss at baseline (HR 4.93; 95% CI: 1.20-20.41), bedridden functional state (HR 4.09; 95% CI: 2.12-7.90), WHO stage IV (HR 3.19; 95% CI: 1.51-6.76), and CD4 <200 are independent predictors of mortality.[33] In a similar study in Arbaminch hospital, the principal predictors of mortality are TLC < 750 vs. ≥ 750/µL (HR 3.6; 95% CI: 1.5 -8.1), WHO stage IV vs. II-III (HR 3.7; 95% CI: 1.6-8.5), and BMI ≤ 18.5 vs. > 18.5 Kg/m2 (HR 2.9; 95%CI: 1.04-8.0)[34]. 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)[35].

According to Johannessen et al., 2008,the independent predictors of mortality were severe anemia (hemoglobin <8 g/dL; AHR 9.20; 95% CI: 2.05–41.3), moderate anemia (hemoglobin 8–9.9 g/dL; AHR 7.50; 95% CI: 1.77–31.9), thrombocytopenia (platelet count <150 × 109/L; AHR 2.30; 95% CI: 1.33–3.99) and severe malnutrition (body mass index <16 kg/m2; AHR 2.12; 95% CI: 1.06 –4.24). A history of oral candidiasis and cryptococcal

meningitis also conferred an increased mortality risk (HR 3.17, 95%CI: 1.70-5.87, P < 0.001 and HR 2.76, 95%CI: 1.07-7.10, P =0.03, respectively) [36].

2.3.3 Drug adherence and treatment failure

Treatment failure is mainly caused by previous exposure to ART, preexisting resistance, limited potency of regimen, imperfect adherence, poor absorption of drug, rapid elimination, and drug-drug interaction, which lead to persistent viral replication and drug failure [26]. According to Mweete et al., 2012, treatment failure and virological failure rates were8.2/ 100 PYO (4.6-14.4) and AHR, 2.06 (95% CI: 1.11-3.81; p= .002), respectively [37]. A similar study from Mozambique reported a treatment failure rate of 14/ 100 PYO (95% CI: 13.0-16.0) and a regimen-switch rate of 0.6/ 100 PYO (95% CI: 0.4-1.1) [38].

Changes in drug concentrations resulting from drug interactions can lead to treatment failure or toxicities. Overlapping toxicities are more of a concern for patients taking NRTIs and anti-tuberculosis medications; for example, the use of either d4T or didanosine with isoniazid should be avoided because of the increased risk of peripheral neuropathy [39]. Early studies showed diminished serum concentrations of AZT when it was given with rifampin. Rifampin decreased serum concentration of EFV (15%-20%) and NVP (20%-30%)[40]. Rifampin also leads to diminished absorption of PIs boosting with increased doses of ritonavir fails to produce adequate PI concentrations and sometimes leads to unacceptable toxicity. In a clinical trial involving HIV/TB-co infected patients, co-administration of rifampin with standard dose (1000/100mg) of SQV/r twice daily, majority (64%) of them developed grade 3 or 4 hepato-toxicity [41]. In a study in Uganda and Zimbabwe, 61%of patients receiving AZT/3TC/TDF had a viral load of < 50 copies of HIV RNA/ml of blood at 48 weeks. TDF-containing quadruple-nucleoside regimens such as TDF/AZT/3TC/ABC may perform even better [42].

Studies of patients with advanced AIDS have found increased concentrations of NVP in patients receiving fluconazole for treatment or prophylaxis of cryptococcal meningitis, and 25% of the subjects developed serious hepatotoxicity [43]. Ketoconazole has significant interactions with NNRTIs: one study has found a bidirectional interaction between ketoconazole and NVP, consisting of a 72% decrease in ketoconazole concentration and a 15%-30% increase in NVP concentration. Ketoconazole increases PI concentrations by 30%-

130%, and PIs can lead up to 3-fold increase in ketoconazole concentrations [44]. In HIV-infected patients, azithromycin and clarithromycin are widely used for the treatment and prevention of Mycobacterium avium-intracellular infections. When azithromycin is co-administered with NFV, it has been found to cause, a 28% decrease in NFV concentration and a 107% increase in azithromycin concentration [45]. Clarithromycin, however, has significant interactions with NNRTIs and with PIs. When clarithromycin is co-administered with EFV or NVP, its concentration is decreased by 39%, and 30% respectively and NVP concentration increased by 26% [44].

Co-administration of NVP and EFV may decrease concentrations of Praziquantel, Albendazole, Mebendazole, and Ivermectin while PIs may increase their concentrations increasing the potential for CNS toxicity esp. with Ivermectin. Peripheral n ephropathy and pancreatitis were reported during co-administration of Metronidazole, Pentamidine, and Suramin with ddl, dT4, and TDF respectively [45]. A study on treatment-naïve PLHIV from Senegal showed that AZT is unsuitable for populations that have a high prevalence of anemia and low CD4+ cell counts, as the incidence of severe anemia (grade IV) was 6.6% during the first 3 months of treatment with AZT + 3TC + tenofovir (TDF). The ddI + 3TC combination is well tolerated, as in industrialized countries [36].

The effectiveness of HIV/AIDS management depends critically on the efficacy of the ARVs against the virus and adherence to medications. Factors predicting adherence include forgetfulness (Adjusted Odds Ratio, AOR 3.29, P = 0.005), social support (AOR 2.42, P = 0.006) and depression at baseline (AOR 2.13, P = 0.011)[46].

A review of similar studies have shown medication-related factors like palatability and adverse effects (e.g., metabolic complication, lipodystrophy); substance abuse like drug abuse and alcohol consumption, the latter accounting for 50-60% non-adherence; socioeconomic and stigma-and discrimination factors as a challenge[47]. Non-adherent patients who initiated HAART when the CD4+ cell count was 200-349 cells/µL, had statistically elevated mortality rates (AHR 2.56; 95% CI: 1.36-4.84,P = 0.004) compared with adherent patients who initiated HAART at a CD4+ cell count of 350 cells/µL or greater[21].

Delaying HAART until the CD4+ cell count falls to a level of 200 cells/µL, does not increase the mortality rate in HIV-infected patients with good medication adherence. In addition, non-adherent patients have higher mortality rates than adherent patients with similar CD4+ cell counts. Above CD4+ 200 cells/µL, medication adherence is the critical determinant of survival, not the CD4+ cell count at which HAART is begun [48].

Retention of patients on treatment is still a challenge in ART programs in resource-limited settings with a considerable proportion of patients lost to follow up. According to Yibeltalet al., 2011, retention rates vary across health facilities, ranging from 51% to 85% after 24 months on ART. An overall attrition rate of 19.8/100 PYO (95% CI: 17.9 –21.9) was reported from a study in Mozambique with 57.2/100 PYO in the first 90 days (95% CI: 49.5–66.4), and 13.2/100 PYO after 90 days (95% CI: 11.7–15.0) [49].

The risk of attrition was higher in patients with WHO stage IV (AHR 1.7; 95% CI: 1.3 –2.4), weight <45 kg (AHR 2.1; 95% CI: 1.6–2.9], and severe anemia (AHR 1.6; 95% CI: 1.2–2.1]). Patients not prescribed CTP were at higher risk for attrition compared with patients who were prescribed this drug (AHR 1.4; 95% CI: 1.0–1.8) [37]. A study from Uganda reported that 19-44% of patients lost to follow up were in fact deaths [50]. In other similar study, more than 71% of the attritions occurred in the 1st year of ART initiation. In addition, 29-59% of patients lost to follow up are those dying at home without being reported [51]

2.2 CONCEPTUAL FRAMEWORK

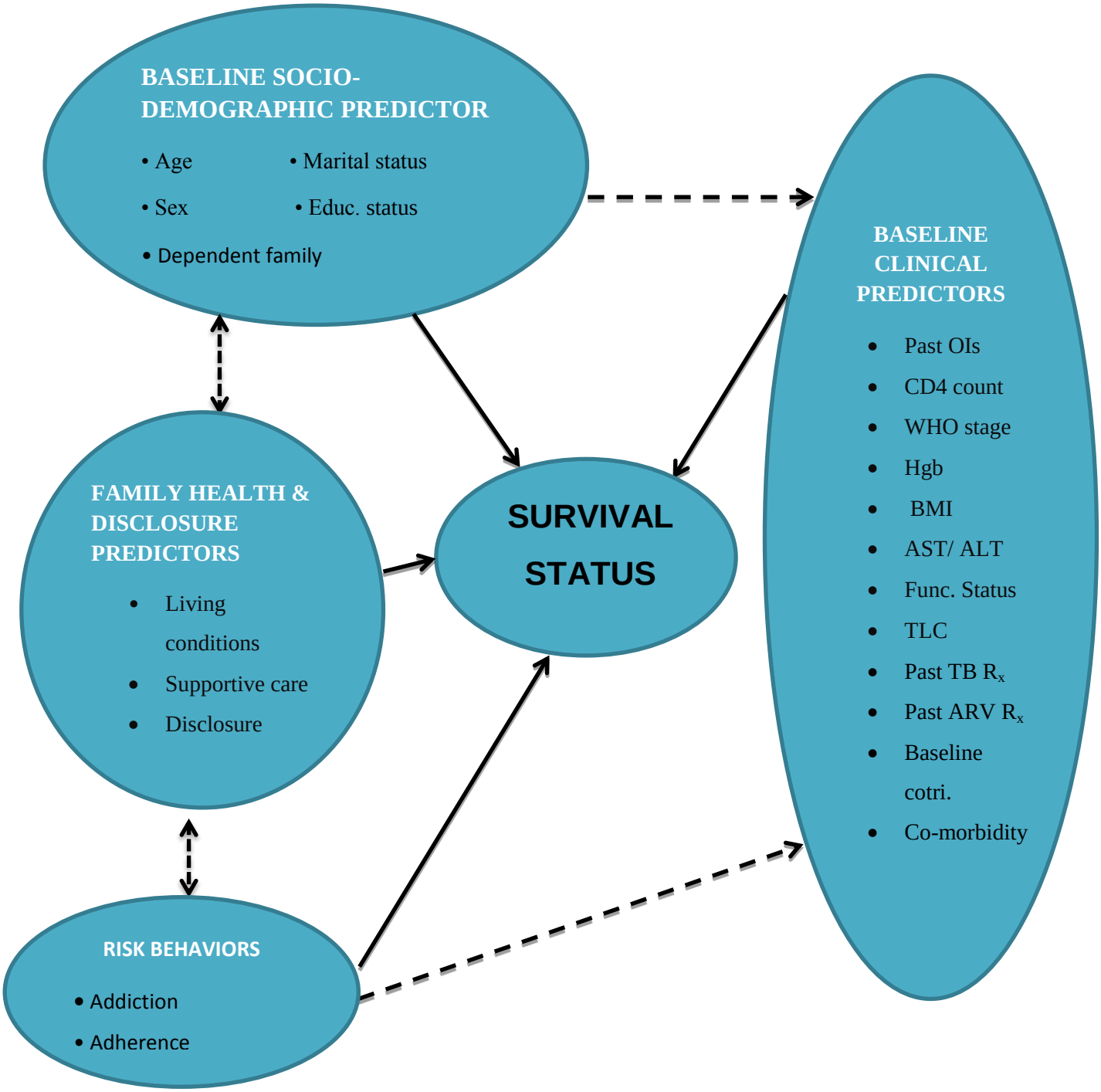

Figure 1: Conceptual framework on predictors of survival status among PLHIV after initiation of ART.

