SURVIVAL STATUS AMONG PATIENT LIVING WITH HIV AIDS WHO ARE ON ART TREATMENT IN DURAME AND HOSSANA HOSPITALS

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SURVIVAL STATUS AMONG PATIENT LIVING WITH HIV AIDS WHO ARE ON ART TREATMENT IN DURAME AND HOSSANA HOSPITALS

A RETROSPECTIVE LONGITUDINAL STUDY

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LIST OF ACRONYMS

AIDS; Acquired Immune Deficiency Syndrome

AHR; Adjusted Hazard Rate

ART; Antiretroviral Therapy

AZT; Zidovudine

BMI; Body Mass Index

CHR; Crude Hazard Rate

CI; Confidence interval

d4t; Stavudine

EFV; Efaviren

EPTB; Extra Pulmonary Tuberculosis

HAART; Highly Active Antiretroviral Therapy

HAPCO; HIV/AIDS Prevention and Control Office

HIV; Human Immunodeficiency Virus

MOH; Ministry Of Health

NNRTI; Non-Nucleoside Reverse Transcriptase Inhibitor

NRTI; Nucleoside Reverse Transcriptase Inhibitor

NVP; Nevirapine

PCP; Pneumocystis Carini Pneumonia

PI; Protease Inhibitor

PLWHA; People Living With HIV/AIDS

PTB; Pulmonary Tuberculosis

SNNPR; Southern Nations Nationalities Peoples Region

3TC; Lamivudine

TLC; Total Lymphocyte Count

VCT; Voluntary Counseling and Testing

WHO; World Health Organization

ABSTRACT

Introduction: The benefits of highly active antiretroviral therapy 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. Factors that limit the success of HAART include poor therapy adherence, regimen complexity, viral resistance, drug tolerability and toxicity, therapy costs, and presence of comorbid conditions such as substance abuse and addiction. The optimal time to start treatment for HIV/AIDS has been a contentious issue since the introduction of Highly Active Antiretroviral Treatment.

Objective: To assess survival in PLWHA and started ART treatment in Durame and Hosanna hospital

Methodology: A retrospective longitudinal study was conducted in Durame and Hosanna hospital. Patient's records enrolled between august, 2006 to July, 2010 was reviewed by using patients ART unique identification number as a reference and the total sample size of the study was 481. Univariate analysis was used to describe patient's baseline characteristics. Actuarial 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 determine independent predictors of time to death.

Result: Four hundred eighty one patients on ART were followed for a median of 24 month (IQR 13, 40). The mean age was 36.4 and the median weight of the cohort at the initiation of ART was 52kg (IQR, 48-57kg).The median CD4 count was 154cells/µl (IQR, 102-224). The estimated mortality was 7%, 8%, 11.3 %, 15.7% and 21% at 6, 12, 24, 36 and 48 months respectively. After adjustment, the independent significant predictors of death in patients living with HIV/AIDS after initiation of ART remain poor ART adherence(AHR=5.09[95%CI=5.51, 49.48]),Advanced WHO staging (AHR=1.5[95%CI= (1.18, 2.16]), positive TB test (AHR=3.9[95%CI= 1.89, 8.07]), not married or single (AHR=10.27[95%CI=1.35, 78.3), male gender (AHR=1.704[95%CI= 1.23, 2.24])and older age(AHR=1.45[95%CI=1.1,1.96).

Conclusion: This study demonstrates that simple laboratory and clinical data, available to health care providers prior to ART initiation, can predict which patients are at increased risk of death when they start therapy.

I.INTRODUCTION

HIV has infected close to 70 million people and more than 30 million have died due to AIDS. More than 66% of the 40 million people living with HIV AIDS are in sub Saharan Africa, where AIDS is the leading cause of death. About 14,000 people in sub Saharan Africa are being infected daily with HIV and 11,000 are dying every day due to HIV AIDS related illnesses (1).

AIDS is one of the most destructive epidemics in the world, Cumulative worldwide mortality associated with HIV and AIDS has been estimated at 3.1 million (2). Although only 10% of the world's population lives in sub Saharan Africa, the region is nevertheless home to around two-thirds of the world's HIV-infected people, In 2007, an estimated 22.5 million adults and children in the region were living with HIV/AIDS and 1.6 million died, representing 76% of global AIDS deaths (3).

The World Health Organization (WHO) had estimated that there were over 1.3 million people receiving anti retroviral therapy (ART) in low and middle income countries, representing 20% of 6.5 million estimated to need it, Great progress has been made in providing access to ART in sub-Saharan Africa; by April 2007, approximately 1.3 million people were receiving ART some 28% of the 4.8 million people estimated to be in need (3).

In Ethiopia more than 1.3 million people living with HIV and an estimated 277,800 people requiring treatment. In 2003 the government of Ethiopia introduced ART program with the goal of reducing HIV related morbidity and mortality, improving quality of life of people living with HIV and mitigating some of the impact of epidemic, In 2005 Ethiopia launched free ART and over 71, 000 were initiated by the end of November 2006 and 241 hospitals and health centers are now providing HIV care and treatment services in regions of the country (4).

In Ethiopia the adult prevalence of HIV was estimated to be 2.2% in 2008. The total number of People Living with HIV/AIDS (PLHIV) in the same period was estimated to be 1,037,267 adults and 68,136 of them were children. Furthermore the number of deaths due to AIDS for the same period was estimated to be 58,290 for adults and 9,284 among children (5).

Ethiopia is currently decentralizing HIV care and treatment services to selected health centers. Decentralization increases access by taking services closer to more people, reducing transport and related costs for patients and families, resulting in improved adherence and enrolment in care and treatment services early in the course of the disease. Decentralization follows the health network model, ensuring linkages between services at hospital, health centre and community levels. Large scale in-service trainings in various programme areas have been carried out to build capacity of different cadres of health care providers. Efforts have been made to demystify HIV care and ART by developing standardized and simplified clinical tools, reference materials, and job aids. Building the capacity of clinical nurses to prescribe first-line ARVs for stable patients and provide primary chronic HIV care including ART was pioneered in 2006. Ethiopia is also piloting the use of trained non-health professional counselors (6).

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,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. Factors that limit the success of HAART include poor therapy adherence, regimen complexity, viral resistance, pharmacodynamic interactions, drug tolerability and toxicity, therapy costs, and presence of comorbid conditions such as substance abuse and addiction (7).

A fundamental component of working towards the goal of providing, by 2010, universal access to antiretroviral treatment for patients with acquired immunodeficiency syndrome (AIDS) is an increased and secured production of antiretroviral drugs (ARTs) in order to meet the increased demand from lower- and middle-income countries. The vast majority of adults (96%) were reported to be receiving first-line regimens. Reporting compliance was very high for this group, with information on the specific regimens used available for 97% of this set of patients. The

programs reported that 95% of all adults receiving first line regimens were using regimens consistent with the preferred first-line approach including: Stavudine (d4T) lamivudine (3TC) Nevirapine (NVP) (61%), Zidovudine (ZDV) +3TC+NVP (16%), ZDV+3TC+ efavirenz (EFV) (9%), and d4T+3TC+EFV (8%) Less than 1% of these groups were reported to be taking either alternative first-line regimens, including the triple nucleoside combinations of ZDV+3TC+abacavir (ABC) and d4T+3TC+ABC, or taking regimens not considered or not recommended by WHO (8).

RATIONALE OF THE STUDY

The survival benefit of highly active antiretroviral therapy (HAART) in HIV infection and its impact on the incidence of opportunistic infections have been well studied in the developed World. 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. As a result, the existing treatment guidelines and recommendations are based on data from the developed world (9).

The study will give 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 basic information on factors affecting survival of PLWHA and started ART treatment

II. LITERATURE REVIEW

3.1 Burden of HIV/AIDS globally and ART in Ethiopia

Globally 39.4 million peoples are living with HIV AIDS. Adults contribute 37.2 million. About 5 million peoples are newly infected of which 4.3 million are adults from these more than 95% of new infections are in developing countries. Over 6 million need ART but 350,000-400,000 is treated in developing countries. By December 2006 two million people in low and middle income countries were receiving ART but this was still only 28% of those estimated to be in urgent need of it (9).

In Ethiopia 47% of the total population is aged 15 to 49 years. The highest prevalence occurs in the age group 15-24, 90% of HIV infection occurs in adults between 15-49 years. In Ethiopia 443,964 PLWHA enrolled, 246,347 PLWHA started treatment and 179,183 are currently on ART. The total persons on 1st line regimen is 166,444 of which 156,083 are adults. The total number of persons on 2nd line regimen is 1000 of which 865 are adult. among adults on the 1st line regimen 64,605 are 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 .6% are on 2nd line regimen from these 132 on ABC-ddI-LPV/R and 733on TDF-ddI-LPV/R and 11,739 are on others and unspecified regimens (10,11).

3.2 Factors affecting survival

Study conducted in south Africa reveals that the strongest predictors of mortality were a 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 a 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 a history of oral candidiasis (HR 2.58, 95% CI 1.37 - 4.88) remained significant in multivariate analysis (12).

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 (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 (15).

Individuals with incomplete CD4 T cell recovery to <500 cells/microL had more advanced HIV-1 infection at baseline. CD4 T cell changes during the first 3-6 months of ART already reflect the capacity of the immune system to replenish depleted CD4 T lymphocytes (16, 17).

In a study of 421 Italian patients with AIDS who were followed for up to 30 months, a hemoglobin level of 8 to, 11g/dL was associated with a relative risk of dying of 1.9 (95%CI 5 1.3–2.8) and a hemoglobin level of 8 g/dL was associated with a relative risk of dying of 2.9 (95% CI 1.9–4.5) compared with patients having a hemoglobin level of above 11 g/dL at the time of diagnosis of AIDS (18).

