GENDER DIFFERENCE IN SURVIVAL STATUS AMONG ANTIRETROVIRAL THERAPY USERS IN YIRGALEM GENERAL HOSPITAL, SIDAMA ZONE, SNNPR, ETHIOPIA

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Jimma Ethiopia

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ABSTRACT

***Background**: HIV infection is one of the most pandemic infectious diseases in the world. Antiretroviral therapy is a lifelong HIV/AIDS treatment for people living with human immune deficiency virus. In Ethiopia ART service has been scaled up and increased in cohort of users but still losses to follow-up and early mortality of patients on ART have been challenges for the success of the program.*

***Objective**: To assess the gender difference in survival status among ART users in Yirgalem General Hospital, Sidama zone, SNNPR, Ethiopia.*

***Method**: retrospective cohort study was conducted from September1st 2010 to August 30th 2015, in Yirgalem general hospital. A sample of **687** ART users was included in the study using simple random sampling technique. Data were collected using structured checklist and entered to EPI data version 3.1 then exported and analyzed by STATA version 13. Descriptive statistics: Proportion, mean, median and standard deviation were used. The Kaplan Meier curves were used to estimate survival function of male and female ART users and biomarkers of ART. Log rank test was employed for the assurance of statistical difference in the Kaplan Meier curves. The Cox-proportional hazards regression model was employed to identify predictors of survival status. Assumption of proportional hazard model was checked using goodness of fit test and Schoenfeld residual plot and also interaction among predictor variable were checked.*

***Result**: The numbers of records reviewed were 412 females and 273 males with retrieval rate of 99.7%. The overall survival probability was 84.5%. Female and male had survival probability of 80.1% and 91.18% respectively. Factors: females (AHR=1.79(1.04, 3.06)), divorce (AHR=2.09(1.10, 3.97)), no education (AHR=2.54(1.29, 4.98)) and primary education (AHR=2.07(1.18, 3.65)), never disclosing of HIV status (AHR=3.62(1.25, 10.46)), bedridden functional status (AHR=2.71(1.24, 5.89)) and TB-co infection (AHR=2.60(1.48, 4.45)) were found to be independent predictors of survival status.*

***Conclusion and recommendation:** overall survival probability was low. Predictors of survival were: sex, educational level, disclosure of HIV status, marital status, functional status and TB-co infection. Intervention to further reduce mortality, should focus on high risk group and expansion of HIV counseling and testing service in facilities and community level.*

***Key words:** HIV, ART, Gender, survival, Yirgalem Hospital*

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ABBREVIATIONS AND ACRONYMS

ADR Adverse Drug Reaction

AIDS Acquired Immune Deficiency Syndrome

ALT Alanine Aminotransferase

AST Aspartate Aminotransferase

ART Anti-Retroviral Therapy

AZT Zidovudine

BMI Body Mass Index

CPT Cotrimoxazole Preventive Therapy

CD4 Type of T-Lymphocyte, White Blood Cells

D4T Stavudine

HAART Highly Active Antiretroviral Therapy

HGB Hemoglobin

HIV Human Immune Deficiency Virus

EDHS Ethiopian Demographic Health Survey

INH Isoniazid

LTF Lost To Follow Up

KM Kaplan Meier

PLWHA People Live With HIV/AIDS

WT Weight

WHO World Health Organization

TB Tuberculosis

TDF Tinofovir

OI Opportunistic Infections

SNNPR South Nations Nationalities People Region

CHAPTER ONE: INTRODUCTION

1.1 Background

Acquired Immune Deficiency Syndrome (AIDS), which is caused by the Human Immunodeficiency Virus (HIV), has been the major problem for the past three decades worldwide. HIV infection is one of the most pandemic infectious diseases in the world. It brings with its profound social, economic and public health consequences (1,2).

Worldwide there are an increasing number of people living with HIV/AIDS, which is consistent with the growth of the epidemic and the availability of lifesaving treatment. Since the start of HIV epidemic, around 78 million people have become infected and 39 million people have died of AIDS related illnesses till 2013 (3). Globally, 36.7 million people live with HIV, of which 2.1 million people became newly infected with HIV and 1.1 million people died from AIDS related illness in 2015 (4). Adolescent girls and young women aged 15–24 years were at particularly high risk of HIV infection. Despite they account 11% of the adult population; they contribute 20% of new HIV infections among adults in 2015 globally. The sex imbalance is more pronounced in HIV prevalence (5).

Sub-Saharan Africa has the most serious HIV and AIDS epidemic in the world. This region accounts for almost 70% of the global total new HIV infections. There were 24.7 million people living with HIV of which women constitute for 58% in 2013. In same year 1.5 million and 1.1 million were new HIV infections & people died of AIDS related causes respectively (3). Nearly 25 million people were living with HIV at the end of 2014, of which 60 percent were women (6).

Ethiopia is in a low generalized HIV epidemic with significant heterogeneity among regions and population groups. Projected adult HIV prevalence was estimated to be 1.1% in 2015 (7). The 2016 projection of HIV prevalence for male and female were 0.7 and 1.4 respectively. Urban are more affected than rural areas while females are twice affected than male population. The HIV prevalence among 15 to 24 years was low for both sexes, but young women have a two to six fold higher HIV prevalence than young men (ranging from 15-17 years: 0% males vs. 0.2% females and those 20-22 years: 0.1% males vs. 0.6% females). In women the HIV prevalence

peaked earlier and became higher, 3.7% between age group 30-34 while in men peaked slowly and reached high, 3% between 35-39 age group (8,9).

In south nation nationality people and region of Ethiopia the prevalence of HIV/AIDS was 0.9% in 2011 (8). The prevalence has sex difference in which females and males were 1.1% & 0.6% respectively. The sex difference in HIV prevalence holds both in the urban and rural areas. Urban women had notably high HIV prevalence rate at 3.6% compared to 2.4% in the males. As well those residing in rural were 0.5% and 0.2% for female and male respectively. This region was the third largest home for people living with HIV/AIDS comprising of 108,000 in 2011. It contributes for 14% of the overall new HIV infection in the country (10).

1.2 Statement of problem

Antiretroviral therapy is a lifelong HIV/AIDS treatment for people living with human immune deficiency virus. Goal of antiretroviral treatment has expanded to include not only prevention of AIDS related morbidity and mortality but also prevention of HIV transmission. However, despite the ongoing scale up of antiretroviral therapy, HIV transmission and AIDS related mortality remain high in many parts of the world (11).

Globally, 17 million people living with HIV were accessing antiretroviral therapy, of which 46% were adults living with HIV in 2015 (4). Despite the absence of curative therapy for HIV/AIDS, the ultimate goal of highly active antiretroviral therapy (HAART) is to reduce HIV related morbidity and mortality, to improve quality of life, preserve immunologic function and suppression of viral load among people live with human immune deficiency virus (11).
Over the past decade, antiretroviral treatment programs have been scaled up dramatically in sub Saharan region. The treatment coverage in this region reached 37%, While 67% of men and 57% of women were not receiving ART in this region in 2013 (3). Among people living with HIV those 15 years and older receiving antiretroviral therapy were 42% in same year (12). Earlier assessments had suggested that 6% of all individuals receiving first line therapy in sub Saharan Africa needed to switch to second line regimens in any given year. As well it is estimated that approximately three quarters of adults living with HIV have not achieved viral suppression (2). Study done in this region in 2013 shows, estimated survival of ART users at one and five year were 0.87 (95% CI, 0.72–0.94) and 0.70 (95% CI, 0.36–0.86) respectively (13).

Ethiopia launched its ART initiative in 2003 based on a subsidized fee based approach. Subsequently, the service was rapidly scaled up with a number of global and national initiatives. With the help of concerted global and national actions, ART became available free of charge since 2005 in the country. As a result there has been a continuous increase in the cohort of HIV infected individuals accessing this life saving intervention. Though the government has done tremendous effort in prevention of HIV transmission and reduction of morbidity and mortality due to AIDS, still lost to follow up and early mortality is a challenge for the success of ART program (14–16). Recently ART service was available in 1047 Health facilities of which 849 were Health centers and ART coverage for adults of fifteen years and above has reached 79.6 % in 2015 (17). By the end of June 2013 the numbers of people ever enrolled in chronic care were

reached 728,874 while the number ever started ART were 439,301 and 317,443 were those on ART. Only 70.3% of individuals who ever started ART were on treatment indicating challenges of patient retention (18).

The possible difference in disease spectrum and prognosis of HIV infection in men and women is a major concern with conflicting reports about the effect of gender related difference on mortality. The progression rates might differ between women and men because of biological and socioeconomic factors (19). Males appear not to access HIV services as often as females and also have worse treatment outcomes, including mortality. The proportion of males enrolled in ART programs is lower than females (20). Other studies found that, women may also be less likely to start ART because they have less time to keep HIV outpatient appointments because of family commitments, fears about pregnancy, or socioeconomic circumstances (21).

Mortality is one reason for PLWHA attrition in ART programs. The mortality rate varies based on sex difference. According to study conducted in Black lion specialized hospital female ART users die at a higher rate as compared to male (22). In contrast study done in Goba hospital revealed males die at a higher rate compared to female (23).

Despite the availability of a large body of research evidence that addresses issues about AIDS in Ethiopia, the level of understanding about survival status difference based on gender as a result of HIV infection, is low and inconsistent across studies. This study addresses estimate of mortality and identify predictors that have impact on the survival of ART users with particular emphasis on gender difference.

CHAPTER TWO: LITERATURE REVIEW

2.1 Survival status of ART users at different point in time

The survival probability of ART users differs with time interval from initiation time of ART. A two year prospective study conducted in India in 2014, shows difference in survival probability with change in time interval after initiation of ART. The probability of survival at 3, 6, 12 and 24 months treatment follow up were 87.5%, 84.1%, 82.7% and 82.3% respectively. The probability of survival was lesser in the first six month. Beyond six month follow up it was nearly similar throughout the study period (24). The study done in Nepal in 2012 shows that, the survival probability of patients at 3 month, 6 month, 1 year, 2 year, and at 5 year were 94.66%, 91.43%, 89.65%, 86.53%, and 82.86%, respectively (25).

According to a study conducted in Uganda in 2011, the survival status at six, twelve, eighteen, and twenty four months were 93%, 88%, 87% and 86%, respectively. As well those at thirty, thirty six and forty two month almost have similar survival probability which was near to 85%. The finding shows higher mortality in the first six month of ART initiation (26).

The study done in Cameron in 2009 shows, the survival probability of ART users at 6, 12 and 24 months of follow up, which was 80%, 77% and 70% respectively. Then at month 36 and 48 it was near to 62.5% and at 60 months of follow up it was 50% of survival probability. (27).

The finding of research employed in Somali region in 2015, revealed that the estimated survival probability of the cohort of ART users at 6, 12, 24, 36 and 48 months were 91.6%, 90.2%, 88.7%, 87.3% and 85.9%, respectively (28). The study done in Jinka, South Omo in 2016 shows that, probability of survival and the retention rate of patients on ART at 72 months of follow up was 64.0% and 79.0% respectively (29). According to study done in Gondar hospital in 2012 shows, 60.4% of the PLWHA were retained on treatment and 10.4% crude death within five year of follow up (30). In support to this study, finding from Hadiya and Kembata zone in 2015 shows that, 12.6% of crude death of ART users and 83.1% of probability of survival within five year treatment follow up (31).

2.2 Gender difference in survival status of ART users

Regarding the relation between gender and survival status among ART users, literatures show three controversies. Since health care seeking behavior of females is high, they will have better

survival than males. On the other hand, though they start treatment at a better clinical stage their immunologic response is lesser than their counterpart, which decreases their survival probability. Some also states gender has no effect on survival of ART users.

A two year prospective study conducted in India in 2014 shows, being male was a predictor of early mortality with a risk almost two times greater than that of female (24). As well a case study in India in 2016 also shows the life time survival of ART users was estimated to be 12.2 years and separately women had 13.0 years which was significantly higher than men that was 11.3 years (32).

A Study done in South Africa in 2012 shows that, cumulative mortality proportion of females was less than that of males in which both curves go up then bend to the right. On month twelve, it was below 0.1 for females but above 0.1 for males. On month 24 & 36, it was 0.11 & 0.13 for females and 0.15 & 0.18 for males respectively (33). According to a study conducted in Malawi in 2010 indicates that, the cumulative probability of survival at 3, 6, 12 and 18 months after ART initiation were 90%, 87%, 83% and 80% for men and 94%, 92%, 90% and 88% for women respectively (34).

According to study done in Dar es salaam, Tanzania in 2013, women were starting ART at a less advanced disease stage but after one year of treatment initiation both women and men had similar clinical and immunological condition (35). Finding from study conducted in Uganda in 2011 shows that, the probability of survival was 91.2% for males and 94.1% for females at 12 months (36). Study done in Malawi in 2008 also revealed, females survival probability was 76.0% which was significantly higher than male survival probability that was 64.6% at two and half year of follow up (37).

The finding of study done in Black lion Specialized Hospital in 2012 shows, females ART users had shorter survival status on average as compared to males (AHR=1.818; 95% CI: 0.365-0.843) (22). In contrast Study done in Goba in 2015 shows, the survival probability of male was significantly less than female. In which males experience two and half (AHR=2.67; 95% CI: (1.74–4.10) times risk of mortality while on ART treatment compared to females (23).

2.3 Determinants for survival status of ART users

Though ART is used in order to improve progression of disease and survival status of ART users, there are a number of factors facilitating and influencing the survival status of ART users.

2.3.1 Socio demographic factor

Different literatures shows the socio demographic factors explained as having contribution in disease progression and outcome and for the difference in survival status. Study employed in USA in 2013 shows, divorced were 4.3 times 95% CI (2.97, 6.26) and Single/never married were 13 times 95% CI (9.65, 17.75) more likely to die earlier when compared to married (38).

Study in south east Uganda in 2011 shows, the risk of dying for females was 41% lower than males. The risk of death increased by 9% for every 10 year increase in age at initiation of ART (26).

Study done in Aksum in 2014 revealed that, those with lower education (no education or primary education) were three times increased risk of mortality than those individual who completed secondary or higher and males were at higher risk of mortality (39). Study in South Wollo northern Ethiopia in 2014 revealed that, patients whose age greater than 41 years was at risk of death at a rate of 48.9% greater than age group (30-40). As well the risk of death of rural residents were about two times greater than urban residents (40).

2.3.2 Psychosocial related factors

Disclosure of HIV status to the others was important predictors of survival status that was identified by numbers of studies. The study done in Jinka, South Omo in 2016 shows that, risk of dying among ART users those not disclosed their HIV status were six times greater when compared to those disclosed (29).

2.3.3 Nutritional status related factor

Nutrition and HIV infection have a complex and dependent interaction. It is often affected by HIV or secondary complications due to opportunistic infections especially those related to gastrointestinal and therapies. Furthermore Poor nutritional status affects immune status, moderates the efficacy of medications, may increase the severity of side effects, and can affect important outcomes.