2.3 SIGNIFICANCE OF THE STUDY

The introduction of HAART has greatly improved the survival of HIV/AIDS infected people. HAART reduces morbidity and mortality by suppression of viral replication, restoration and preservation of immune function, and prevention of drug resistance. Mortality among patients on HAART is associated with high baseline levels of HIV RNA, WHO stage III or IV at the beginning of treatment, low body mass index, severe anemia, low CD4 cell count, type of ART treatment, cotrimoxazole prophylaxis, gender, resource-poor settings and poor adherence to HAART[49]. This gives us the opportunity to act on modifiable risk factors that are identified. However, as far as the knowledge of the researcher, the availability of information on such issues is minimal in Ethiopia. So this study is helpful in identification of predictors of survival status among PLHIV after the initiation of ART.

The aim of this study is to identify survival status and the different potential predictors of survival status in HIV patients after the initiation of the ART treatment. The study findings can also be used for planning and implementing an effective service for HIV/AIDS patients that is focused on important aspects that can improve survival. In addition, it will enable different organizations working in this area to improve their aid and support and also provide them with additional program monitoring and evaluation tools. The study result will also help health facilities that are providing ART service to focus on factors that have an impact on the outcome of the treatment during the patient's follow up.

Finally, the study result enables patients to be entertained by the best of their treatment outcomes and improve their quality of life by creating awareness on the factors that are detrimental to their therapy. This study will also serve as a reference material for future other studies to be conducted on related topics.

3. OBJECTIVES

3.1 General Objective

- To investigate the survival status and identify the potential predictors of mortality status after initiation of ART among PLHIV at Jigjiga, Karamara hospital, Jigjiga zone, Somali region, Eastern Ethiopia.

3.2 Specific Objectives

- To determine the prevalence of mortality among PLHIV after initiation of ART
- To estimate the median survival time of PLHIV after initiation of ART
- To identify the independent predictors of survival status of PLHIV after initiation of ART

4. METHODS AND MATERIALS

4.1. Study Area and Period

The study was conducted in Somali region, located in the eastern part of the country. The region's population size is estimated to be 4.56 million. The age structure of the population is typical as other regional states of the country, with 55.6% of the population are 15 years and above [53].

The health profile of the region is trailing behind other regions. The potential health service coverage in the region is 42.3%. Although the adult HIV prevalence in the region (0.8%) is below the national average, there are an estimated 29,282 PLHIV. There were 2,891 new HIV infections and 1,985 annual AIDS-related deaths. A total of 9,637 PLHIV ever enrolled in ART clinic among whom, 1,312 ever started, and 1,295 (13.6%) currently on ART in seven health facilities in the region [54].

Kharamara hospital is one of the zonal hospitals in the region. In the comprehensive HIV care and treatment service at the hospital there are 2960 patients enrolled, of which 2007 ever-started ART, and 1144 currently on ART. The hospital uses intake form, follow up form, registers (Pre-ART register and ART register), monthly report form, cohort report form, pharmaceutical and laboratory report form and different referral paper tool to monitor the patients. Patients are seen at two weeks after ART initiation and then routinely every month for clinical assessment and ART dispensing. The study was conducted from February 2014 to March 2014.

4.2. Study design

A retrospective follow up study with record review was conducted to assess survival status and potential factors of mortality among PLHIV receiving antiretroviral therapy in Kharamara hospital from January 1st, 2009 up to December 31st, 2013.

4.3. Population

People living with HIV/AIDS aged ≥18 years, and who started ART treatment in Kharamara hospital between January 1st 2009 and December 31st 2013 fulfilling the inclusion criteria.

4.4 Inclusion and exclusion criteria

Inclusion criteria:

- ✓ HIV positive adults aged 18yrs or older who started ART in Kharamara hospital from January 1st, 2009 up to December 31st, 2013.
- ✓ HIV positive adults with complete baseline data in the intake forms, pre-ART registers and follow-up form.

Exclusion criteria:

- ✓ Transfer ins with incomplete baseline data.
- ✓ HIV positive adults whose end status is not recorded.
- ✓ Competing cause of death.

4.5. Study variables

4.5.1. Dependent variable

- ✓ Time to event status

4.5.2. Independent variable

The independent variables are:

- ✓ **Socio-demographic** characteristics as Age, Religion, Sex, educational level, Ethnicity, Marital status and occupation.
- ✓ **Risk behaviors** such as smoking, Alcohol and Drug use.
- ✓ **Baseline clinical, laboratory and ART** information as Past opportunistic illness, Tb test and treatment, Treatment regimen, CD4count, Chemoprophylaxis (cotrimoxazole, INH…), BMI, WHO clinical staging, Hgb, T-cell lymphocyte count, and ALT/AST.
- ✓ **Follow up** information like duration since initiation of ART, Adherence, and Side effects.

4.6. Data collection procedure

4.6.1. Data collection instrument

The checklist consists of the following data:

- ✓ Socio-demographic data
- ✓ Baseline clinical, Laboratory and ART data
- ✓ Baseline social support and Condition
- ✓ Knowledge on HIV and ART
- ✓ Risk behaviors
- ✓ ART and other Treatments
- ✓ ART Follow-up data

4.6.2. Data collection and quality control

To compile the required information a data collection form was developed from ART entry and follow-up forms that are being used in the ART clinic. Prior to the actual data collection, the data collection form was validated by a pre-test at the ART clinic in Jigjiga health center and subsequent modifications have been done.

The data was collected by reviewing pre-ART register, ART intake form, laboratory request, monthly cohort form, and follow up form. The most recent laboratory results before starting ART would be used as a baseline value. If there is no pre-treatment laboratory test, results obtained within one month of ART initiation would be used. Deaths was confirmed by reviewing the death certificates, medical registration in the hospital, or registration by ART adherence supporter through calling using the registered phone number and individuals alive and on ART at the end of the study period was censored.

Problems encountered at the time of data collection were reported immediately and appropriate actions were taken. The collected data was checked out for the completeness, accuracy and clarity by the principal Investigator and Supervisor.

4.6.3 Data collection personnel

The data was collected by experienced ART nurses who were trained on comprehensive HIV care and involved in patient follow ups in the ART clinic. A supervisor was supervising the data collection process. The data collectors and the supervisor were trained on the data

collection procedures for two days. The investigator followed the overall data collection process.

4.7. Data quality assurance

All completed data collection forms were examined for completeness, consistency and clarity during data management, storage, and analysis. The data was coded, entered, and cleaned by the principal investigator before analysis. Data exploration was carried out to check for any inconsistencies, coding error, outliers, and missing values and appropriate treatment was made. Data analyses was then made using SPSS version 16.0 for windows.

4.8. Data analysis

The outcome of each subject was dichotomized as censored and death. Descriptive analysis of the continuous and categorical data describing the cohort's characteristics at baseline and during follow-up was made and presented by tables and graphs. After checking for the assumptions of KM curves and Cox PH model, Kaplan-Meier model was used to estimate survival probability after ART initiation and log rank tests was used to compare the difference of the survival curves. Cox-proportional hazard model was used to identify independent predictors of survival. Multivariate analysis was conducted for those variables which were found to be significant in the bivariate analysis with P value <0.25 were entered using stepwise method. Finally, all variables significant at $P < 0.05$ level were included in the final multivariable model. All analyses was made using SPSS version 16.0 for windows (SPSS Inc., Chicago, IL, USA).

4.9. Operational definitions and definition of terms

Ambulatory: An individual able to perform activities for daily living.

Attrition: defined as discontinuation of ART for any reason. It includes death, loss to follow up, and stopping ARV medications while remaining in care**.**

Bedridden: An individual unable to perform activities for daily living**.**

CD4 count: a way of measuring immune-competency by counting the lymphocyte that carry the CD4 molecules.

Drop out: if a patient discontinued ART for at least three month as recorded by ART physician.

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

Immunodeficiency: break down in immune competence to resist or fight off infections.

Incomplete record: if data on Pre-ART knowledge and Risk behaviors, baseline characteristics (Age, Sex, WHO stage), and follow up data for 3 consecutive visits are not available.

Lost to follow up: If patients failed to return to the clinic after 90 days from their expected clinic appointment date.

Opportunistic infections: are illnesses caused by various organisms, some of which usually do not cause disease in persons with healthy immune systems but these organisms take advantage of the opportunity provided by immunodeficiency.

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.

Survival: lack of experience of death. It is being alive (on ART or not) and not experiencing AIDS related death during the study period.

Switching: is a change in treatment regimen from first-line to second-line ART, excluding change in treatment dose.

