Gender Disparities in Late Presentation and Survival among HIV Patients on Antiretroviral Therapy in Public Health Facilities of Arba Minch Town, Southern Ethiopia: Eight Years Retrospective Cohort Study

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Jimma, Ethiopia

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ABSRACT

Background: There is a conflicting report about gender-related differences in enrolment and survival both in developed and developing countries. Where differences have been reported in resource poor countries particularly in Ethiopia, evidences showing the effect of gender in presentation to care and survival of peoples on an antiretroviral therapy are not well studied.

Objective: To assess gender disparity in presentation for HIV/AIDS care and survival among patients on antiretroviral therapy (ART) in Arba Minch town, Southern Ethiopia.

Methods: A facility based - retrospective cohort study design was carried out. By using simple random sampling method a total of 520 subjects were included in the study. Gender differences in presentation to HIV/AIDS care and survival was assessed using data from medical records of patients. Focus group discussion was also conducted for a better understanding of reasons for late presentation to HIV/AIDS care. Survival analysis and Kaplan-Meier test was used to see the association of variables with time of ART initiation and follow up. Life table and log rank test was used to compare survival curves. Cox proportional-hazards regression model was used to compare independent determinants of time to death between male and female.

Results: A total of 520 HIV infected patients who were on highly active antiretroviral therapy (HAART) in the antiretroviral therapy clinic of Arba Minch hospital and health centre from Feb.1, 2006 to Jan.30, 2014 were included in the analysis. Men initiated ART with lower CD4 cell counts compared to women (median baseline CD4 175 cells/mm3, inter quartile range (IQR): (130-201) versus 181 cells/mm3, inter quartile range (IQR): 146–247, P-value < 0.009). Substance abuse, fear of stigma and low awareness to HIV/AIDS were among the reasons that lead men to initiate ART late. Men were at an increased risk of death compared to women (adjusted hazard ratio: 2.05, 95% CI: 1.33–3.15 at P-value < 0.001).

Conclusion and recommendation: In this study there is a marked increase in risk of mortality for men than women and it might be attributed to their late engagement in to HIV/AIDS care. Therefore, more effort is required to engage men in HIV/AIDS care in a timely manner.

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ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AHR	Adjusted Hazard Rate
AMH	Arba Minch Hospital
AMHC	Arba Minch Health Center
ART	Antiretroviral Therapy
ARV	Antiretroviral
BMI	Body Mass Index
CDC	Centers for Disease Control
CHR	Crude Hazard Rate
CI	Confidence interval
FHAPCO	Federal HIV/AIDS Prevention and Control Office
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
MOH	Ministry of Health
OIS	Opportunistic Infections
PCP	Pneumocystis Carini Pneumonia
PLHIV	People Living with Human Immune deficiency Virus
SNNPR	Southern Nations Nationalities Peoples Region;
SPSS	Statistical Package for Social Sciences
STI	Sexually transmitted infection
SSA	Sub-Saharan Africa
TB	Tuberculosis
UNAIDS	United Nations Joint Program on Acquired Immune Deficiency Syndrome
UNICEF	United Nations Children's Emergency Fund
VCT	Voluntary Counseling and Testing
WHO	World Health Organization

1. INTRODUCTION

1.1. Background

Human Immunodeficiency Virus/ acquired immunodeficiency syndrome (HIV/AIDS) remains an important public health problem despite significant worldwide efforts to combat the disease. Globally, an estimated 35.3 million peoples were infected with HIV in 2012, the majority in developing countries(1). Of these, 2.3 million were newly infected and 1.6 million lost their lives(1). Not only does the epidemic cause tremendous human suffering, it has also become a major cause of social and economic instability. Sub-Saharan Africa (SSA), with about 69% of the global population with HIV and constituting 70% of HIV/AIDS deaths worldwide, is the most affected region in the world(1). The projected national HIV prevalence estimated for 2013 is 1.3 %(0.9% for male and 1.7% for females).The number of adults living with HIV in 2013 is estimated at 734,048(285,183 male and 448,865 female) and of this 154,084 are children under the age of 15(2).

The introduction of ART has offered hope to people living with HIV (PLHIV) and has been credited with improving the quality of life significantly and reducing mortality. In low- and middle-income countries, the estimated number of people receiving ART in the region, increased from 100,000 people in 2003 to 9.7 million by the end of 2012, reaching an estimated 61% of those in need. In most regions, including SSA, HIV treatment coverage for men is lower than coverage among women. In the region, 57% of treatment eligible men received ART in 2012, compared to 73% of treatment eligible women(1). Despite these successes, there remain persistent challenges to optimizing the effectiveness of HIV care and treatment scale-up in the region. Among the most important of these are very high rates of late ART initiation (i.e., in the advanced stages of HIV disease), which in turn is associated with high rates of mortality soon after initiation of ART (early mortality)(3). According to the latest consensus definition from the HIV in Europe study group, late presenters are defined as persons presenting to a clinic that can prescribe ART with a CD4 count of less than 350/mm^3 or an AIDS defining illness(4). While early treatment is now recommended by guidelines, many patients continue to engage in care with regrettably late stage disease(3, 5)

Delays in HIV/AIDS care have serious public health implications due to loss of opportunities to prevent further transmission through effective ART, and initiating treatment for HIV infection at an advanced stage leads to poorer patient outcomes than with early treatment. In addition, Late ART

initiation is associated with a longer infectious period, leading to higher onward HIV transmission, considering that earlier presentation and HIV-suppressing treatment might otherwise reduce viral load and risk of transmission and the cost of treating and caring for patients with late presentation is much higher than if they had been diagnosed and treated early(3, 6).

Early HIV diagnosis and timely administration of ART can not only reduce morbidities and mortalities in HIV-infected patients, but also decrease the patients' viral loads and risk of HIV transmission. Moreover, health education and counseling accompanied by early HIV diagnosis may induce HIV-infected patients to practice safe sex, which may translate into a lower chance of HIV transmission(7-9).

1.2. Statement of the Problem

Most patients in SSA, home to 70% of all new HIV infection in the world, initiate ART at very low CD4 counts with substantial variability in the CD4 count at ART initiation across sites and settings and its persistence over time points to the complex and multi-level nature of the problem(10-11). The median CD4 count at ART initiation in this region is about 122 cells/μL (IQR 53–194)(5). The very low CD4 counts at which populations in SSA are initiating ART reflects, among other things, the emergency nature of HIV scale-up in the region, treatment prioritization of the sickest individuals, and absorptive capacity of the health care system to meet the overwhelming demand for treatment through scale-up and decentralization(12). As a result, there is a very high rates of early mortality in SSA; between 8 to 26 % of patients die in the first year of ART with most deaths occurring in the first few months(13). Initiation of ART in advanced stage of the disease is also common phenomena in Ethiopia particularly in Arba Minch town; with 52.2% of adult patients in Arba Minch hospital engage in to care in WHO Stage III and Stage IV(14).

Mortality among patients on highly active antiretroviral therapy (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 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 (13-15). However, the durability of the effectiveness of HAART remains to be delineated. In addition, there

are factors that limit the success of HAART including poor therapy adherence, regimen complexity, viral resistance, pharmacodynamic interactions, drug tolerability and toxicity, therapy costs, and presence of co- morbid conditions such as substance abuse and addiction(16).

Factors related with the residual deaths seem to vary significantly across populations(17) and there is a particular gender differences in ART programme access and survival. Disproportionately more women than men have accessed ART in SSA(18-19) whereas, a different report from the developed world suggests a higher risk of death on ART for women than men(20) ; however, according to studies across SSA, men experience greater mortality than women on treatment(21-22). Men's early mortality appears mainly to be due to presentation with more advanced HIV disease, (23-24), although compliance with therapy and other health facility related factors also contribute(25). Men's position of responsibility within the family and the shame they feel when accessing ART have been described as barriers to seeking care(26-27). In contrast, maternal and child health policies which reinforce women's HIV testing and their role in children's health facilitate earlier attendance for women(28).

During the early years of introduction of ART in resource-limited settings, late presentation was inevitable because of lack of access to antiretroviral drugs (ARVs). In recent years, however, access to ARVs has improved and lack of drugs cannot be taken as reasons for late initiation of treatment(29). The Ethiopian Ministry of Health (MOH) introduced ART in 2003 on subsidized, fee-based scheme, and ART became freely available since 2005. Further, ART was decentralized to health centers in 2006, which marked the rapid scale-up phase in the history of the Ethiopian ART programme(30). Though it is being modified currently, the national ART initiation criteria for both adults and adolescents states that, in places where CD4 cell count is available, WHO clinical stage IV, irrespective of CD4 cell count, WHO stage III and if CD4 cell count is less than 350 and all WHO clinical stages, if CD4 cell count is less than 200 were criteria for eligible patients to start ART(15).

In settings with high disease burden and resources limited areas of Ethiopia such as Gamo Gofa Zone, evidence regarding late presentation to HIV/AIDS care and gender differences in late presentation and survival is not well documented. Even though, a study regarding the effect of improved availability of HIV services on patient presentation to care and subsequent pre-ART and on-ART outcomes was done in Arba Minch hospital, it focuses on the general outcomes after ART

initiation(14, 31). Moreover, there is mixed evidence about effect of gender in timely initiation to HIV/AIDS care and survival, and the possible reason to gender difference in presentation to care and survival has not been reported yet(20, 32). Therefore, the objective of this study is to compare gender disparities in enrolment to HIV/AIDS care and to identify risk factors for gender differences in mortality among patients on ART in Arba Minch town, Gamo Gofa Zone, southern Ethiopia.

2. LITERATURE REVIEW

2.1. Overview of Late Presentation to HIV/AIDS Care and survival status

The Use of Antiretroviral Drugs, which are designed to achieve and sustain viral suppression among the people receiving ART, take maximum advantage and multiple benefits in scaling-up access to HIV care and treatment. The health status of patients at the time of ART initiation plays a crucial role in the success of treatment and patients with advanced HIV disease at the time of ART initiation are less likely to respond to treatment; thereby placing financial strain on health services and a higher mortality rate compared with those who initiate earlier (6, 33).

In the developed world, a large proportion of HIV-infected individuals, roughly 15%–43%, present at clinics for care with advanced or severe disease (WHO stage 3 and 4 or CD4 < 200 cells/µl)(34). For example, a recent study assessing the impact of late presentation on AIDS and mortality from Europe found that the incidence of AIDS/death increased in the first year after HIV diagnosis, with a 13-fold and a 6-fold increased incidence of AIDS/death in Southern and Eastern Europe respectively(35).

Furthermore, characteristics associated with late presentation in the developed world include male sex, older age, risky behaviour (including injection drug and alcohol use), lower income, and low degree of education(34, 36). However, little is known about the proportion or characteristics of HIV-infected individuals who present late for care at clinics in low-income countries, particularly those in SSA.

In 2013, a systematic review of literature that was conducted to identify the magnitude of late ART initiation problem in SSA reported late ART initiation as a major contributor to the problem of early mortality and morbidity. Moreover according to this review most patients in SSA initiated ART at the median CD4 count of 122 cells/µL, which is below international and national guidelines recommendations levels(5).