Finding from far western Nepal in 2013 revealed that, for a one kilogram decrease in the baseline bodyweight at initiation of ART, the mortality risk increased by 4% (41). Study in Cameron in 2009 shows body mass index below 15kg/m^2 and 15-18.5kg/m^2 were 3 times and 1.57 times more likely to die compared to those above 18.5kg/m^2 (27).

According to study done in Aksum in 2014 shows that, people who start ART with weight of less than 40 kg do have about two and half times higher risk of mortality than those who have baseline body weight of > 60 kg (39).

2.3.4 Medical condition related factors

The major aim of ART program is for improvement of patient clinical response and hindering of AIDS related deaths and complications. Medical condition at baseline and afterwards determine survival status of ART users.

According to study conducted in Zimbabwe in 2014, males had poorer clinical status during initiation of ART with regard to current and previous TB illness when compared to females. As well among few ART users who had hemoglobin measurements taken, anemia was more prevalent among males than females, and anemia has been shown to be a strong risk factor for deterioration of disease progression and earlier death independent of CD4 count and viral load (42). Study in Malawi in 2008 shows, those with stages 1 and 2 have 85.0%, stage 3 have 72.1% and stage 4 have 60.1% survival probability (37).

Different literatures shows as functional status of people live with HIV at baseline deteriorates their probability of surviving lowers (22,24,29,31,32,43,44). Study done in Jimma University Teaching Hospital in 2015 revealed that, the problem of high mortality among TB/HIV co infected ART users. It shows more than 1 in 5 TB-HIV co-infected (20.2%) individuals died during TB treatment. On the other hand PLWHA on WHO stages 2, 3 and 4 compared to stage 1 were found protective for mortality risk (45).

Finding of study done in armed force of Addis Ababa in 2012 yields that, PLWHA who suffered from Opportunistic Infections (OI) had nearly a nine times risk of mortality than those who were free of OIs. As well functional status was a determinant factor for the survival difference in which those ambulatory were twice and those bedridden nearly three and half times at higher risks of dying as compared to those had working functional status (44). As well study done in

debre markos hospital shows those had ambulatory (AHR=2.7; 95% CI: 1.9-3.9) and bedridden (AHR=2.4; 95% CI: 1.3-4.2) functional status were at higher risk of death compared to those with working functional status (43). Finding in Jinka south Omo shows those with history of TB treatment had about two times risk of death than those free of TB history at baseline (29). Other literatures also shows those having TB at baseline were at higher risk of mortality compared to those with no history of TB co infection (23,26,28,44).

According to study conducted in Arba minch town, southern Ethiopia in 2014 shows, the initiation of HAART was associated with a dramatic effect in the overall reduction of incidence rates of increased WHO clinical stage among ART users (46).

2.3.5 Behavior related factor

Adherence to ARV drug is a key to sustain HIV suppression, risk reduction of drug resistance, improved overall health, quality of life, and survival, as well as decreased risk of HIV transmission (11).

Study done in Brazil in 2013 indicates the incidence of poor adherence was 1.5 times greater among women compared to men (47).

Finding from study in Debre markos in 2014 indicates impact of level of adherence to pills on survival. ART users those had fair and poor ART adherence were 2.15 and 1.89 times at high risk of mortality than those with good adherence respectively (48). The study conducted in Harar and Dire Dawa town in 2015 indicates the level of adherence to pill was 85 % which was lower than the 95% recommended level of adherence (49).

2.3.6 Medication related factor

The primary goal of antiretroviral therapy is improving clinical and immunologic response. Antiretroviral therapy regimen can be changed based on certain stated factors. According to the Standard Treatment Guideline of Ethiopia, ART regimen can be changed if a patient develops treatment failure, new TB, drug side effect and other problems (50).

Finding of study conducted in Nekemt in 2013 shows, the main reason for regimen change were toxicity/side effects (80.3%), pregnancy (6.3%), new TB (5.6%), drug stock out (4.9%) and treatment failure (2.8%). Most common toxicity reported were lipoatrophy (58.8%) followed by rash (12.3%) and CNS toxicities (11.4%) (51). According to study conducted in Fitche hospital in 2014, the major reasons for regimen change were toxicity followed by treatment failure (52).

Study done in Shashemene and Assela hospitals in 2010 shows, CPT initiations before or after ART initiation reduce risk of mortality by 86% when compared to those not taking CPT at all (53).

2.3.7 Baseline laboratory result

The finding from different studies showed lower CD4 cell count at the initiation of the ART have been associated with increased risk of mortality.

Study employed in South Africa in 2010 shows, severe anemia (<11mg/dl) was a risk factor of mortality of ART users (54). Finding of research employed in Aksum in 2014 shows, those with baseline hemoglobin level of less than 11mg/dl were 2.25 times at a higher risk of mortality in the follow up time compared to those having above 11mg/dl. This study also shows those with smear positive TB were 2.62 time at higher risk of mortality than smear negative (39). Study conducted in University of Gondar specialized hospital in 2012 revealed those with baseline CD4 cell count less than 200cells/dl were 5 times at higher risk of mortality in the follow up time compared to those with greater than 200cells/dl (30).

2.3.8 Others

Early initiation of ART is proved to improve life expectancy of ART users. Study done in South Africa in 2013 shows, HIV positives those started taking ART have life expectancies around 80% of normal life expectancy, provided that they start treatment before their CD4 count drops below 200 cells/ml. Life expectancies was 15%–20% higher among ART users who survived to 24 month after starting ART than those had just started ART (55).

Finally during review of literatures, some flaws of previous studies were observed. For instance, most of the studies didn't consider sample size determination for cox-proportional hazard model during sample size calculation even though cox-regression model was employed to identify predictor variables. The other during sampling technique most studies included transferred outs those probably overestimate probability of survival since its outcome is not known.

Conceptual framework

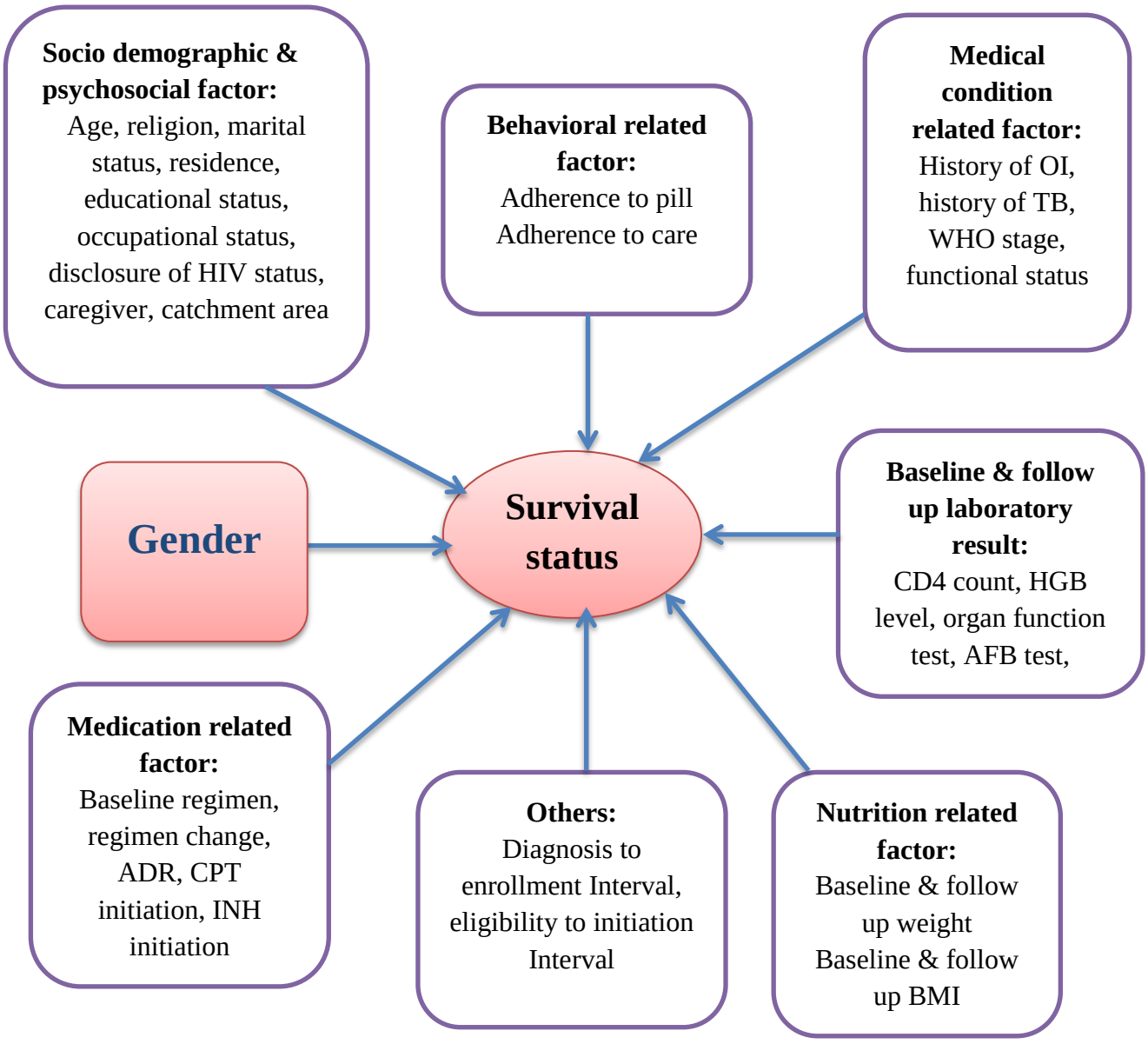

Figure 1: Conceptual framework for gender difference in survival status and its predictors among ART users adapted from different literature

Significance of the study

Despite extensive studies and intervention efforts have been done so far, still early mortality as a result of HIV/AIDS remains public health problem and a challenge for ART program. Evidence related to gender difference in survival status still under studied in Ethiopia as far as investigator reviewed.

So as this study assessed the Gender difference in survival status among ART users in Yirgalem general hospital and will add up to date information to existing knowledge and will help for additional interventions.

For partners working on HIV/AIDS, the findings of the study will help for evidence based intervention. The study will add relevant knowledge to the scientific community and fill the research gap of the study area to this specific issue.

Ministry of health and regional health bureau can use the finding as baseline for evidence based planning.

CHAPTER THREE: OBJECTIVE

3.1 General objective

To assess gender difference in survival status among ART users in Yirgalem General Hospital, Sidama zone, SNNPR, Ethiopia, 2017

3.2 Specific objectives

1. To determine survival status of ART users in Yirgalem general hospital
2. To test the gender difference in survival status of ART users in Yirgalem general hospital
3. To identify factors affecting survival status of ART users in Yirgalem general hospital

CHAPTER FOUR: METHODS AND MATERIALS

4.1 Study area and study period

This study was conducted in Yirgalem General Hospital, which is, one of the earlier hospital found in SNNPR. It is located in Yirgalem Town at 45kms from Hawassa city. The Hospital is launched by Norwegian missionaries on January 1966. The facility has been providing inpatient and outpatient service in the four departments since its establishment. Antiretroviral therapy service provision in the hospital was started fee based in 2003 and free of charge was started since 2005.

Today the hospital is offering ART service, voluntary counseling and testing of HIV and it is one of the treatment initiating center for multidrug resistant tuberculosis in south of Ethiopia since 2013. Currently, there are 2015 adult ART users in the hospital. Among these 839 are adult ART users those start treatment from Sep 1st 2010 to Aug 30th 2015 comprising of 506 female and 333 males.

The study was conducted from March 15 to April 15, 2017.

4.2 Study design

Institutional based retrospective cohort study design was employed.

4.3 Population

4.3.1 Source population

All adult ART users' records, those enrolled to ART service in ART center of Yirgalem general hospital from September 1st, 2010 to August 30th, 2015

4.3.2 Study population

Adult ART users' records selected during sampling and included in the study, among those enrolled from September 1st, 2010 to August 30th, 2015

4.4 Sample size determination

Sample size was calculated for each objective separately in order to attain maximum sample size.

For objective one: The sample size was calculated online (56) based on the assumption that type I error 5 %, power of 90 %, and parameters used from similar study:

Incidence rate 0.057death per year

Median survival time 0.54 year

Censored rate 1.32 censored per year

Planned follow up period 5year (33).

Sample size became 170 then adding ten percent non retrieval rate finally it gives **187**.

For the second objective which is to test gender difference in survival status, the estimate of survival status difference was used to calculate sample size. The required Sample size was determined based on hazard ratio of similar study using STATA version 13 considering the following assumptions. Level of confidence 95% (α =0.05) and a power of 90% were considered. According to study conducted in Black Lion specialized Hospital in 2012 revealed that female (the four year survival was 88.14%) has a lesser survival as compared to males (the four year survival was 91.7%) with adjusted hazard ratio of female was 1.818. The standard deviation was 0.23 and probability of failure observed was 90% (22). Then taking probability of withdrawal 10% the calculated sample size became **687** records of ART users'.

For the third objective which is identifying factors associated with survival status of ART users, different predictors were used to determine maximum sample size [Table 1].

Table 1: Predictor variables used for sample size determination using STATA version 13, software with the parameters used and the total sample size, February 2017

Sir.no	Predictors	Parameters	Sample size	Reference
1.	WHO stage IV	AHR=3.19 Standard deviation =0.5 Probability of failure observed = 88%	33	(57)
2.	Functional status	AHR=2.67 Standard deviation =0.243 Probability of failure observed = 90%	228	(22)
3.	Opportunistic infection	AHR= 3.35 Standard deviation =0.5 Probability of failure observed = 82%	32	(31)
4.	TB co-infection	AHR= 1.43 Standard deviation = 0.5 Probability of failure observed = 82%	366	(31)
5.	Adherence to ART	AHR= 2.7 Standard deviation = 0.5 Probability of failure observed = 82%	48	(31)

After challenging for the three objectives the final Sample size became 687.

4.5 Sampling method and procedure

4.5.1 Sampling frame

Adult HIV positive ART users' unique record identification number found on registration book for those enrolled in the given follow up period in ART center of Yirgalem hospital separately for males and females, is sampling frame in order to recruit those eligible participants.

4.5.2 Sampling procedure

Having a total of 839 records of adult ART users' from September 1st, 2010 to August 30th, 2015, the population in each year was stratified by sex and enrollment year. Then the calculated sample size was proportionally distributed to males and females of each year separately. By using ART unique record identification number, simple random sampling technique was applied to recruit study participants records from each stratum separately. Then sampling frame that were generated using unique record ART number were entered into SPSS and the required sample size were selected randomly by using SPSS select case procedure. Finally 414 females and 273 males ART users' records were recruited [Figure 2].