Transferred out: If patient moved to another health facility with confirmed written documentation of transfer out

Treatment failure: is defined by one of the three WHO criteria:

i. **Clinical:** new or recurrent WHO stage 4 or certain stage 3 conditions (e.g. PTB, severe bacterial infections);
ii. **Immunological:** fall of CD4 count to pre-therapy baseline (or below), a 50% fall from the on-treatment peak value (if known), or persistent CD4 levels <100 cell/μL; or
iii. **Virological:** plasma viral load > 10,000 copies/μL

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

Working/ functional - An individual able to perform usual work in and out of the house, harvest, go to school for children, normal activities or playing

4.10. Ethical considerations

The study was carried out after getting approval from the ethical clearance committee of Jimma University, collage of public health and Medical sciences through Department of biostatistics and epidemiology .Then, data was collected after getting written consent from Kharamarah Hospital. As the study was conducted through review of medical records, there was no harm to individual patients. Extraction of data from medical records was done by trained staff working in the ART clinic at Kharamara hospital in order to preserve confidentiality. The data obtained was not be accessed by a third person, except the principal investigator, and will be kept confidential.

4.11. Dissemination of Research finding

Findings of the study will be submitted and presented to Department of biostatistics and Epidemiology College of public health and Medical science of Jimma University. The dissemination will also goes to the Kharamara hospital, Somali Regional Health Bureau, different NGOs and the Zonal HAPCO. Furthermore efforts will be made to present the finding at different professional meeting and manuscript will be sent to different journals for publication.

5. RESULTS

5.1. Socio demographic factors

Study subjects were 822 adult patients who started ART of which 345(42%) male and 477 (58%) were female. They were followed for a median of 22 months. Baseline and follow-up information of the patients were gathered from the ART clinic records of the patients to identify the independent predictors of their survival status.

The mean age of the patients was 32yrs (SD±9.75). Regarding their marital status 107(13%) were never married and 382(46.3%) were married, 233(28.3%) of them were divorced and the rest 100(12.1%) were widowed. Out of the study subjects, 365 (44.7%) were muslin, 430(52.3%) orthodox and the rest 27 (3.3%) were protestants.

Regarding the educational and occupational status 302(36.7%) have had no education, 203(24.6%) have at least completed primary education only 72(8.7%) have attended college or above level and 400(48.7%) were not employed. Five hundred seventy eight (70.1%) have dependent children at home (Table 1).

Table 1: Socio demographic characteristics of study population who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

Variables	Frequency	Percent
Sex		
Male	345	42.0%
Female	477	58%
Age		
18-24	96	11.7%
25-44	594	72.3%
45-64	124	15.0%
65+	8	1.0%
Religion		
Muslim	365	44.7%
Orthodox	430	52.3%
Protestant	27	3.3%
Marital status		
Single	107	13%
Married	382	46.3%
Divorced	233	28.3%
Widowed	100	12.1%
Educational status		
Not education	302	36.7%
Primary	203	24.6%
Secondary	231	28.1%
College/Above	72	8.7%

Dependent children at home		
Yes	578	70.1%
No	244	29.1%
Employment status		
Merchant	32	3.9%
Gov't employee	72	8.8%
NGO employee	96	11.7%
Military	23	2.8%
Day Laborer	174	21.2%
Driver	19	2.3%
Jobless	400	48.7%
Others	6	0.7%

5.2. Baseline clinical and laboratory related factors

Two hundred thirty nine (29.1%) of the study subjects had BMI less than 18.5Kg/m^2 and 121 (14.7%) had BMI greater than 25Kg/m^2. The median weight of the subjects at the base line was 50kg (IQR, 43-57). The median CD4 count at the beginning of ART was 147cells/µl (IQR, 76-219). Out of the study subjects, 239 (29.1%) were co infected with TB and 176(21.4%) of them were infected by other opportunistic infections. Cotrimoxazole for 779(88.3%), INH for 156(11.7%) and fluconazole for 17 (2%) was given to the study subjects.

At baseline 490(59.6%) had working, 246(30%) ambulatory and 83(10.1%) bed ridden functional status and 120(14.6%) were at WHO stage IV, while 374(45.5%), 174(21%) and 149(18.2%) were on WHO stage III, stage II and stage I respectively. During the initiation of ART 199(24.4%), 219(26.7%) and 404(49.2%) were taking Stavudine-based, Zidovudine-based, Tenofovir-based and 2nd line ART regimens respectively (Table 2). And 781(95%) had good adherence, 26(3%) fair and 14(2%) poor adherence. Only 509(61.8%) of the subject had disclosed their HIV status for their close ones.

Table 2: Base line Clinical and laboratory characteristics of study population, who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

. Variables	Frequency	Percent
Functional Status		
Working	490	59.6%
Ambulatory	246	29.9%
Bedridden	83	10.1%
WHO Staging		
Stage I	149	18.2%
Stage II	174	21.1%
Stage III	374	45.5%
Stage IV	120	14.6%
BMI Category		
< 18.5 Kg/M^2	239	29.1%
18.5-24.99Kg/M^2	446	50.6%
>=25 Kg/M^2	121	14.7%
Weight(Kg) (Median (IQR))	50(43-57)kg	
CD4 Count(Median(IQR))(Cells/µl)	147 (76-218)cells/ µl	
ART Regimen		
Stavudine Based	199	24.2%
Zidovudine Based	219	26.7%
Tenofovir Based	404	49%
2nd-Line	-	
Cotrimoxazole		
Given	804	97.8%
Not Given	12	1.5%
Inh Given		
Yes	191	23.2%
No	627	76.3%
TB Co-Infected		
Yes	239	29.1%
No	583	70.9%
Other Opportunistic Infections		
Yes	646	78.6%
No	176	21.4%
Art Adherence		
Good	753	91.8%
Fair	39	4.7%
Poor	29	35%

5.3. Risk behavior factors

Among the study subjects, 422(51%) had regular sexual partner while 138(16.9%) had casual sexual partner and 676(82%) of the subjects never used condom. With regard to substance use 78(9.4%), 72(9.8%), 81 (10.1%), and 14 (1.7%) had been using tobacco, alcohol, soft drug and hard drugs moderately or more, respectively (Table 3).

Regarding the general condition of spouse, the status of 651(73.8%) of their spouse condition is unknown and 25(3.0%) while 92(11.2%) of their spouses are already dead. Regarding the HIV status of the spouse of the patients 633(77%) had unknown HIV status and 130(15.8%) are tested to be HIV positive but only 5(1%) started ART and out of their spouses 782(94%) of them had unknown TB result and 110(13.3%) were on TB treatment.

Table 3: Base line risk behavior characteristics of study population, who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

Variables	Frequency	Percent
Tobacco use		
Yes	78	9.4%
No	740	90.2%
Alcohol use		
Yes	72	9.8%
No	750	91.2%
Soft Drugs use		
Yes	81	10.1%
No	741	89.9%
Hard Drug		
Yes	14	1.7%
No	752	91.4%
Had regular partner		
Yes	422	51.4%
No	400	49.6%
Had casual partner		
Yes	138	16.9%
No	684	83.1%
Condom use		
Yes	49	5.9%
No	760	92.2%

Finally, 224(27.3%) of the study cohort have had poor understanding of HIV disease and 230(28.0%), 173(21.0%) and 169(21.0%) had poor understanding of HIV/AIDS transmission, prophylaxis and treatment of Opportunistic illness, and ART medication and adherence respectively (Table 4).

Table 4: Base line understanding of study population, who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

Variables	Frequency	Percent
Understand HIV disease		
Yes	596	72.5%
No	224	27.3%
Understand HIV transmission		
Yes	590	71.8%
No	230	28.0%
Understand of Rx of OIs		
Yes	647	78.7%
No	173	21.0%
Understand ART adherence		
Yes	647	78.7%
No	169	21.0%

5.4. Survival Analysis

A total of 822 patients were followed for an average of 22 months. The minimum follow up time was 1week and the maximum was 60months**.** During the follow-up period, 69(8.4%) patients died, with 37(60.6%) of the deaths occurring in the first 3 months (HR: 0.022). The remaining 753(91.6%) were right censored due to being active, LTFUP, drop out being transferred out to other health facilities during the follow up period. The estimated mortality of the study cohort was 7.4%, 8.6%, 9.8 %, 12 % and 13.1% at 6, 12, 24, 36 and 48 months respectively (Table 5).

Table 5: Actuarial Table estimates of the cumulative occurrence of mortality of study population after starting ART between Jan. 2009- Dec.2013.until censored in February 2014.

Interval Start Time	Number Entering Interval	Number With drawing	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion at End of Interval	Hazard Rate
0	822	178	733.000	36	.05	.95	.95	.01
6	608	66	575.000	14	.02	.98	.93	.004
12	528	61	497.500	6	.01	.99	.92	.002
18	461	85	418.500	2	.00	1.00	.91	.001
24	374	95	326.500	4	.01	.99	.90	.002
30	275	62	244.000	3	.01	.99	.89	.002
36	210	42	189.000	3	.02	.98	.88	.003
42	165	46	142.000	1	.01	.99	.87	.0012
48	118	53	91.500	0	.00	1.00	.87	.00
54	65	47	41.500	0	.00	1.00	.87	.00

Out of the total 822 study subjects who started ART at jigjig, Kharamar hospital between January 1st 2009 to December 31st 2013 by the end of the 60 months follow up period 390(47.4%) were still active and under ART care, 69(8.4%) were dead, 212(25.8%) were lost to follow up, 7(0.9%) were drop outs and 144(17.5%) transferred out to other health facilities (fig.2).