2.2. Factors associated with late presentation to HIV/AIDS care

Importantly, very few studies have examined factors that determine late ART initiation. A systematic review of different literatures on determinants of late ART initiation in SSA, identified

pathways to late ART initiation which includes, delays in HIV diagnosis, late enrollment in care, while HIV status is known and Late ART initiation despite early enrollment into care(5). In a study conducted in 2010 Nigeria, for example, 50% of HIV-infected individuals had CD4 <200 cells/μL at HIV diagnosis(37). A retrospective study in Zambezia province, Zimbabue reported low CD4 at ART initiation and high mortality rates. Among those ART eligible at enrollment (21%), only 58% initiated ART within 90 days of enrollment, and older age and higher level of education were strongly predictive of ART initiation(38). Similarly, in a peri-urban community near Cape Town, South Africa, 36% of HIV-infected individuals had CD4 <200 cells/μL and 31% presented HIV-related symptoms (WHO stage 3/4) at the time of diagnosis(39).

Furthermore, despite the increase in the annual population HIV testing rates in this community from 4% in 2001 to 20% in 2006, the proportion that was diagnosed late did not change with time. Another retrospective sex-specific analysis of data from adult patients who started ART between January 2005 and June 2009 in mozambique, demonstrated that though, HIV testing and ART coverage increase, a suboptimal steady state have been reached in the rates of late ART initiation in the catchment areas of 25 clinics(3). According to analysis of a national cross-sectional cohort of Cameroonian HIV-positive adults in 2008, a delays of three months in 30% of participants and more than six months in 15% were reported, before enrolling in care(40).

A case - control Study conducted in Dessie referral and Borumeda district hospitals from March 1 to 31, 2010, northern Ethiopia, observed that HIV-positive adults who lived with their families, lived in a rented house, perceived many ART side effects or HIV-related stigma, tested with sickness/symptoms, did not disclose their HIV status to their partner, or had frequent alcohol use were more likely to enroll in care late(41). HIV positive individuals who live with parents were 3.29 times more likely to present late to HIV/AIDS care than HIV positive individuals who live alone. HIV positive individuals who live with renting house were 2.52 times more likely to present late to HIV/AIDS care than HIV positive individuals who live with owning house. Non-pregnant women were 9.3 times more likely to present late to HIV/AIDS care than pregnant women(41).

2.3. Gender difference in late presentation

The first entry point to HIV/AIDS care is HIV testing, which is often accessed through provider-initiated testing at the health facilities. In many settings, provider-initiated testing has favored

women and children, this resulted in women to have more regular contact with the health care system and associated opportunities for HIV testing, especially via antenatal care, or holding different health-related beliefs. There has been recent growing recognition that men are disadvantaged because no equivalent routine testing opportunity exists for them(42) and this is considered at least partly to account for the fact that men initiate ART later than women(26-27, 43).

Those Patients with young children in their household and pregnant women have more contact with the health care system and thus initiate HIV care earlier in the course of their disease(44). Though, antenatal care programs are a key difference in how men and women access care and are often cited as a plausible cause for observed differences in health outcomes. Based on finding from an observational cohort study that was done to identify survival differences between sexes explained by late ART initiation in Uganda, this difference did not appear to have a large impact or access to care via antenatal services did not explain differences in outcome(45). According to Qualitative interviews with male and female participants in an ART cohort study at a treatment site in Malawi between January 2008 and September 2009, women's frequency of testing, health awareness and commitment to children led to earlier ART uptake and that men's commitment to wider social networks of influence, masculine ideals of strength, and success with sexual and marital partners led them to refuse treatment until they were sick(46).

A study conducted in Mozambique found that Male patients enrolled at rural clinics and clinics were less likely to initiate ART late, although in this study men in rural sites represented only 8% of the men included in their analysis. Women initiating ART at clinics that also had an onsite PMTCT program were significantly less likely to initiate ART late, independently of whether individual women entered the program via PMTCT(3). The reason suggested was, ease of referral of HIV infected women from PMTCT to HIV care and treatment services when both are co-located at the same facility. Concerning to marital status, among women, being married/in union or widowed was associated with lower risk of late ART initiation when compared to those who were single(3, 44). The death of a spouse could prompt an individual to seek an HIV test prior to the onset of symptoms, especially if HIV is suspected as a possible cause death in the spouse, and further motivate an individual to seek HIV care for already known HIV infection(3).

A Cameroonian cohort study, using a large number of study participants, with baseline assessment between 2007 and 2008, and follow-up until June 2012, found that being a male younger than 45 years was 1.49 times more likely to initiate ART late than a female younger than 45 years was associated with higher odds of late ART initiation(17).

2.4. Survival Differences in HIV/AIDS Care and Follow up

Though, the provision of ART has improved the survival of peoples enrolled in to HAART, there is still a conflicting reports about gender-related differences in mortality among men and women both in developed as well as, in developing world(20, 32, 47-48). Gender differences inherent in the health-seeking behaviors of men and women, and the historical gender-specific efforts in HIV-related public health campaigns in Africa, impact health outcomes, including mortality(21,49-50). For instance, recent cohort studies conducted among individuals starting ART in SSA have indicated that men tend to access ART at a later disease stage than women, and the risk of mortality once on ART is much higher for men than women, even when adjusting for disease state(24, 51). Specifically, in Uganda, evidence from a large, nationally representative cohort study indicates that men are (hazard ratio, HR) 1.43 (95% confidence interval: 1.31–1.57) times more likely to die than women(24), and in South Africa, evidence from a large cohort study indicates that men are 1.47 (HR, 95% confidence interval: 1.27–1.72) times more likely to die than women(51). But these differences are only partly explained by more advanced HIV disease at the time of ART initiation, differential LTF and subsequent mortality, and differences in responses to treatment. This study demonstrated the observed difference in mortality on ART is best explained by background differences in mortality between men and women in the South African population unrelated to the HIV/AIDS epidemic(51). However, this study is only partly being generalized because there was a high proportion of missing values for WHO stages and viral load.

In contrast to this study, the finding of a cohort study done in Uganda using a mediational analysis, that considered gender as the initial variable, time to death as the outcome, initial CD4 count as the mediator, and age as a covariate, reported that there is a marked increase in risk of mortality for men and approximately half of it is attributed to their later engagement in care(45).

Unlike other studies where men had a comparably higher mortality than women(45, 47-48) a facility- based retrospective cohort study which was conducted from January 1, 2006 to 2008, in Oromiya Ethiopia, reported that there was no significant difference in survival rates between the sexes and CD4 count was not found to be associated with survival. It was explained by the fact that the majority of patients (82%) had a CD4 count below 200 cells/ml, which could have made the comparison with higher CD4 counts statistically unstable(15).

2.5. Risk factors for gender differences in mortality

Mortality among patients on HAART might be associated with Base line clinical, laboratory and anti-retroviral treatments(15-16, 31). In sub-Saharan Africa, men appear to initiate ART at older ages and with more advanced HIV disease than women(18, 22), and markers of advanced HIV disease at the time of ART initiation strongly predict early mortality on ART(45). A study on baseline risk behaviors among HIV Patients in Kenya, Namibia, and Tanzania, 2013 reported that, men had significantly lower CD4 counts than women. Nearly two-thirds of men had CD4 counts less than 350 cells/mm3 compared to less than half of women (64% vs. 46%, p- value =0.001)(52) and men tend to be at higher risk of death and the leading cause was the lower CD4 cell counts at which men on average present themselves for ART initiation(45).

Another study of Gender differences in retention and survival on antiretroviral therapy among HIV-1 infected health care workers, teachers, police/army personnel, who accessed ART in Malawi by June, September and December 2006 respectively, examined men have higher mortality on ART than women(22). After Controlling for age, WHO clinical stage and occupation, men experienced nearly 2 times the mortality of women RR 1.90 [95% CI: 1.57- 2.29]. A higher proportion of men initiated ART in WHO stage 4 ($p<0.001$). According to this study possible reasons were unclear but could have been biological or because men present for ART at a later clinical stage or have poorer adherence to therapy(22).

Recently, an observational cohort study using an accelerated failure time model with a Weibull distribution to explore survival differences between sexes explained by late initiation among patients who initiated ART between January 2004 and April 2011was done in Uganda. This study examined whether single men had differing baseline risk, according to baseline CD4, compared with other groups, they found that single men had significantly lower CD4 (median 99, IQR 30–

190) than married men (120, IQR 48–199) [*P* = 0.03] and compared to single women (144, IQR 68–209) [*P* < 0.001](45). The median age in this study was 33 (interquartile range [IQR] 27–39), and 1676 (35.1%) were men (p< 0.001).

Another Cohort study with baseline assessment between 2007 and 2008, and follow-up during 5 years in Cameroon revealed the median of 38 (31–45) years overall, 40 (34–47) years in men and 35 (30–43) years in women, (p <0.0001). In all, 85.6% of participants were urban dwellers and about the same proportion were started on ART at WHO stages III–IV of disease severity, similarly among men and women. The main opportunistic infection was tuberculosis, which was found in 428 (29.6%) patients, and was more frequent in men than in women (34.7% vs 27.9%, p=0.0003)(17). In support of these studies a multi-center cohort study in south Africa reported that crude mortality of participants on ART was higher for men than women: 8.5 versus 5.7/100 person-years, unadjusted HR 1.46 (1.37–1.56), (p,0.001)(48). In multivariable analysis, after adjusting for baseline age, cohort, CD4+ cell count, WHO stage, log viral load, anaemia, and weight, men had a 31% higher risk of death than women (adjusted HR [AHR] 1.31, 95% (CI 1.22–1.41)(48). Other study have shown that adherence prescribed ART was better in women than in men(53) which can explain differing rates of mortality between men and women started on ART. However, a retrospective cohort study conducted among ART attendees enrolled between July 2005 to January 2012 in Nekemte Referral Hospital, Western Ethiopia demonstrated that, there was no association between gender and ART adherence, rather majority of the patients (95.9%) had good ART adherence(31).

A study conducted to assess antiretroviral treatment outcome in public hospitals South Nations Nationalities and Peoples Region, Ethiopia in 2011 revealed that, gender, WHO stage, CD4 cell count, functional status and the existence of NVP-ARV drug as a combined regimen at base-line have significant effect on determining the mortality and permanent discontinuation of treatment in a longer follow up period. Having a higher risk of death for males than female, with AHR of 1.632 (CI: 1.309-2.034) p-value < 0.001(54).