WHO stage IV diseases, however, was found to be a strong predictor of mortality in all studies reporting on this. 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 a doubling in the hazard of death (summary hazard ratio, 2.2; 95% CI, 1.5–3 (1).

The mortality hazard ratio (HR) of those with a baseline BMI <18 compared with those with a baseline BMI >18 was 3.4 (95% CI, 3.0–3.9). The median survival time of those presenting with a BMI <16 was 0.8 years, in contrast to a median survival of 8.9 years for those with a baseline BMI >22. Baseline BMI <18 remained a highly significant independent predictor of mortality after adjustment for age, sex, co-trimoxazole prophylaxis, tuberculosis, reported wasting at diagnosis, and baseline CD4+ cell count (adjusted HR = 2.5, 95% CI 2.03.0) (19).

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 (20).

Compared with younger patients, older patients were more likely to be on non nucleoside reverse transcriptase inhibitors based versus protease inhibitor based regimens (42 vs. 29%, P<0.01). Older patients had fewer AIDS-defining opportunistic infections (22 vs. 31%, P<0.01), but higher mortality (36 vs. 27%, P=0.04) and shorter survival (25^{th} percentile survivor function 36.2 vs. 58.5 months, P=0.02) than younger patients (11).The analysis in Nigeria demonstrates Male gender (HR,1.77, CI,1.15_2.75, P<0.010), age less than 30 years old (HR ,1.65, CI ,1.07_2.53, P<0.023), CD4 count less than 50 (HR,3.28, CI,2.20_4.89, PB=0.0001), co-infection with HIV and TB (HR,3.53, C,_2.36_5.28, PB=0.0001), and unemployment/ unknown occupation (HR,1.79, CI,1.21_2.66) were significantly associated with increased risk of death (21,22).

Significant risk factors associated with mortality included WHO stage IV disease, a base line CD4 cell count under 50 cells/mul and increasing grades of malnutrition. Individuals who were severely malnourished [body mass index (BMI) < 16.0 kg/m] had a six times higher risk of dying in the first 3 months than those with a normal nutritional status (23).

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) (23).

Study conducted in the far north province of Cameroon showed that survival probability was 77% at 1 year [95% CI: 75–80] and 47% at 5 years [95% CI: 40–55]. The median survival time was 58 months. CD4 count, haemoglobin, BMI, sex and clinical stage at enrolment were independent predictors of mortality. 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). 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 haemoglobin <8.5 g / dl had two times more risk of death than those with a haemoglobin rate >8.5 g / dl (24).

Study conducted in zewuditu hospital showed that estimated mortality 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 CD4 count (AHR=1.85[95%CI=1.35, 2.52]) (25).

3.3 Adherence and ART regimen

Study in India showed that 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. 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 Asian study result showed that type of regimen used at treatment initiation significantly predicted the rate ratios of subsequent changes (with NNRTI and no PI; RR 1.64 (1.38 – 1.96) $p < 0.001$, with PI no NNRTI; RR 3.39 (2.76 – 4.16) $p < 0.001$, NRTI only; RR 6.37. (4.51 – 9.00) $p < 0.001$, reference regimen is d4T/3TC/NVP). Moreover, being on a second or a third combination regimen was associated with a reduced rate ratio of change in ART, as compared with being on a first prescribed combination therapy (second RR 0.82 (0.68 – 0.99) $p = 0.039$,third RR 0.77 (0.61 – 0.97), $p = 0.024$) (27).

In collaborative analysis of prospective studies Antiretroviral therapy substantially reduces mortality rate among HIV/TB-co infected patients. Initiation of ART within 6 months of TB diagnosis is associated with greater survival. 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 the corresponding figures were 4.1-99% for AIDS or death and 1.3-96% for death alone .triple ART, detectable viral load,CD4 count at base line, and change in CD4 count were important in predicting CD4 counts <200 cells/µl (28, 29).

Study conducted in native American adults shows that the main Factors associated with the greatest reduction in risk of death from time of study entry were current use of HAART, HR 0.13 (0.06–0.30, p<0.001), and CD4 count 200 at entry, HR 0.16 (0.08–0.35, p 0.001). Current use of HAART was the strongest predictor of survival from time of AIDS diagnosis, HR 0.11 (0.05–0.25, p< 0.001). The use of HAART therapy and CD4 count were primary predictors of survival (Under the hypothesis that the patients lost to follow-up were dead, study in Senegal shows the probabilities of dying were respectively 13.4% (95% CI, 10.4–17.1%) and 21.0% (95% CI, 17.4 25.4%) at 12 and 24 months of follow-up. Mortality rate decreased from 12.5 deaths/100 person-years (95% CI, 9.4–16.7) during the first year of treatment to 6.6/100 person-years (95% CI, 4.3–10.0) during the second year [hazard ratio (HR), 1.9; 95% CI, 1.1–3.1 P< 0.01] and kept decreasing thereafter (4.5, 2.3 and 2.2/100 person-years for years 3, 4 and 5, respectively) (20). For 0-3, 3-9 and >9 months from ART start mortality rates were 24, 13 and 6/100 pyrs respectively. 43% of the deaths were in the first 3 months of treatment. Adjusted hazard ratios (aHRs) for participants with hemoglobin <8, 8.1-9.9, >11.9(f)/12.9 (m) g/mL were 4.99, 3.05 and 0.12 respectively comparing to 10-11.9 (f)/12.9 (m)g/mL in the first 3 months of ART. AHRs for CD4 counts were 0.40, 0.38 and 0.34 for 50-99, 100-200 and >200/µL comparing to <50/µL (30).

The optimal time to start treatment for HIV/AIDS has been a contentious issue since the introduction of Highly Active Antiretroviral Treatment (HAART). In the revised 2009 guidelines, it is recommended that HAART is initiated on all HIV patients with CD4 counts < 350 cells/µl, regardless of symptoms (31).

According to Degu J, mortality rate in ART+ group was 15.4/100PYO and most of the death occurred during the first three month. Robert etal in other hand revealed the cumulative mortality rate at 12 months was 2.9%.Frank J. etal estimated mortality rates ART +were 15.4 and 56.4 deaths per 1000 person-year (32,33).

Non-adherent patients who initiated HAART when the CD4+ cell count was 0.200 to 0.349 x 10(9) cells/L had statistically elevated mortality rates (adjusted relative hazard, 2.56 [95% CI, 1.36 to 4.84]; P = 0.004) compared with adherent patients who initiated HAART at a CD4+ cell count of 0.350 x 10(9) cells/L or greater, However, compared with adherent patients who initiated HAART at a CD4+ cell count of 0.350 x 10(9) cells/L or greater, adherent patients who initiated HAART when the CD4+ cell count was 0.200 to 0.349 x 10(9) cells/L had statistically similar mortality rates (adjusted relative hazard, 0.82 [CI, 0.45 to 1.49]; P > 0.2). Delaying HAART until the CD4+ cell count falls to 0.200 x 109 cells/L does not increase the mortality rate in HIV-infected patients with good medication adherence. Mortality rates increase if HAART is initiated below 0.200 x 10(9) cells/L. Also, non adherent patients have higher mortality rates than adherent patients with similar CD4+ cell counts. Above a CD4+ cell count of 0.200 x 10(9) cells/L, medication adherence is the critical determinant of survival, not the CD4+ cell count at which HAART is begun(34)

III.OBJECTIVE

2.1 GENERAL OBJECTIVE

To assess survival status among PLWHA who are under ART treatment in Durame and Hosanna hospitals.

2.2 SPECIFIC OBJECTIVES

- To estimate time to death of PLWHA who are on ART
- To determine factors affecting survival in PLWHA after initiation of ART

IV. METHODOLOGY

4.1 Study area and period

The study was conducted in Durame and Hosanna hospital from December 28 to February 05. Kembata Tembaro and Hadiya zones are two zones from 13 zones of SNNPR .there are 7 woredas and one town administration in Kembata Tembaro zone and there are 10 woredas and one town administration in Hadiya zone. Durame town is administrative center for Kembata Tembaro zone and it is 362 km away from Addis Ababa. In Durame town there is one zonal hospital, one health center and one maternal and child center which give preventive, curative and rehabilitative service for the catchment area population. ART clinic in Durame hospital gives ART service for HIV patients, a total of 656 patients have been enrolled, 310 ever started ART and 212 are currently on ART. Hosanna town is administrative center for Hadiya zone and it is 235 km away from Addis Ababa, in Hosanna town there is one hospital and health center which gives preventive, curative and rehabilitative service for the catchment area population. ART clinics in Hosanna hospital and health center give an ART service for HIV patients, a total of 1,745 have been enrolled, 910 ever started ART and 623 patients are currently on ART and there are 835 ART attendants currently in both hospitals.

4.2 Study design

A retrospective longitudinal study was conducted in Durame and Hosanna hospital to assess survival in PLWHA and who are on ART.

4.3 Population

4.3.1 Source population

Person living with HIV/AIDS, age ≥15years and started ART treatment in Durame and Hosanna hospital.