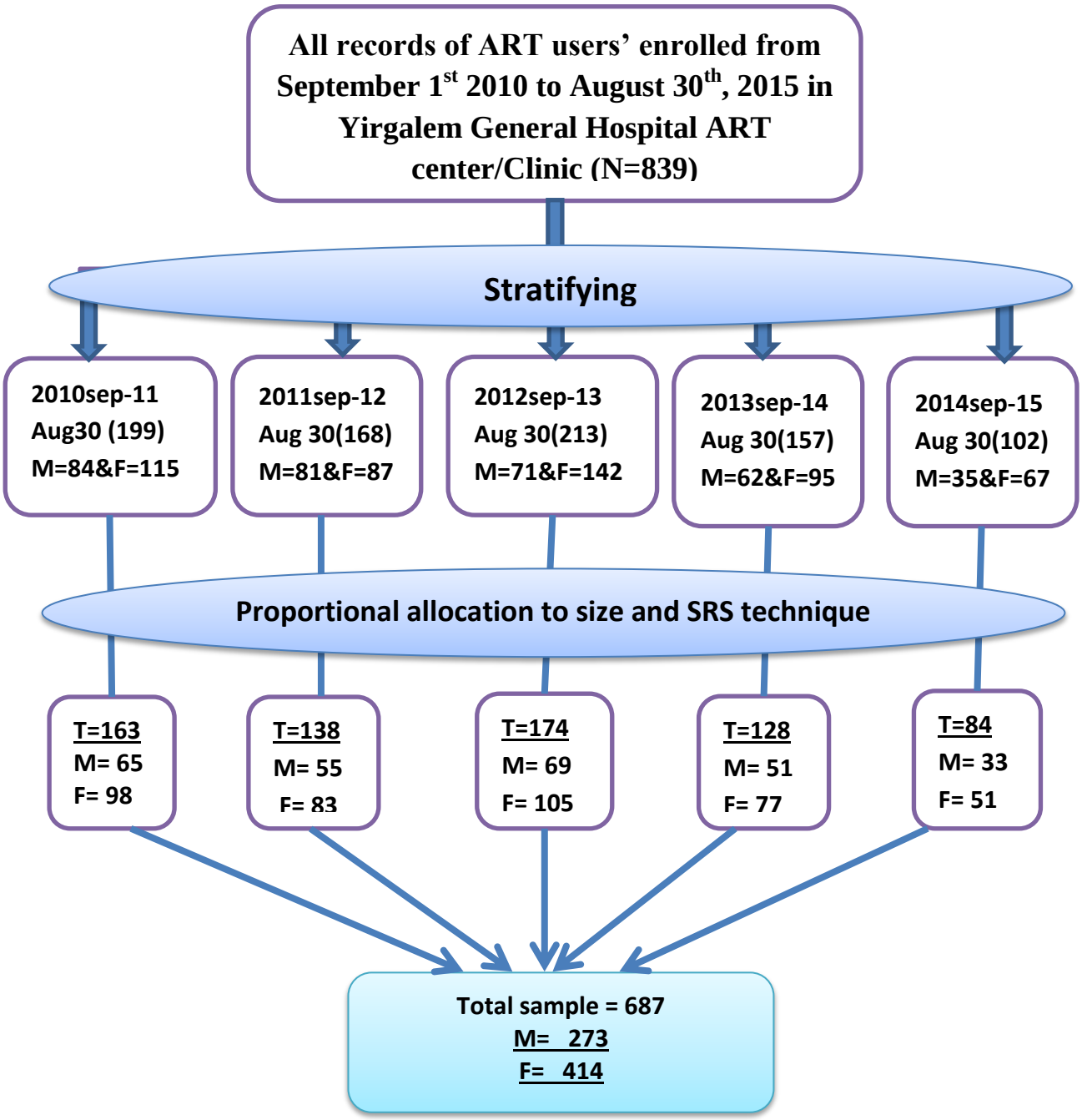

Figure 2: Schematic presentation of sampling procedure

4.6 Inclusion criteria

Records of adults those age 15 and above at initiation of ART

Records of HIV positive individuals' those start ART at least one year prior in Yirgalem hospital

4.7 Exclusion criteria

Records of those transferred out ART users'

4.8 Variables of the study

4.8.1 Dependent variable

- Survival status

4.8.2 Independent variable

- Socio demographic and psychosocial related factor:
  - Age, religion, marital status, level of education, residence, occupational status, disclosure status, caregiver, catchment area
- Gender
- Behavioral related factor:
  - Adherence to pill, adherence to care
- Nutritional status:
  - Baseline weight, follow up weight, baseline BMI, follow up BMI
- Medical condition related factor:
  - History of OI, history of TB, WHO stage, functional status
- Medication related factor:
  - Baseline regimen, history of regimen change, CPT initiation, INH initiation, adverse drug reaction
- Baseline and follow up laboratory result:
  - HGB level, CD4count, liver function test (ALT/AST), renal function test(Cr/BUN), AFB test, TLC, WBC, NEUT, PLT
- Others:
  - Interval of diagnosis to enrollment date, interval of eligible to initiation date

4.9 Data collection procedure and technique

Data were extracted by using a structured standardized checklist. The standardized checklist was prepared based on the ART patient monitoring chart which is employed by the ART center.

Two clinical nurses were recruited for data extraction. They were given two day training on data extraction, how to fill the prepared checklist from patient follow up card. The first day of training which focuses on the purpose of research and how to extract the data from records were held in class room of Yirgalem medical college. On the next day practical attachment of extracting data from records was held in Leku district hospital.

Then data collectors extract ART users' information from records of ART users' follow up card. The incomplete records were cross checked with electronic data base and ART registration log book before they were dropped. The data collectors were closely supervised by the principal investigator and supervisor.

4.10 Operational definition

- Adherence to pill:
  - Good : > 95% (of 30 dose if forgot <=2 dose or out of 60 dose if forgot <=3 dose)
  - Fair : 85-94% (of 30 dose if forgot 3-5 dose or out of 60 dose if forgot 3-9 dose)
  - Poor : < 85% (of 30 dose if forgot >=6 dose or out of 60 dose if forgot >9 dose)
- ART users: adult HIV positives those started ART at least one year prior to study period
- Baseline laboratory result: results recorded at time of ART initiation, but if not available result within one month of ART initiation considered as baseline laboratory result
- Censored: those lost to follow up, drop-out and on follow up
- Drop-out: ART users not seen for more than 3 month starting from date of last schedule
- Gender: explained in this study as male or female
- Functional Status:
  - Working functional status: able to perform usual work in or out of the house, harvest and go to workplace.
  - Ambulatory functional status: unable to perform usual work of living but able to carry out self-care activities
  - Bedridden functional status: unable to perform activities of daily living
- Incomplete card: when one of the independent variable is not registered namely, CD4 cell count, WHO stage, weight and functional status
- Lost to follow up: ART users not seen for >= 1 month but less than 3 month starting from date of last schedule
- Side effect: as recorded by physician/nurse on the patient card
- Survival: when the ART user is known to be alive as evidenced by his/her clinical follow up
- Survival time: the period that ART users stays alive after initiation of ART to end of event occurs
- Retention: refers to ART users known to be alive and receiving ART at the end of a follow-up period.

4.11 Data quality assurance

To ensure the quality of data, data collectors were recruited from facilities other than the study area and they were given two day training on how to fill the checklist. As well they were given training on practical skill how to extract data from follow up card and then what they extract were rechecked with the actual follow up card. This practical training was held in Leku district hospital.

The entire filled checklists were checked for consistencies and completeness of the data on daily bases. The incompletes were returned back to respective data collectors for cross check with the actual records based on unique record number. After data collection, data were cleaned manually then each checklist were given a unique code and entered to prepared template scheme in EPI Data version 3.1 by controlling skip patterns and legal values. Ten percent of the entered data were rechecked by comparing the entered data with the actual checklist. Finally data were exported to STATA version 13 and explored to check for missing values and outliers for data cleaning.

4.12 Data processing and analysis

The cleaned and compiled data were prepared for final analysis. Descriptive statistics such as proportions, means, medians, and standard deviation (±SD) were computed for categorical and continuous variables as supposed necessary. Trend analysis was done to see the change in the biomarkers of ART over the five year treatment follow up period.

Kaplan Meier survival function was done to estimate the probability of survival of ART users for gender category and biomarkers of ART. Log rank test was used to test the statistical difference in the KM curves. Then, 6, 12, 24, 36, 48, 54 and 60 months probability of survival were determined using life table.

To identify predictors of survival status first Bivariate Cox regression analysis was done to estimate the unadjusted Hazard Ratios (HRs). Each independent variables having $P<0.2$ in bivariate analysis was candidate for multivariable Cox regression model. Then multivariable Cox regression analysis was performed to estimate the adjusted hazard ratios. Adjusted Hazard ratio with 95% confidence interval was used to measure the existence of significant association and strength between predictor variables and the outcome. Variables that were statistically significant at $p < 0.05$ were considered as independent predictors of survival status of ART users. Then results were presented using tables, graphs and narration.

Assumption of proportional hazard model was checked using Schoenfeld residual plot, Goodness of fit test using global test at $p>0.05$ were used to declared model is fit and time dependent covariates when there is no significant interaction between covariate and time variable, the effect of covariate not vary with time change. So cox-PH model is reasonable. Interaction was checked at p value >0.05 to declare no interaction among variables.

4.13 Ethical clearance

Ethical clearance for the study was obtained from ethical Review Board (IRB) of Jimma University Institute of Health science (JUIH). Permission letter was obtained from chief executive officer and medical director of Yirgalem General Hospital. Finally the objective of the study was explained to coordinator and staffs of ART clinic of Yirgalem hospital.

There were no unique identifiers of ART users on the checklist and all the data collected were handled confidentially and were discarded at the end of data collection safely.

4.14 Dissemination plan of the results

The finding of the study will be presented to Jimma university school of public health to department of population and family health.

As well it will be presented to Sidama zone health office and Yirgalem general hospital and also through different workshops and seminars will be disseminated to relevant stakeholders found at regional and zonal level. It will be accessed to interested researchers and academicians through the department of population and family health and library of Jimma University. Finally, efforts will be made to publish on scientific journal.

CHAPTER FIVE: RESULTS

A total of 685 records were reviewed giving a retrieval rate of 99.7%.

5.1 Socio demographic and psychosocial Characteristic

There were 412 and 273 records of females and males ART users' included in the study respectively. The mean age of participants at the time of ART initiation was 32.90 years (±SD 9.24) (females 31.75(±SD 8.55) and males 34.65(±SD 9.96)). Nearly half, 326 (47.60%) ART users were within the age group of 25 – 34 consisting 210 (64.42%) females and 116(35.58%) males ART users. Three hundred thirty (48.18%) ART users were married comprising of 195 (59.09%) females and 135(40.91%) males. Two hundred forty two (35.33%) have primary level of education among these 154 (63.64%) were females and 88(36.36%) were males. Nearly half, 310 (45.26%) were unemployed consisting of 244 (78.71%) females and 66 (21.29%) males ART users. Three hundred fifty six (51.97%) follow orthodox religion and among these 212 (59.55%) were females and 144 (40.45%) were males ART users. Nearly three fourth of ART users, 504 (73.58%) were reside in urban of which 305 (60.52%) were females and 199 (39.48%) were males [Table 2]

Table 2: Baseline Socio-demographic and psychosocial characteristics of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

Socio demographic characteristics	Female		Male		Total (%)
	Frequency	Percent	Frequency	Percent	
Age group					
15-24	65	69.15	29	30.85	94 (13.72)
25-34	210	64.42	116	35.58	326 (47.60)
35-44	103	55.68	82	44.32	185 (27.01)
45-54	25	42.37	34	57.63	59 (8.61)
>55	9	42.86	12	57.14	21 (3.06)
Marital status					
Never married	62	47.33	69	52.67	131 (19.12)
Married	195	59.09	135	40.91	330 (48.18)
Divorced	75	70.09	32	29.91	107 (15.62)
Widowed	80	68.38	37	31.62	117 (17.08)
Level of education					
No education	90	68.18	42	31.82	132 (19.27)
Primary	154	63.64	88	36.36	242 (35.33)
Secondary	124	57.41	92	42.59	216 (31.53)
Tertiary	44	46.32	51	53.68	95 (13.87)
Religion					
Orthodox	212	59.55	144	40.45	356 (51.97)
Protestant	154	61.11	98	38.89	252 (36.79)
Muslim	40	58.82	28	41.18	68 (9.93)
Catholic	6	75.00	2	25.00	8 (1.17)
Other	0	0.00	1	100	1 (0.15)
Occupation					
Employed	56	42.11	77	57.89	133 (19.42)
Self employed	66	49.25	68	50.75	134 (19.56)
Unemployed	244	78.71	66	21.29	310 (45.26)
Other	46	42.59	62	57.41	108 (15.77)
Residence					
Urban	305	60.52	199	39.48	504 ((73.58)
Rural	107	59.12	74	40.88	181 (26.42)
Catchment area					
Reside within catchment	271	58.79	190	41.21	461 (67.30)
Reside out of catchment	141	62.95	83	37.05	224 (32.70)
Care giver					
Yes	322	59.41	220	40.59	542 (79.12)
No	90	62.94	53	37.06	143 (20.88)
Disclosure					
Yes	330	59.46	225	40.54	555 (81.02)
No	82	63.08	48	36.92	130 (8.98)

5.2 Baseline Medical condition and nutrition related factor

Nearly three fourth, 519 (75.77%) of ART users had at least one opportunistic infection at baseline and among these 297 (57.23%) were females and 222 (42.77%) were males. Four hundred forty six (65.11%) had no history of TB at baseline comprising 271 (60.76%) females and 175 (39.24%) males. Three hundred ninety four (57.52%) had working functional status at initiation of ART of which 231 (58.63%) were females and 163 (41.37%) were males. Two hundred thirty nine (34.9%) ART users were on WHO stage III at baseline of which 129 (53.97%) were females and 110 (46.03%) were males. The overall mean weight at baseline was 53.51Kg (±SD 11.72) where females had 51.66 (±SD 11.87) and males had 56.31 (±SD 10.94) [Table 3].

Table 3: Baseline medical and nutritional status of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

Medical and nutrition related factor	Female		Male		Total (%)
	Frequency	Percent	Frequency	Percent	
Past history of OI					
Yes	297	57.23	222	42.77	519 (75.77)
No	115	69.28	51	30.72	166(24.23)
History of Tuberculosis					
None	271	60.76	175	39.24	446 (65.11)
INH prophylaxis	69	60.00	46	40.00	115 (16.79)
TB-Rx	72	58.06	52	41.94	124 (18.10)
Baseline AFB result					
Negative	344	59.93	230	40.07	574 (83.80)
Positive	68	61.26	43	38.74	111 (16.20)
Eligibility criteria					
Clinical only	18	72.00	7	28.00	25 (3.65)
Cd4 count only	218	61.06	139	38.94	357 (52.12)
Clinical and cd4 count	141	55.95	111	44.05	252 (36.79)
Transferred in	22	59.46	15	40.54	37 (5.40)
Pregnancy	14	100	0	0.00	14 (2.04)
Functional status					
Working	231	58.63	163	41.37	394 (57.52)
Ambulatory	135	64.29	75	35.71	210 (30.66)
Bedridden	46	56.79	35	43.21	81 (11.82)
WHO clinical stage					
Stage I	114	69.51	50	30.49	164 (23.94)
Stage II	105	57.38	78	42.62	183 (26.71)
Stage III	129	53.97	110	46.03	239 (34.9)
Stage IV	64	64.65	35	35.35	99 (14.45)
Weight category					
≤40kg	87	76.99	26	23.01	113 (16.50)
40-60kg	242	60.96	155	39.04	397 (58.00)
>60kg	83	47.43	92	52.57	175(25.50)
Body mass index at baseline					
Not malnourished	108	56.54	83	43.46	191 (27.90)
Moderate malnutrition	31	68.90	14	31.10	45 (6.56)
Severe malnutrition	37	66.07	19	33.93	56 (8.17)
Missing	236	60.05	156	39.95	393(57.37)

The leading adverse drug reaction/side effect at the first one month of follow up were chronic diarrhea 111 (18.2%), fatigue 104 (17.05%) and numbness 89 (14.59%). The commonest opportunistic infection at baseline were herpes zoster 145 (21.16%), pulmonary tuberculosis 124 (18.10%) and bacterial pneumonia 107 (15.62%) [Figure 3].