Similarly, a study in 2010 reported from Arbaminch Hospital, Ethiopia, revealed the survival of patients on ART associated with improvement in patients starting treatment earlier and higher mortality was associated with advanced clinical stage at start of treatment (HR [95%CI] =2.4 [1.5, 4]), age over 45 years at presentation (HR [95%CI] =1.7 [1.2, 2.4]) and men had higher mortality

rates than women (HR [95%CI] =1.4 [1.1, 1.8]) though, it is contrasted with a study that was done using data collected during the follow-up time from 2005 to 2008 in Tikur Anbessa hospital, Addis Ababa Ethiopia. According to this study, males have significantly higher survival rate than females and the estimated HR for females was 0.55 (CI: 0.365-0.843)(32). However, in this study unlike the other studies conducted in South Nations Nationalities and Peoples Region and western Ethiopia(31, 54), random sampling method was not employed during selection the study subjects.

In Ethiopia different studies on determinants of mortality and anti-retro viral treatment outcomes were reported (14-15, 31-32, 54). Some revealed that no significant gender difference in survival among patients on ART(15, 31), and others reported higher rate of males than females die(14, 54). However, unlike many studies in Africa, higher rate of death was observed in females from a study conducted in Addis Ababa, Ethiopia(32). Though different findings have been observed, none of these studies tried to identify the reason for existing disparities among gender and survival rate. Rather most underlines, the need for further study, in particular they emphasizes the necessity to explore possible reasons for higher mortality among males(14, 32).

Based on the above literatures difference in enrolment to HIV/AIDS care for males and females could be observed due to difference in socio-demographic characteristics. Again status of patients during initiation of ART, including presence of opportunistic infections, past history of medications taken, functional status and so on has a relation with HIV/AIDS patients' status during follow up period. Furthermore, gender difference in survival exists after they have started ART. This might happen because of the different socio- demographic characteristics that males and females have, and the other can be difference in status of patients during the time they initiate ART and their status during follow up times. The following figure shows the conceptual framework based on reviewed literatures.

Conceptual framework

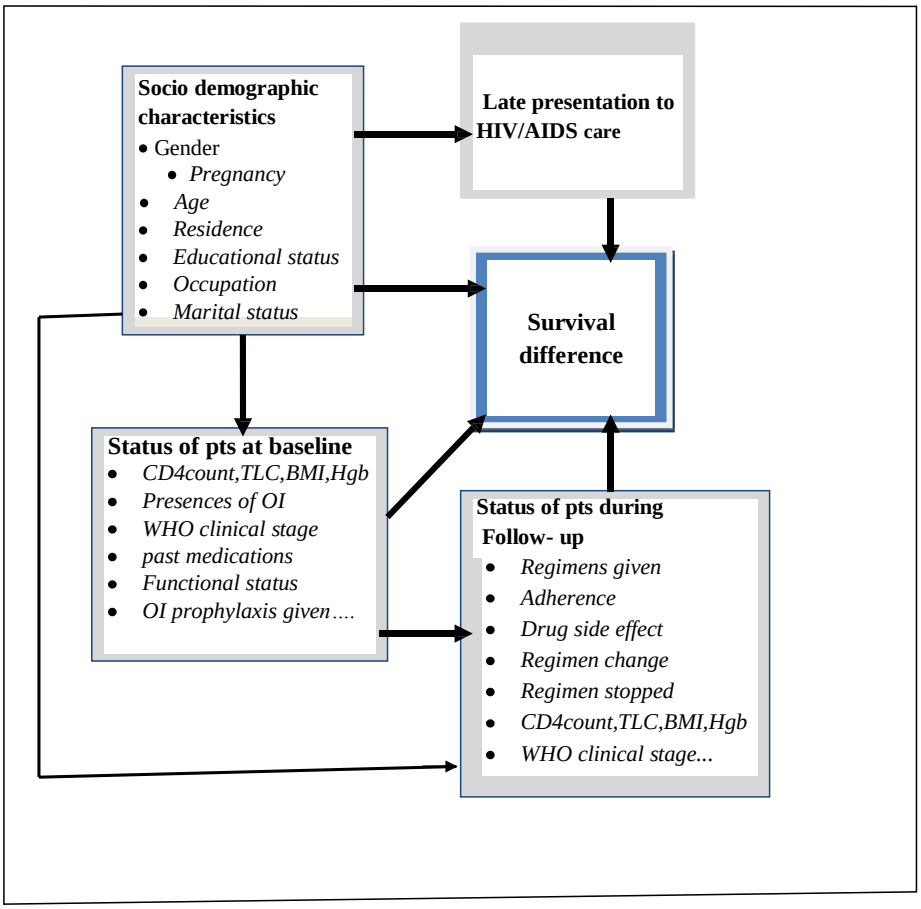

Figure 1 Conceptual framework for the assessment of gender difference in presentation to HIV/AIDS care and survival in public health facilities in Arba Minch town, Southern Ethiopia (reviewed from different literatures).

SIGNIFICANCE OF THE STUDY

Since the advent of antiretroviral therapy (ART), mortality rates for people living with HIV/AIDS have decreased substantially both in resource rich and resource-limited settings with conflicting reports about gender-related differences in enrolment and mortality. Where differences have been reported, little is known about the reasons. Exploring the reasons underlying any difference could inform strategies designed to address these differences and interventions that ultimately increase the effectiveness of HIV care and treatment scale-up. This will benefit service providers, Zonal Health Desk and Health facilities to develop suitable strategies for awareness creation to people living with HIV so that people living with the virus come early to the HIV/AIDS care and remain in care until timely treatment commencement decisions are made and, thereafter, maintaining high fidelity to essential long-term care and treatment contact.

Thus, generating gender specific and locally consumable data will serve as stepping board for further study in the country. Furthermore, it will provide evidence for organizations working on HIV/AIDS and ART at national, regional, and district levels on late presentation to HIV/AIDS care and risk factors determining the mortality of HIV positives attending HAART.

3. OBJECTIVES

3.1. General objective

To assess gender disparities in presentation to the HIV/AIDS care and survival among patients on highly active antiretroviral therapy in public health facilities of Arba Minch town, southern Ethiopia, 2014

3.2. Specific objectives

- To compare gender difference in presentation to the HIV/AIDS care among patients on anti retroviral therapy
- To determine survival difference in HIV care and follow up among patients enrolled into anti retroviral therapy between men and women
- To identify risk factors for gender differences in mortality among patients enrolled into anti retroviral therapy

4. METHODOLOGY

4.1. Study area and period

The study was conducted in Arba Minch town, Gamo Gofa Zone, Southern Nations, Nationalities and Peoples' Regional State of Ethiopia for one month from February 30, 2014.

Arba Minch town, the capital town of Gamo Gofa Zone, is located 505 km south of Addis Ababa; the capital of Ethiopia and 275 km from Hawassa, the capital of the SNNPR region. According to the 2007 census result it has a population of 81,451 and of this 42,670 were males and 38,844 were females. There is one general hospital and 3 health centres offering health care services for the population of the town. Among the health facilities in the town, only AMH and AMHC are currently providing ART. There is no private health facility that provides ART to population of the town. The hospital started providing ART in August 2003 with financial support from the Norwegian Lutheran Mission. When Ethiopia launched the 'free' ART programme in 2005, the hospital became part of the national scheme for ARV delivery. Clinical and total lymphocyte count (TLC) as criteria for starting treatment and follow-up had been used until CD4 testing was available in mid-2006. Total number of adult HIV/AIDS patients who are on ART in Arbaminch hospital (AMH) are 2526 and 406 adult HIV/AIDS patients initiated ART in Arbaminch health center (AMHC). Among these women accounts 1374 (54.3%) and 268 (66%) in AMH and AMHC(55).

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4.2. Study Design

A facility-based retrospective cohort study was employed.

4.3. Population

4.3.1. Source Population

All HIV/AIDS patients who were on HAART from Feb.1, 2006 to Jan.30, 2014 at the AMH and AMHC HIV/AIDS clinic

4.3.2. Study Population

All randomly selected HIV/AIDS patients who were on HAART from Feb.1, 2006 to Jan.30, 2014 at AMH and AMHC HIV/AIDS clinic

4.4. Inclusion criteria and Exclusion criteria

All HIV/AIDS patients on HAART from Feb.1, 2006 to Jan.30, 2014 whose ages were more than or equal to 15 years and had received ART on at least two clinical visits, and have complete registration, intake and follow up forms were included in the study. However, those patients diagnosed and started treatment in other places, had previous ART history, and were with incomplete information were excluded from the study.

4.5. Sample Size and Sampling Techniques

4.5.1. Sample size determination

The sample **s**ize was calculated to detect the difference in survival curves and to allow comparisons using gender. Based on the assumption of 95% two sided confidences level, 80 % power, 1:1 ratio of male to female, hazard ratio of 1.60 when the proportion surviving females is 0.929 and 0.083 & 0.082 lost follow up rate for females and male respectively (14). Using the above assumption, PASS (power analysis and sample size system) by Dr. Jerry L. Hintze and NCSS(56). Produces the following sample size:

Table 1 Sample size using Log-rank Test Analysis for assessment of gender differences in enrolment to HIV/AIDS care and survival in public health facilities in Arba Minch Town, Southern Ethiopia, 2014

Numeric Results in Terms of Sample Size when the Test is Two-Sided and T0 is 1

Power	N1	N2	N	(HR)	Female Prop (S1)	Male Prop (S2)	Accr Pat'n	Acc time /total time	Female Loss	Male loss	alpha
0.8004	260	260	520	1.60	0.9290	0.8888	Equal	8 /8	0.083	0.082	0.050

Numeric Results in Terms of Events when the Test is Two-Sided and T0 is 1

Power	Femal events(F	male even	total event	(HR)	Female Propsur	Male Propsu	Accr Pat'n	Acc time /total	Female Loss	male loss	alpha
0.8004	58.3	85.1	143.3	1.60	0.929	0.8888	Equa	7 /8	0.083	0.08	0.050

A two-sided log-rank test with an overall sample size of 520 subjects (260 females and 260 males) achieves 80.0% power at a 0.05 significance level to detect a hazard ratio of 1.60 when the proportion surviving in the control group is 0.929(14). The study lasts for 8 time periods of which subject accrual (entry) occurs in the 7 time periods. The accrual pattern across time periods was uniform (all periods equal). The proportion dropping out of the control group and the treatment group was 0.083, 0.082 respectively(14).

4.6. Sampling Procedure

Profile of all patients on ART Between February 1, 2006 and January 30, 2014, were evaluated. Then, subjects with incomplete data were excluded. For those who fulfil inclusion criteria, unique ID number was given in increasing order for both male and female ART groups separately. The total study participants were distributed proportionally to the hospital and health centre, based on the total number of HIV positive females and males receiving ART. Then, simple random sampling technique was employed separately to select samples from both groups using computer-generated random number table. Study subjects for qualitative data were recruited using a purposive sample of patients on antiretroviral therapy (ART), from strata defined by gender and grouped according to WHO clinical stage at presentation, and were invited to participate in FGDs. Four FGD groups, each with 8 -12 participants who have been receiving antiretroviral therapy (ART) starting from January 1, 2014 in antiretroviral clinic of both health facilities were recruited. First two groups were females whose age is eighteen years or older. The rest were males aged eighteen years or older.