4.3.2 Study population

Those patients fulfilling the following criteria

Inclusion criteria

- HIV positive adults aged 15yrs or older who started ART
- HIV patients with complete intake form, registers and follow up form

Exclusion criteria

- Diagnosis is made outside of health institution
- Loss to follow up
- Women who were pregnant at the time of ART initiation and lactating mother

4.4 Sample size determination and sampling technique

4.4.1 Sample size determination

The sample size was calculated based on the assumption that type I error 5%, power of 80% one exposure(being on ART treatment) and two outcome (cumulative survival rate) allocation ratio, median survival time was taken from previous study.

$$n = \left(Z_{\frac{\alpha}{2}} + Z_{\beta}\right)^2 \left(\frac{1 + \frac{1}{m}}{\frac{p}{\ln(r)^2}} \right)$$

$$p = 1 - p_a \exp\left(-\ln(2)\frac{F}{m}\right) \quad (35)$$

$$pa = 1 - \frac{\exp\left(-\ln(2)\frac{A}{m}\right)}{\ln(2)\frac{A}{m}}$$

$$m = (C + E)/2$$

Where;

C=median survival time for non exposed group (the value is 48)

E=median survival time for exposed group (the value is 27.9) (36)

F=follow up time (4years)

A= accrual time during which subjects are recruited to the study (the value is 2)

M=number of non exposed group per exposed group

r=ratio of median survival times

α=level of significance

Zα/2=1.96 at 95% confidence interval

Power=1-β=90%, Zβ=1.282

n=minimum sample size required for each group

The sample size is 292 for n_1 (being on ART treatment) and146 for n_2 (cumulative survival time), the 10% contingency is added and the final sample size is 321for n_1 and161for n_2 finally resulting the total sample size of 481.

4.4.2 Sampling technique

study participant were selected by using systematic random sampling method by which one random number in the Patient's ART unique identification numbers as a starting point and every number next to random number will be taken as a study participant if the data in registration book is incomplete the next number will be taken as a study participant. The sample was taken proportionally from both hospitals 128 from Durame hospital and 353 from Hosanna hospital. Profiles of all patients on ART between August 2006 and July 2010 were evaluated. Then after loss to follow up, drop out, PMTCT and transfer out or patients Started ART since July 2010 or before August 2006 or with incomplete data were excluded.

4.5 data collection procedure

4.5.1variable

4.5.1.1 Independent variable

The independent variables are

- Socio demographic characteristics(age, sex, religion, ethnicity ,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, BMI, Hgb, T-cell lymphocyte count,CD4count, side effects)
- ART treatment

4.5.1.2 Dependent variables

The main outcome measure is survival status from the initiation of ART to November 2010

4.5.2 Questionnaire

The checklist consists of the following data

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

4.5.3 Data collection and quality control

A data collection form was developed from ART entry and follow up form being used in the ART clinic. The data was collected by reviewing pre-ART register, laboratory request, monthly cohort form, and follow up form, ART intake form, patients' card and death certificate complemented by registration by home visitors. The most recent laboratory results before starting ART was used as a base line value. If there is no pre-treatment laboratory test, results obtained within one month of ART initiation was used .if two results obtained within a month the mean was used. A total of three day training was given for all supervisors and data collectors. The overall activity was controlled by the principal investigator of the study. Data quality was controlled by designing the proper data collection materials and through continuous supervision. All completed data collection form was examined for completeness and consistency during data management, storage and analysis. The data was entered and cleaned by trained data clerk and principal investigator respectively before analysis.

4.6. Data processing and analysis

Data was entered to Epi-Info 3.3 for windows and analyzed using SPSS version 15.0 for windows.

The data was cleaned and edited before analysis. Data exploration was undertaken to see if there were odd codes or 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. 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 were censored. Finally, the outcome of each subject was dichotomized into censored or death. Univariate analysis was used to describe patient's baseline characteristics. Actuarial table had been 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 determine independent predictors of time to death.

4.7. Ethical Considerations

The proposal was submitted to the Institutional Review Board (IRB) of Addis Ababa University, Faculty of Medicine for approval. Following the approval by IRB, Official letter of co-operation was written to concerned bodies by the School of Public Health AAU. As the study had been conducted through review of medical records, the individual patients had not subjected to any harm as far as the confidentiality is kept. To preserve the confidentiality, nurses working in ART clinic of Durame and Hosanna hospital have extracted the data from the medical records. Moreover, no personal identifier was used on data collection form. The recorded data has not accessed by a third person except the principal investigator, and had been kept confidentially.

4.8. Operational Definition

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

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

HAART; The name given to treatment regimens recommended by leading HIV experts to aggressively suppress viral replication and progress of HIV disease.

Immunodeficiency; break down in immuno-competence to resist or fight off infections.

Lost; if a patient discontinued ART for at one to three month as recorded by ART physician

Opportunistic infections; illness caused by various organisms, some of which usually do not cause disease in persons with healthy immune systems.

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

Reverse transcriptase; enzyme of HIV converts the single –stranded viral RNA in to DNA

Protease Inhibitor **(PI)**; antiviral drugs that act by inhibiting the virus protease enzyme.

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.

V.RESULT

The study was conducted between December and April 2011, 1,220 HIV on patients ever started ART.

Four hundred eighty one (381 active and 100 death) adult patients were included in the present study. Base line and follow up predictors of survival among HIV patients who started ART were assessed. Patients on ART were followed for a median of 24 month.

Among the study subjects, 45.1% (217) of them were males and the mean age was 31.9 (SD=8.52). Forty seven Percent (227) of them had primary education, and 57.2% of the study subjects were on marriage. Thirty point six percent (147) were unemployed. The median weight of the study subjects at the initiation of ART was 52 kg (IQR, 48kg-57kg). The mean Hemoglobin was 12.7(IQR, 11-14). The median CD4 count was 158cells/µl (IQR, 101-224). Among the study subjects, 96.7 %(465) were given cotrimoxazole at the time of ART initiation, 22.9 %(110) had TB co infection and three percent (15) were poorly adhered. Initial ART regimen was d4t (30)-3TC-NVP in 155 patients (32.2%), AZT-3TC-NVP in 114 patients (23.7%), TDF-3TC-EFV in 79 patients (16.4%) and 62 patients (12.9%) on AZT-3TC-EFV.at ART initiation, 227(47.2%) adults were in WHO stage III, 73 (15.2%) were in WHO stage IV and 125(26%) were in WHO stage II. adverse side effects to ART were reported in 117(14.3%) patients including 34 cases of nausea,22 cases of numbness, 14 cases of rash and 14 cases of fat change. Regimen change was reported in 61(12.7%) patients from these 36 cases due to side effects/toxicity, 10 due to new TB infection and 9 due to clinical failure. Poor/fair adherence were reported in 27(4%) patients from these 12 patients poorly adhered due to forgetting,9 patients by travelling problem and 3 patients by fear of stigma.

Table1 Baseline comparison of socio-demographic characteristics of 481 patients Initiated ART At Durame and Hosanna hospital during 2006-2010.

Variables	Frequency(n=481)
Sex	
Male	217(45.1%)
Female	264(54.9%)
Age	
<40years	308(64%)
≥40	73(15%)
Religion	
Protestant	296(61.5%)
Catholic	24(5%)
Orthodox	104(21.6%)
Muslim	55(11.4%)
Others	2(0.5%)
Ethnicity	
Kembata	174(36.2%)
Hadiya	175(36.4%)
Amhara	46(9.6%)
Gurage	42(8.7%)
Others	44(9.1%)
Marital status	
Single	73(15.2%)
Married	275(57.2%)
Divorced	72(15.2%)
Widowed	30(6.2%)
Separated	31(6.2%)
Educational status	
Primary	226(47%)
Secondary	116(24.1%)
Tertiary	47(9.6%)
Not educated	92(19.1%)
Dependent children at home	
Yes	364(75.7%)
No	117(24.3%)
Employment status	
Farmer	122(25.4%)
Merchant	46(9.6%)
Gov't employee	83(17.3%)
Driver	13(2.7%)
Day laborer	28(5.8%)
Unemployed	147(30.6%)
Others	42(8.6%)

Table 2 Base line Clinical and laboratory information of 481 patients Initiated ART at Durame and Hosanna hospital during 2006-2010.

Variables	Frequency(n=481)
Cotrimoxazole	
Given	465(96.7%)
Not given	16(3.3%)
Weight at presentation (median (25th - 75th quartiles)) (kg)	52(48-57)kg
CD4 count (median (25th -75th quartiles)) (cells/µl)	158(101.75-224.25)cells/ µl
Haemoglobin (g/dl)	12(11-14)g/dl
Functional Status	
Working	264(54.9%)
Ambulatory	178(37%)
Bedridden	38(7.9%)
WHO staging	
Stage I	55(11.4%)
Stage II	125(26%)
Stage III	227(47.2%)
Stage IV	74(15.8%)
ART regimen	
D4T-3TC-NVP	155(32.2%)
D4T-3TC-EFV	57(11.9%)
AZT-3TC-NVP	114(23.7%)
AZT-3TC-EFV	62(12.9%)
others	93(19.3%)
Past TB test	
Positive	110(22.9%)
negative	371(77.1%)
ART Adherence	
Good	453(94.2%)
Poor	28(5.8%)