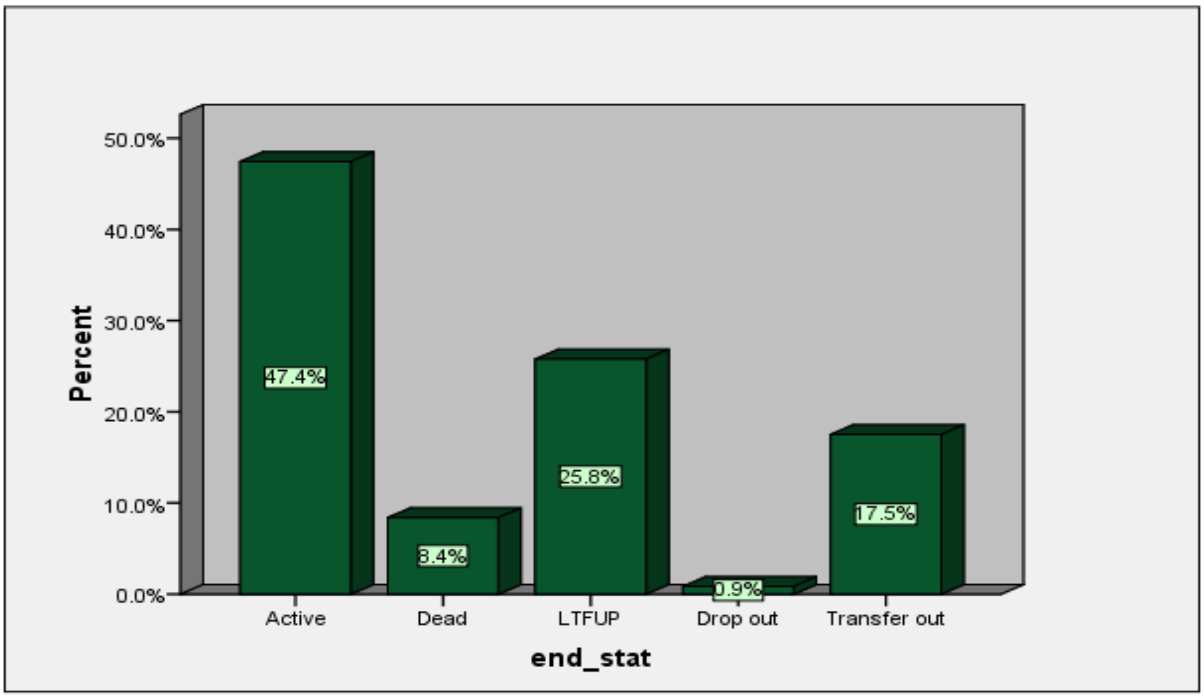

Figure 2: End status of study subjects after initiation of ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

In bivariate Cox regression analysis male sex(CHR=2.121,95%(1.31-4.31), single and married marital status ((CHR=4.25, 95%CIs(1.59-11.39), CHR=1.76, 95%CIs(0.68-4.53)), no education and primary education level((CHR=1.997, 95% CIs(1.36-23.16),(CHR=2.85, 95%CIs (0.65-12.4)), jobless occupational status(CHR= 3.775, 95% CIs (0.519-27.47) ambulatory & bedridden baseline functional status((CHR=2.48,95%CIs(1.422-4.32),(CHR=6.92, 95%CIs (3.80-12.61)), advanced WHO clinical stage III & IV ((CHR=3.54, 95% CIs(1.38-9.0),(CHR=6.45, 95%CIs (2.42-17.19)), lower BMI(CHR= 8.375, 95% CIs(2.98-23.52)), baseline CD4 count< 200((CHR=7.52, 95% CIs(3.36-16.85),(CHR=6.2, 95%CIs (2.74-14.01)), past TB co-infection(CHR=2.24, 95% CIs(1.39-3.59)), other opportunistic infection(CHR=2.34, 95% CIs (1.106-4.95)), fair & poor ART adherence((CHR=11.92, 95% CIs(6.4-22.16),(CHR=19.19, 95%CIs (11.35-34.06)), INH not given (CHR=5.68, 95% CIs(2.27-a4.19)), and smoking(CHR= 1.805, 95% CIs(.922-3.53)) were all associated with survival (Table 6,7,&8).

In this study Age, religion, occupational status, and dependent children at home, baseline ART regimen, cotrimoxazole initiation, baseline understanding of HIV disease and transmission, baseline understanding of treatment of opportunistic infections, alcohol use, and hard drug use were not associated with survival in the bivariate analysis.

Table 6: Bivariate Cox-regression analysis of predictor of survival among PLHIV initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

VARIABLES		SURVIVAL STATUS		CRUDE HR	95%CI	P-Value
		DEAD	CENSORED			
Sex						
	Male	**41(11.9%)**	**304(88.1%)**	**2.121**	**(1.311-4.31)**	**.002**
	Female	**28(5.9%)**	**449(94.1%)**	-	-	-
Age						
	18-24	**4(4.2%)**	**92(95.8%)**	.341	(0.038-3.05)	.336
	25-44	**55(9.3%)**	**539(90.7%)**	.704	(0.097- 5.09)	.728
	45-64	**9(7.3%)**	**115(92.7%)**	.507	(0.064- 4.03)	.519
	65+	**1(12.5%)**	**7(87.5%)**	-	-	-
Religion						
	Muslim	**27(7.4%)**	**338(92.6%)**	.615	(.164-2.911)	.615
	Orthodox	**39(9.1%)**	**391(90.9%)**	.635	(.171-2.937)	.635
	Protestant	**3(11.1%)**	**24(88.9)**	-	-	-
Marital status						
	Single	**19(17.8%)**	**88(82.2%)**	**4.250**	**(1.59-11.39)**	**.004**
	Married	**31(8.1%)**	**351(91.9%)**	1.760	(.684-4.53)	.241
	Divorced	**14(6.0%)**	**219(94.0%)**	1.279	(.460-3.55)	.637
	Widowed	**5(5.0%)**	**95(95.0%)**	-	-	-
Educational status						
	No education	**44(14.4%)**	**262(85.6%)**	**1.997**	**(1.36-23.16)**	**.017**
	Primary	**16(7.5%)**	**197(92.5%)**	2.853	(.656-12.41)	.162
	Secondary	**7(3%)**	**224(97%)**	1.090	(.226-5.25)	.886
	College/Above	**2(2.8%)**	**70(97.2%)**	-	-	-

[1]

[1] * Variables significantly associated at the Bivariate analysis

Table 7: Bivariate Cox-regression analysis of predictor of survival among PLHIV initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

VARIABLES		SURVIVAL STATUS		CRUDE HR	95% CIs	P-Value
		DEAD	CENSORED			
Employment status						
	Merchant	**1(3.1%)**	**31(96.9%)**	-	-	-
	Gov't employee	**5(6.9%)**	**67(93.1%)**	2.806	(.338-23.306)	.340
	NGO employee	**7(6.9%)**	**95(93.1%)**	2.387	(.294-19.405)	.416
	Military	**1(4.3%)**	**22(95.7%)**	1.289	(.081-20.615)	.857
	Day Laborer	**12(6.9%)**	**162(9301%)**	2.576	(.335-19.817)	.364
	Driver	**2(10.5%)**	**17(89.5%)**	3.996	(.362-44.093)	.258
	Jobless	**41(10.2%)**	**359(89.2%)**	3.775	(.519-27.475)	.190
Base line fun. Status						
	Working	**25(5.1%)**	**465(94.9%)**	-	-	-
	Ambulatory	**25(10.2%)**	**221(89.8%)**	**2.480***	**(1.422-4.325)**	**.001**
	Bedridden	**19(22.9%)**	**64(77.1%)**	**6.924***	**(3.80-12.616)**	**<.0001**
Baseline WHO						
	Stage I	**5(3.4%**	**144(96.6%)**	-	-	-
	Stage II	**7(4.0%)**	**167(96.0%)**	1.273	(.404-4.01)	.680
	Stage III	**37(9.9%)**	**337(90.1%)**	**3.535***	**(1.38-9.00)**	**.008**
	Stage IV	**20(16.7%)**	**100(83.3%)**	**6.447***	**(2.42-17.19)**	**<.0001**
BMI category						
	< 18.5 Kg/m^2	**54(22.4%)**	**185(77.8%)**	**8.375***	**(2.98-23.52)**	**<.0001**
	18.5-24.9 Kg/m^2	**11(2.6%)**	**405(97.4%)**	1.610	(.244-2.48)	.674
	≥25 Kg/m^2	**4(3.3%)**	**117(96.7%)**	-	-	-
CD4 category						
	<50 cells/μL	**25(18.5%)**	**101(81.5%)**	**7.529***	**(3.36-16.85)**	**<.0001**
	50-99cells/μL	**20(14.3%)**	**120(85.7%)**	**6.200***	**(2.74-14.01)**	**<.0001**
	100-199cells/μL	**16(5.5%)**	**275(94.5%)**	1.780	(0.76-4.16)	.183
	≥200 cells/μL	**8(3.1%)**	**248(96.9%)**	-	-	-

Table 8: Bivariate Cox-regression analysis of predictor of survival among PLHIV initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

VARIABLES		SURVIVAL STATUS		CRUDE HR	95% CIs	P-Value
		DEAD	CENSORED			
Cotrimoxazole	Yes	**67(8.3%)**	**737(91.7%)**	-	-	-
	No	**1(8.3%)**	**11(91.7%)**	.992	(.138-7.15)	0.994
INH Given						
	Yes	**5(2.6%)**	**185(97.4%)**	-	-	-
	No	**64(10.2%)**	**564(89.8%)**	**5.68***	**(2.27-14.19)**	**<0.0001**
TB co-infected						
	Yes	**34(14.2%)**	**205(85.8%)**	**2.24***	**(1.39-3.59)**	**.001**
	No	**35(6.0%)**	**548(94.0%)**	-	-	-
Oppo. Infections						
	Yes	**593(91.8%)**	**53(8.2%)**	**2.34***	**(1.106-4.950)**	**.024**
	No	**160(90.9%)**	**16(9.1%)**	-	-	-
ART regimen						
	Stavudine based	**18(9.0%)**	**181(91.0%)**	.747	(.351-1.590)	.450
	Zidovudine based	**13(5.9%)**	**206(94.1%)**	1.210	(.655-2.235)	.543
	Tenofovir based	**38(9.4%)**	**366(90.6%)**	-	-	-
ART Adherence						
	Good	**33(4.4%)**	**720(95.6%)**	-	-	-
	Fair	**15(38.5%)**	**24(61.5%)**	**11.92***	**(6.41-22.18)**	**<.0001**
	Poor	**21(72.4%)**	**8(27.6%)**	**19.19***	**(11.35-34.46)**	**<.0001**
Understand HIV Ds						
	Yes	**52(8.7%)**	**544(91.3%)**	1.23	(.702-2.16)	.470
	No	**16(7.1%)**	**208(92.9%)**	-	-	-
Understand HIV trans.	Yes	**52(8.8%)**	**538(91.2%)**	1.269	(0.72-2.2)	.405
	No	**16(7.0%)**	**214(93.0%)**	-	-	-

[2]

[2] * Variables significantly associated at the Bivariate analysis

Table 9: Bivariate Cox-regression analysis of predictor of survival among PLHIV initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

VARIABLES		SURVIVAL STATUS		CRUDE HR	95%CIs	P-Value
		DEAD	CENSORED			
Understand of OIs RX						
	Yes	**55(8.5%)**	**592(91.5%)**	.876	(.479-1.604)	.668
	No	**13(7.5%)**	**160(92.5%)**	-	-	-
Understand ART adh.						
	Yes	**55(8.5%)**	**595(91.5%)**	.894	(.489-1.64)	.717
	No	**13(7.7%)**	**156(92.3%)**	-	-	-
Alcohol use						
	Yes	**9(12.5%)**	**63(87.5%)**	1.73	(.859-3.49)	.125
	No	**60(8.0%)**	**690(92.0%)**	-	-	-
Smoking						
	Yes	**10(12.5%)**	**68(87.2%)**	1.81	(.922-3.53)	.085
	No	**59(8.0%)**	**681(92.0%)**	-	-	-
Soft Drugs use						
	Yes	**7(8.6%)**	**74(91.3%)**	1.268	(.577-2.789)	.554
	No	**62(8.3%)**	**679(91.7%)**	-	-	-
Hard Drugs use						
	Yes	**6(42.8%)**	**8(57.2%)**	1.490	(.641-3.463)	.354
	No	**63(8.4%)**	**689(91.6%)**	-	-	-

[3]

[3] * Variables significantly associated at the Bivariate analysis

This study found that the independent significant predictors of death in patients living with HIV/AIDS after initiation of ART were being male gender, bedridden functional status, advanced WHO staging (III and IV), low CD4 count, lower BMI, and poor ART adherence.