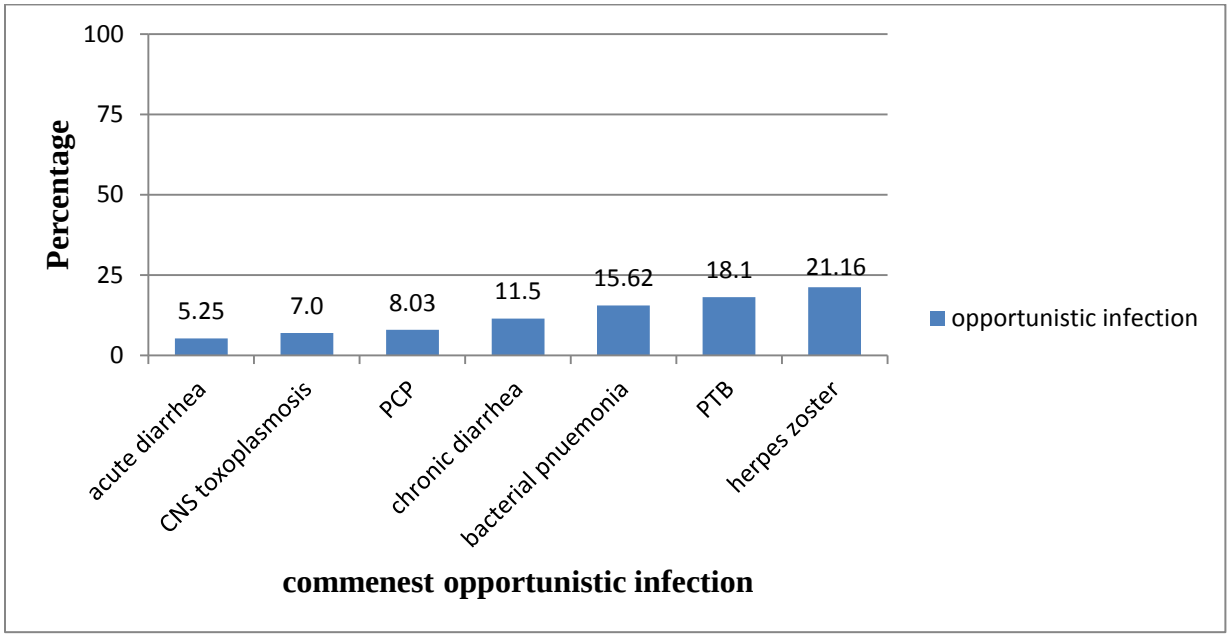

Figure 3: Common baseline opportunistic infection of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

5.3 Baseline laboratory result, medication and behavior related factor

On the first six month follow up 677 ART users reach of which 406 were females and 271 were males. More than three fourth, 514 (75.92%) had good adherence to ART drug at six month of follow up of which 304 (59.14%) were females and 210 (40.86%) were males. The baseline overall mean hemoglobin level was 12.12mg/dl (±SD 2.8) where males had 12.64mg/dl (± SD 2.89) and females had 11.76mg/dl (± SD 2.7). Four hundred twenty (61.32%) had hemoglobin level between (11-17mg/dl) of which 250 (59.52%) were females and 170(40.48%) were males. The baseline mean CD4 cell count was 197.7 (± SD 117.3). Nearly half of ART users, 344(50.22%) were grouped under CD4 cell count of below 200cells/µl, of which 200 (58.14%) were females and 144 (41.86%) were males. At baseline ART regimen 1e (TDF+3TC+EFV) was prescribed for 357 (52.12%) of PLWHA consisting of 216 (60.50%) females and 141(39.50%) males [Table 4].

Table 4: Baseline laboratory result, medication and behavior related factors of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

Baseline laboratory result, medication and behavior related factor	Female		Male		Total (%)
	Frequency	Percent	Frequency	Percent	
Adherence to pills (ART) at 6month (n=677)					
Good	304	59.14	210	40.86	514 (75.92)
Fair	91	61.90	56	38.10	147 (21.71)
Poor	11	68.75	5	31.25	16 (2.37)
Adherence to care at 6 month (n=677)					
Below mean	291	58.78	204	41.22	495 (73.11)
Above mean	115	63.18	67	36.82	182 (27.60)
Hemoglobin category					
<11mg/dl	122	65.24	65	34.76	187 (27.30)
11-17mg/dl	250	59.52	170	40.48	420 (61.32)
>17mg/dl	27	45.76	32	54.24	59(8.61)
Missing	13	68.42	6	31.58	19 (2.77)
CD4 category					
≤ 200	200	58.14	144	41.86	344(50.22)
201 – 350	147	63.09	86	36.91	233 (34.02)
>350	65	60.19	43	39.81	108 (15.76)
ALT (LF test)					
Normal (0-50)	179	63.48	103	36.52	282(41.17)
Abnormal (>50)	42	60.87	27	39.13	69 (10.07)
Missing	191	57.19	143	42.81	334 (48.76)
Cotri-prophylaxis at 0 month					
Yes	348	58.29	249	41.71	597 (87.15)
No	64	72.73	24	27.27	88 (12.85)
Adherence to cotri at 6month (if taken) (n=677)					
Good	292	58.40	208	41.60	500 (89.45)
Fair	33	56.90	25	43.10	58 (10.55)
Poor	0	0	0	0	0
ART regimen					
1a (d4T + 3TC + NVP)	13	72.22	5	27.78	18 (2.63)
1b (d4T + 3TC + EFV)	4	66.67	2	33.33	6 (0.88)
1c (AZT + 3TC +NVP)	85	57.43	63	42.57	148 (21.61)
1d (AZT + 3TC + EFV)	38	58.46	27	41.54	65 (9.49)
1e (TDF + 3TC + EFV)	216	60.50	141	39.50	357 (52.12)
1f (TDF + 3TC + NVP)	56	61.54	35	38.46	91 (13.28)

The overall mean days of confirmation to enrollment date were 17.39 (± SD 116) where females had 17 (± SD 92.48) and male had 17.9 (± SD 144.7). The overall mean days of eligible date to start date of ART were 38.18 (± SD 144.12) where females had 39.96 (± SD 154.37) and males had 35.49 (± SD 127.31). ART drug regimen prescribed at the first six month were 1a 15(2.22%), 1b 4 (0.59%), 1c 120 (17.73%), 1d 58 (8.57%), 1e 370 (54.65%) and 1f 110 (16.25%). Reason for regimen change at the first six month were toxicity/side effect 49(87.50%), new tuberculosis 6 (10.71%) and risk of pregnancy 1 (1.79%).

From baseline complete blood count result of ART users the mean white blood cell count were 5.8 (± SD3.04) where females had 5.6 (± SD 3) and males had 3.1 (± SD 6.1). The mean neutrophil count were 56.5 (± SD13.5) where females had 56 (± SD13.57) and males had 57.2(± SD13.5). The mean platelet count were 249.3(± SD101.8) where females had 252.7(± SD103.8) and males had 244(± SD98.7).

From baseline organ function test result, the mean aspartate amino transaminase/AST were 37.6 (± SD28) where females had 36.7(± SD27.8) and males had 39(± SD28.3). The mean blood urea nitrogen (BUN) were 22(± SD12.2) where females had 21.8(± SD13.3) and males had 22.4(± SD10.2). The mean creatinine level were 0.81(± SD0.3) where females had 0.79(± SD0.32) and males had 0.85(± SD0.31).

5.4 Biomarkers of ART

The mean weight change over time shows improvement. The mean weight at baseline and at the end of five year was 51.5kg and 59.9kg for females and 57kg and 64kg for males respectively. Weight change over five year treatment follow-up was 8.4kg for females and 7kg for males [Figure 4].

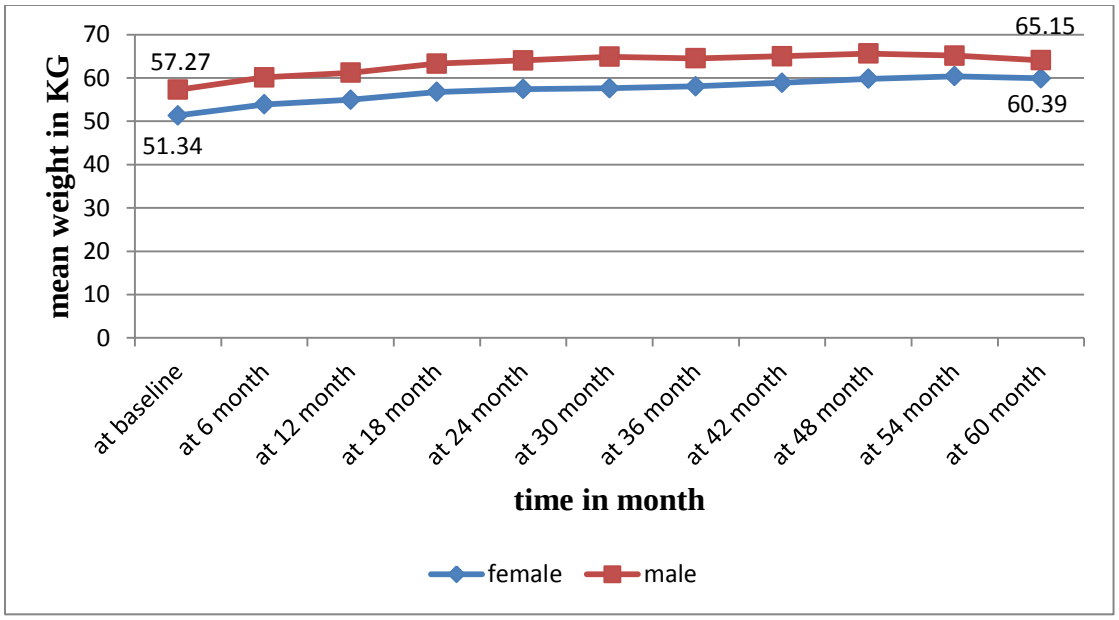

Figure 4: Trends of mean weight change based on sex category of ART users, Sep 2010 – Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685)

The percentages of WHO stage one shows better progress for both females and males over the five year treatment follow up period. The baseline and at the end of five year percentage of WHO stage one for females were 22% and 96% and for males were 27% and 97.9% respectively. The change in the percentage of WHO stage one at baseline and at the end of five year treatment follow up for females and males were 74% and 70.9% respectively [Figure 5].

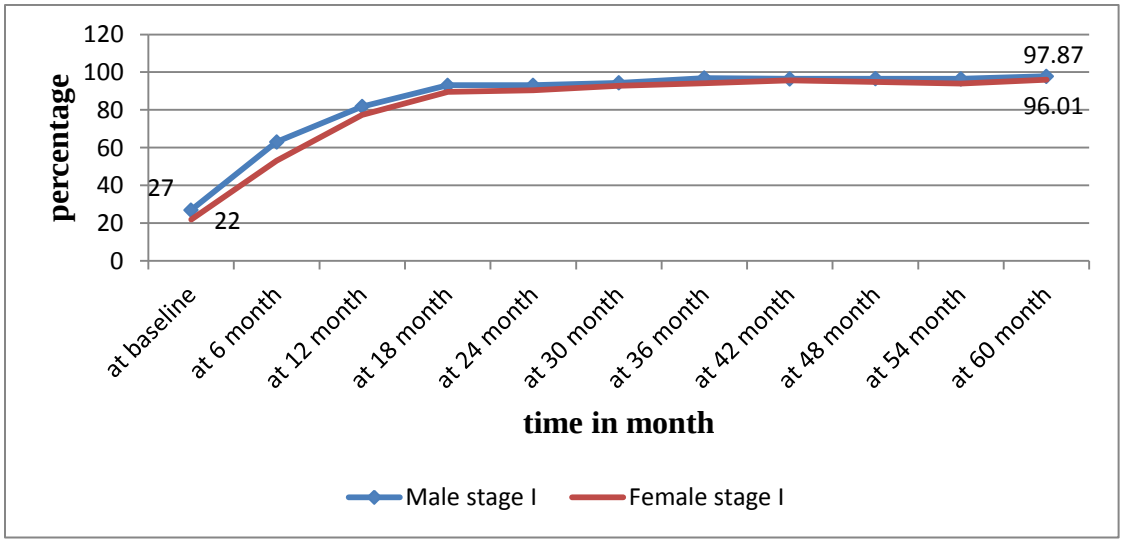

Figure 5: Trends of WHO clinical stage one based on sex category of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The overall percentages of working functional status over the five year treatment follow up period shows better progress. The baseline and at the end of five year percentage of working functional status for females were 56% and 97.94% and for males were 59.71% and 99.8% respectively. Change in the percentage over the five year treatment follow up period was 41.94% and 40.09% for females and males respectively [Figure 6].

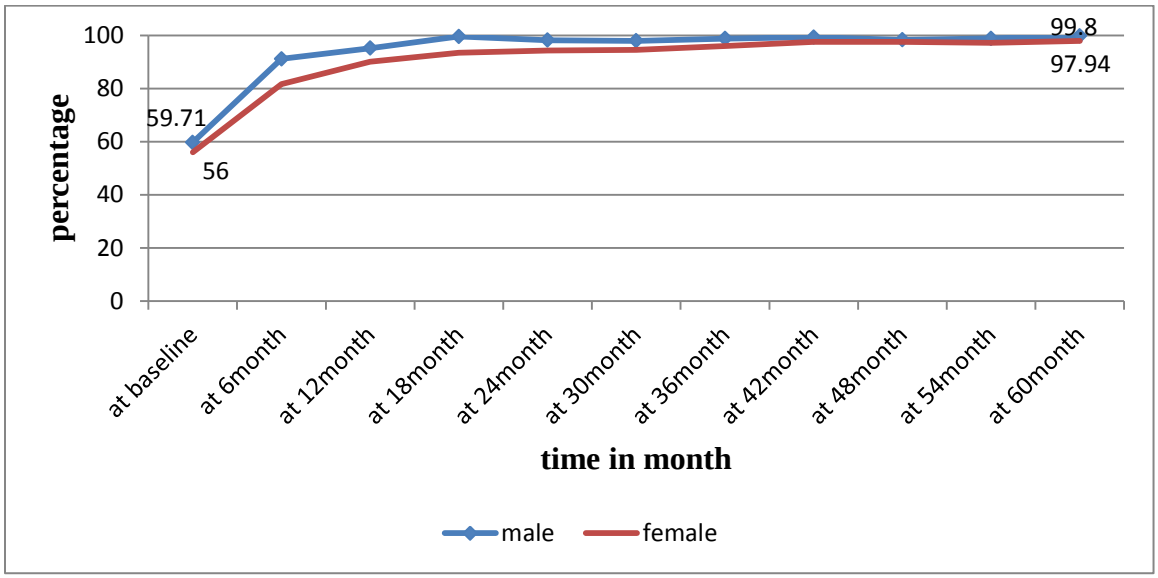

Figure 6: Trends of working functional status based on sex category of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The mean CD4 cell count over the different time interval shows better improvement for both females and males. The overall mean CD4 cell count at baseline and at the end of five year treatment follow up time were 195.8 and 512.56 where females had 182.5and 501.4and males had 203.2 and 514 respectively. The change in the mean CD4 cell count over the five year treatment follow up time for females and males were 318.9 and 310.8 respectively [Figure 7].