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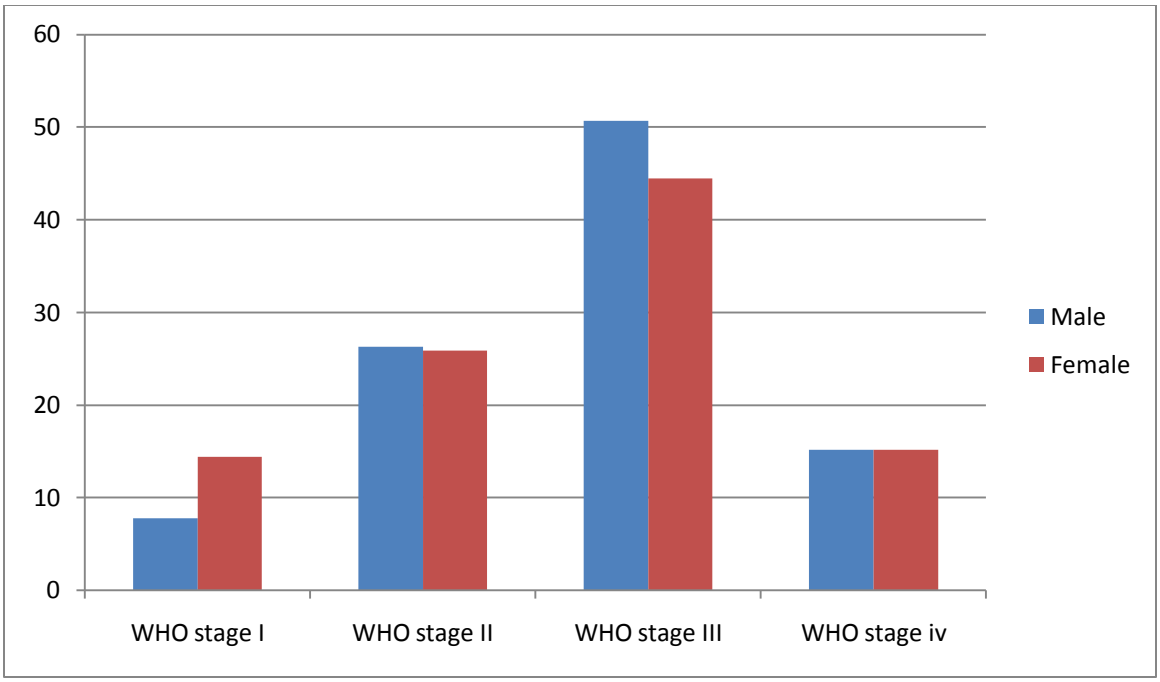

Figure1 WHO clinical staging at base line stratified by sex of the study subjects studied (N = 481 patients**)** in Durame and Hosanna hospital, SNNPR, from August 2006 to April 2010.

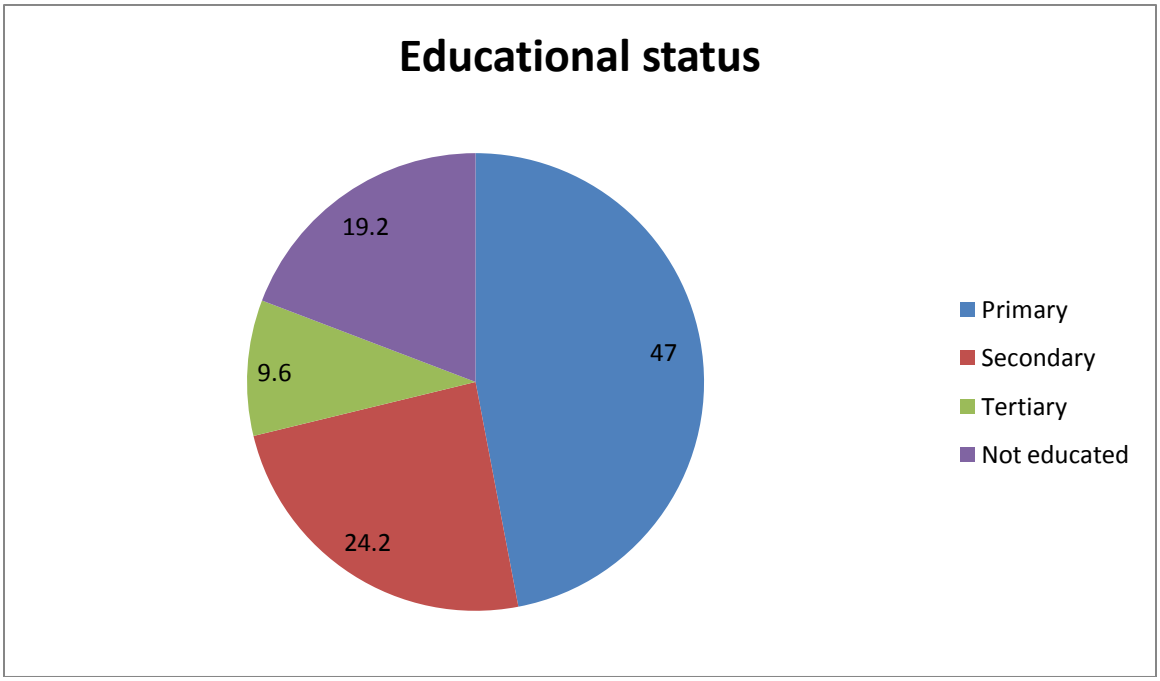

Figure2 Educational status of the study subjects studied (N = 481 patients**)** in Durame and Hosanna hospital, SNNPR, from August 2006 to April 2010.

Survival Analysis

A total of 481 patients were followed for median of 24 month. The minimum follow up time was 1 month and the maximum was 48 month**.** One hundred (20.4%) subjects died, from these 31.6 %(31) died within 5 month and the rest 79.6% were active up to the end of last censored date. The estimated mortality was 7%, 8%, 11.3 %, 15.7% and 21% at 6, 12, 24, 36 and 48 months respectively.

Table3 Actuarial Table estimates of the cumulative progression to death for 481 study subjects Starting ART b/n 2006- 2010

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Cumulative Proportion Surviving at End of Interval	Hazard Rate
0	477	24	.92	.02
5	453	41	.87	.01
10	412	74	.66	.06
15	338	43	.60	.02
20	294	59	.44	.06
25	235	51	.34	.05
30	184	41	.34	.00
35	143	24	.31	.02
40	119	45	.28	.02
45	74	40	.17	.09
50	34	20	.09	.13
55	14	2	.09	.00

a. The median survival time is 60

When analysis of Univariate predictors of death include single by marital status (HR=17.3, 95%CI 2.27, 133.21), positive past TB test (HR=2.82 95%CI 1.324, 6.02), WHO clinical stage III (HR=1.551 95%CI 1.153, 2.086), Age >40 yrs (HR=1.138 95%CI 1.883, 2.466), being WHO clinical stage IV shows less pronounced with (HR=1.304 95%CI 1.195, 1.707).

Using the multivariate Cox proportional hazard adjusted model, factors such as single by marital status HR=10.27(95%CI 1.348- 78.38, P=0.001), poor ART adherence HR=5.06(5.51-49.48, p=0.043), positive past TB test HR=3.906(95%CI 1.889-8.075 P=<0.001) Male gender HR=1.704(95%CI 1.29-2.24 P=<0.001), age >40yrs HR=1.458(95%CI1.081, 1.966 P=0.014) and WHO clinical stage III HR=1.502(1.07, 2.104 P=0.018).were confirmed as significant independent predictors of death after controlling for other factors(Table6 and 7).

Table6 Multivariate Cox regression analysis of socio demographic characteristics among 481 patients initiated ART at Durame and Hosanna hospital during 2006-2010

Variables	AHR	95%CI	P-value
Sex			
Male	**1.704**	**(1.292, 2.246)**	**<0.001**
Female	-	-	-
Age			
≥40 yrs	**1.458**	**(1.081, 1.966)**	**0.014**
<40 yrs	-	-	-
Religion			
Protestant	0.473	(0.115, 1.949)	0.3
Catholic	0.484	(0.111, 2.1)	0.332
Orthodox	0.689	(0.165, 2.873)	0.609
Muslim	0.868	(0.201, 3.755)	0.85
Others	-	-	-
Ethnicity			
Kembata	1.483	(1.002, 2.195)	0.049
Hadiya	0.956	(0.654, 1.397)	0.815
Amhara	0.8	(0.498, 1.287)	0.359
Gurage	0.621	(0.381, 1.013)	0.056
Others	-	-	-
Marital status			
Single	**10.279**	**(1.348, 78.383)**	**0.001**
Married	1.228	(0.755, 1.995)	0.408
Divorced	0.792	(0.519, 1.21)	0.281
Widowed	0.794	(0.454, 1.388)	0.418
Separated	-	-	-
Educational status			
Primary	1.047	(0.787, 1.393)	0.751
Secondary	0.961	(0.696, 1.326)	0.808
Tertiary	1.094	(0.733, 1.633)	0.661
Not educated	-	-	-
Dependent children at home			
Yes	0.757	(0.596, 0.963)	0.024
No	-	-	-
Employment status			
Farmer	0.411	(0.236, 0.717)	0.002
Gov't employee	0.327	(0.184, 0.581)	<0.001
Unemployed	0.548	(0.327, 0.919)	0.023
Merchant	0.539	(0.302, 0.963)	0.037
Driver	-	-	-

Table7 Multivariate Cox regression analysis of Clinical and laboratory information among 481 patients initiated ART at Durame and Hosanna hospital during 2006-2010

Variables	AHR	95%CI	P-value
WHO staging			
Stage I	-	-	-
Stage II	1.28	(0.852, 1.922)	0.234
Stage III	**1.502**	**(1.071, 2.104)**	**0.018**
StageIV	0.652	(0.430, 0.988)	0.044
Past TB test			
Positive	**3.906**	**(1.889, 8.075)**	**<0.001**
Negative	**-**	**-**	**-**
Cotrimoxazole			
Given	1.262	(0.638, 2.499)	0.504
Not given	-	-	-
Functional Status			
Working	1.443	(0.935, 2.227)	0.098
Ambulatory	1.164	(0.745, 1.817)	0.504
Bedridden	-	-	-
ART regimen			
D4T-3TC-NVP	0.228	(0.167, 0.311)	<0.001
D4T-3TC-EFV	0.26	(0.112, 0.605)	0.002
AZT-3TC-NVP	0.324	(0.22, 0.477)	<0.001
AZT-3TC-EFV	-	-	-
ART Adherence			
Good	-	-	-
poor	**5.069**	**(5.519, 49.485)**	**0.043**
CD4 count			
<50	0.907	(0.588, 1.399)	0.659
50-99	0.891	(0.605, 1.313)	0.559
100-199	0.907	(0.683, 1.205)	0.501
≥200	-	-	-
Hemoglobin level			
<7	1.333	(0.884, 2.01)	0.170
7-9.9	1.072	(0.701, 1.641)	0.748
10-11.9	1.08	(0.828, 1.425)	0.55
≥12	-	-	-