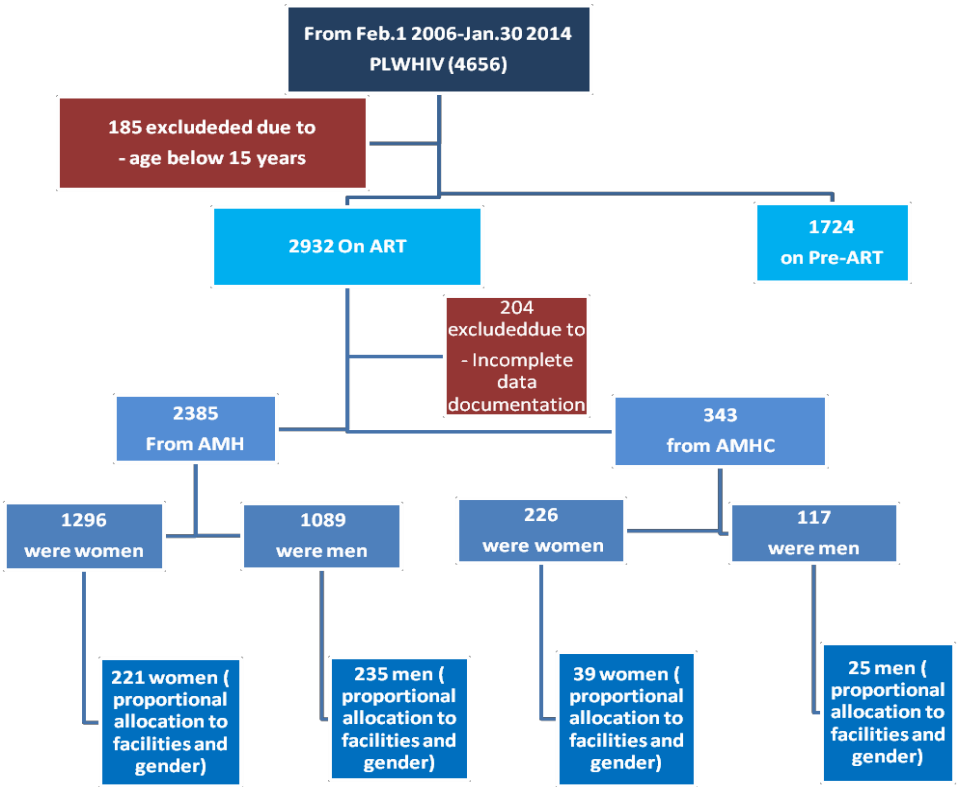

Figure 2 Schematic presentation of sampling techniques for the assessment gender differences in presentation to HIV/AIDS care and survival in public health facilities in Arba Minch town, Southern Ethiopia

4.7. Data Collection Procedures

The data source for study variable was both medical and electronic records of patients kept at the health facilities. The medical and electronic records of each individual have a unique patient identifier that can be used to construct a longitudinal history of medical care utilization for each patient.

The medical and electronic records contain routinely collected clinical and laboratory report data. These documents contain information on age, gender, date of HIV screening and ART initiation, history of opportunistic infections (OIs) and concurrent medical conditions, immunological responses, and therapy-related to prevention of mother to child transmission of HIV, ARV drugs, Cotrimoxazole and INH prophylaxis. Data abstraction form was used to retrieve relevant data from medical records of patients. A form adapted from previous similar study (31) was used and Change on the format was done by the investigator after reviewing relevant literatures on the phenomenon under study and with consideration of the research problem, specific research questions and Health Information System of the country.

The data was collected by two nurses who were trained and had been working at ART clinic of each hospital and health center 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 were obtained within a month the mean was used.

To better understand reasons for late presentation to HIV/AIDS care in patients on ART cohort. Information was collected from four FGD groups consisting, 8-12 participants using a semi-structured FGD guide prepared in Amharic to assess common factors such as behavioural, institutional and personal related barriers to early HIV/AIDS care. After selecting the participant, appropriate time and comfortable place of meeting was selected and organized. During conducting the FGDs explanation and elaboration of the need to do the FGD was made and the participants were asked their willingness to participate in the FGD. Note taker and recorder was assigned for note- taking and tape recording while the subgroup facilitators facilitates the discussion; and discussion was lasts an average of 1-1:30 hrs for each male and female groups. Then after, the data was transcribed and was translated in to English by language experts. Two health officers supervised the data collectors and checked the completeness and consistency of the collected data. Data quality was controlled by designing the proper data collection materials and through continuous supervision.

4.8. Study Variables

- Independent variables
  - Socio demographic characteristics (age, 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

- Dependent variable
  - Survival difference in HIV/AIDS care from the initiation of ART to January30, 2014

4.9. Operational Definition

- Early presentation to HIV/AIDS care: - HIV positive individuals who had WHO clinical stage I or II or a CD4 count of >200/µL at the time of presentation to the ART clinic(44, 57)
- Late presentation to HIV care: – HIV positive individuals who had WHO stage III or IV clinical stage or a CD4 lymphocyte count of ≤ 200/µL at the time of first presentation to the ART clinics(44, 57).

4.10. Data Processing and Analysis Procedure

The data was entered into EPI INFO Version 3.5.1. Then it was exported to SPSS for windows version 20.0 for performing statistical analysis. For comparison of treatment group female group was selected as references (none exposed) group. In the analysis process, Descriptive statistics was used to describe the data, assess normality, and identify missing values and outliers. Then frequencies, cross tabs, measures of central tendencies and variations were computed to see the nature of the data. Gender difference was assessed after the baseline clinical and demographic characteristics of patients were described in terms of mean/median value for continuous data and percentage for categorical data.

Analysis was done separately for men and women. Recorded responses collected from the male and female FGD groups were transcribed and content analyzed & thematized in the main thematic area. It was then, triangulated with analysis of baseline clinical and demographic data for individuals attending sequentially for ART. Gender specific data on death was confirmed by reviewing medical and electronic registrations in the hospital and health centre, registration by ART adherence supporters, or by calling using the registered phone number. Individuals who had been lost during follow up, and those who are alive and on ART until the end of the study period were censored. Then, the outcome of each subject was dichotomized in to censored or death. Finally, survival analysis and Kaplan-Meier test were used to assess the association of baseline clinical and demographic characteristics of patients from ART initiation with survival. Life table was used to estimate survival for male and female patients after initiation of ART, and log rank test was used to

compare survival curves. To ascertain the association; variables found to be significant at ($p<0.25$) in a bivariate analysis was included in the final model. Cox proportional-hazards regression model was used to determine independent predictors of survival for both male and female. To assess the Proportional hazards assumptions, Covariates that change in value over the course of the follow up period (time-dependent covariates) were incorporated in the Cox model (was extended to contain product (interaction) terms). The bivariate and adjusted hazard rate and its 95% CI were estimated.

4.11. Data Quality Management

To check correctness and consistency of data collection tool, the research instrument was pre-tested with 5% of the study subjects, using records of patients with antiretroviral therapy in the hospital, before the actual data collection. A two days training had been given for two health officers who supervised the data collectors and for four nurses who collected the data. The overall activity was controlled by the principal investigator of the study. The supervisors were responsible for supervising the data collectors; check for the completed questionnaire; and correct any mistake or problem encountered. Discussion with all supervisors and data collectors at the end of each day was performed to get feedback and to solve problems. Data consistency was assured throughout data collection, entry and analysis. The overall data collection process was coordinated by the principal investigator. Double data entry was done and data was compared for inconsistency and checked against the hard copy if there is any difference between the two entered data.

4.12. Ethical Consideration

Ethical clearance was secured from the Institutional Review ethical committee of Jimma University, and permission from the Gamo gofa Zonal Health Desk, Arba Minch hospital, Arba Minch town Health office and Arba Minch Health center was obtained. The objectives, and importance of the study was explained to all concerned bodies. To preserve the confidentiality, nurses working in ART clinic of AMH and AMHC extracted the data from the medical records. Moreover, no personal identifier was used on data collection form. The recorded data was not accessed by a third person except the principal investigator, and it was kept confidentially. Regarding participants for FDG, Participation in the study was on a voluntary basis.

Again consent was taken for those participants who were agreed to participate for interview by trained nurse. Thus, participants who were not willing to participate in the study and those who wish to quit from the study at any point in time were informed to do so without any restriction.

4.13 Dissemination Plan

The study will be used primarily for the partial fulfilment for the requirement of degree of Masters in public health/ population and family health/ in Jimma University. So, the finding will be submitted to the Department of population and family health and publicly defended; and the result of the study will be submitted to the department and advisors. After the approval of the advisors, examining board, and the department, the study result and findings will also be submitted to relevant bodies such as AMH and AMHC, Arba Minch town Health Office, SNNPR Health Bureau, and Federal Ministry of Health. Finally, attempts will be made to present the results on scientific conferences and to publish the results of the study on local or international journal

5. RESULT

A total of 520 adult patients were recruited in this study. Among these, 260(50.0%) were females. The median follow up period for both men and women was 38 months with Inter quartile range (IQR) of (22-59 month). There was a statistically significant mean differences on the follow up period of women and men (P-value <0.001) (42.0 months, IQR 24.25-64.75 months vs. 34 months, IQR 20-53 months for women and men respectively). During this period of time, 403(77.5%) complete follow up (52.35% were females), 89(17.1%) died with the follow up period (57.3% were males), 28(5.4%) lost to follow up (67.3% were males).

5.1 Socio-Demographic characteristics of the study participants

Women were on average 4 years younger than men at ART initiation (median age 31 years for women (IQR 28-38 years) and 35 years for men (IQR 28-41 years)). Men tended to be better educated and were more likely to be married. Regarding to occupational status, majority of females were Housewives 130(50.0) followed by governmental employers 31(12.0). Whereas, the majority of men were private employ 54(20.8). Of the total study subjects, 306(58.8%) were Orthodox by religion (62.7% for men), and 440(84.6%) were urban residents (85.8% for women). Table 2 shows socio-demographic characteristics of the study participants by gender.