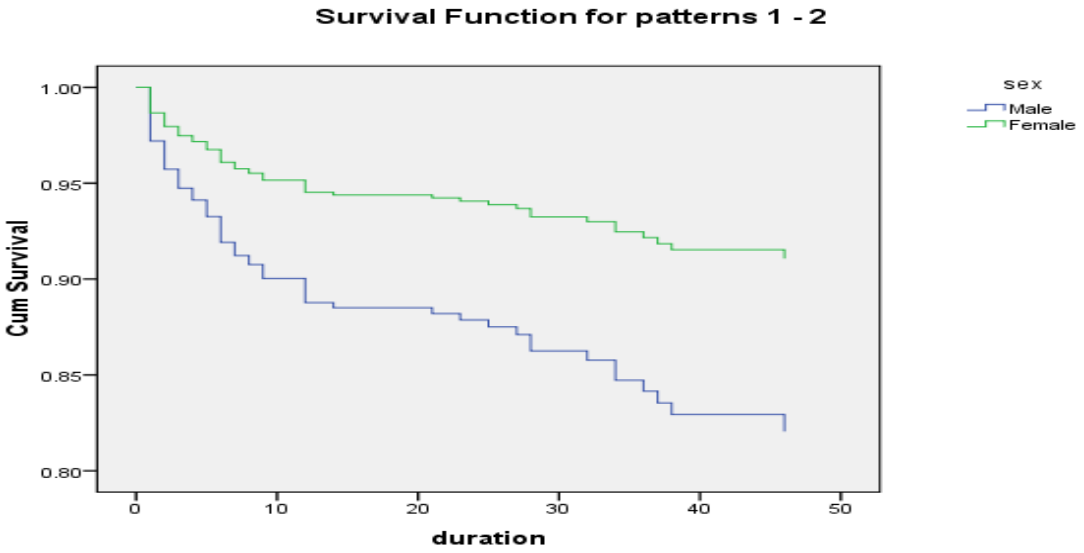

Figure 3: Survival status by Sex ofpatients at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

Based on the study result males are at higher risk of death when compared with females(HR=2.12, 95%CIs(**(1.31- 4.31)**) (fig.3) and regarding marital status never married marital groups had a higer risk of mortality when compared to the widowed groups((HR=**4.25, 95%CIs (1.59-11.39))** during the bivariate analysis (fig 4).

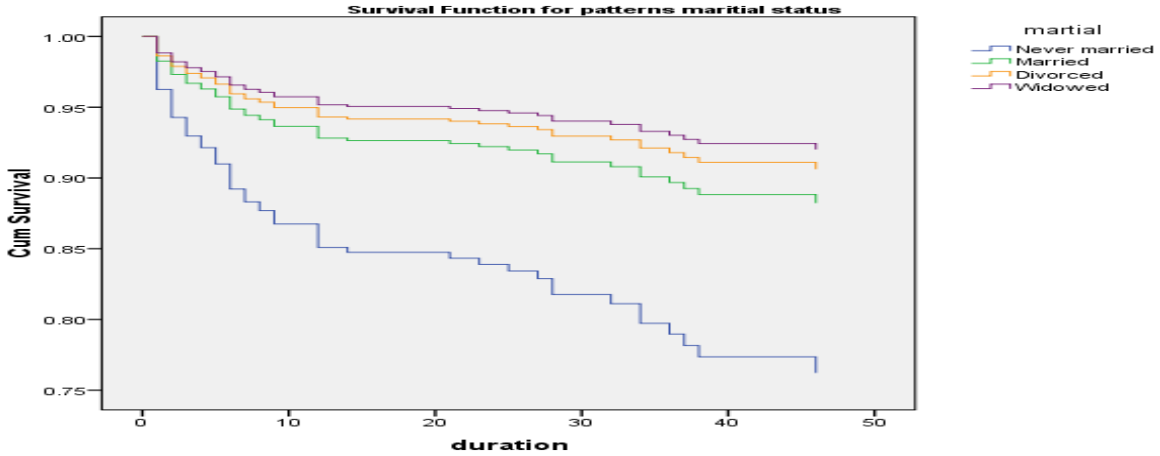

Figure 4: Survival function for marital status of study subjects who initiated at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

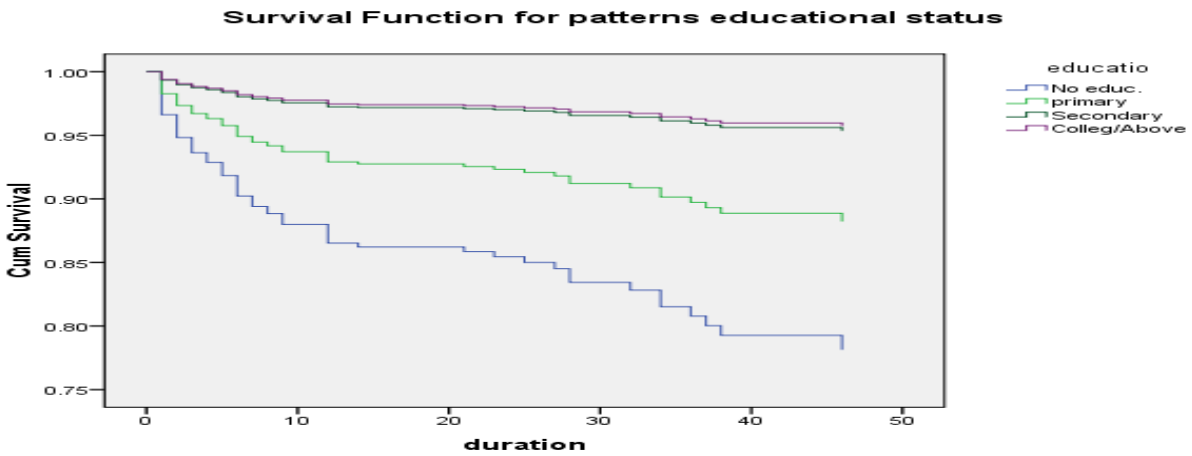

Figure 5: Survival function by educational status ofpatients study subjects who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

As shown in fig.5 patients with illiterate and primary educational status were at higher risk of death when compared to patients with secondary education and college level.

Out of the clinical and laboratory data bedridden functional, advanced WHO stage III & IV, lower BMI, CD4 lower than 200cell/μL and poor ART were shown to have a difference on the risk of death among the others in their group (fig.6 & 7).

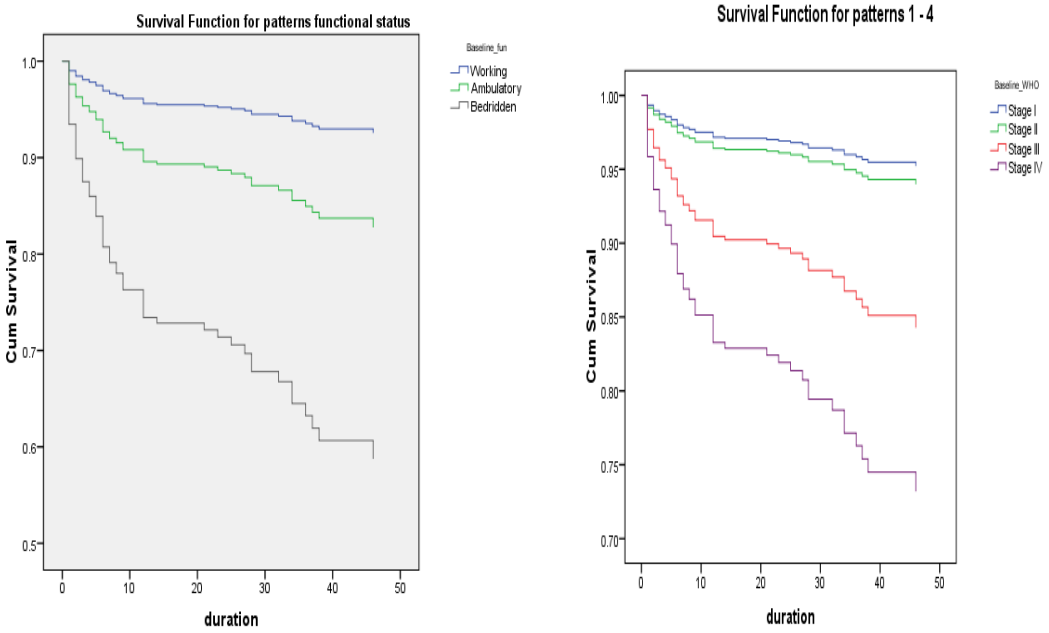

Figure 6: Survival function by functional status and WHO stage study subjects who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