AHR=Adjusted hazard ratio

CI=Confidence Interval

Older age study subjects are at higher risk of death when compared to the younger age groups especially in the later time of treatment. Age >40yrs HR=1.458(95%CI1.081, 1.966 P=0.014) (figure3)

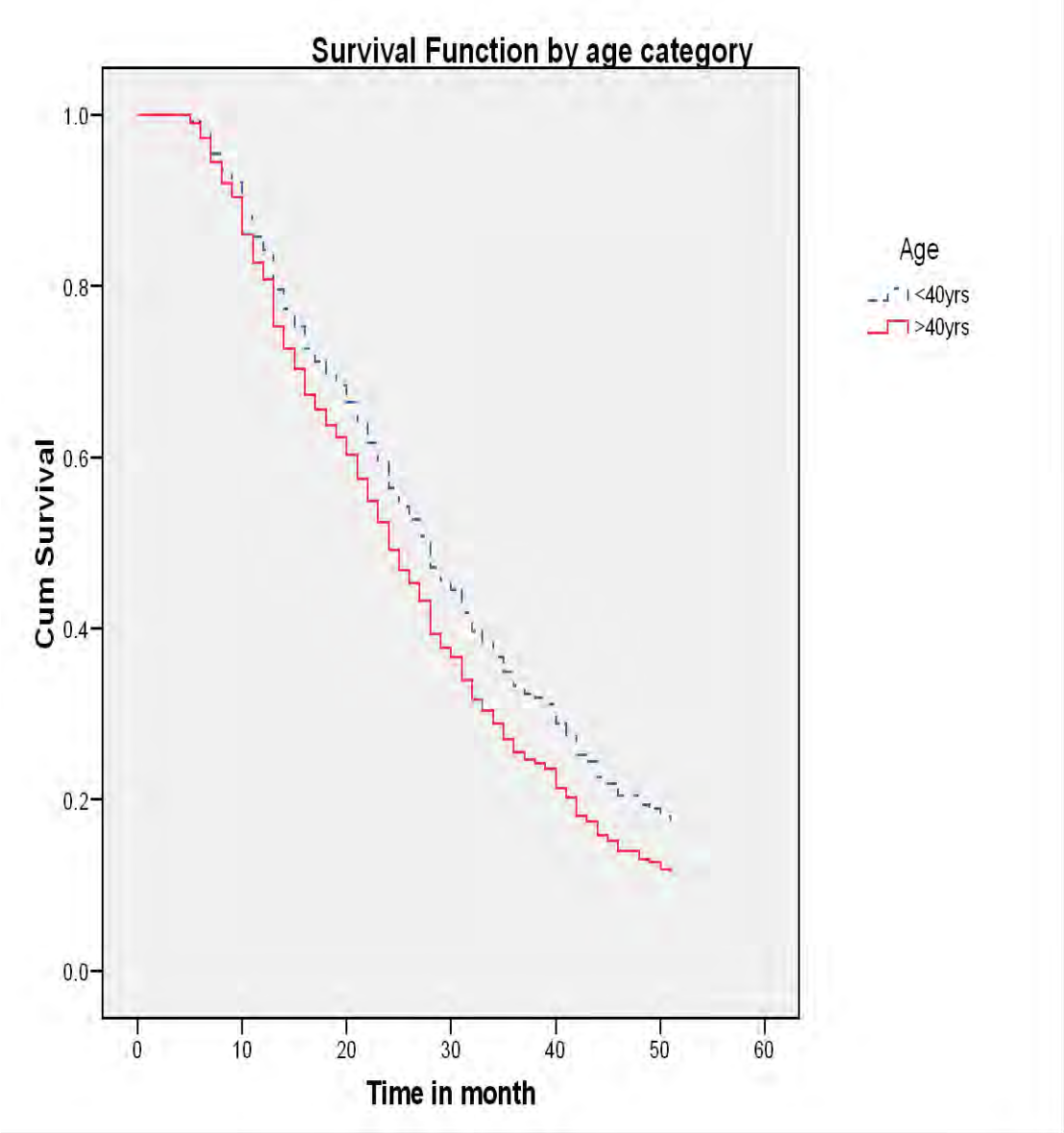

Figure 3 survival curves of HIV infected patients on antiretroviral therapy according to age category at the time of initiation of ART, in Durame and Hosanna hospital, 2006-2010

Our study result showed male sex was a predictor of mortality with a risk almost doubles that of female sex (AHR 1.704: 1.29-2.25 log rank<0.001) (figure4)

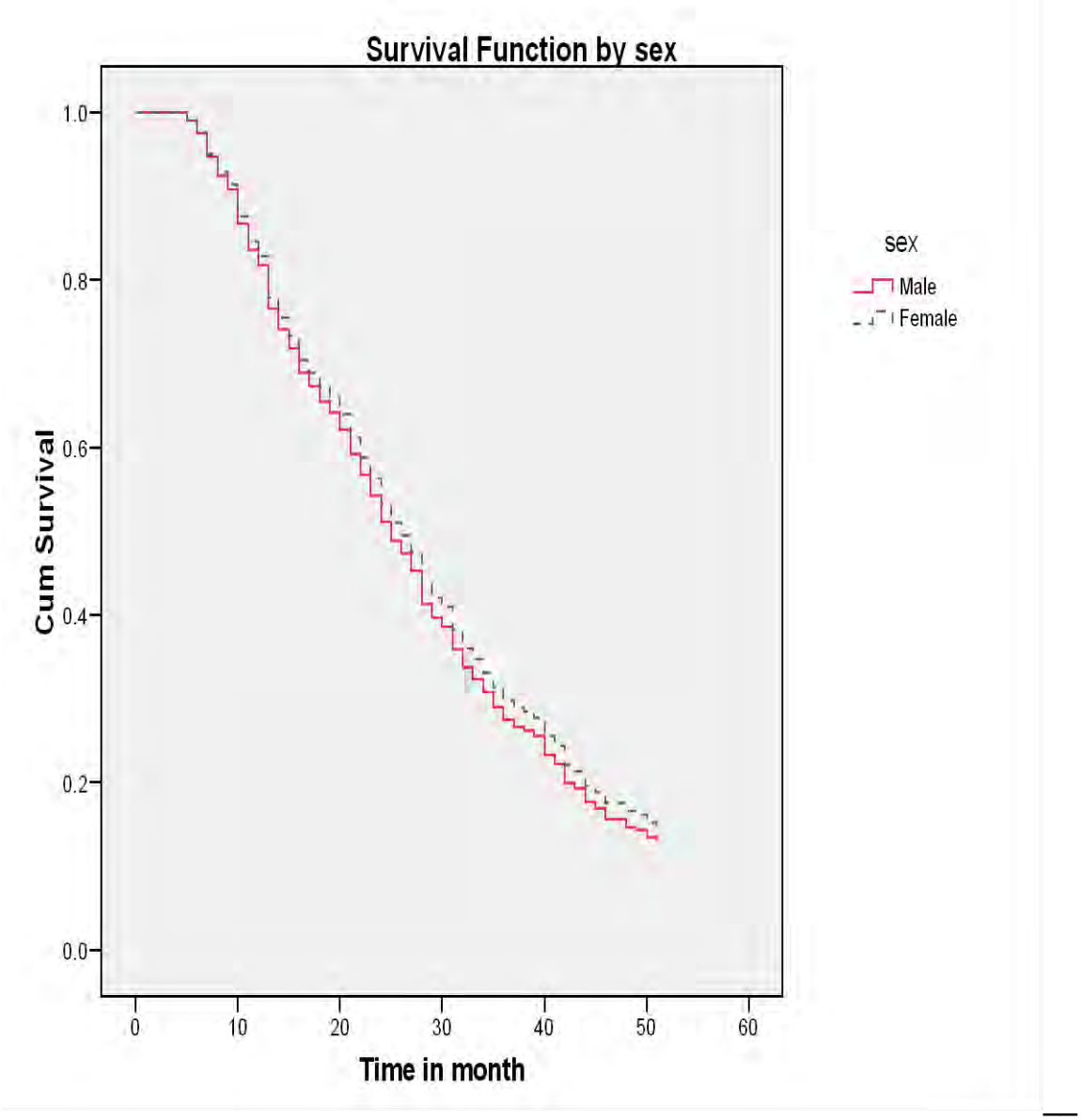

Figure 4 survival curves of HIV infected patients on antiretroviral therapy according to sex category at the time of initiation of ART, in Durame and Hosanna Hospital, 2006-2010

According to our study result being single or unmarried is a strong predictor of mortality with an AHR =10.27(95%CI 1.348- 78.38, log rank<0.001) (figure5)