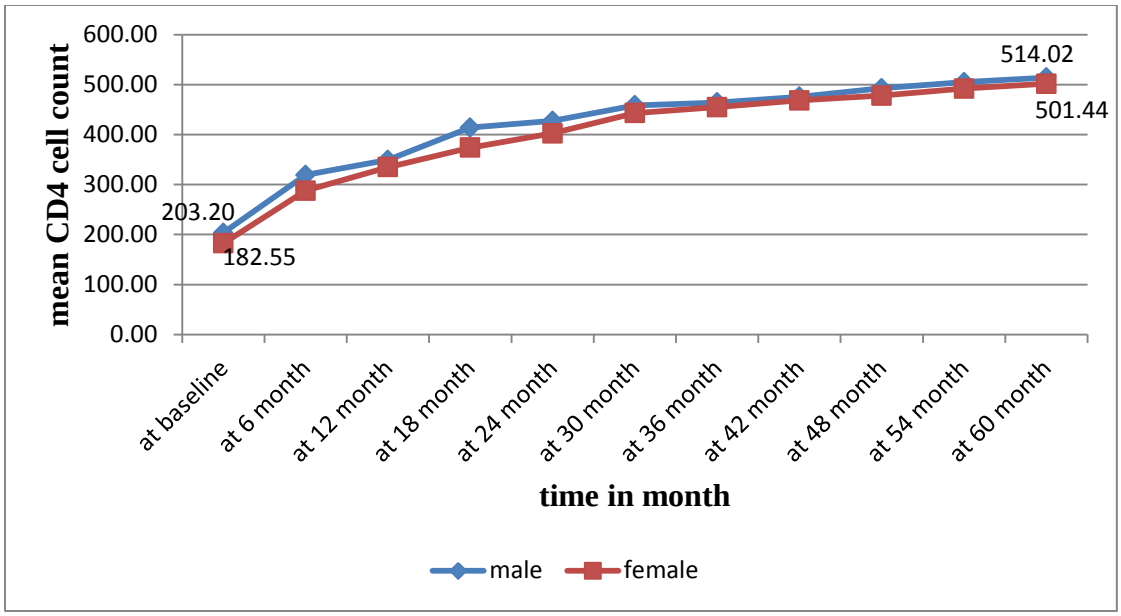

Figure 7:Trends of mean CD4 cell count based on sex category of ART users, Sep 2010 – Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

5.5 Retention rate of ART users

The total median follow up period was 42 months. Females had 42 month and males had 43 month median follow up time. Overall estimated mean follow up of ART users were 39.66 (±SD=16.7) months. Females had 38.9 (±SD=16.4) and males had 40.8 (±SD=17) months of mean follow up months. Overall retention rate was 66.13 % making attrition rate of 33.87%. Females were 65.05% and males were 67.77% to retain on treatment over the five year follow up period. Drop-outs, death and lost to follow up accounted for 49.14%, 36.21% and 14.66% of attrition rate respectively.

5.6 Survival status of ART users

The total extents of follow up were 27,209 person-months with overall incidence rate of 3 deaths per 1000 person-months observation. Females and males incidence rate were 3.9 deaths per 1000 person-months observation and 1.8 deaths per 1000 person-months observation respectively. A total death of 20 males and 64 females ART users were observed during the five year treatment follow up period. The overall survival probability of ART users were 84.53% [Figure 8].

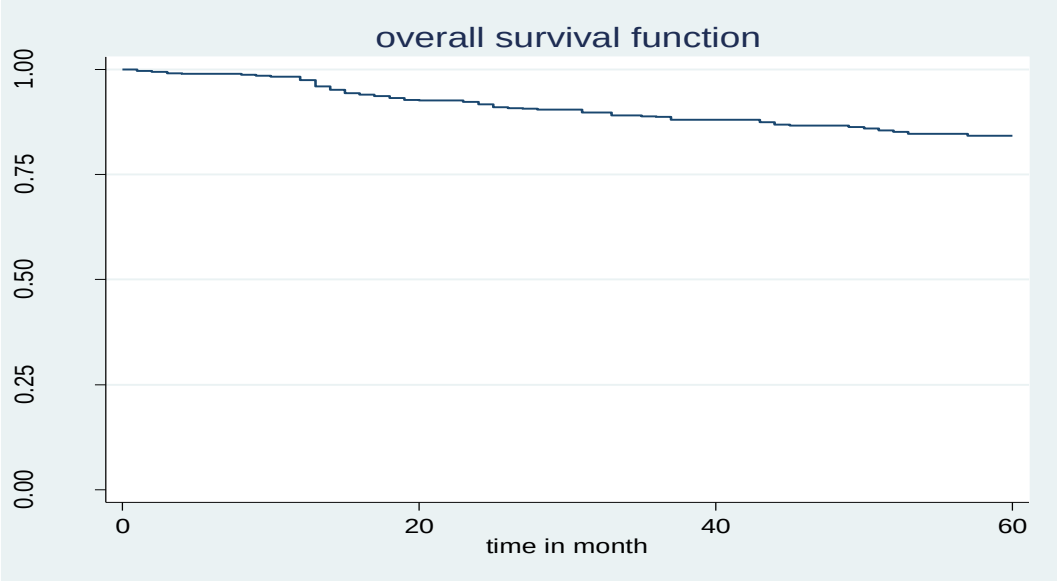

Figure 8: Kaplan Meier survival curve of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

Probability of surviving over the five year treatment follow up period was 80.10% for females and 91.18% for males [Figure 9].

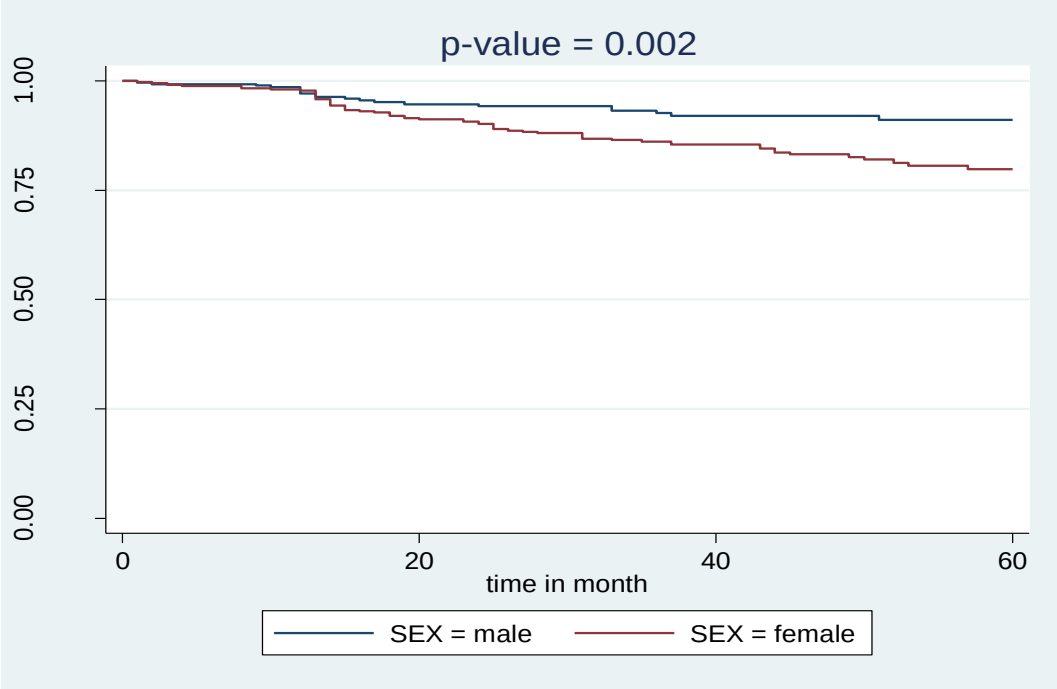

Figure 9: Kaplan Meier survival curve by sex category of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The overall probabilities of survival of ART users, those at baseline were working, ambulatory and bedridden functional status, were 93.29%, 80.82% and 47.51% respectively. Females had 90.25%, 77.11% and 37.43% and males had 97.50%, 87.30% and 63.59% probability of surviving those at baseline were working, ambulatory and bedridden functional status respectively [Figure 10].

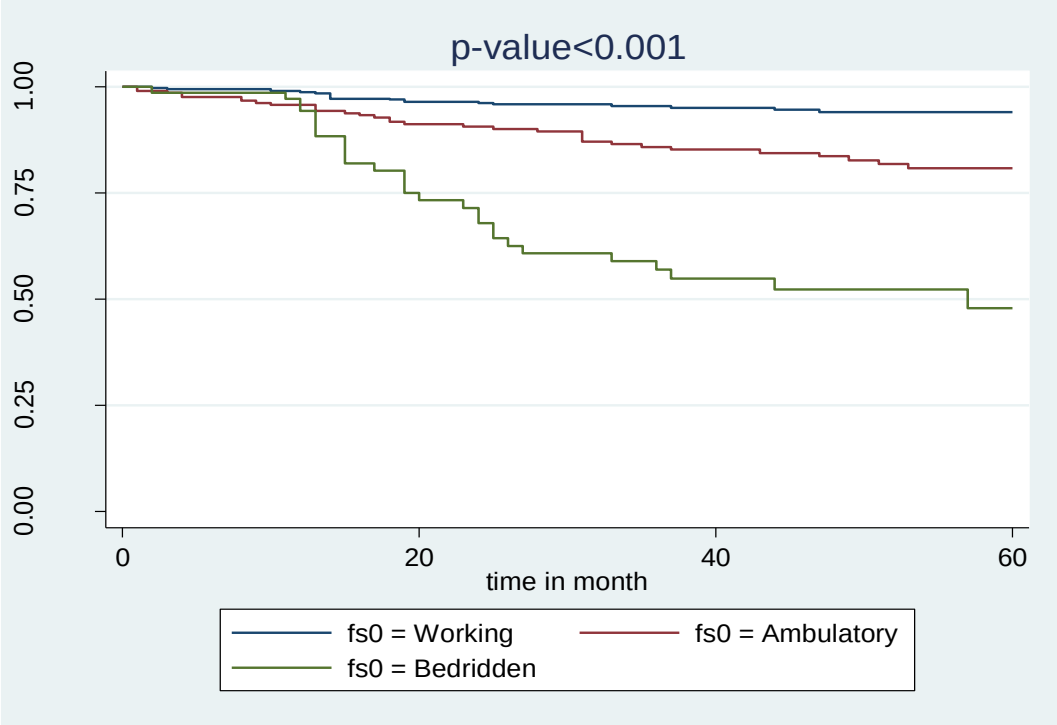

Figure 10: Kaplan Meier survival curve by functional status of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The overall probability of survival of ART users, those at baseline were on WHO stage I, II, III and IV, were 98.53%, 92.29%, 81.83% and 51.05% respectively. Females had 97.64%, 92.26%, 75.16% and 42.09% whereas males had 100%, 92.51%, 90.53% and 71.12% probability of surviving among those at baseline were stage I, II, III and IV respectively [Figure 11].

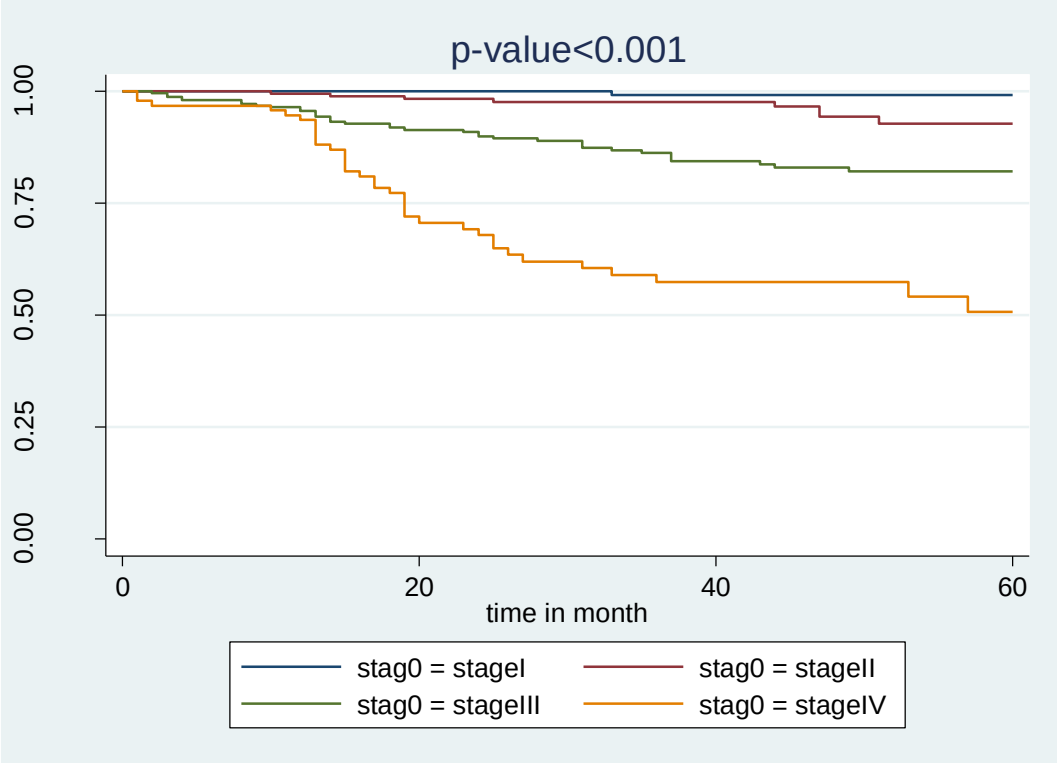

Figure 11: Kaplan Meier survival curve by baseline WHO stage of ART users, Sep 2010 – Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The overall survival probability of ART users those had baseline CD4 cell count of less than 200cells/dl, 200-350cells/dl and above 350cells/dl were 79.35%, 87.74%, and 93.40%, respectively. Females had 72.53%, 86.72% and 85.13% whereas males had 89.53%, 89.66% and 100% probability of surviving for those with baseline CD4 cell count of less than 200cells/dl, 200-350cells/dl and above 350cells/dl respectively [Figure 12].