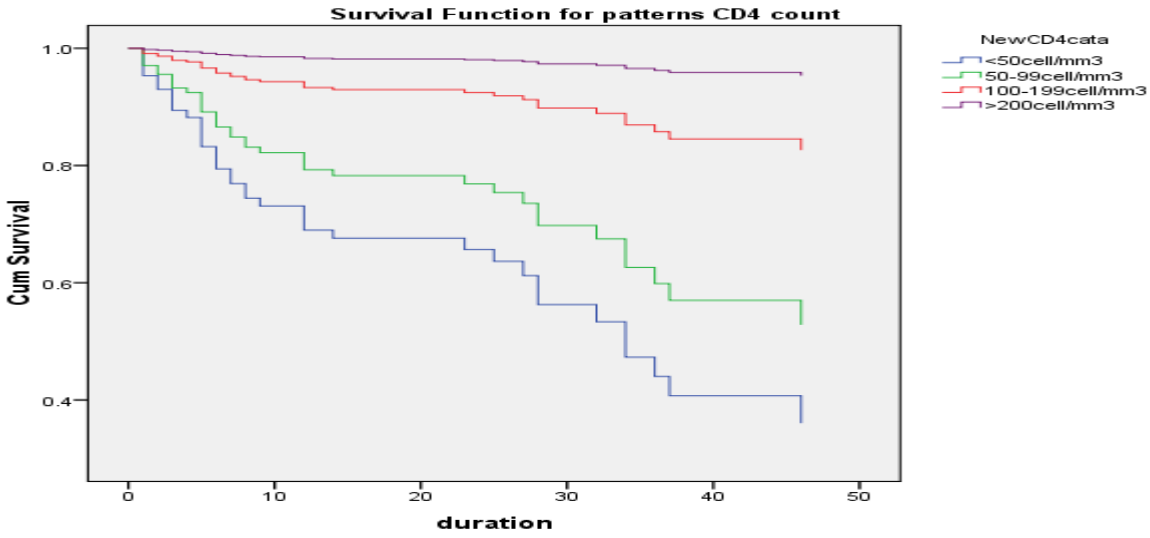

Figure 7: Survival function by CD4 counts of study subjects who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

Out of the 822 patients those patients with fair and poor adherence were found to have a markedly high risk of mortality when compared to patients with good adherence level (fig.8).

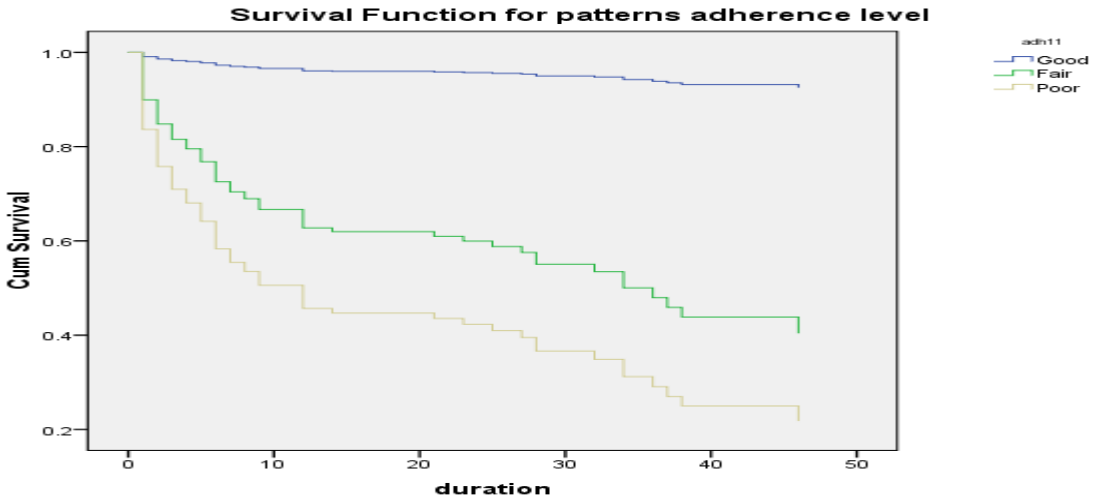

Figure 8: Survival function by adherence level study subjects who initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 -Dec.2013.

A multivariate Cox regression analysis was then done, with only those variables associated with survival with P-value <0.25 in the bivariate analysis and not collinear being entered in to the multivariate model. In the multivariate Cox regression analysis, each variable was checked to fit the model by adjusting for all remaining variables. Age of the cohort was also included in the model irrespective of its association during the bivariate analysis.

Using the multivariate Cox proportional hazard adjusted model, factors such as sex ((AHR=2.547, 95%CIs (1.23-5.72)) showing that males have twice higher risks of mortality when compared to females. With regard of the baseline clinical and laboratory data indicated subjects with bed ridden baseline functional status ((AHR=3.74, 95%CI (1.33-10.59) are four times more likely to die than those who had working functional status at baseline. Advanced WHO clinical stage III and IV had 3 and 4 times higher risk of mortality ((AHR=3.48, 95% CI (1.05-11.54)) and ((AHR=4.127, 95%CI (1.21-14.10)) when compared with those at stage I.

Lower BMI ,<18.5Kg/m^2 is shown to increase the risk of mortality six times when compared to those who have BMI ≥25Kg/m^2 (AHR=6.11, 95% CI (2.06-18.14)) and also lower CD4 count <50cells/μL & 50-99 cells/μL ((AHR=7.57, 95% CI (3.38-16.9)) & (AHR=5.85, 95% CI (2.57-13.3) had a marked effect on the survival status of PLHIV by increasing the risk of mortality by seven and six times when compared to those with CD4 count >200 cells/μL. Regarding adherence, poor ART adherence ((AHR=9.59, 95% CI (5.03-18.2)) increases risk of mortality ten times than good ART adherence.

In this study of the independent significant predictors of survival status of patients living with HIV/AIDS after initiation of ART, variables as being male gender, bedridden functional status, advanced WHO staging (III and IV), lower BMI, low CD4 count, and poor ART adherence were confirmed as significant independent predictors of death after controlling for other factors (Table 10).

Table 10: Multivariate Cox-regression analysis of predictor of survival among PLHIV initiated ART at Jigjiga, Kharamara hospital, Somali region, Eastern Ethiopia, Jan. 2009 - Dec.2013.

VARIABLES	SURVIVAL STATUS		AHR	(95% CI)
	DEAD	CENSORED		
Sex				
Male	**41(5.0%)**	**304(37.0%)**	**2.58**	**(1.02-5.72)****
Female	**28(3.4%)**	**449(54.6%)**	1	1
Baseline Functional Status				
Working	**25(5.1%)**	**465(94.9%)**	1	1
Ambulatory	**25(10.2%)**	**221(89.8%)**	2.24	(0.89-5.63)
Bedridden	**19(22.9%)**	**64(77.1%)**	**3.75**	**(1.33-10.59)****
Baseline WHO staging				
Stage I	**5(3.4%**	**144(96.6%)**	**1**	**1**
Stage II	**7(4.0%)**	**167(96.0%)**	.294	(.030-2.84)
Stage III	**37(9.9%)**	**337(90.1%)**	**3.48**	**(1.05-11.54)****
Stage IV	**20(16.7%)**	**100(83.3%)**	**4.13**	**(1.21-14.10)****
BMI				
< 18.5 Kg/m^2	**54(22.4%)**	**186(77.8%)**	**6.11**	**(2.06-18.14)****
18.5-24.9 Kg/m^2	**11(2.6%)**	**405(97.4%)**	.984	(.301-3.22)
>=25Kg/m^2	**4(3.3%)**	**117(96.7%)**	**1**	**1**
CD4 category				
<50 cells/μL	**25(18.5%)**	**101(81.5%)**	**7.57**	**(3.38-16.9)****
50-99 cells/μL	**20(14.3%)**	**120(85.7%)**	**5.85**	**(2.57-13.3)****
100-199 cells/μL	**16(5.5%)**	**275(94.5%)**	**1.78**	**(.761-4.16)**
< 200 cells/μL	**8(3.1%)**	**248(96.9%)**	**1**	**1**
ART Adherence				
Good	**33(4.4%)**	**720(95.6%)**	**1**	**1**
Fair	**15(38.5%)**	**24(61.5%)**	**6.15**	**(3.16-11.98)**
Poor	**21(72.4%)**	**8(27.6%)**	**9.59**	**(5.03-18.20)****

6. DISCUSSION

6.1. Discussion

According to this study, 69(8.4%) of the cohort died during the 60 months follow-up period, and out of the total many of the deaths 36 (52.2%) occurring in the first 3 months of follow up. This figure is similar with the result of a study conducted in Arbaminch hospital which also estimated mortality rate in ART+ group to be higher during the first three month of follow up [8]. Other studies done in different setting in Ethiopia and other African countries also proved that high mortality of PLHIV after ART initiation occurred during the early phase of treatment [55, 56, 57, 58, and 59]. Even though, the studies did not indicate the exact cause of high mortality at initial phases of treatment, it might be due the fact that most of the patients in the current study took longer time to initiate treatment and most of the study had advanced HIV stage (67.9% had CD4 < 200 cells/μL and 60.5% were in WHO stage III & IV) at baseline presentation and this can increases their risk of mortality due to the presence of opportunistic infection including TB..

The estimated probability of surviving in this study at 6, 12, 18 , 24, 36,and 48 months were 92.6%, 91.4%, 91%, 91.2%, 88 and 87.9% which is in line with a study conducted at public hospitals in Harar that showed the estimated survival probability to be 91.7%, 90.3% and 88.4% at 12, 24, and 36 months[34]. The result is slightly higher than the studies conducted in other African countries. For instance according to a study carried out in Malawi, the probability of being alive on ART at 6, 12 and 18 months was 89.8%, 83.4% and 78.8%[22]. But this difference can be explained by the differences in the frequency of events occurred, sample size, socio demographic and baseline characteristics of the of study participants. Other than this the growing understandings of HIV disease, its transmission and about the importance of ART might play a great role in improving the survival of PLHIV. The result of estimated probability indicates that as follow up time increases the estimated probability of surviving declines from time to time due to occurrence of death and the withdrawal of patients from the ART clinic due to different conditions.

Based on the results of this study conducted in Kharamara hospital Jigjiga town the independent significant predictors of death in patients living with HIV/AIDS after initiation of ART were being male gender, bedridden functional status, advanced WHO

staging (III and IV), low CD4 count, and poor ART adherence.