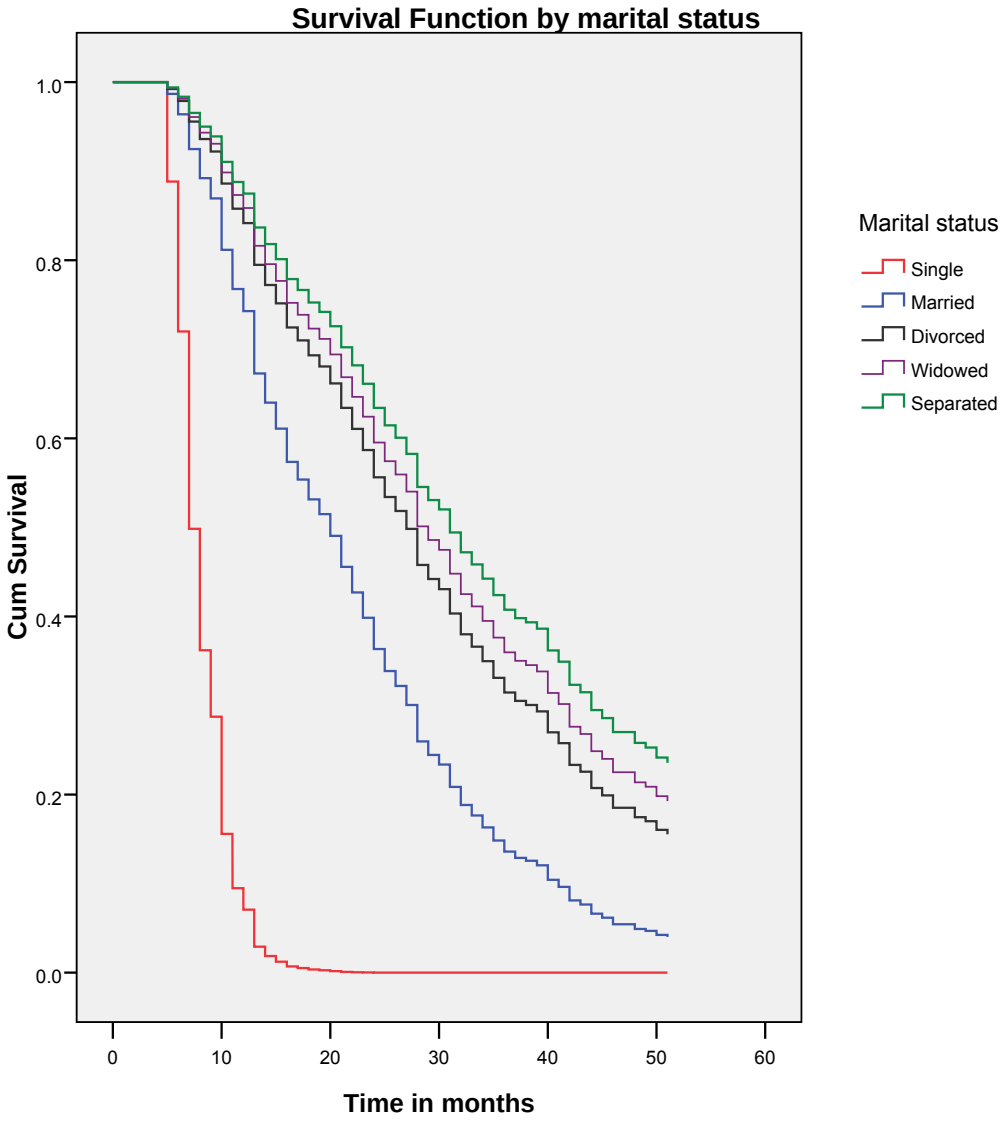

Figure5 survival curves of HIV infected patients on antiretroviral therapy by marital status category at the time of initiation of ART, in Durame and Hosanna hospital, 2006-2010

There was a decrease in survival rate of patients with positive past TB test after initiation of ART. The probability of surviving for positive past TB test patients declines sharply in the first five months (figure 6).

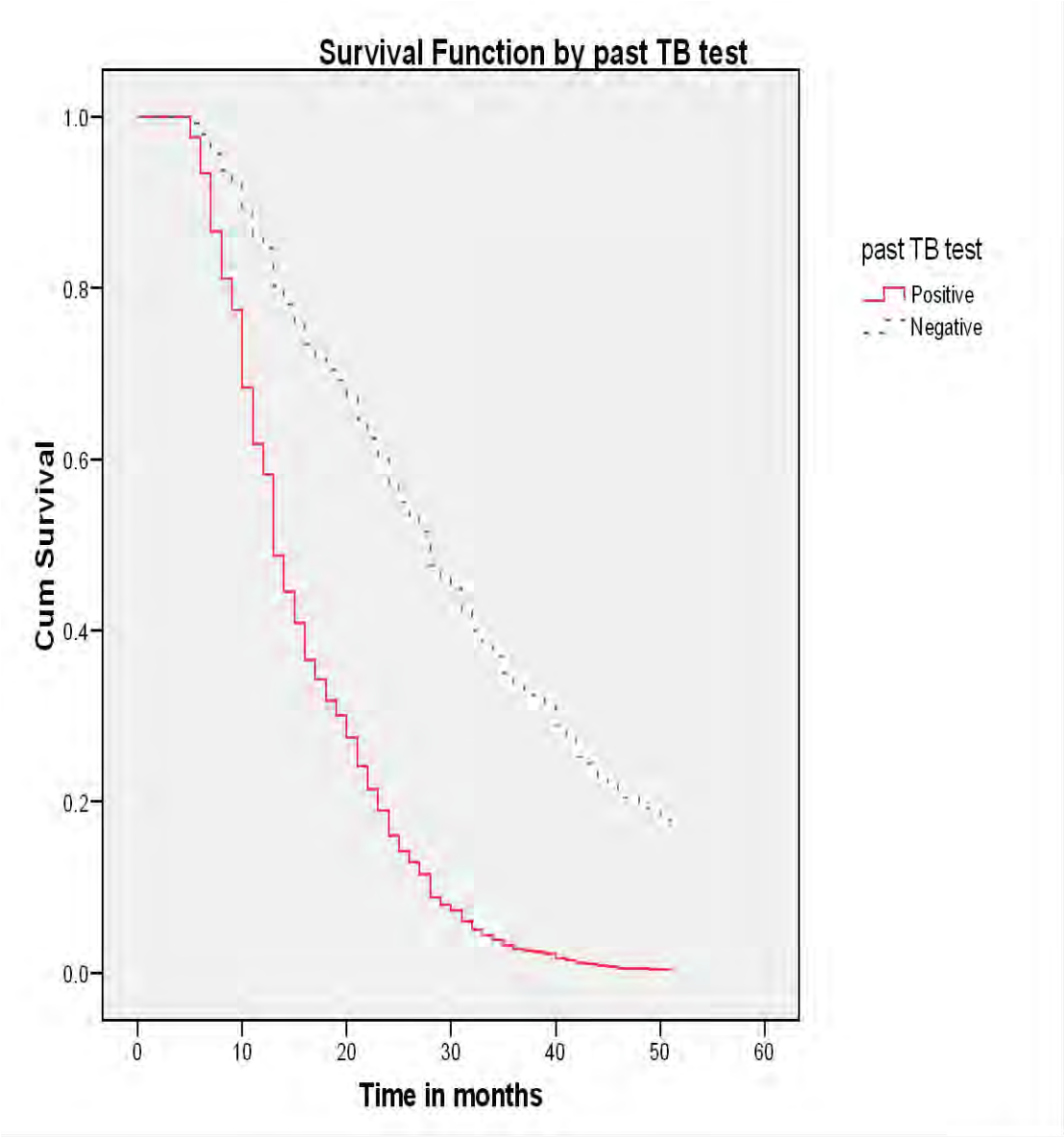

Figure 6 survival curves of HIV infected patients on antiretroviral therapy according to past TB test category at the time of initiation of ART, in Durame and Hosanna hospital, 2006-2010

VI. DISCUSSION

In this historical longitudinal study, we found that the independent significant predictors of lesser survival in patients living with HIV/AIDS after initiation of ART were being single or unmarried, male gender, older age, past positive TB test, advanced WHO staging (III) and poor adherence.

Our study result confirm the relationship between male gender and mortality after controlling for confounding (AHR 1.704; 1.29-2.25 P<0.001), which is in agreement with a study in Malawi which shows females had a significantly higher survival rates than males (37) .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: 1.37-2.19) Majority of recent studies showed females have significantly higher survival than males (20,21, 23,28). This may be due to more women (54.9%) receive ART than men (45.1%) in Durame and Hosanna hospital, men may be more reluctant to undergo VCT and then seek treatment because infection with HIV still attracts stigma in Ethiopia and another reason may be the men come for ART usually at a more advanced clinical stage and suffer from higher mortality.

Study conducted in Tanzania shows anemia as a strong predictor of mortality, patients with severe anemia had nearly 15 times higher risk of dying during the first year on ART compared to those with a normal hemoglobin level(9). Another study conducted in Cameroon indicated patients with haemoglobin ≤ 8.5g/dl had two times more risk of death than those with haemoglobin rate >8.5g/dl.

Johanssen etal found high mortality with the majority of death occurring within three months of starting ART They estimated mortality rate 19.2% and 24.5% at 3 and 6 months, in a South African court, the mortality rate in the first 4 months of ART was 19.1 deaths per 100 person-years, decreasing to 2.9 deaths per 100 person- years beyond four months and 1.3 deaths per 100 person years beyond one year (38). Degu J etal estimated mortality rate in ART+ group was 15.4/100PYO and most of the death occurred during the first three month (33). Our study result also shows majority of death occurred within first five months of starting ART.