Table 2 A comparisons of Base line socio-demographic characteristics between men and women on ART at the AMH and health center from Feb. 1, 2006 and Jan. 30, 2014

Variables		Women	Men	Total	P-value
Age	Median	31.00	35.000.04	32.00	0.04
Marital Status (N=520)	Married	147(56.5)	180(69.2)	327(62.9)	0.006
	Divorced	43(16.5)	19(7.3)	62(11.9)	
	Never married	30(11.5)	27(10.4)	57(11.0)	
	Separated	26(10.0)	26(10.0)	52(10.0)	
	Widow	14(5.4)	8(3.1)	22(4.2)	
Education Status (N=520)	No education	91(35.0)	74(28.5)	165(31.7)	0.093
	Primary	104(40.0)	100(38.5)	204(39.2)	
	Secondary and above	65(25)	86(33.1)	151(29)	
Religion (N=520)	Orthodox	143(55.0)	163(62.7)	306(58.8)	0.021
	Protestant	100(38.5)	70(26.9)	171(32.7)	
	Muslim	11(4.2)	21(8.1)	32(6.2)	
	Others	6(2.3)	6(2.3)	10(2.3)	
Residence (N=520)	Urban	223(85.8)	217(83.5)	440(84.6)	0.239
	Rural	37(14.2)	43(16.5)	80(15.4)	
Occupation (N=390)	Private employ	24(9.2)	54(20.8)	78(15.0)	0.002
	Gov't employ	31(12.0)	47(18.0)	78(15.0)	
	Farmers	14(5.4)	48(18.4)	62(11.9)	
	Merchant	28(10.8)	31(12.0)	59(11.3)	
	Driver	2(0.8)	26(10.0)	28(5.4)	
	Teachers/Militar	6(2.4)	17(6.6)	23(4.4)	
	Other	25(9.2)	37(14.2)	62(11.9)	

Note; housewife 130 (50.0%) (Women), from occupation were removed b/c it was not comparable with men

5.2. Baseline Clinical Characteristics

At ART initiation, men had lower median CD4 cell count than women (175cells/µL Vs 181cells/µL and were more likely to initiate ART in WHO clinical stage 4 than women (49(18.8%) Vs. 30(11.5%) respectively; and 174(66.9%) men and 175(67.3%) women were in stage 1 or 2 with a CD4 count below 200 cells/µl. More men than women likely had previous opportunistic infections and tended to have higher positive TB test. The median haemoglobin and BMI level were similar for men and women (12.5 g/dl vs. 12.0g/dl) and (20.2K.g/m^2 vs. 20.4K.g/m^2) respectively. (Table 2)

Table 3 A comparison of Base line clinical, laboratory and ART information in men and women on ART at the AMH and health centre from Feb. 1, 2006 and Jan. 30, 2014

Variable		Women	Men	Total	P-Value
Presences of OIs	No	170(65.4)	161(61.9)	331(63.7)	0.437
	Yes	90(34.6)	99(38.1)	189(36.3)	
TB Test	Yes	12(4.6)	23(8.8)	35(6.7)	0.089
	No	248(95.4)	237(91.2)	485(93.3)	
TB Test Result	Negative	2(5.7)	3(8.6)	5(14.3)	0.068
	Positive	6(17.1)	18(51.4)	24(68.6)	
	Not determined	4(11.4)	2(5.7)	6(17.1)	
Functional Status	Working	225(86.5)	215(82.7)	440(84.6)	
	Ambulatory	28(10.8)	37(14.2)	65(12.5)	0.463
	Bed ridden	7(2.7)	8(3.1)	15(2.9)	
ART Eligibility Criteria	CD4 cell count	175(67.3)	174(66.9)	349(67.1)	0.011
	WHO stage IV	30(11.5)	49(18.8)	79(15.2)	
	WHO stage III with TLC	55(21.2)	37(14.2)	92(17.7)	
Starting HAART Regiment	1a(30)=d4t(30)-3TC-NVP	78(30.0)	128(49.2)	206(39.6)	0.001
	1a(40)=d4t(40)-3TC-NVP	3(1.2)	1(0.4)	4(.8)	
	1b(30)=d4t(30)-3TC-EFV	38(14.6)	44(16.9)	82)15.8)	
	1b(40)=d4t(40)-3TC-EFV	15(5.8)	14(5.4)	29(5.6)	
	1c=AZT-3TC-NVP	20(7.7)	14(5.4)	34(6.5)	
	1d=AZT-3TC-EFV	6(2.3)	17(6.5)	23(4.4)	
	TDF-3TC-NPV	0	1(0.4)	1(0.2)	
	TDF-3TC-EFV	100(38.5)	41(15.8)	141(27.1)	
Baseline CD4	Median(IQR)	181(146-247)	175(130-201)	179(138-222)	0.009
Baseline BMI	Median(IQR)	20.4(18.8-20.5)	20.2(18.3-21.7)	20.3(18.6-22.1)	0.063
Baseline Hemoglobin	Median(IQR)	12.00(10.8-13.0)	12.50(11.013.6)	12.0(11.0-13.3)	0.022

Concerning to provision of prophylaxis, cotrimoxazole was give for a total of 466(89.6%) patients While INH and fluconazole was given for 266(51.2%) and 50(9.6%) respectively. In terms of sex difference, less number of women had taken cotrimoxazole prophylaxis 229(88.1%) women Vs 237 (91.2%) men. Similarly a large number of men had taken INH prophylaxis and fluconazole; (137(52.7%) and 26(10.0%) for INH and fluconazole respectively).

One hundred and eighty nine (36.3%) patients were having opportunistic infections, of whom 96 (18.6%) had more than one opportunistic infections at the time of initiation of antiretroviral therapy. Concerning the type of opportunistic infections, candidiasis is the most common type of OI in both sexes (Fig. 3 describes the detail).

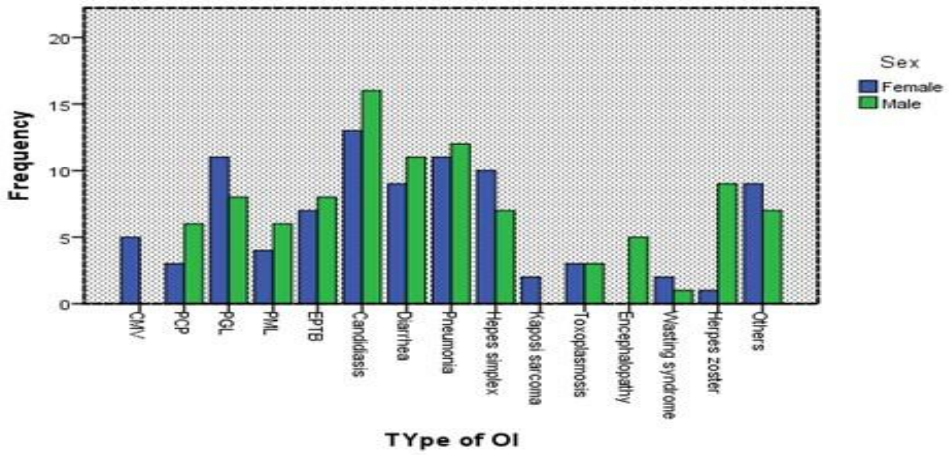

Figure 3 The distribution of OIs type among HIV/AIDS patients at the initiation of antiretroviral therapy at AMH and AMHC, from Feb. 1, 2006 and Jan. 30, 2014

5.3. Follow up Condition of the Study

Regarding to duration of time on Pre-ART period there was no significant difference among women and men. The median time between entry to HIV/AIDS chronic care and initiation of ART was 30(IQR, 13-48) and 30(IQR14-51) month for women and men respectively.

During the follow up period, only 275(52.9%) study participants were eligible to determine adherences status. From these participants 257(93.5%) had good drug adherences status. Both women and men didn't show significant differences on their adherences status (P-Value 0.512). In the follow up period antiretroviral drug was changed for 184(35.2%) of patients, because of new drug available for 136(73.9%), toxicity for 35 (19.0%), development of new tuberculosis infection

for 4(2.2%), pregnancy for 3 (1.6%), drug out of stock for 2(1.09) and other unknown reason for 4 (2.2%) of patients. Regimen change was not comparable (P-value 0.713) among the study groups.

5.4. Gender difference in presentation to HIV/AIDS care

More than two-third (68.6%) of the study participants, were presented late to HIV/AIDS chronic care. Among these 193(54.1%) were male in gender whereas from the early presenting group 96(58.9%) were females. This finding is supported by FGD, *participants from the group described that;* men have *low awareness to HIV/AIDS than women and one participant from the group stated that:*

"...I didn't realize that I should have come to the health facility early. I came to health facility only when I had serious health problem."A 46 year old male participant from AMH

Three hundred thirty one (89.1%) the study participants were diagnosed for late presentation based on their CD4 count. In connection to this, significant difference was observed at gender on presentation to HIV care. Women had a 41% less risk to be present late compared to men (P-Value 0.008, 95% CI 0.408- 0.863). This finding was also supported by focused group discussion which s*ome participants described that: fear of stigma, and substance abuse, were the common factors that affect men to attend ART early in the course of the disease and one male participant from the group said that:*

"....By the time I knew my sero-status, I didn't disclose this to anyone, because I thought that people would affect my social relation, affect my job and loss respect from my close friends and families." A 42 year old male participant from AMH

In this study, a total of 43(16.5%) of women were pregnant. Of these, about 20 (12.5%) had initiated ART early. This finding was strengthened by focused group discussion*; participants across the groups described Women access health services more frequently than men because women have frequent contact with health professionals especially during child vaccination and antenatal visit and they receive advice from them and seek care early when they get illness*

5.5. Gender Differences in Survival

Study participants were stayed for different length of time in the cohort which makes the general population at risk of the event (i.e. death) 21, 797person month or 1816 person years (i.e. person time). The total survived within the follow up period was 439 persons; this makes the rate of death after initiation of ART is 4.7 persons per 100 per year. The death rate was 6.2 and 4.9 persons per 100 person years for among males and females respectively. The mean survival time for the study participant was 77.5 months (95% CI74.5-80.4). The distribution of mean survival time was 81.2 months (95%CI of 77.5-84.8) for women and 71.8 months (95% CI of 67.3-76.3) for men. The median survival time was 94 month for the overall cohort group. It was not determined for female study group within the follow up period; this means that more than 50% of female study participants were still alive at the end of study period. Whereas, it was 91 months for male study participants

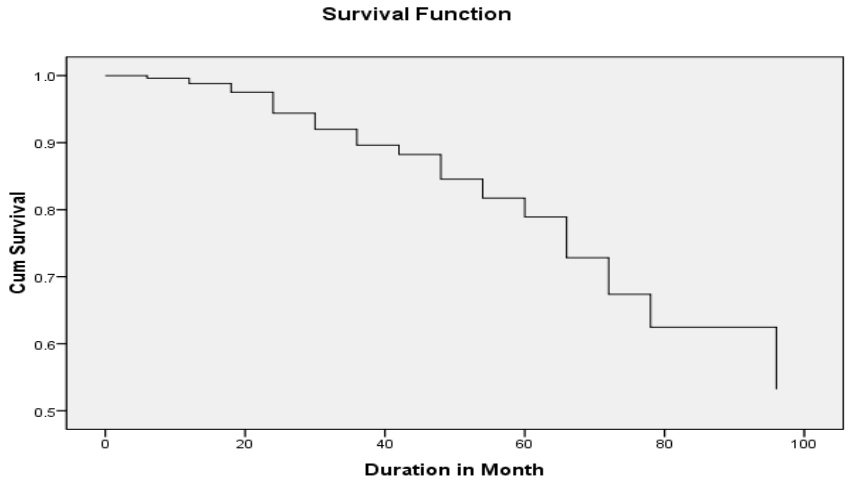

Figure 4 The survival graph showing probability of survival of HIV infected patients taking ART at AMH and AMHC from Feb. 1, 2006 and Jan. 30, 2014

The cumulative probability of survival at 12, 24, 36, 48 60, 72, 84 and 92 months after ART initiation was 0.97, 0.87, 0.83, 0.76, 0.63,0.57 and 0.57 for men and 0.98, 0.96, 0.93, 0.87, 0.81, 0.67 and 0.67 for women.