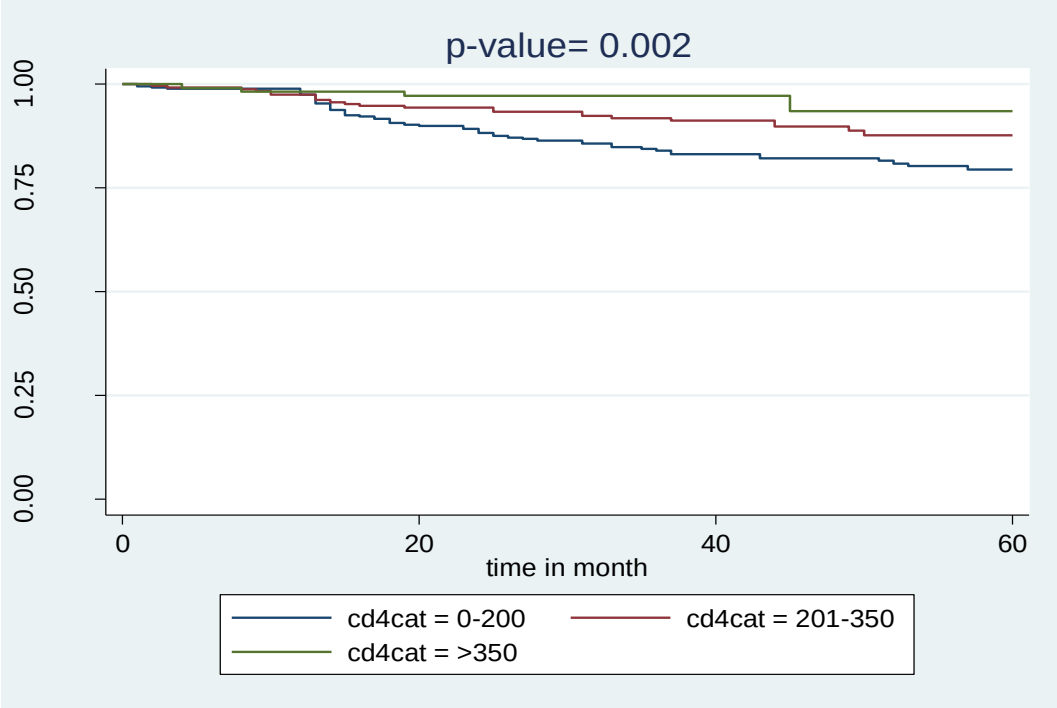

Figure 12: Kaplan Meier survival curve by baseline CD4 cell count of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The overall probability of survival of ART users those had baseline weight of less than 40kg, 40-60kg and above 60kg were 52.80%, 86.22% and 98.26% respectively. Females had 46.59%, 85.29% and 95.61% whereas males had 74.89%, 87.89% and 100% probability of surviving for those with baseline weight of less than 40kg, 40-60kg and above 60kg respectively [Figure 13].

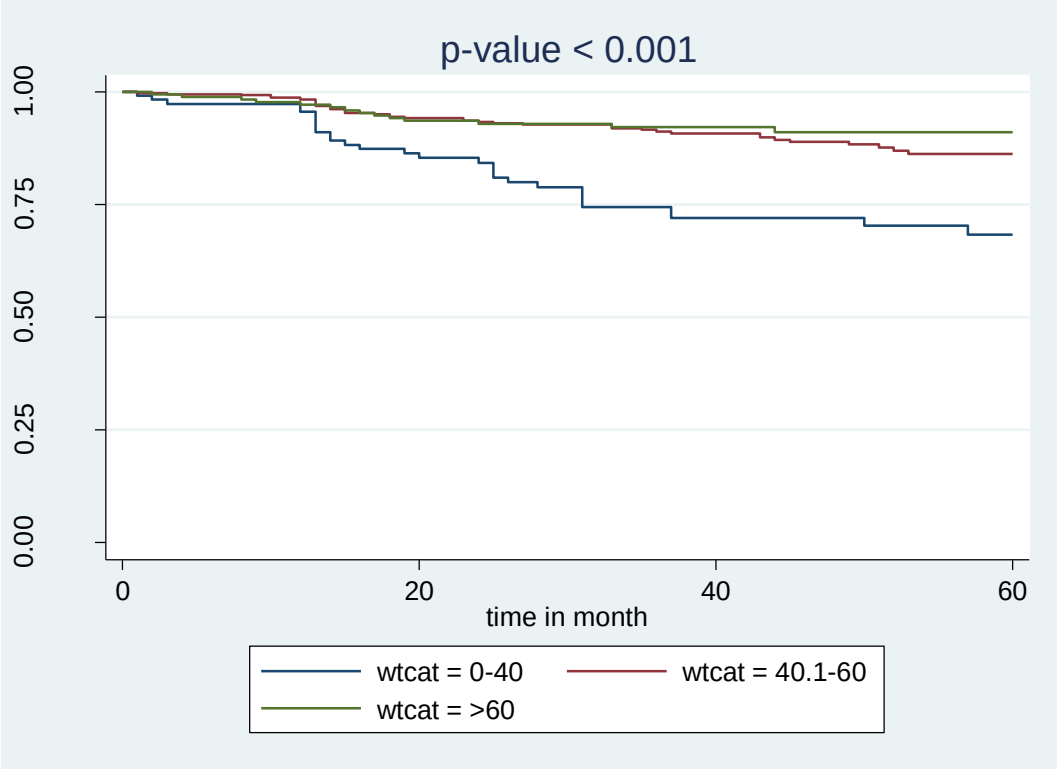

Figure 13: Kaplan Meier survival curve by baseline weight of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The standard case scenario analysis yields the overall survival probability of 82% where females had 77.07% and males had 89.53% [Figure 14].

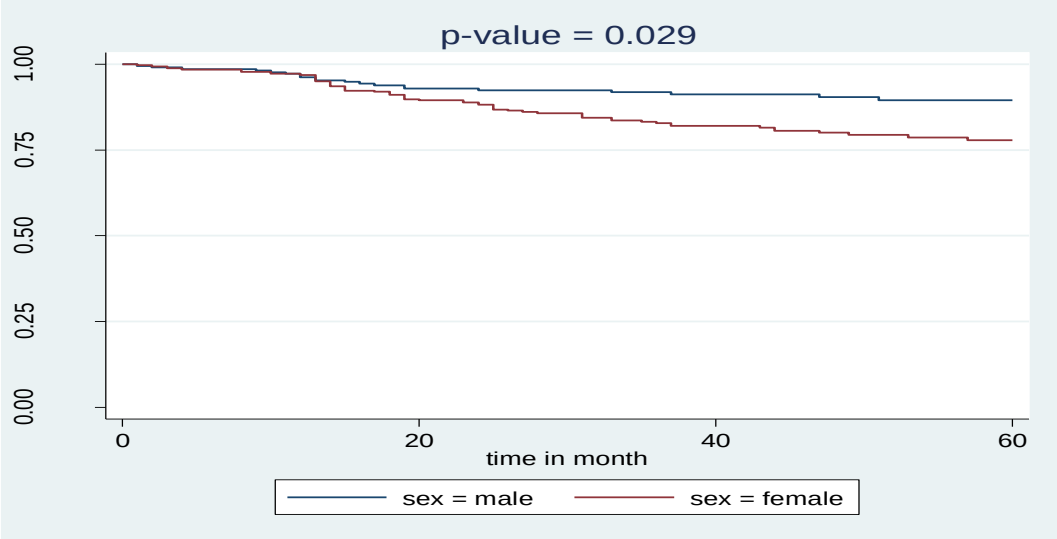

Figure 14: Kaplan Meier survival curve based on standard case scenario by sex category of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=537).

The worst case scenario analysis yields overall survival probability of 58.7% where females had 55.03% and males had 64.37% [Figure 15].

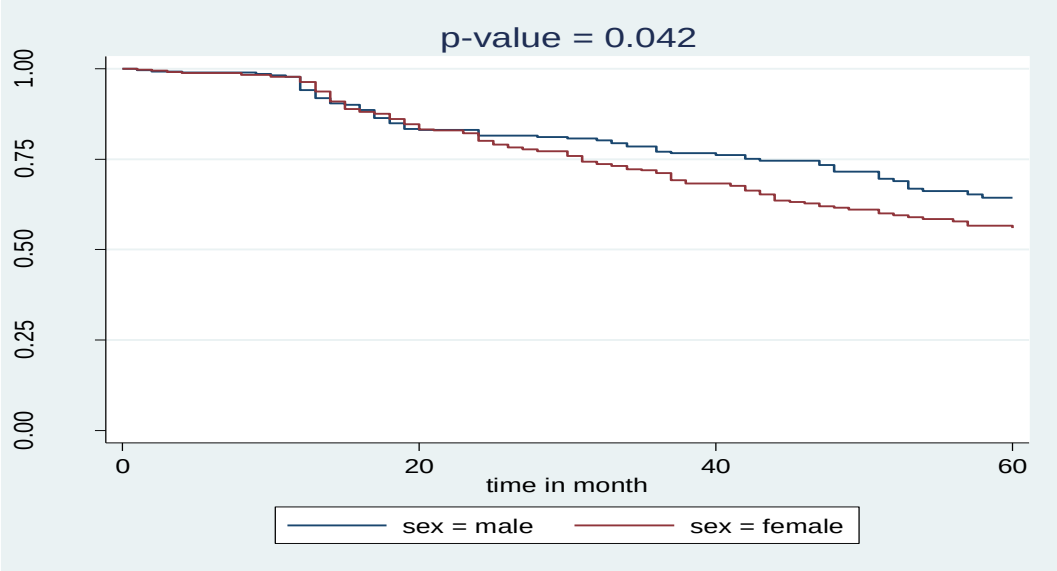

Figure 15: Kaplan Meier survival curve based on worst case scenario by sex category of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n=685).

The highest mortalities were observed during 12 to 18 months of follow up. Mortalities among males were high between 12 to 18 months whereas among females were high between 18 to 24 months of follow up. For both females and males the number of death goes declining [Table 5&6].

Table 5: Overall Life table of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

Interval	Beginning total	Death	Lost	Survival	Standard error	95% CI	
0-6	685	8	0	0.9883	0.0041	0.9768	0.9941
6-12	677	7	0	0.9781	0.0056	0.9639	0.9867
12-18	670	24	54	0.9416	0.0091	0.9209	0.9570
18-24	592	13	43	0.9201	0.0106	0.8965	0.9386
24-30	536	10	42	0.9023	0.0118	0.8763	0.9230
30-36	484	8	63	0.8863	0.0129	0.8582	0.9091
36-42	413	5	55	0.8748	0.0137	0.8451	0.8992
42-48	353	5	76	0.8609	0.0148	0.8289	0.8874
48-54	272	3	71	0.8500	0.0159	0.8157	0.8784
54-60	198	1	39	0.8453	0.0165	0.8096	0.8748

Table 6: Life table of ART users based on sex category, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

Interval	Beginning total	Death	Lost	Survival	Standard error	95% CI	
Male							
0-6	273	3	0	0.9890	0.0063	0.9663	0.9964
6-12	270	3	0	0.9780	0.0089	0.9517	0.9901
12-18	267	7	27	0.9510	0.0133	0.9171	0.9713
18-24	233	2	15	0.9426	0.0144	0.9065	0.9650
24-30	216	1	17	0.9380	0.0150	0.9007	0.9616
30-36	198	1	30	0.9329	0.0158	0.8940	0.9579
36-42	167	1	17	0.9270	0.0168	0.8860	0.9537
42-48	149	1	23	0.9203	0.0180	0.8767	0.9489
48-54	125	1	32	0.9118	0.0197	0.8642	0.9433
54-60	92	0	20	0.9118	0.0197	0.8642	0.9433
Female							
0-6	412	5	0	0.9879	0.0054	0.9711	0.9949
6-12	407	4	0	0.9782	0.0072	0.9584	0.9886
12-18	403	7	27	0.9355	0.0122	0.9066	0.9556
18-24	359	11	28	0.9056	0.0148	0.8720	0.9308
24-30	320	9	25	0.8791	0.0168	0.8418	0.9082
30-36	286	7	33	0.8563	0.0184	0.8157	0.8885
36-42	246	4	38	0.8412	0.0196	0.7984	0.8757
42-48	204	4	53	0.8223	0.0213	0.7759	0.8599
48-54	147	2	39	0.8094	0.0229	0.7597	0.8497
54-60	106	1	19	0.8010	0.0241	0.74860	0.8436

5.7 Factors associated with survival status of ART users

In bivariate cox regression Sex, residence, educational status, marital status, catchment area, disclosure of HIV status, caregiver, baseline Weight, baseline WHO stage, baseline functional status, baseline CD4 cell count, and tuberculosis co infection at baseline were found significant in bivariate analysis and chosen as candidate variable for multivariable cox regression model.

In multivariable cox regression analysis: sex, marital status, educational status, disclosure of HIV status, functional status and TB-co infection were found to be independent predictors of survival status of ART users.

Female ART users were nearly two times (AHR=1.79; 95% CI: 1.04, 3.06) more likely to die in treatment follow up period compared to male. Those who were divorced had two times (AHR=2.09; 95% CI: 1.10, 3.97) risk of dying within five year ART initiation when compared to those married. Among ART users those have no education were two and half times (AHR=2.54; 95% CI: 1.29, 4.98) and those having primary level of education were two times (AHR=2.07; 95% CI: 1.18, 3.65) at higher risk of dying within five year treatment follow up period as compared to those with secondary and tertiary level of education.

Among ART users those never disclosed about their HIV status had three and half times (AHR=3.62; 95% CI: 1.25, 10.46) risk of dying within five year treatment follow up period when compared to those disclosed their HIV status. For those functional status at baseline were bedridden, they had nearly three times (AHR=2.71; 95% CI: 1.24, 5.89) risk of dying within five year treatment follow up period compared to those with working functional status. ART users those had pulmonary tuberculosis at baseline were 2 and half times (AHR=2.60; 95% CI: 1.48, 4.45) at higher risk of dying within five year treatment follow up period compared to those with no history of tuberculosis at baseline [Table 7].

Table 7:Bivariate and Multivariable Cox-regression analysis of factors associated with survival status of ART users, Sep 2010 –Aug 2015, in Yirgalem General Hospital, Southern Ethiopia, Mar, 2017 (n = 685).