Study conducted in zewuditu hospital shows the estimated mortality was 24.9%, 29%, 31.7%, 33.1%, 33.5, and 34% at 6, 12, 18, 30, and 48 months respectively (25). However according to a study carried out by Alfred C etal in Malawi, the probability of being alive on ART at 6, 12 and 18months was 89.8%, 83.4% and 78.8% respectively(17). our study result shows estimated mortality was 7%, 8%, 11.3 %, 15.7% and 21% at 6, 12, 24, 36 and 48 months respectively This survival difference might be due to majority of the patients start ART at WHO stage I and II; good follow up, low default rate, high drug access while in our study, almost half of the cohort at WHO stage III and high default rate and the study is conducted in rural hospital most of listed problems are observed in most of times.

Study conducted in Uganda shows after adjusting for age, sex, tuberculin skin test status, CD4 lymphocyte count and history of HIV related infections ,the overall relative hazard for death associated with tuberculosis was 1.81 (95% CI,1.24-2.65) . According to Chottanapund S etal, the survival rate at 1,2 and 3 years after TB diagnosis were 96.1%,94%,and 87.7% for ART+ group and 44.4%,19.2% and 9.3% for ART- group(log ran test<0.001). Manosuthi etal also showed patients who delayed ART for greater than 6 months after TB diagnosis had a higher mortality rate than those who initiated ART less than 6 months after TB diagnosis (28). Our study also show similar result patient with positive TB test has AHR 3.9 (1.88, 8.07 log rank test <0.001). This may be because TB is the leading cause of death worldwide in HIV infection and mycobacterium tuberculosis is a virulent organism that can produce disease in HIV-infected persons at any stage of disease even when the immuno suppression is minimal.

Study conducted in Singapore showed that patients of older age at diagnosis had a significantly higher risk of progression compared to younger patients' in addition older patients has higher mortality (36 vs. 27%p=0.04) and shorter survival 25th percentile survivor function (36.2 vs. 58.5 months, p=0.02) than younger patients(39). Our study result also shows similar progression this may be due to older aged patients progressed to AIDS at a faster rate and older patients may have a reduced capacity to generate new CD4 cells in response to viral killing.

Patients who were educated at most primary level had high risk compared to those secondary or above(21) (log ran test, P<0.001).But these is not consistent result both in bivariate and multivariate analysis indicating educational level is not a strong predictors of survival in our study. Our study showed no difference in survival by religion, ethnicity and presence of dependent children, Likewise a study carried out in California showed risk of death is similar among ethnic groups. In our study, single not married patients had high risk of death than married patients. More over single not married patients were at high risk of mortality compared to married patients (log ran test, P<0.01). This difference might be due to married patients psychologically ready and get social support from their partner in adapting the illness and taking the drug correctly.

Study in Cameroon shows patients with a base line CD4 count ≤ 50cells/mm^3 presented a mortality risk twice as high as those with >50cells/mm^3(24). Another study in Canada shows the hazard for the low CD4 count strata were higher CD4<50cells/mm^3, RH=6.07, 95% CI 4.11-8.97 relative to counts ≥200 cells/mm^3.Majority of the previous studies (12: 13: 31) identified Low CD4 count was one of the independent predictors of mortality. our study result contradict this finding and there is no hazard difference for low and high CD4 count this may be due to majority of the patients have CD4 count above 200 cells/mm^3.

Study conducted in rural Malawi shows individuals who were severely malnourished [Body Mass Index (BMI) <16kg/m^2] had a six times higher risk of dying in the first three months than those with a normal nutritional status (17). Another Study in Cameroon shows BMI ≤15kg/m^2 was related to three times higher risk of death than a BMI>18.5kg/m^2in addition different previous studies demonstrated BMI as one of the strong predictors of mortality (19, 30), we excluded it since only the weight not height of the patients has been recorded at base line. As a result we couldn't calculate BMI for each patient. Study conducted in Thailand clearly documented TLC was significantly associated with survival (40).

Study conducted in Uganda shows non adherent participants had a mortality of 42.5 deaths per 1000 person-years and after adjusting for age, sex and educational level were two times as likely to die as adherent participants (16, 41). In addition study conducted in Ethiopia the risk of death in non- adhered patients is 4 times higher compared to adhered patients (25). This was in agreement with our study results which indicate there is strong association between mortality and ARV adherence.

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7.1 STRENGTH

- Our study was carried out in a rural hospital
- Strong power
- Retrospective longitudinal study
- The study gives an insight for researchers especially in carrying out prospective study.

7.2 LIMITATION

- Using secondary data which might have incomplete data
- Selection bias is possibly introduced during secondary data collection because patients with incomplete records were excluded
- Mortality might be underestimated lost to follow up patients probably includes more individuals dying at home without being reported
- Generalizabilty is questionable as important predictors of survival in other studies such as viral load and BMI were not considered.

VIII.CONCLUSION AND RECOMMENDATION

As more patients present for care, it is critical for health care providers to be aware of those at highest risk of mortality in order to maximize clinical outcomes. This study demonstrates that simple laboratory and clinical data, available to health care providers prior to ART initiation, can predict which patients are at increased risk of death when they start therapy.

This study has identified the independent significant predictors of survival in patients living with HIV/AIDS after initiation of ART. These factors include being not married or single, male gender, positive TB test, advanced WHO staging, older age and poor adherence.

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

To hospitals and health centers with ART clinic

- A careful monitoring of patients with advanced WHO staging, positive TB test result and elder patients are necessary particularly during the first 5 months of ARTintiation.
- Careful follow up for poorly adhered patients and giving them drug counseling is crucial to improve survival
- Develop a way to control the completeness and reliability of base line and follow up data being collected especially hemoglobin and TLC count.
- Preventive efforts should focus on high risk groups.
- The ART care should be further improved to decrease the current mortality rate.

To kembata tembaro and hadiya zone health bureau

- Giving in-service training for the health care giver on HIV/AIDS care and support especially on how to recognize and manage patients with high risk.
- Integrating the HIV care with other developmental organizations like NGOs, Religious leaders and community supporters.
- Undergo further observational studies especially prospective study to complement this study.
- Developing a multi sectoral approach to improve patients survival

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Annex-I QUESTIONNAIRE

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

Name of the hospital----------

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

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

Part-I SOCIO DEMOGRAPHIC CHARACTERISTICS

101. Age (----------) years

102. Sex 1.male

2. Female

103. Religion

1. Protestant 2. Catholic

3. Orthodox 4. Muslim

99. Others specify----------

104. Ethnicity

1. Kembata 2. Hadiya

3. Amhara 4. Gurage

99. Others specify----------

105. Marital status

1. Single 2. Married

3. Divorced 4. Widowed

5. Separated

106. Educational status

1. Primary 2. Secondary

3. Tertiary 4. Not educated

107. Dependent children at home

1. Yes

2. No

108. Occupational status

1. Farmer 2. Merchant

3. Government employee 4. Non government employee

5. Day laborer 6. Driver

7. Commercial sex worker 8. Jobless

99. Other specify----------

Part-II Base line clinical, laboratory and ART information

201. past opportunistic illness

1. No 2. CMV 3. PCP

4. PGL 5. PML 6. EPTB

7. Candidiasis 8. Diarrhea 9. Pneumonia

10. Herpes simplex 11. Kaposi sarcoma

12. Toxoplasmosis 13. Encephalopathy

14. Wasting syndrome 15.Herpes zoster

16. Other specify-------

202. Weight at base line (----------) kg

203. Height at base line (----------) cm

204. Functional status at base line

1. Working 2. Ambulatory

3. Bed ridden

205. WHO clinical staging of HIV at base line

1. Stage II

2. Stage III 3. Stage IV

206. Past TB test

1. No 2. Not determined

3. Positive 4. Negative

207. Past TB treatment

1. No 2. 2SRHZ/6EH

3. 2HRZES/1HRZE/5HRE 4.2HRZE/6HE

208. Past medication

1. No 2. Cotrimoxazole

3. INH 4. Other specify----------

209. CD4 count at base line (----------) date----------/----------/----

210. Hgb count at base line ----------

211. TLC count at base line----------

Part-III ART treatment

301. ART eligibility criteria

1. CD4<200
2. WHO stageIV
3. WHO stage II and III with TLC<1200

302. OI prophylaxis given

1. Not given 2. Cotrimoxazole
3. INH 4. Fluconazole
5. Others specify----------

303. Regimens given at follow up time

1. la(30)=d4t(30)-3TC-NVP 2. la(40)=d4t(40)-3TC-NVP
3. lb(30)=d4t(30)-3TC-EFV 4. lb(40)=d4t(40)-3TC-EFV
5. lc=AZT-3TC-NVP 6. ld=AZT-3TC-EFV
7. 2nd line regimens

Part-IV patient follow up information (filled from ART follow up form) recent results