The study showed that males are at a higher risk of mortality as compare to females (AHR= 2.547 (1.02, 2.52)), which is in agreement with a study conducted in Durame and Hossana hospital that confirmed the relationship between male gender and mortality (AHR 1.704; 1.29-2.25) [70]. Similarly a study conducted in Malawi showed females had a significantly higher survival rates than males [59]. In addition study conducted in Cameroon showed male sex was a predictor of mortality with a risk almost double that of female sex (HR= 1.73: 95% CIs (1.37-2.19)). Majority of recent studies showed that males had significantly higher risk of mortality than females [22, 39 & 59], but a study conducted in Zambian adults showed higher mortality in women (HR=1.29) [60], while a study done in Uganda showed no difference in mortality by age or sex [61]. The difference in the result of the current study and those done in other african countries might have occured as a result of socio demograohic and environmental factor diffrenc of the study populatoins included in the study.

The difference in risk of death related to sex might be due to more women (58%) were receiving ART than men (42%) in Kharamara hospital at the time of this study. Even though there is no association between sex and adherence in this study, some studies justified this sex difference in survival can be due to more men are lost to follow up and poorly adhered than females [58].

Never married patients had high risk of mortality compared to the other marital status groups (CHR=4.25; 95%CI: **(1.59-11.39)**). This difference might be due to married patients' psychological preparedness to seek partners' and social support, conceive the facts, and adhere to ART.

Regarding educational status those study subjects who were not educated had high risk of mortality (CHR: 1.997; 95%CI: **(1.36-23.16)**) compared to those who attended college/above. Not educated groups had twice higher risk of mortality than those in college/above level. It is similar with the study done in Durame and Hosanna hospital that stated Patients who were educated at most primary level had high risk compared to those secondary or above (log ran test, P<0.001) [70]. This could be due that educational level may have an impact on adherence to therapy. The higher educational level groups may have a better understanding of the importance of ART treatment and adherence resulting

in increased survival. But both these results on marital and educational status were not consistent results in multivariate analysis indicating marital status and educational level are not strong predictors of survival in this study. Our study showed no difference in survival by religion, ethnicity and presence of dependent children, ART regimen that was similar to the studies conducted in different parts of our country [67, 68, 69 & 70].

In this study out of the baseline clinical predictors functional status, advanced WHO stages, lower BMI(< 18.5Kg/m^2), lower CD4 count and poor ART adherence were found to be associated with early mortality. A study conducted in Senegal also revealed a high mortality in poor countries was linked to lower base line CD4 count, concomitant TB infection, and lack of free care [37].

The result of this study revealed that patients with BMI <18.5 kg/m^2 had a higher risk of mortality (AHR= 6.11, 95% CI(2.06-18.14)) when compared with those with BMI ≥25 kg/m^2 but those groups 18.5-24Kg/m^2 (AHR=.984, 95% CIs (.301-3.22)) indicating that there is no difference in risk of mortality between the latter group (18.5-24Kg/m^2) and the subjects in the reference groups (≥25 kg/m^2). Different previous studies demonstrated BMI as one of the strong predictors of mortality.

A study conducted in rural Malawi also showed individuals who were severely malnourished (BMI <16kg/m^2) had six times higher risk of dying in the first three months than those with a normal nutritional status [62]. Another Study in Gambia shows the mortality hazard ratio (HR) of those with a baseline BMI <18 compared with those with a baseline BMI ≥18 was 3.4 (95%CIs: 3.0, 3.9) [64]. This implies that individual with BMI <18.5 kg/m^2 are more likely to die HIV related death. This might be due to lower BMI is common among patients with advanced WHO stage IV which are commonly affected by opportunistic infections including TB that are known increases the risk of death among PLHIV.

Regarding their functional status, patients in bedridden functional status (AHR=3.74, 95% CIs (2.06-18.14)) were 4 times more likely to die than patients in working functional status. This finding is consistent with many studies done in Ethiopia; for example, study done in eastern Ethiopia showed a 4.09 time of mortality risk for patients in bedridden functional status than working ones [34]. As stated in a study conducted in southern Ethiopia, the risk of death among working patients is lowered by 55% than bedridden patients during ART initiation [65]. The mortality risk of patients in ambulatory and

bedridden functional status is 2.11 and 3.35 times compared to working patients in Military Hospital in Addis Ababa, Ethiopia [66]. Another study done in Arbaminch hospital also concluded that risk of mortality was increased in bedridden patients by 2.99 times than working patients [67]. Based on a study done in Uganda Ambulatory and bedridden functional status were found to be 2.87 and 6.90 times at risk of death than the working status patients [55]. Therefore, patients who are on bedridden functional status should get due attention in order to reduce their risk of mortality.

In this study patients with advance WHO stages III and IV of patients had an increased the risk of death by 3 and 4 times than patients at stages I. Also, different studies in Ethiopia like the study done in the Armed Forces General Teaching Hospital, Addis Ababa supported this finding [68]. Moreover patients in advanced clinical stages are prone for TB and other opportunistic infection that calls an attention for routine screening and provision of prophylaxis as per the guideline [67].

Results of this study showed patients with a CD4 count of <50 cells/μL (AHR=7.5, 95%CIs (3.38-16.9) and 50-99 cells/μL (AHR=5.8, 95%CIs (2.57-13.)) having a higher risk of mortality when compared to those with a CD4 count of ≥200 cells/μL. The result is similar with study in Cameroon that showed patients with a base line CD4 count ≤ 50cells/mm^3 presented a mortality risk twice as high as those with >50 cells/mm^3 . Another study in Canada showed the hazard for the low CD4 count strata were higher CD4<50 cells/mm^3 (HR=6.07, 95% CI 4.11-8.97) relative to counts ≥200 cells/mm^3.[72] Majority of the previous studies identified Low CD4 count was one of the independent predictors of mortality [33, 36].

In this study, patients with poor and fair ART adherence were at high risk of death (AHR=**9.594** and AHR= 6.15) than those with good adherence. This result is in line with a study done in Addis Ababa, patients who have poor adherence were at risk of death by 3.92 times than with those who have good adherence patients [68]. Study conducted in Uganda also shows non adherent participants had a mortality of 42.5/ 1000 PYO and after adjusting for age, sex and educational level, were two times more likely to die than adherent participants [61].

In addition, adherence was significantly associated with immunologic recovery, especially in patients with AIDS defining disease. Poor adherence was a significant predictor of death. This could be used for further studies of the reasons for poor adherence and also to

increase the survivals of patients with poor ART adherence that need to be followed more frequently to decrease risk of death.

6.2. Limitations of the study

The study used secondary data, which had incomplete information on some important predictor factors such as Hgb level that may have an impact on the outcome variable. Those uncovered factors may have a marked significant impact on the outcome of interest. The unavailability of information on important predictors of survival may put the studies generalizability at stake.

Excluding of those study participants who do not have complete CD4 count and WHO clinical stage records may cause under/over estimation of health outcome. The exclusion of patients with incomplete information during data collection might also result in selection bias. Mortality might be underestimated by lost to follow up and drop out patients that probably included more individuals dying at home without being reported. The difficulty to ascertain the causes of death for deaths occurring for those deaths occurring outside of the health facility may lead to the over or under estimation of the outcome variable.

7. CONCLUSION AND RECOMMENDATION

7.1 CONCLUSION

The study revealed those different factors that determine the survival status of PLHIV after the initiation of ART. The identified predictor of survival includes sex, functional status, WHO staging, BMI, lower CD4, poor adherence etc. Even if ART plays a vital role in reducing HIV/AIDS related death in most settings including our country still the above mentioned factors are shown to be having a significant effect on the outcome of treatment on the survival status of the patients after the initiation of ART.

Other than the above mentioned factors level adherence to treatment, risky behaviors like tobacco use and educational status of the subjects are also shown to have a marked effect on the effectiveness of ART on averting HIV related death.

Generally the study cohort had lower mortality rate when compared to other earlier studies conducted in Ethiopia and other African countries. This emphasizes the importance of ART in reducing morbidity and mortality among PLHIV. The results of the study revealed that different factors can determine the outcome of ART treatment on improving the survival status of PLHIV.

The improvement or modification of these individual, organizational or environmental factors affecting the survival of the PLHIV can lead to improvement of the quality of life and increasing of the survival status of the PLHIV. However, a lot needs to be done regarding patient retention and adherence. Also further studies are needed to understand the underlying causes of patient attrition.

7.2 RECOMMENDATION

Based on this study finding, the following recommendations can be forwarded to concerned authorities to improve the effectiveness of the ART service;

TO JIGJIGA REGIONAL AND ZONAL HEALTH BUREAU

- Policy makers and programmers at national and regional level has to work on increasing access to ART in collaboration with non-governmental stake holders.
- Planning and implementing an effective service for HIV/AIDS patients that is focused on important aspects that can improve survival.
- Integrating the HIV care with other developmental organizations like NGOs, Religious leaders and community supporters.

TO KHARAMAR HOSPITAL

- Ongoing monitoring of patients with advanced WHO staging, bedridden functional status, positive TB test result and lower BMI are necessary particularly during the first few months of ART initiation.
- Health care providers working in ART clinic should give greater attention for data recording since data are crucial in patient monitoring and follow up.
- Careful follow up for patients with poor adherence and giving them drug counseling is crucial to improve survival. Health care providers working in ART clinic should work with the patients to enhance adherence towards ART because adherence barriers are significant in predicting survival.
- Develop a way to control the completeness and reliability of base line and follow up data being collected especially on important clinical and laboratory records.
- Behavioral factors are known to have an impact on the health status of patients and working on these factors can improve the quality of life of the patients.
- Collaborated efforts should focus on improving the survival of high risk groups.
- Extensive studies are needed to assess underlying causes for patients declared as LTFU at ART clinics.

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9. ANNEXES

9.1. Annex

I. Questionnaire

INTRODUCTION

This patient information collection sheet is intended to assess predictors of survival of HIV/AIDS patients after initiating antiretroviral treatment at ART clinic of Kharamara Hospital, Jijiga, Ethiopia. The study will be conducted through reviewing secondary data and visiting the home/calling if the status of the patient is not recorded or found in the ART follow up form. 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 predictors 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 PLWHA.