Variables	Level	Death	Censored	Unadjusted HR (95%)	Adjusted HR (95%)	P value
Sex	Male	20 (7.3)	253(92.7)	1	1	
	Female	64 (15.5)	348 (84.5)	2.14(1.29, 3.54)	1.79(1.04, 3.06)	0.034*
Marital status	Married	22 (6.7)	308(93.3)	1	1	
	Never married	15 (11.5)	116(88.5)	2.03(1.05, 3.91)	1.46(0.69, 3.04)	0.314
	Divorced	23 (21.5)	84 (78.5)	4.03(2.24, 7.24)	2.09(1.10, 3.97)	0.024*
	Widowed	24 (20.5)	93(79.5)	3.70(2.07, 6.60)	1.46(0.72, 2.97)	0.289
Level of education	No education	32 (24.2)	100(75.8)	5.76(2.24, 14.82)	2.54(1.29, 4.98)	0.007*
	Primary	28 (11.6)	214 (88.4)	2.54(0.98, 6.57)	2.07(1.18, 3.65)	0.011*
	Secondary and Tertiary	24 (5.3)	287(94.7)	1	1	
Disclosure	Yes	41 (7.4)	514(92.6)	1	1	
	No	43 (33.1)	87 (66.9)	6.75(4.37, 10.42)	3.62(1.25, 10.46)	0.017*
Functional status	Working	21 (5.3)	373 (94.7)	1	1	
	Ambulatory	37 (17.6)	173(82.4)	3.33(1.95, 5.68)	1.74(0.92, 3.29)	0.089
	Bedridden	26 (32.1)	55 (67.9)	7.11(3.99, 12.64)	2.71(1.24, 5.89)	0.012*
TB-co infection	No TB	32 (7.2)	414(92.8)	1	1	
	INH prophylaxis	12 (10.4)	103 (89.6)	1.61(0.83, 3.13)	1.57(0.79 3.13)	0.198
	TB treatment	40 (32.3)	84(67.7)	5.50(3.45, 8.77)	2.60(1.48, 4.45)	0.001***
Weight	<40kg	30 (26.5)	83 (73.5)	3.56(1.88, 6.72)	0.76(0.37, 1.58)	0.470
	40-60kg	40 (10.1)	357 (89.9)	1.29(0.70, 2.37)	0.68(0.35, 1.30)	0.250
	>60kg	14 (8.0)	161 (92.0)	1	1	
WHO stage	Stage I&II	17(4.90)	330(95.0)	1	1	
	Stage III	40 (16.7)	199(83.3)	3.62(2.05, 6.39)	1.53(0.74, 3.15)	0.248
	Stage IV	27 (27.3)	72 (72.7)	7.05(3.83, 12.95)	1.77(0.74, 4.21)	0.196
CD4 count	<200	57 (16.6)	287 (83.4)	4.10(1.48, 11.32)	2.23(0.78, 6.35)	0.133
	200-350	23 (9.9)	210 (90.1)	2.30(0.79, 6.63)	1.67(0.56, 4.96)	0.351
	>350	4 (3.7)	104 (96.3)	1	1	
Catchment	Within catchment	50 (10.8)	411 (89.2)	1	1	
	Outside catchment	34 (15.2)	190 (84.8)	1.60(1.035, 2.48)	1.06(0.65, 1.70)	0.813
Caregiver	Yes	40 (7.4)	502(92.6)	1	1	
	No	44 (30.8)	99(69.2)	5.99(3.88, 9.23)	1.12(.38, 3.26)	0.834
Residence	Urban	52 (10.3)	452 (89.7)	1	1	
	Rural	32 (17.7)	149(82.3)	1.86(1.19, 2.88)	0.68(.38, 1.21)	0.191

*p value <0.05

CHAPTER SIX: DISCUSSION

This study gives highlight on gender difference in survival status and its determinants among ART users in Yirgalem general hospital. The overall probability of survival was 84.5%. This finding is comparable with study conducted in Nepal in 2012 (82.86%) (25). But higher than study conducted in Jinka South, Omo in 2016 which was 64% (29). This difference might be methodological difference in which this study considered the drop-outs as censored that might increase probability of survival.

Probability of surviving among females was 80.1% which was lower than males 91.18%. The risk of dying within five year treatment follow up was nearly two times among females compared to males. This finding is consistent with a study conducted in black lion specialized hospital in 2012 (22).This might be because of the fact that their biological difference of females lost their time and energy on the triple burden of household tasks, child care, agricultural work and community management roles that limits time for rest and self-care activities of women. Also this might be HIV among women is not only driven by gender inequality, but it might also entrenches gender inequality, leaving women more vulnerable to its impact. However, findings of this study were in controversy with study done in Goba in 2015, Aksum in 2014 and South east Uganda in 2011 (23,26,39). This difference could be the fact that males might be engaged in risky behaviors like alcohol consumption, smoking and poor adherence to treatment than women.

In this study marital status was significantly associated to the survival status of ART users. Those who divorced were two times at risk of dying within five year treatment follow up compared to married. This finding is in agreement with study done in USA in 2013 (38). This might be divorced are high risk group and they might have fear of stigma and discrimination which can lead to poor compliance to drug and treatment follow up schedule. As well they might loss support of their partner and least socially integrated compared to married. On the other hand they might have wider sexual network which leads to acquisition of HIV and other sexually transmitted disease that can result to risk of mortality.

Among ART users those have no education were two and half times and those having primary level of education were two times at higher risk of dying within five year treatment follow up when compared to those having secondary and tertiary level of education. This finding is in line

with study conducted in Aksum Hospital Northern of Ethiopia in 2014 (39). This could be due to the fact that educated persons have exposure to different source of information like internet, written materials and better understanding about the disease and its treatment.

Among ART users those never disclosed about their HIV status were three and half times at higher risk of dying within the five year treatment follow up compared to those disclosed their HIV status. This finding is in line with study done in Jinka, South Omo in 2016 (29). This might be the fact that disclosure of HIV status to others might avoid disease related depression, fear of stigma and discrimination, freedom to take their pill regularly and good compliance. As well they would have chance of memorization from others about their schedule and can get supportive care.

This study found that, those had bedridden functional status at baseline were nearly three times more likely to die in the five year treatment follow up period compared to those had working functional status. This finding is consistent with Studies done in Armed forces general teaching hospital in 2012, in Eastern Uttar Pradesh India in 2014, Debre Marcos referral hospital in 2014, Black lion specialized hospital in 2012, Hadiya and Kembata zone public health facility in 2015, Jinka south Omo in 2016 and Andhra Pradesh state of India in 2016, were in agreement with this finding (22,24,29,31,32,43,44). This might be the immune status of PLWHA deteriorates before treatment initiation which might result to lesser survival.

In this study those with TB-co infection at baseline were 2 and half times at higher risk of dying within the five year treatment follow up period when compared to those with no history of tuberculosis. This finding is in line with studies conducted in Armed force teaching hospital in 2012, Goba hospital in 2016, Jinka hospital in South Omo in 2016, Jinja in South east of Uganda in 2011and Kharamara hospital of Somali region in 2015 were in agreement with this finding (23,26,28,29,44). This could be the fact that TB-co infection is the commonest infectious disease among HIV positives. It might badly deteriorates the immune system of ART users and further exacerbate their clinical condition. As well there will be poor appetite, and as there is burden of drug, this might cause drug intolerance, gastro intestinal upset, drug-drug interaction and adverse drug reaction which might lead to early death.

In this study CD4 cell count was not significant. However it was significant independent predictors of mortality in studies conducted in Gondar hospital in 2012 (30). It is the fact that as CD4 cell count decreases, the functional status deteriorates. As a result CD4 cell count might be confounded by functional status when it was adjusted.

So the implication of these findings support the current WHO and Ethiopia policy regarding initiation of ART at a better clinical stage. HIV counseling and testing is a gateway for treatment provision. Since HCT service is targeted to high risk group, patients visit health facility at poor clinical stage. This can result to poor quality of life, early mortality, increment in dependency ratio, negative economic and political impact to the country. As well it is against to achieve sustainable development goal "3" which states "Ensure healthy live and well-being for all at all age".

The other is the lower survival probability of female needs to assess the gender roles and responsibilities. This might be because of their lower status.

Strength and Limitation

Strength:

- The study estimates five year survival status of ART users which is longer as compared to other studies
- This study gives emphasis to the gender difference in survival status

Limitation

- Mortality might be overestimated since the real cause of death was not ascertained so that all deaths were considered as HIV/AIDS related.
- To the opposite it might be underestimated due to the lost to follow up and drop-outs those probably include more ART users dying at home without being reported
- Due to secondary nature of data some variables inadequate (BMI) which could have significant effect and their effect cannot be seen in this study. As well some variables lost that need to be studied like income, alcohol consumption, substance use

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

The study revealed a lower estimated survival probability and retention rate of ART users. Drop-outs contribute for a higher attrition rate of ART users during the five year treatment follow up period.

Females had lower five year survival probability compared to males. Additionally marital status, educational level, disclosure of HIV status, functional status and TB co-infection at baseline were found to be independent predictors of survival.

7.2 Recommendations

Depending on the finding, the following recommendations were forwarded:

Ministry of Health (MOH)

- Empowering women and provision of especial attention tailored to their need
- Collaborate with ministry of education and strengthening the newly started adult learning
- Mobilize mass media on social behavioral change communication (SBCC) on benefit of using ART, disclosure of HIV status and the negative consequences of treatment interruption

Program level

- Mass media promotion on treatment and its impact using templates and health information dissemination at community level
- Expand HIV counseling and testing service at the community level to provide opportunities for earlier diagnosis with timely linkage to care before immune status deteriorates
- Strengthening TB prevention and control program

Researcher and academic institute

- In-depth qualitative studies to investigate why gender difference in survival status among ART users exist and searching for the true difference

Facility

- Special consideration should be given for high risk groups such as divorced, females
- Required baseline and follow up laboratory investigation should be done as per guideline and height should be measured and recorded
- ART users retention mechanisms have to be strengthened using trace back mechanism
- Strengthen counseling at initiation of ART to retain ART users on treatment
- Provider initiative testing and counseling service for all

Community level

- Strongly address issue of disclosure, adherence to pill and care, risk of drug interruption among HIV positives through open discussion, community conversations and mobilizations using health extension workers, women development army, religious leaders

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Annexes

Annex 1 data collection tool

PART I SOCIO DEMOGRAPHY AND PSYCHOSOCIAL RELATED FACTORS:

Question NO.	Question	Response category	Remarks
q101	Unique ART record number	__ ____	
q102	Age at the start of ART	_____ years	
q103	Sex of the patient	1. Male 2. Female	
q104	Patient's residence	1. Urban 2. Rural	
q105	Marital Status	1. Never Married 2. Married 3. Divorced 4. Widow	
q106	Educational level	1. No education 2. Primary 3. Secondary 4. Tertiary	
q107	Religion	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 5. Other specify _____	
q108	Occupation	1. Employed 2. Self employed 3. Unemployed 4. Other Specify _____	
q109	Client resides within catchment area?	1. Yes 2. No	
q110	Has the patient disclosed his/her HIV status?	1. Yes 2. No→skip to q115	
q111	Has the patient disclosed to His/her Family member	1. Yes 2. No	
q112	Has the patient disclosed to his/her Friend	1. Yes 2. No	
q113	Has the patient disclosed to Relative	1. Yes 2. No	
q114	Write if disclosed to any other	_____	
q115	Does patient has care giver?	1. Yes 2. No	

Part-II: HIV Care and ART Information

Question NO.	Question	Response category	Remarks
q201	Date of confirmed HIV positive	__ __/__ __/__ __ __ __	
q202	Date of enrolment	__ __/__ __/__ __ __ __	

q203	Date of eligibility	__ __/__ __/__ __ __ __	
q204	Why eligible for ART	1. Clinical only 2. CD4 3. Transfer in 4. pregnancy	
q205	Date of ART start	Date __ __, Month __ __, Year __ _	
q206	Interval of confirmed to start of ART	_____ in month	
q207	How long on HAART (in months)	_____ in month	

Part-III: Follow up information from patient card

Q.No.		Questions	Record			Remark
q301	wt0	Weight at the start of ART	_____kgms			99. Not done
q302	wt6	Weight at the 6 months of start of ART	_____kgms			99. Not done
q303	wt12	Weight at the 12months of start of ART	_____kgms			99. Not done
q304	wt18	Weight at the 18 months of start of ART	_____kgms			99. Not done
q305	wt24	Weight at the 24 months of start ART	_____kgms			99. Not done
q306	wt30	Weight at the 30 months of start of ART	_____kgms			99. Not done
q307	wt36	Weight at the 36 months of start of ART	_____kgms			99. Not done
q308	wt42	Weight at the 42 months of start ART	_____kgms			99. Not done
q309	wt48	Weight at the 48 months of start of ART	_____kgms			99. Not done
q310	wt54	Weight at the 54 months of start ART	_____kgms			99. Not done
q311	wt60	Weight at the 60 months of start ART	_____kgms			99. Not done
		1. Not malnourished (>18.5kg/m^2) 2. Moderate mal^n(16-18.5) 3.Severe mal^n (<16kg/m^2)				
q312	bmi0	Body mass index at 0 month	1	2	3	99. Not done
q313	bmi6	Body mass index at 6 month	1	2	3	99. Not done
q314	bmi12	Body mass index at 12 month	1	2	3	99. Not done
q315	bmi18	Body mass index at 18 month	1	2	3	99. Not done
q316	bmi24	Body mass index at 24 month	1	2	3	99. Not done
q317	bmi30	Body mass index at 30 month	1	2	3	99. Not done
q318	bmi36	Body mass index at 36 month	1	2	3	99. Not done
q319	bmi42	Body mass index at 42 month	1	2	3	99. Not done
q320	bmi48	Body mass index at 48 month	1	2	3	99. Not done
q321	bmi54	Body mass index at 54 month	1	2	3	99. Not done
q322	bmi60	Body mass index at 60 month	1	2	3	99. Not done
q334	fs0	Functional status at the start of ART	1. Working 2. Ambulatory 3. Bedridden			99. Not done
q335	fs6	Functional status at 6 months	1	2	3	99. Not done
q336	fs12	Functional status at 12 months	1	2	3	99. Not done

q337	fs24	Functional status at 18 months	1 2 3	99. Not done
q338	fs30	Functional status at 24 months	1 2 3	99. Not done
q339	fs36	Functional status at 36months	1 2 3	99. Not done
q340	fs42	Functional status at 42 months	1 2 3	99. Not done
q341	fs48	Functional status at 48 months	1 2 3	99. Not done
q342	fs54	Functional status at 54 months	1 2 3	99. Not done
q343	fs60	Functional status at 60 months	1 2 3	99. Not done
q344	stag0	WHO staging at the start of ART	1. Stage-I 2. Stage-II 3. Stage-III 4. Stage-IV	
q345	stag6	WHO staging at 6 months	1 2 3 4	99. Not done
q346	stag12	WHO staging at 12 months	1 2 3 4	99. Not done
q347	stag18	WHO staging at 18 months	1 2 3 4	99. Not done
q348	stag24	WHO staging at 24 months	1 2 3 4	99. Not done
q349	stag30	WHO staging at 30 months	1 2 3 4	99. Not done
q350	stag36	WHO staging at 36 months	1 2 3 4	99. Not done
q351	stag42	WHO staging at 42 months	1 2 3 4	99. Not done
q352	stag48	WHO staging at 48 months	1 2 3 4	99. Not done
q353	stag54	WHO staging at 54 months	1 2 3 4	99. Not done
q354	stag60	WHO staging at 60 months	1 2 3 4	99. Not done
q355	tb0	TB status at the start of ART	1. No sign 2. INH 3. TB RX	99. Not done
q356	tb6	TB status at the 6 months	1 2 3	99. Not done
q357	tb12	TB status at the 12 months	1 2 3	99. Not done
q358	tb18	TB status at the 18 months	1 2 3	99. Not done
q359	tb24	TB status at the 24 months	1 2 3	99. Not done
q360	tb30	TB status at the 30 months	1 2 3	99. Not done
q361	tb36	TB status at the 36 months	1 2 3	99. Not done
q362	tb42	TB status at the 42 months	1 2 3	99. Not done
q363	tb48	TB status at the 48 months	1 2 3	99. Not done
q364	tb54	TB status at the 54 months	1 2 3	99. Not done
q365	tb60	TB status at the 60 months	1 2 3	99. Not done
q366	spt0	If sputum at start, what was the result	1.Negative 2.Positive	
q367	spt6	If sputum at 6 month, what was the result	1 2	99. Not done
q368	spt12	If sputum at 12 month, what was the result	1 2	99. Not done
q369	spt18	If sputum at 18 month, what was the result	1 2	99. Not done
q370	spt24	If sputum at 24 month, what was the result	1 2	99. Not done
q371	spt30	If sputum at 30 month, what was the result	1 2	99. Not done
q372	spt36	If sputum at 36 month, what was the result	1 2	99. Not done
q373	spt42	If sputum at 42 month, what was the result	1 2	99. Not done
q374	spt48	If sputum at 48 month, what was the result	1 2	99. Not done
q375	spt54	If sputum at 54 month, what was the result	1 2	99. Not done
q376	spt60	If sputum at 60 month, what was the result	1 2	99. Not done