Table 4 A life table for a cohort ART patients at the AMH and AMHC from Feb. 1, 2006 up to Jan.

30, 2014 by their gender

Sex	Time in months	Number at start	Withdr	Number at Risk	No of	Probability of death	Probability of Surviving	Cumulative Probability of Surviving	
	0	260	1	259.5	1	0	1		1
	6	258	11	252.5	1	0	1	0.99	
	12	246	27	232.5	2	0.01	0.99	0.98	
	18	217	16	209	0	0	1	0.98	
	24	201	16	193	4	0.02	0.98	0.96	
Female	30	181	11	175.5	4	0.02	0.98	0.94	
	36	166	31	150.5	2	0.01	0.99	0.93	
	42	133	12	127	5	0.04	0.96	0.89	
	48	116	20	106	3	0.03	0.97	0.87	
	54	93	12	87	2	0.02	0.98	0.85	
	60	79	13	72.5	3	0.04	0.96	0.81	
	66	63	4	61	7	0.11	0.89	0.72	
	72	52	15	44.5	3	0.07	0.93	0.67	
	78	34	7	30.5	0	0	1	0.67	
	84	27	8	23	0	0	1	0.67	
	90	19	18	10	1	0.1	0.9	0.60	
	0	260	7	256.5	1	0	1		1
	6	252	8	248	3	0.01	0.99	0.98	
	12	241	28	227	4	0.02	0.98	0.97	
	18	209	27	195.5	13	0.07	0.93	0.90	
	24	169	15	161.5	5	0.03	0.97	0.87	
Male	30	149	27	135.5	4	0.03	0.97	0.85	
	36	118	23	106.5	2	0.02	0.98	0.83	
	42	93	9	88.5	4	0.05	0.95	0.80	
	48	80	13	73.5	3	0.04	0.96	0.76	
	54	64	12	58	3	0.05	0.95	0.72	
	60	49	9	44.5	6	0.13	0.87	0.63	
	66	34	3	32.5	0	0	1	0.63	
	72	31	14	24	2	0.08	0.92	0.57	
	78	15	5	12.5	0	0	1	0.57	
	84	10	4	8	0	0	1	0.57	
	90	6	5	3.5	1	0.29	0.71	0.41	

A statistically significant difference was observed at (P-value = 0.007) for the survival of HIV infected adult patients during comparison by gender. Figure 4 shows the cumulative survival probabilities for men and women, illustrating the significantly lower survival among men group.

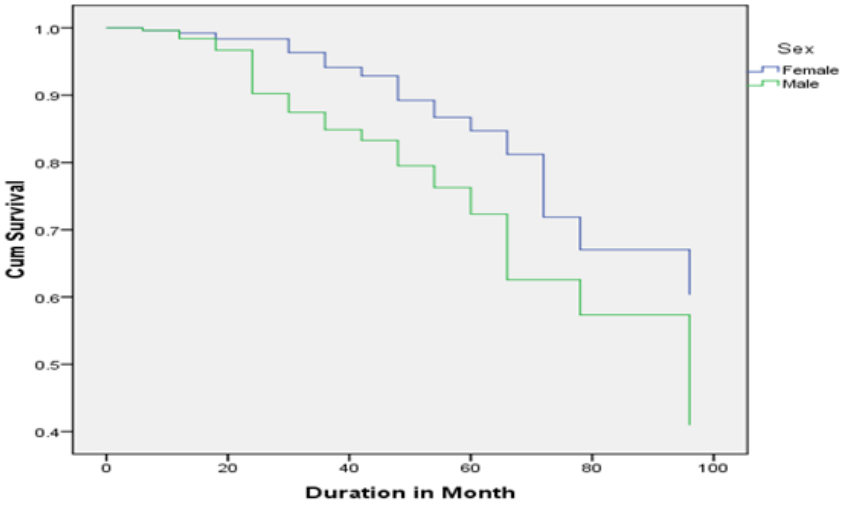

Figure 5 The survival graph showing comparison of probability of survival among HIV infected patients taking ART at AMH and AMHC, Feb. 1, 2006 and Jan. 30, 2014

During Bivariate analysis of Cox-proportional hazard regression only six baseline variables have showed significant association with death at a 5% level of significance. By this analysis, variables: education status, taking prophylaxis, and baseline HgB level were significant at P-value of less than 0.25. Therefore, these variables were retained for multi variable analysis in addition to the above four variables (Table 5). Factors strongly associated with mortality in bivariate analysis were gender men vs. women (p=0.004) marital status, divorced vs. never married (p=0.05) baseline functional status, bed ridden vs. working (p=0.001) late vs. early ART initiation (p=0.003) and baseline CD4 count (p=0.001). After adjustment baseline functional status (p=0.001), baseline CD4 count (p=0.001) remained significantly associated with mortality. Male gender had 2.05 (95 % CI =

1.33-3.15; p=0.001) times higher risk to death compared to female. Among all death recorded in this cohort group, about 79(88.3%) were occurred among the late presentation group. Late presenters were 1.97 (P-Value 0.009, 95% CI 1.41- 2.74) times more risk to death compared to early presenters. (Table 5)

Table 5 Bivariate and Multivariable Cox regression analysis of baseline characteristics HIV patients initiated ART at AMH and AMHC during 2006-2014

Variable		No. death	Bivariate analysis		Multi variable analysis		
			CHR	P-value	AHR	95% CI	P-value
Age	15-24year	10	1.01	0.943	.923	0.55-1.54	0.76
	25-34 year	42	0.93	0.664	1.045	0.75-1.44	0.79
	35-44 year	20	0.774	0.198	.756	0.50-1.12	0.16
	≥45year	17	1				
Gender	Male	51	1.79	0.004	2.05	1.33 -3.15	0.001
	Female	38	1		1		
Residences	Urban	78	1.38	0.313			
	Rural	11	1				
Marital Status	Never married	12	1		1		
	Married	43	0.275	0.119	2.13	1.23-3.67	0.021*
	Separated	12	0.837	0.613	0.49	0.33-0.72	0.03*
	Divorced	17	3.44	0.05	1.57	0.92-3.56	0.19
	Widowed	5	0.264	0.02	1.03	0.47-2.47	0.57
Education	No education	28	1.51	0.12	1.37	0.32-3.24	0.097
	Primary	38	1.38	0.26	1.23	0.48-2.50	0.49
	Secondary and above	23	1		1		
	WHO stage only	17	2.31	0.21	1. 26	0.72-3.15	0.313
Eligibility	Clinical and TLC	13	0.59	0.03	0.61	0.28-1.17	0.076
	CD_4	59	1		1		
Functional status	Working	62	1		1		
	Ambulatory	17	1.417	0.20	1.51	0.70-3.24	0.289
	Bedridden	10	2.589	<0.001	6.02	2.62-13.81	<0.001
Prophylaxis	Use	27	0.31	0.19	0.54	0.28 -0.81	0.061
	Not Use	64	1				
Presentation	Early	10	1				
	Late	79	1.58	0.003	1.97	1.41-2.74	<0.001
Adherences Status	Good	34	0.72	0.287			
	Poor	3	1				
CD_4 count		89	0.99(B= -0.009)	<0.001	0.991	0.998-0.995	<0.001
Hemoglobin		89	0.911(B= -093)	0.089	0.888	0.805-0.981	0.019*

After conducting separate analysis for the two cohort (Men vs. Women) (Table 6), predictors of mortality was determined for each group. Baseline CD4 count remained statistically significant with mortality in each gender group (AHR=0.98, 95% CI=0.97-0.99). Men aged ≥45 years had 3.78 (95% CI=1.21-4.46; *P*=0.001) times more risk to death compared to those aged 15-24 and men having history of any regimen change were 2.24 times (*P*=0.005; 95% CI=1.28-3.92) more risk compared to those who had not. In addition to women's baseline CD4 count, their baseline functional status was predictor of mortality. Where, women with bed ridden as functional status had more than six times (*P*=0.001; 95% CI=2.87-14.83) risk to death than women who had working as functional status. .

Table 6 Multi variable Cox regression analysis of baseline and follow up characteristics HIV patients initiated ART atAMH andAMHC grouped by gender during 2006-2014

		Female					Male				
		Bivariate analysis		Multi variable analysis			Bivariate analysis		Multi variable analysis		
Variable		CHR	P value	AHR	95%CI	P-value	CHR	P-value	AHR	95%CI	P-value
Age	15-24year										
	25-34 year	0.09	0.474	0.12	0.03-0.57	0.122	2.26	0.186	1.74	0.26-11.51	0.566
	35-44 year	0.05	0.327	0.06	0.01-0.40	0.062'	1.72	0.393	0.73	011-503	0.747
	245year	0.42	0.638	0.24	0.04-1.62	0.242	3.13	0.08	3.78	1.21-4.46	0.001'
Residences	Urban	1.00									
	Rural	1.05	0.837	1.10	0.18-6.82	0.922	1.31	0.259	0.61	0.024-1.61	0.241
Marital Status	Never married										
	Married	0.29	0.011	0.29	0.06-1.33	0.11	0.90	0.807	0.99	0.15-6.55	0.995
	Separated	0.44	0.208	0.38	0.04-3.51	0.391	1.88	0.247	3.98	0.56-28.08	0.166
	Divorced	0.92	0.861	0.74	0.11-4.89	0.755	1.11	0.87	0.49	0.03-8.51	0.624
	Widowed	0.16	0.091	0.06	0.98-1.78	0.984	3.56	0.051	1.54	0.13-18.38	0.734
Education	No education	0.94	0.799				1.08	0.721			
	Primary	1.04	0.857				0.96	0.823			
	Secondary and above										
Eligibility	WHO stage only										
Criteria	Clinical and TLC	0.97	0.944				0.99	0.973			
	CD_4	0.70	0.413				0.71	0.442			
Functional status	Working										
	Ambulatory	1.86	0.154	1.67	0.70-4.00	0.249	1.11	0.762	0.76	0.26-2.17	0.603
	Bed ridden	7.19	0.001	6.52	2.87-14.83	0.001'	0.43	0.407	0.64	0.08-5.48	0.686
Regimen	Yes	1.00									
Change	No	1.20	0.26	1.32	0.77-2.28	0.331	1.18	0.067	2.24	1.28-3.92	o.oo5'
Adherences	Good										

ww

6. DISCUSSION

In this cohort, analyses demonstrate that among patients initiating ART between 2006 and 2013 at public health sectors of Arba Minch town in Southwest Ethiopia, gender difference and survival ratio were examined. In most of previously conducted studies a large proportion of HIV-infected individuals, present at clinics for care with advanced stages of the disease (WHO stage 3 and 4 or CD4 < 200 cells/µl)(5,34,37,41). In this study, more than two third (68.6%) of the study participants were late presenter to HIV/AIDS chronic care. Of these, the majority (54.1%) were male in gender. Compared to studies conducted in Africa and the developed world, late initiation to HIV/AIDS care is high. In a South African cohort, 36% of HIV-infected individuals had a CD4 count <200 cells/µL and 31% presented HIV-related symptoms (WHO stage 3/4) at the time of diagnosis(39). Whereas only 15-45% of study participants in the developed world presented late for HIV/AIDS care(34). The problem will become even worse, if we consider ART eligibility criteria, in which HIV infected individuals in the developed world initiate ART early in the course of the disease than developing countries(10-11).