401. Date confirmed HIV positive (----------/----------/-------)

402. Eligible date (----------/----------/----------)

403. Last follow up date (----------/----------/----------)

404. Duration since initiation of ART (---------- month)

405. Recent weight (---------- kg)

406. Recent functional status

1. Working 2. Ambulatory

3. Bedridden

407. Recent WHO staging

1. Stage II

2. Stage III 3. Stage IV

408. TB prophylaxis

1. No

2. Yes

409. TB screened

1. No 2. Negative

3. Positive

410. TB treatment

1. No

2. Yes

411. opportunistic infections

1. No 2. Zoster 3. Pneumonia

4. Pulmonary TB 5. EPT 6. Oral trush

7. genital/oral ulcer 8. Diarrhea

9. Cryptococcal meningitis 10. CNS toxoplasmosis

11. PCP 12. Others specify------

412. Cotrimoxazole

1. Given

2. Not given

413. Recent ARV adherence

1. Good 2. Fair

3. Poor

414. Reason for fair/poor adherence

1. Toxicity/SE 2. Share with others

3. Forgot 4. felt better

5. Too ill 6. Stigma

7. Drug stoke out 8. Travelling problem

9. unable to pay 10. Alcohol

11. Depression 12. Others specify-----

415. Drug side effect

1. No 2. Nausea 3. Diarrhea

4. Fatigue 5. Headache 6. Numbness

7. Rash 8. Anemia 9. Fat change

10. Night mare 11. Dizziness

12. Others specify----------

416. Reason for regimen change

1. Not change 2. Toxicity/SE

3. Pregnancy 4. Risk of pregnancy

5. New drug available 6. Drug out of stoke

7. Clinical failure 8. NewTB

9. Other specify----------

417. Reason for stopping regimen

1. Not stopped 2. Pregnancy

3. toxicity/SE 4. Treatment failure

5. Poor adherence 6. Drug out of stock

7. Lack of finance 8. Other patient decision

9. Planned treatment interruption 10. Other specify----------

418. Recent CD4 count (----------date----------/---------/------)

419. Recent TLC count (----------)

420. Recent Hgb count (----------)

421. Current status 1.alive

2. Dead

Annex-II consent form (English version)

My name is _____, I am an ART clinic nurse working in Durame or Hosanna hospital ART clinic and now I am collecting data from our patients ART logbook for the research being conducted to assess survival of HIV/AIDS patients after initiation of antiretroviral treatment, by Ato Gezahegn Abose who is the MPH student 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 basic information on factors affecting survival of PLWHA and 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 Gezahegn Abose E-mail: abosegezahegn@yahoo.com

TELEPHONE: 0913814848

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

1. Yes 2. No

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

Annex-III Consent form (Amharic version)

ለጥናቱ ተሳታፊዎች የፈቃደኝነት መጠየቂየ ቅጽ

ስሜ _____ ይባላል፡፡ በዚህ ሆስፒታል ቲቢ ክሊኒክ ውስጥ የሚሠራ የጤና ባለሙያ ስሆን አሁን የኤች.አይ.ቪ/ኤድስ ተዕዕኖ በቲቢ ዓይነትና ሕክምናው ላይ በሚል ርዕስ በአዲስ አበባ ዩኒቨርሲቲ ድህረ ምረቃ ተማሪ የሆኑት ለሚሰሩት ጥናት መረጃ ከቲቢ ታካሚዎች መዝገብ ላይ እየሰበሰብኩ ነው፡፡ አንተ/ቺ የጥናቱ አካል በመሆን ተመርጠሃል/ሻል፡፡ አጥኚው እዚሁ መዝገብ ላይ የሚሠራውን እኔን ለመረጃ ሰብሳቢነት ሲመርጠኝ የመረጃውን ምስጢራዊነት ለመጠበቅ ብሎ ነው፡፡ ማለትም ከክሊኒኩ ውጪ ያሉት በመረጃ ስብሰባ ወቅት ስምዎንና ሌሎች መረጃዎችን እንዳያዩ ሲባል ነው፡፡

የጥናቱ ውጤት ሳይንሳዊ ሂደትን የተከተለ መረጃ በማቅረብ የቲቢ/ኤች.አይ.ቪ መከላከያና መቆጣጠሪያ ፕሮግራሞችን ለመገምገምና ለኤች.አይ.ቪ እና ቲቢ ታካሚዎች የተለየ ጥንቃቄ እንዲደረግ አስተዋጽኦ የጐላ እንደሚሆን ይታመናል፡፡ በመሆኑም ለጥናቱ አስፈላጊ የሆኑ መረጃዎች ከእርስዎ ቲቢ መዝገብ ላይ ይወሰዳል፡፡ ጥናቱ የሚደረገው ከቲቢ ሕክምና መዝገብ ላይ ስለሆነ በእርስዎ ላይ ምንም ዓይነት ጉዳት አያመጣም፡፡ መረጃዎ እንዲወሰድ መፍቀድ ለተጠቀሰው የጥናቱ ዓላማ መሳካት የጐላ አስተዋጽኦ ይኖረዋል፡፡ ከሕክምና መዝገብዎ ላይ መረጃ ሲወሰድ የእርስዎን ማንነት የሚገልጽ ስም እና ሌላ ምንም ዓይነት ነገር ወደ መጠይቁ አይሞላም፡፡ የተወሰደውም መረጃ ምስጢራዊነቱ ተጠብቆ ሙሉ በሙሉ ለምርምር ሥራ ብቻ ይሆናል፡፡ የሕክምና መረጃዎ ለምርምር ሥራ እንዳይውል የማድረግ መብት አለዎት፡፡ ነገር ግን መረጃዎ ለምርምር ሥራው ቢውል ጠቀሜታው የጐላ ነው፡፡ በጥናቱ ለመሳተፍ ፈቃደኛ ባይሆኑ በሕክምናዎት ላይ ምንም ዓይነት ጉዳት አይፈጠርም፡፡ በሌላ በኩል መረጃዎን በመስጠትዎ የሚያገኙት የተለየ ጥቅም አይኖርም፡፡ ጥናቱን በተመለከተ ጥያቄ ካለዎት እኔን ወይም አጥኚውን አቶ መጠየቅ ይችላሉ፡፡

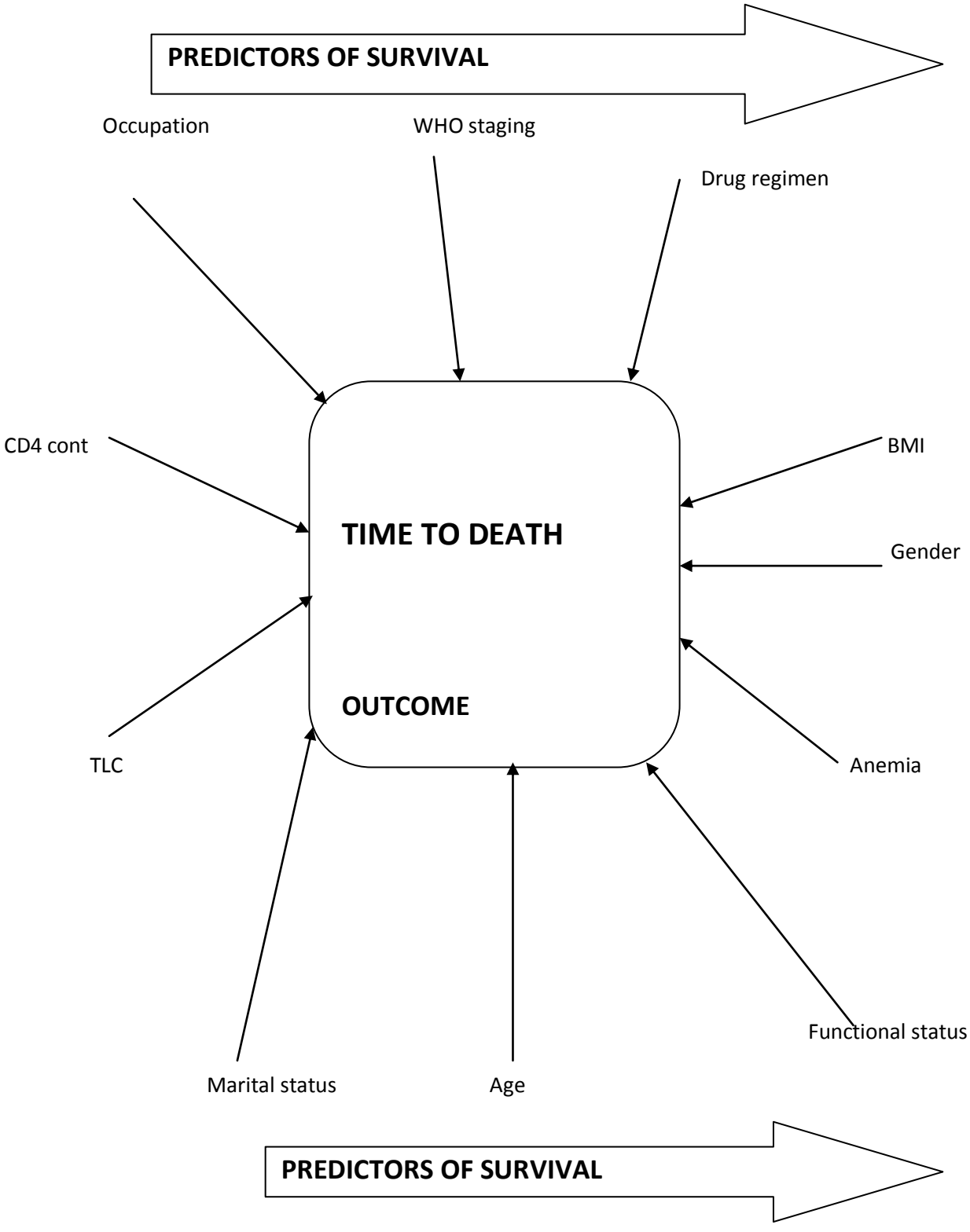
መረጃው ለምርምር ሥራ ቢውል ፈቃደኛ ነዎት?

1. **አዎ** 2. **አይደለም**

መረጃቸውን ለጥናቱ ሥራ እንዲውል ፈቅደዋል፡፡ የመረጃው ሰብሳቢ ስምና ፊርማ_____

_____

Annex IV; Conceptual frame work for the project.



Declaration

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

Name Gezahegn Abose

Signature_____

Date _____

This thesis work has been submitted for the examination with my approval as a university advisor

Name Fikre Enquselassie (PhD)

Signature_____

Date_____