	1. NOI 2. Z 3. BP 4. PTB 5. EPTB 6. TO 7. TE 8. UM 9. DC 10. DA 11. PCP 12. CT 13. CM 14. NHL 15. KS 16. CCa 17. O			
	Use the options listed above for the q377-q387 (multiple answers are possible)			
q377	oi0	OIs at the start of ART	_____	99
q378	oi6	OIs at 6 months	_____	99
q379	oi12	OIs at 12 months	_____	99
q380	oi18	OIs at 18 months	_____	99
q381	oi24	OIs at 24 months	_____	99
q382	oi30	OIs at 30 months	_____	99
q383	oi36	OIs at 36 months	_____	99
q384	oi42	OIs at 42 months	_____	99
q385	oi48	OIs at 48 months	_____	99
q386	oi54	OIs at 54 months	_____	99
q387	oi60	OIs at 60 months	_____	99
q388	cotr0	Cotrimoxazole at the start of ART	1. Yes 2. No	99
q390	cotr6	Cotrimoxazole at 6 months	1. Yes 2. No	99
q391		If yes, adherence at 6 months	1. G 2. F 3. P	99
q392	cotr12	Cotrimoxazole at 12 months	1. Yes 2. No	99
q393		If yes, adherence at 12 months	1. G 2. F 3. P	99
q394	cotr18	Cotrimoxazole at 18months	1. Yes 2. No	99
q395		If yes, adherence at 18months	1. G 2. F 3. P	99
q396	cotr24	Cotrimoxazole at 24months	2. Yes 2. No	99
q397		If yes, adherence at 24months	1. G 2. F 3. P	99
q398	cotr30	Cotrimoxazole at 30months	3. Yes 2. No	99
q399		If yes, adherence at 30months	1. G 2. F 3. P	99
q400	cotr36	Cotrimoxazole at 36months	4. Yes 2. No	99
q401		If yes, adherence at 36months	1. G 2. F 3. P	99
q402	cotr42	Cotrimoxazole at 42months	5. Yes 2. No	99
q403		If yes, adherence at 42months	1. G 2. F 3. P	99
q404	cotr48	Cotrimoxazole at 48 months	1. Yes 2. No	99
q405		If yes, adherence at 48months	1. G 2. F 3. P	99
q406	cotr54	Cotrimoxazole at 54 months	1.Yes 2. No	99
q407		If yes, adherence at 54months	1. G 2. F 3. P	99
q408	cotr60	Cotrimoxazole at 60 months	1.Yes 2. No	99
q409		If yes, adherence at 60 months	1. G 2. F 3. P	99
q410	cd40	CD4 count at the start of ART	_____(cells/mm^3)	99
q411	cd46	CD4 count at 6 month	_____(cells/mm^3)	99
q412	cd412	CD4 count at 12 month	_____(cells/mm^3)	99
q413	cd418	CD4 count at 18 month	_____(cells/mm^3)	99
q414	cd424	CD4 count at 24 month	_____(cells/mm^3)	99
q415	cd430	CD4 count at 30 month	_____(cells/mm^3)	99
q416	cd436	CD4 count at 36 month	_____(cells/mm^3)	99
q417	cd442	CD4 count at 42 month	_____(cells/mm^3)	99

q418	cd448	CD4 count at 48 month	_____(cells/mm^3)	99
q419	cd454	CD4 count at 54 month	_____(cells/mm^3)	99
q420	cd460	CD4 count at 60 month	_____(cells/mm^3)	99
q421	tlc0	Total lymphocyte count at the start of ART	_____(cells/mm^3)	99
q422	tlc6	Total lymphocyte count at 6 months	_____ (cells/mm^3)	99
q423	tlc12	Total lymphocyte count at 12 months	_____(cells/mm^3)	99
q424	tlc18	Total lymphocyte count at 18 months	_____(cells/mm^3)	99
q425	tlc24	Total lymphocyte count at 24 months	_____(cells/mm^3)	99
q426	tlc30	Total lymphocyte count at 30 months	_____(cells/mm^3)	99
q427	tlc36	Total lymphocyte count at 36 months	_____(cells/mm^3)	99
q428	tlc42	Total lymphocyte count at 42 months	_____(cells/mm^3)	99
q429	tlc48	Total lymphocyte count at 48 months	_____(cells/mm^3)	99
q430	tlc54	Total lymphocyte count at 54 months	_____(cells/mm^3)	99
q431	tlc60	Total lymphocyte count at 60 months	_____(cells/mm^3)	99
	If there is regimen change at 6, 12, 18, 24, 30, 36, 42, 48, 54 or 60 months, consider the following options for reasons (multiple response is possible) 1. Toxicity/side effect 2. Risk of pregnancy 3. due to new TB 4. New drug available 5. Drug out of stock 6. Other reason 7. Clinical treatment failure 8. Immunologic failure 9. Virologic failure			
q432	reg0	ART drug regimen started	_____	99
q433	reg6	ART drug regimen at 6 months	_____	99
		If change in regimen at 6months, reason for change (describe type)	_____	99
q434	reg12	ART drug regimen at 12 months	_____	99
q435		If change in regimen at 12 months, reason for change (describe type)	_____	99
q436	reg18	ART drug regimen at 18 months	_____	99
q437		If change in regimen at 18 months, reason for change (describe type)	_____	99
q438	reg24	ART drug regimen at 24 months	_____	99
q439		If change in regimen at 24 months, reason for change (describe type)	_____	99
q440	reg30	ART drug regimen at 30 months	_____	99
q441		If change in regimen at 30 months, reason for change (describe type)	_____	99
q442	reg36	ART drug regimen at 36 months	_____	99
q443		If change in regimen at 36 months, reason for change	_____	99
q444	reg42	ART drug regimen at 42 months	_____	99

q445		If change in regimen at 42 months, reason for change	_____	99
q446	reg48	ART drug regimen at 48 months	_____	99
q447		If change in regimen at 48 months, reason for change	_____	99
q448	reg54	ART drug regimen at 54 months	_____	99
q449		If change in regimen at 54 months, reason for change	_____	99
q450	reg60	ART drug regimen at 60 months	_____	99
q451		If change in regimen at 60 months, reason for change	_____	99

	If the adherence status for ARV at any of the 6, 12, 18, 24, 30, 36, 42, 48, 54 or 60 is either poor or fair, use the following options to fill q453, q455, q457, q459, q461, q463, q465, q467, q469, q471 1. Toxicity/side effect 2. Share with others 3. Forgot 4. felt better 5. Too ill 6. Stigma, disclosure or privacy issue 7. Drug stock outs 8. Patient lost/run out of pills 9. Delivery/travel problems 10. Inability to pay 11. Alcohol 12. Depression 13. other (multiple response is possible)			
q452	adhr6	Adherence status at 6 months	1. G (Good) 2. F (Fair) 3. P (Poor)	99
q453	reason6	If poor/fair adherence at 6month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q454	adhr12	Adherence status at 12 months	1. G 2. F 3. P	99
q455	reason12	If poor/fair adherence at 12 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q456	adhr18	Adherence status at 18 months	1. G 2. F 3. P	99
q457	reason18	If poor/fair adherence at 18 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q458	adhr24	Adherence status at 24 months	1. G 2. F 3. P	99
q459	reason24	If poor/fair adherence at 24 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q460	adhr30	Adherence status at 30 months	1. G 2. F 3. P	99
q461	reason30	If poor/fair adherence at 30 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99

q462	adhr36	Adherence status at 36 months	1. G 2. F 3. P	99
q463	reason36	If poor/fair adherence at 36 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q464	adhr42	Adherence status at 42 months	1. G 2. F 3. P	99
q465	reasn42	If poor/fair adherence at 42 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q466	adhr48	Adherence status at 48 months	1. G 2. F 3. P	99
q467	reasn48	If poor/fair adherence at 48 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q468	adhr54	Adherence status at 54 months	1. G 2. F 3. P	99
q469	reasn54	If poor/fair adherence at 54 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q470	adhr60	Adherence status at 60 months	1. G 2. F 3. P	99
q471	reasn60	If poor/fair adherence at 60 month, reason(s) for poor/ fair adherence (multiple response possible)	_____ _____ _____	99
q472	adhrcar6	Interval of Scheduled to actual date of visit at 6 month in day	_____ _____	99
q473	Adhrcar12	Interval of Scheduled to actual date of visit at 12 month in day	_____ _____	99
q474	adhrcar18	Interval of Scheduled to actual date of visit at 18 month in day	_____ _____	99
q475	Adhrcar24	Interval of Scheduled to actual date of visit at 24 month in day	_____ _____	99
q476	Adhrcar30	Interval of Scheduled to actual date of visit at 30 month in day	_____ _____	99
q477	Adhrcar36	Interval of Scheduled to actual date of visit at 36 month in day	_____ _____	99
q478	Adhrcar42	Interval of Scheduled to actual date of visit at 42 month in day	_____ _____	99
q479	Adhrcar48	Interval of Scheduled to actual date of visit at 48 month in day	_____ _____	99
q480	Adhrcar54	Interval of Scheduled to actual date of visit at 54 month in day	_____ _____	99
q481	Adhrcar60	Interval of Scheduled to actual date of visit at 60 month in day	_____ _____	99

q492	**wbc/neut 0**	WBC total & Neutrophil % at the start of ART	_____ _____	99
q493	**wbc/neut 6**	WBC & neutrophil % at 6 months	_____ _____	99
q494	**wbc/neut 12**	WBC & neutrophil % at 12 months	_____ _____	99
q495	**wbc/neut 18**	WBC & neutrophil % at 18 months	_____ _____	99
q496	**wbc/neut 24**	WBC & neutrophil % at 24 months	_____ _____	99
q497	**wbc/neut 30**	WBC & neutrophil % at 30 months	_____ _____	99
q498	**wbc/neut 36**	WBC & neutrophil % at 36 months	_____ _____	99
q499	**wbc/neut 42**	WBC & neutrophil % at 42 months	_____ _____	99
q500	**wbc/neut 48**	WBC & neutrophil % at 48 months	_____ _____	99
q501	**wbc/neut 54**	WBC & neutrophil % at 54 months	_____ _____	99
q502	**wbc/neut 60**	WBC & neutrophil % at 60months	_____ _____	99
q503	**hgb/plt0**	Hemoglobin & platelet at the start of ART	_____ _____	99
q504	**hgb/plt6**	Hemoglobin & platelet at 6 months	_____ _____	99
q505	**hgb/plt12**	Hemoglobin & platelet at 12 months	_____ _____	99
q506	**hgb/plt18**	Hemoglobin & platelet at 18 months	_____ _____	99
q507	**hgb/plt24**	Hemoglobin & platelet at 24 months	_____ _____	99
q508	**hgb/plt30**	Hemoglobin & platelet at 30 months	_____ _____	99
q509	**hgb/plt36**	Hemoglobin & platelet at 36 months	_____ _____	99
q510	**hgb/plt42**	Hemoglobin & platelet at 42 months	_____ _____	99
q511	**hgb/plt48**	Hemoglobin & platelet at 48 months	_____ _____	99
q512	**hgb/plt54**	Hemoglobin & platelet at 54 months	_____ _____	99
q513	**hgb/plt60**	Hemoglobin & platelet at 60months	_____ _____	99

q514	**sgot/sgpt0**	SGOT & SGPT at the start of ART	_____ _____	99
q515	**sgot/sgpt6**	SGOT & SGPT at the 6 months	_____ _____	99
q516	**sgot/sgpt12**	SGOT & SGPT at the 12 months	_____ _____	99
q517	**sgot/sgpt18**	SGOT & SGPT at the 18 months	_____ _____	99
q518	**sgot/sgpt24**	SGOT & SGPT at the 24 months	_____ _____	99
q519	**sgot/sgpt30**	SGOT & SGPT at the 30 months	_____ _____	99
q520	**sgot/sgpt36**	SGOT & SGPT at the 36 months	_____ _____	99
q521	**sgot/sgpt42**	SGOT & SGPT at the 42 months	_____ _____	99
q522	**sgot/sgpt48**	SGOT & SGPT at the 48 months	_____ _____	99
q523	**sgot/sgpt54**	SGOT & SGPT at the 54 months	_____ _____	99
q524	**sgot/sgpt60**	SGOT & SGPT at the 60 months	_____ _____	99
q525	**bun/creat0**	BUN & creatinine at start ART	_____ _____	99
q526	**bun/creat6**	BUN & creatinine at 6 months	_____ _____	99
q527	**bun/creat12**	BUN & creatinine at 12 months	_____ _____	99
q528	**bun/creat18**	BUN & creatinine at 18 months	_____ _____	99
q529	**bun/creat24**	BUN & creatinine at 24 months	_____ _____	99
q530	**bun/creat30**	BUN & creatinine at 30 months	_____ _____	99
q531	**bun/creat36**	BUN & creatinine at 36 months	_____ _____	99
q532	**bun/creat42**	BUN & creatinine at 42 months	_____ _____	99
q533	**bun/creat48**	BUN & creatinine at 48 months	_____ _____	99
q534	**bun/creat54**	BUN & creatinine at 54 months	_____ _____	99
q535	**bun/creat**	BUN & creatinine at 60 months	_____ _____	99

	60			
1no side effect 2 nausea 3 diarrhea 4 fatigue 5 headache 6 numbness 7 rash 8 anemia 9 abdominal pain 10 jaundice 11 fat change 12 dizzy/anxiety 13 other				
q536	ADR6	Side effect at one month follow up		99
q537	Otcom	Patient outcome	1. On follow up 2. Died 3. Lost 4. drop	99
q538	Dtwhn	If outcome is death when?	Day __ month __ year __	99