In our study, a significant gender differences at entry in to HIV/AIDS care was observed. Compared to men, women had a 41% reduction to be present late to HIV/AIDS care (P-Value 0.008, 95% CI 0.408- 0.863). Again women had a better baseline median CD4 count than men. This finding is comparable with a study which was done in Cameroon where, being a male was 1.49 times more likely to initiate ART late than a female(17).

When asked about reasons for late initiation to HIV/AIDS care, participants from focussed group discussion expressed that; fear of stigma, substance abuse, and low awareness to HIV/AIDS were the common factors that hinder men to attend ART early. Whereas women's responsibility for children, being pregnant and having frequent contact with health professionals lead women to familiar with the health care system and thus, they will initiate HIV/AIDS care earlier in the course of their disease. This finding is comparable with a study conducted in Malawi (using qualitative data collection method) and Ethiopia. In these studies, women's frequency of testing, health awareness and commitment to children led to earlier ART uptake and that men's commitment to wider social networks of influence, masculine ideals of strength, and success with sexual and marital partners led them to refuse treatment until they were sick(41, 46).

Compared to women, more than twice higher rate of death was observed in men (p-value=0.001, 95% CI1.33 - 3.15). High rates of death among men than women was also reported in Uganda and South Africa studies, indicating that men are 1.43 and 1.47 times more likely to die than women, respectively (24,51). However, no significant difference in survival rates between the sexes was reported in a study conducted in Oromiya, Ethiopia (15).

Differences in survival among the gender groups might be the fact that, late presenters had nearly twice (1.97; P-Value 0.001, 95% CI: 1.41–2.74) more risk to death compared to early presenters. This difference might be due to disparities observed in some demographic and HIV disease characteristic at entry in to HIV/AIDS care. Like more men than women likely had previous opportunistic infections and tended to have higher positive TB test and also had lower CD4 cell counts and were older than women.

In multivariable analysis, using Median CD4 count, age, PMTCT, residence and ART drug adherence, regimen change, level of Hgb, functional status; an increased risk of mortality was found among men than women. Men in advanced age groups (age ≥45 years) were found to have more than three times risk of death compared to those within 15-24 age groups. Having lower baseline CD4 count and previous history of any regimen change were also independent predictors of mortality in men. However, functional status of women and lower level of CD4 count at baseline were independent predictors of mortality in women. This finding was similar to studies from sub-Saharan Africa which reported; men appear to initiate ART at older ages and with more advanced HIV disease stage than women(18,22), and markers of advanced HIV disease at the time of ART initiation strongly predict early mortality on ART(45).

Our study revealed that, there was no association between gender and ART adherence, rather majority of the patients (93.5%) were found to have good ART adherence status. This finding is similar to a study conducted in Nekemte Referral Hospital, Western Ethiopia(31), but in contrast to a study from rural South Africa that reported adherence to prescribed ART was better in women than in men and explains differing rates of mortality between men and women on ART(53). This difference might be related to the existing instruments used in the study area for measuring adherence status.

This study has its own limitations; the outcome of the study was measured from data that was obtained from secondary data sources. Information which were not included in the study might have affected the true result of the research. It is possible that there is systemic difference between ART patients who were and were not included in the study. Gender difference in mortality could be under- or overestimated, as data on death were non cause specific. So some deaths could have been non-HIV related.

7. CONCLUSION AND RECOMMENDATION

Conclusion

In our study, late initiation to HIV/AIDS care was high and a significant gender differences at entry in to HIV/AIDS care was documented. Compared to women, more men present to HIV/AIDS care late in the course of the disease. Similarly, women had a better baseline median CD4 count than men. Again, differences in survival among the gender groups were observed.

Recommendation

Reducing gender disparity and improving HIV/AIDS testing and linkage to care, may have a large impact on mortality reduction, control of new infections, and the economic impact of HIV/AIDS.

- Organizations working in HIV/AIDS care should continuously evaluate their targeted campaigns and recognize that males and females are both severely affected by the epidemic in differing ways, and should plan for interventions that engage men.
- HIV/AIDS prevention and control programs in Gamo gofa zonal health desk should develop suitable strategies, like arrangement of campaigns in areas frequented by men, in order to enhance men's early engagement to HIV/AIDS care.
- Besides the care provided to HIV/AIDS patients in the health facilities, in the Arbaminch town as static services, they should also organize awareness creation programs to people living with HIV, to come early to the HIV/AIDS care and remain in care.
- Finally further prospective cohort studies should be conducted to have a detail understanding on gender disparities in ART access and health outcome.

8. REFERENCES

1. UNAIDS. UNAIDS report on the global AIDS epidemic 2013. Geneva, Switzerland: UNAIDS; 2013.

2. National AIDS resource center: HIV/AIDS estimates and projections in Ethiopia, 2011-2016.Addis Ababa, Ethiopia; 2013.

3. Lahuerta M, Lima J, Nuwagaba-Biribonwoha H, Okamura M, Alvim MF, et al. Factors Associated with Late Antiretroviral Therapy Initiation among Adults in Mozambique. PLoS ONE.2012; 7(5):1-10 e37125. doi:10.1371/journal.pone.0037125.

4. Antinori A, Coenen T, Costagiola D, Dedes N, Ellefson M, et al. Late presentation of HIV infection: a consensus definition. HIV Med . 2011; 12: 61- 64. .

5. Maria L, Frances U, Susie H, Batya E,Sarah G et al.The Problem of Late ART initiation in Sub-Saharan Africa: A Transient Aspect of Scale-up or a Long-term Phenomenon? J Health Care Poor Underserved. 2013; 24(1): 359-383. doi:10.1353/hpu.2013.0014.

6. Krentz H. B. and Gill M. J. The DirectMedical Costs of Late Presentation (<350/mm3) of HIV Infection over a 15-Year Period. AIDS Research and Treatment.2012 , ID 757135, doi:10.1155/2012/757135

7. Girardi, E., MS. Aloisi and C. Aloisi . Delayed Presentation and Late Testing for HIV: Demographic and Behavioural Risk Factors in a Multicenter Study in Italy. Journal Acquir Immune Defic Syndr. 2004; 36:951-959.

8. Marks, G, N. Crepaz and JW. Senterfutt. Meta-analysis of high-risk sexual behaveior in persons aware and unaware they are infected with HIV in the United States: implicateons for HIV prevention programs. Journal Acquire Immune Deific Snyder.2005; 39: 446-53.

9. Castilla, J., J. Del Romero and V. Hernando. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. Journal Acquire Immune Deific Snyder. 2005; 40: 96-101.

10. Boulle A, Van Cutsem G, Hilderbrand K, et al. Seven-year experience of a primary care antiretroviral treatment programme in Khayelitsha, South Africa. AIDS. Feb 20; 2010 24(4):563- 572. [PubMed: 20057311].

11. Charurat M, Oyegunle M, Benjamin R, et al. Patient retention and adherence to antiretrovirals in a large antiretroviral therapy program in Nigeria: a longitudinal analysis for risk factors. PLoS One. May 11.2010 5(5):e10584. [PubMed: 20485670].

12. El-Sadr WM, Hoos D. The President's emergency plan for AIDS Relief-is the emergency over? N Engl J Med. 2008 359(6):553-555. [PubMed: 18669420].

13. Stephen D, Anthony D, Xavier A, Landon M, Robin W. Early mortality among adults accessing antiretroviral treatment programs in sub-Saharan Africa. 2008; 22:1897-1908

14. Mulissa Z, Jerene D, Lindtjørn B Patients Present Earlier and Survival Has Improved, but Pre-ART Attrition Is High in a Six-Year HIV Cohort Data from Ethiopia. PLoS ONE. 2010;5(10):1-9 e13268. doi:10.1371/journal.pone.0013268.

15. Andinet W and San Sebastia´ n M. Determinants of survival in adult HIV patients on antiretroviral therapy in Oromiyaa, Ethiopia. Global Health Action. 2010;3: 5398 - DOI: 10.3402/gha.v3i0.5398.
16. Good adherence to HAART and improved survival in a community, HIV/AIDS treatment And care program; the experience of the AIDS support organization (TASO), Kampala, Uganda. BMC health services research. 2008;8:241

17. Poka-Mayap V, Pefura-Yone EW, Kengne AP, et al. Mortality and its determinants among patients infected with HIV-1 on antiretroviral therapy in a referral centre in Yaounde, Cameroon: a retrospective cohort study. BMJ Open. 2013;3:e003210. doi:10.1136/bmjopen-2013-003210.

18. Braitstein P, Boulle A, Nash D, Brinkhof M, Dabis F, et al. Gender and the use of antiretroviral treatment in resource-constrained settings: findings from a multicenter collaboration. J Womens Health. 2008;17: 47-55. .

19. Muula A, Ngulube T, Siziya S, Makupe C, Umar E, et al. Gender distribution of adult patients on highly active antiretroviral therapy (HAART) in Southern Africa: a systematic review. BMC Public Health. 2007;7: 63.

20. Stenehjem E, Shlay JC. Sex-specific differences in treatment outcomes for patients with HIV and AIDS. Expert Rev Pharmacoecon Outcomes Res. 2008; 8: 51-63.

21. Hawkins C, Chalamilla G, Okuma J, Spiegelman D, Hertzmark E, et al. Gender differences in antiretroviral treatment outcomes among HIV-infected adults in Dar es Salaam, Tanzania. AIDS. 2011;25: 1189-1197

22. Taylor-Smith K, Tweya H, Harries A, Schoutene E, Jahn A. Gender differences in retention and survival on antiretroviral therapy of HIV-1 infected adults in Malawi. Malawi Med J 2010;22: 49-56.

23. Kipp W, Alibhai A, Duncan Saunders L, Senthilselvan A, Kaler A, et al. Gender differences in antiretroviral treatment outcomes of HIV patients in rural Uganda. AIDS Care. 2010;22: 271-278.

24. Mills EJ, Bakanda C, Birungi J, Chan K, Hogg RS, et al. Male gender predicts mortality in a large cohort of patients receiving antiretroviral therapy in Uganda. J Int AIDS Soc. 2011;14: 15-30.

25. Zachariah R, Fitzgerald M, Massaquoi M, Pasulani O, Arnould L, et al. Risk factors for high early mortality in patients on antiretroviral treatment in a rural district of Malawi. AIDS. 2006;20: 2355-2360.3.

26. Mills EJ, Beyrer C, Birungi J, Dybul MR. Engaging Men in Prevention and Care for HIV/AIDS in Africa. PLoS Med. 2012;9(2): e1001167. doi:10.1371/journal.pmed.1001167.