Date of review [___/___/_____]

Name of the reviewer _____Signature _____

Time (Started/ Ended) [_____/_____]

Supervisor Name _____

Signature _____ Date [___/____/_____]

Total number of records reviewed _____

Reviewed Patient's card No. from _____to_____

Available Data: I. Complete____ II. Incomplete_____ III. Excluded____

Action taken for the incomplete data:

_____

_____

_____

_____

_____

_____

_____

_____

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

Part I. Study Subjects Baseline Information (from ART Clinic Intake form)

SECTION 1: Socio-Demographic Characteristics

101. Patient ID Number_____

102. Unique ART Number_____

103. Age _____

104. Sex _____

1. Male 2. Female

105. Ethnicity

1. Somali 3. Amhara
2. Oromo 4. Gurage 99. Others(specify)_____

106. Religion

1. Muslim 3. Protestant
2. Orthodox 4. Catholic 99. Others(specify)_____

107. Educational status

1. No education 3. Secondary
2. Primary 4. College/ Above

108. Occupational status

1. Merchant 5. Day laborer
2. Gov't employee 6. driver
3. Non gov't employee 7. Jobless
4. Military 8. Others(specify)_____

109. Marital status

1. Never married 4. Divorced
2. Married 5. Widowed
3. Separated

110. Dependent children at home

101. Yes 2. No

SECTION 2: Baseline Clinical, Laboratory &Art Information

201. Confirmed HIV+ date____ /____ /_____

202. Date Eligible for ART ____ /____ /_____

203. ART start date____ /____ /_____

204. Duration since initiation of ART_____(months)

205. Adherence level for ART

1. Good 2. Fair 3. Poor

206. Past opportunistic illnesses

0. No
1. Candidiasis
2. CMV
3. Crypt. Meningitis
4. Kaposi sarcoma
5. Cryptosporidiosis
6. Diarrhea > 1 month1
7. Diss. Atyp. Mycoses
8. Encephalopathy
9. Wasting syndrome
10. Herpes simplex
11. Mycosis
12. Fever
13. PGL
14. PCP
15. PML
16. Pneumonia
17. Salmonellosis
18. EPTB
19. Toxoplasmosis
99. Other (specify) _____

207. Past TB smear test and result

1. Not determined
2. Negative
3. Positive
4. Pos+
5. Pos++
6. Pos+++

208. Past TB treatment

1. Not determined
2. 2SRHZ/6EH
3. 2HRZES/1HRZE/5HRE
4. 2HRZE/6HE

209. ARV eligibility criteria

1. CD4 below 200
2. WHO stage IV
3. WHO stage I, II, and III with TLC <1200
4. Residence of catchment area

210. Past ARV treatment

0. No
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)
8. Others (specify) _____

211. Past CD4 test

1. Yes, Date [___ /___ /_____]
2. No

212. Past medication (check all)

0. No
1. Cotrimoxazole
2. INH
3. Fluconazole
99. Other (specify) _____

213. Height at baseline _____(cm)

214. Weight _____(Kg.)

215. Baseline Functional status at baseline

1. Working
2. Ambulatory
3. Bedridden

216. Baseline WHO clinical stage

1. Stage I
2. Stage II
3. Stage III
4. Stage IV

217. Hgb at baseline _____(g/dl)

218. CD4 at baseline_____ (count/ µL) Date: [___ /___ /_____]

219. ALT at baseline_____

220. AST at baseline_____

SECTION 3: Baseline Social Conditions

301. Current employment

1. Working full time
2. Working part time
3. Not working
4. Unemployed
99. Other (specify) _____

302. Religious / supportive care

1. Yes
2. No

303. HIV serostatus disclosure

1. Yes
2. No

304. Spouse information

a. Condition of the husband /wife

1. Heathy
2. Chronically ill
3. Dead
4. Unknown

b. HIV tested

1. Not asked
2. Negative
3. Positive
4. Unknown

c. TB tested

1. Not asked
2. Negative
3. Positive
4. Unknown

d. Was/is on ART treatment

1. Yes
2. No

e. Was/iso on TB treatmnet

1. Yes
2. NO

305. General concern identified

1. Financial issue
2. About the children
3. Marital relation ship
4. Family relations
5. Bereavement/ Grief
6. HIV status disclosure
7. Adherence to treatment
8. Dietary problems
99. Other (specify) _____

SECTION 4: Knowledge on HIV and ART

401. Attended HIV related health education in the past

1. Yes
2. No

402. Attended HIV related counseling in the past

1. Yes
2. No

403. Understanding of HIV disease

1. NA 2. - 3. + 4. ++ 5. +++

404. Understood of HIV transmission

1. NA 2. - 3. + 4. ++ 5. +++

405. Understood prophylaxis and OIs

1. NA 2. - 3. + 4. ++ 5. +++

406. Understood of ART medication adherence

1. NA 2. - 3. + 4. ++ 5. +++

SECTION 5. Risk Behavior

501. Had regular partner

1. Yes 2. No

502. Had causal sexual Partner

1. Yes 2. No

503. Condom use

1. NA
2. Never
3. Rarely
4. Sometimes
5. Mostly
6. Always
7. No response

504. Addiction

a. Tobacco

1. NA 2. - 3. + 4. ++ 5. +++

b. Alcohol

1. NA 2. - 3. + 4. ++ 5. +++

c. Soft drugs (e.g.- Khat, shisha etc)

1. NA 2. - 3. + 4. ++ 5. +++

d. Hard drugs (Cocaine, Morphine, IV drugs, etc)

1. NA 2. - 3. + 4. ++ 5. +++

505. Barriers to ART adherence

1. Stigma (from family and friends)
2. Afraid of medications side effects
3. Doubt that medications will work
4. Depressed/anxious
5. Will forget to take medications
99. Other (specify)_____

Part II. Patient's Recent information (from ART follow up form).

601. Latest follow-up date [___ /____ /_____]

602. Recent weight _____ (kg), Date [___ /___ /_____]

603. Recent functional status

1. Working 2. Ambulatory 3. Bedridden

604. Recent WHO clinical stage

1. Stage I 2. Stage II 3. Stage III 4. Stage IV

605. TB screened recently

1. No 2. Positive 3. Negative

606. Recent TB prophyiaxis

1. Yes 2. No

607. Recent TB treatment

1. Yes 2. No

608. Recent opportunistic infections

0. No
1. Zoster
2. Bacterial pneumonia
3. Pulmonary TB
4. Extra-pulmonary TB
5. Oral/Vaginal trash
6. Mouth/ Genital ulcer
7. Chronic or acute diarrhea
8. Pneumocystis carini pneumonia
9. CNS toxoplasmosis
10. Cryptococcal meningitis
11. Other (specify)_____

609. Recent ARV adherence

1. Good 2. Fair 3. Poor

610. If (2 or 3) for 609, Reason for Fair or Poor adherence

1. Forgot
2. Share with others
3. Drug stock out
4. Felt better
5. Too ill
6. Delivery/travel problems
7.Toxicity/side effect
8.Lost/run out of pills
9.Stigma disclosure
10.Inability to pay
11.Alcohol
12.Depression
99. Other (specify) _____

611. Recent dispense

. 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)
8. 1f=TDF / 3TC / NVP
9. 1e=TDF / 3TC / EFV
99. Other (specify)_____

612. Reason for regimen change

0. Not changed
1. Toxicity/side effect
2. Pregnancy
3. Risk of pregnancy
4. Due to new TB
5.New drug available
6. Drug out of stock
7.Clinical failure
8.Immunologic failure
9.Virological failure
99. Other (specify) _____

613. Side effects

. 0. No side effects
1. Nausea
2. Fatigue
3. Diarrhea
4. Anemia
5. Jaundice
6. Headache
7.Abdominal pain
8.Rash
9.Fat change
10.Numbness/tingling
11. Anxiety, Nightmare

614. Recent CD4 count_____ (Cell/ µL) Date: ___/___/_____

615. CD4 Level (Cell/µL) at Follow up visits

At Baseline _____ Date: ___ ___/_____
At 6 month _____ Date: ___/___/_____
At 12 month _____ Date: ___/___/_____
At 18 month _____ Date: ___/ ___/ _____
At 24 month _____ Date: ___/ ___/ _____
At 30 month _____ Date: ___/ ___/ _____
At 36 month _____ Date: ___/ ___/ _____
At 42 month _____ Date: ___/ ___/ _____
At 48 month _____ Date: ___/ ___/ _____
At 54 month _____ Date: ___/ ___/ _____
At 60month _____ Date: ___/ ___/ _____

616. Recent weight _____(Kg) , Date: ___/ ___/ _____

617. Patient weight (Kg) at Follow up visits

At Baseline _____ Date: ___ ___/_____

At 6 month _____ Date: ___/___/_____

At 12 month _____ Date: ___/___/_____

At 18 month _____ Date: ___/ ___/ _____

At 24 month _____ Date: ___/ ___/ _____

At 30 month _____ Date: ___/ ___/ _____

At 36 month _____ Date: ___/ ___/ _____

At 42 month _____ Date: ___/ ___/ _____

At 48 month _____ Date: ___/ ___/ _____

At 54 month _____ Date: ___/ ___/ _____

At 60month _____ Date: ___/ ___/ _____

618. Recent Hgb _____ , Date: ___/ ___/ _____

619. Recent ALT _____ , Date: ___/ ___/ _____

620. Recent AST_____ , Date: ___/ ___/ _____

621. Was Isoniazid prophylaxis initiated?

1. Yes 2. NO

622. If yes to Qu. 621, Start Date: ___/ ____/ _____, Duration: _____ (Weeks/Months).

623. Was cotrimoxazole prophylaxis initiated?

1. Yes 2. NO

624. If yes to Question 623, Start Date: ___/ ____/ _____, Duration: _____ (Weeks/Months).

625. Status of the participant at the end of follow up period

1. Active, Date: ___/ ___/ _____
2. Dead, Date: ___/ ___/ _____
3. LTFUP, Date: ___/ ___/ _____
4. Drop out, Date: ___/ ___/ _____
5. Transfer out,Date: ___/ ___/ _____

Declaration

I, the undersigned, declare that this Research thesis is my original work and has not been presented for a degree in this or any other university, and all sources of materials used for this thesis have been fully acknowledge.

Name of the student: _____

Signature: _____

Name of the institution: Jimma University

Date:_____

Approval of the first advisor:

This thesis has been submitted with my approval as the University advisor.

Name of the first advisor:_____

Date_____ Signature_____

Approval of the second advisor:

This thesis has been submitted with my approval as the University advisor.

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