27. Bila B, Egrot M. Gender asymmetry in healthcare-facility attendance of people living with HIV/AIDS in Burkina Faso. Social Science and Medicine. 2009;69: 854-861.

28. Obermeyer CM, Sankara A, Bastien V, Parsons M. Gender and HIV testing in Burkina Faso: an exploratory study. Social Science and Medicine.2009;69: 877-884.

29. WHO/UNAIDS/UNICEF (2009) Towards Universal Access: scaling up priority HIV/AIDS interventions in the health sector: progress report 2009.

30. Assefa Y, Jerene D, Lulseged S, Ooms G, Van Damme W. Rapid scale-up of antiretroviral treatment in Ethiopia: successes and system-wide effects. PLoS Med. 2009; 6: e1000056.

31. Teshome M., Ali A., Dessie Y. Determinants of Mortality among HIV Positives after Initiating Antiretroviral Therapy in Western Ethiopia: ISRN AIDS. 2013, ID 491601, <http://dx.doi.org/10.1155/2013/491601>.

32. Assefa T, Wencheko E. Survival analysis of patients under chronic HIV-care and antiretroviral treatment at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Ethiop. J. Health Dev. 2012;26(1):22-29

33. Badri, M., Lawn SD. and Wood R. Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study. Lancet.2006.*;368:1254-1259.*

34. Mugavero MJ., Castellano C. and Edelman D. Late diagnosis of HIV infection: the role of age and sex. Am Journal Med. 2007*;120:370-373.*

35. Mocroft A, Lundgren JD, Sabin ML, Monforte Ad, Brockmeyer N, et al. Risk Factors and Outcomes for Late Presentation for HIV-Positive Persons in Europe: Results from the Collaboration of Observational HIV Epidemiological Research Europe Study (COHERE). PLoS Med. 2013;10(9): e1001510. doi:10.1371/ journal.pmed.1001510.

36. Schwarcz S., Hsu L. and Dilley JW. Late diagnosis of HIV infection: trends, prevalence, and characteristics of persons whose HIV diagnosis occurred within 12 months of developing AIDS. Journal Acquir Immune DeficSyndr. 2006;43:491-494.

37. Forbi JC, Forbi TD, Agwale SM. Estimating the time period between infection and diagnosis based on CD4+ counts at first diagnosis among HIV-1 antiretroviral naive patients in Nigeria. J Infect Dev Ctries. Oct 28; 2010;4(10):662-667. [PubMed: 21045361.

38. Moon TD, Burlison JR, Blevins M, Shepherd BE, Baptista A, et al. Enrolment and programmatic trends and predictors of antiretroviral therapy initiation from president's emergency plan for AIDS Relief (PEPFAR)-supported public HIV care and treatment sites in rural Mozambique. Int J STD AIDS. 2011;22: 621-627. doi: 10.1258/ijsa.2011.010442]. .

39. April MD, Walensky RP, Chang Y, et al. HIV testing rates and outcomes in a South African community, 2001-2006: implications for expanded screening policies. J Acquir Immune Defi Syndr. Jul 1; 2009;51(3):310-316. [PubMed: 19582895])

40. Ongolo-Zogo, P.; Loubiere, S.; Boyer, S., et al. Determinants of delayed first consultation afterdiagnosis of HIV infection in Cameroon: results from the ANRS EVAL 12-116 study; Presentedat: Conference on AIDS; Nov 2008; Mexico City (Mexico). 21356115.

41. Abaynew Y, Deribew A, Deribe A. Factors associated with late presentation to HIV/AIDS care in South Wollo ZoneEthiopia: a case-control study. AIDS Res Ther. Feb 28.2011 8(1):8. [PubMed: 21356115].

42. Mills EJ, Ford N, Mugyenyi P. Expanding HIV care in Africa: making men matter. Lancet. 2009;374:275-276.

43. Ford N, Kranzer K, Hilderbrand K, et al. Early initiation of antiretroviral therapy and associated reduction in mortality, morbidity and defaulting in a nurse-managed, community cohort in Lesotho. AIDS. Nov 13; 2010 24(17):2645-2650. [PubMed: 20980868]). .

44. Kigoz, LM. , Dobkin LM. and Martin JN.. Late-Disease Stage at Presentation to an HIV Clinic in the Era of Free Antiretroviral Therapy in Sub-Saharan Africa. Journal of Acquired Immune Deficency Syndrome. 2009; 52(2): 280-289.

45. Kanters S., Nansubuga M., Mwehire D. et al . Increased mortality among HIV-positive men on antiretroviral therapy: survival differences between sexes explained by late initiation in Uganda .HIV/AIDS - Research and Palliative Care. 2013;5 :111-119.

46. Parrott FR, Mwafulirwa C, Ngwira B, Nkhwazi S, Floyd S, et al. Combining Qualitative and Quantitative Evidence to Determine Factors Leading to Late Presentation for Antiretroviral Therapy in Malawi. PLoS ONE. 2011;6(11): e27917. doi:10.1371/journal.pone.0027917.

47. Chen SC, Yu JK, Harries AD, et al. Increased mortality of male adults with AIDS related to poor compliance to antiretroviral therapy in Malawi. Trop Med Int Health. 2008; 13: 513-519

48. Cornell M, Schomaker M, Garone DB, Giddy J, Hoffmann CJ, et al. Gender Differences in Survival among Adult Patients Starting Antiretroviral Therapy in South Africa: A Multicentre Cohort Study. PLoS Med. 2012,9(9): e1001304. doi:10.1371/journal.pmed.1001304.

49. Johannessen A. Are men the losers of the antiretroviral treatment scale-up? AIDS. 2011;25: 1225-1226.

50. Ingle SM, May M, Uebel K, Timmerman V, Kotze E, et al. Differences in access and patient outcomes across antiretroviral treatment clinics in the Free State province: a prospective cohort study. S Afr Med J. 2010;100: 675-681.

51. May M, Boulle A, Phiri S, Messou E, Myer L, et al. Prognosis of patients with HIV-1 infection starting antiretroviral therapy in sub- Saharan Africa: a collaborative analysis of scaleup programmes. Lancet 2010;376: 449-457.

52. Kidder DP, Bachanas P, Medley A, Pals S, Nuwagaba-Biribonwoha H, et al. HIV Prevention in Care and Treatment Settings: Baseline Risk Behaviors among HIV Patients in Kenya, Namibia, and Tanzania. PLoS ONE. 2013;8(2): e57215. doi:10.1371/journal.pone.0057215.

53. Mac Pherson P, Moshabela M, Martinson N, et al. Mortality and loss to follow-up among HAART initiators in rural South Africa. Trans R Soc Trop Med Hyg 2009;103:588-93.

54. Tsegaye E., Worku A.Assessment of antiretroviral treatment outcome in public hospitals, South Nations Nationalities and Peoples Region, Ethiopia. Ethiop. J. Health Dev. 2011;25 (2):102-109.

55. Gamo Gofa Zone Health department . Annual health report 2013 ,Gamo Gofa Ethiopia.

56. Dr. Jerry L. Hintze and NCSS . PASS (power analysis and sample size system) (http://www.ncss.com.26/11/13.

57. Federal HIV/AIDS Prevention and Control Office,2008. Progress towards Implementation of the UN Declaration of Commitment on HIV/AIDS. Federal Ministry of Health Ethiopia, Addis Ababa, Ethiopia, Progress Report :2008.

58. Crawford and Maracek 1989; Balmer 1994; Cook 1994.

9. APPENDICES

DECLARATION

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

Name: _____

Signature: _____

Name of the institution: _____

Date of submission: _____

This thesis has been submitted for examination with my approval as University advisor

Name and Signature of the first advisor _____

_____

Name and Signature of the second advisor _____

_____

Appendix:- A. Participant information sheet and consent form

Participant information sheet and consent form prepared for leader of selected Health Institution.

Title**:** gender disparities in enrollment to HIV/AIDS care and survival among patients on anti retroviral therapy in Arba Minch town Gamo Gofa, Ethiopia

Name of Principal investigator**: Andamlak Gizaw**

Name of the organization: Jimma University, College of public Health and Medical sciences

Introduction

This information sheet and consent form is prepared to explain the study, which your institute is being asked to join. Please listen carefully and ask any questions about the study before you give permission to conduct the study in your organization. You may ask questions at any time after joining the study.

Purpose of the Research Project

The main purpose of this research is to acquire master degree in Public Health. As an outcome the study will evaluate **gender disparities in both (enrollment to HIV/AIDS care and survival).** The research will be helpful in comparing gender differences in presentation to HIV/AIDs care and in determining the survival differences between gender groups. This will help in exploring the reasons underlying. Any difference could inform strategies designed to address these differences and interventions that ultimately increase the effectiveness of HIV care and treatment scale-up. It will also serve as a springboard for subsequent studies in the country.

Procedure

The study will be conducted in Arba Minch town among patients on HAART. Data necessary for the research will be collected by revision of patients' medical records. At the end pattern of Enrollment to HIV/AIDS care and survival status will be compared. Arba Minch hospital and Health center are selected to the study. Those patients who fulfill the inclusion criteria of the

study in both health institutes will be included in the study. To selected eligible study units and to collected important data for the study patients medical record will be reviewed. Your organization is one of the health facility selected for this research. If you are willing to give permission to conduct the study in your organization, you need to understand and sign the agreement form. All collected data and the results obtained will be kept confidentially by using coding system whereby no one will have access to the data.

Risk/ Discomfort

By participating in this research project, you may feel that it has some discomfort especially on confidentiality of patient's information. We hope you will give permission to conduct the study for the sake of the benefit of the research result and we will keep confidentiality of the patients' information.

If your organization participates in this research project, there may not be direct benefit to you or your organization but participation is likely to help us in assessing immunological responses of HAART patients. Ultimately, this will help us to contribute something on HIV treatment in the study area.

Compensations

You will not be provided any payment or incentives to take part in this project; because there is no any cost or resource you will miss due to participation in the research

Confidentiality:

The information collected from this research project will be kept confidential and information about any patient collected by this study will be stored in a file, without patients' name, but a code number assigned to it. In addition, it will not be revealed to anyone except the principal investigator and will be kept locked with key.

Right to refuse or withdraw:

You have full right to refuse from participating in this research. You have also the full right to withdraw from this study at any time you wish, without losing any of your right. If you would like to know more, please contact:

Address of the Principal investigator Andamlak Gizaw Mob. 0912 038993

E-mail gizandal@gmail.com

Po.box _____Jimma University College of Public Health and Medical sciences

I thank you in advance for taking your time to answer our questions.

Would you be willing to give permission to participation of your organization in the study?

If no, please stop here

If yes, sign below.

Consent of the participant:

I the undersigned have been informed that the purpose of this research project. Based on the above information I give permission to conduct the research in this institution voluntarily.

_____ _____

Signature of Participant Date

Thank you for your cooperation

Appendix B :.- Data abstracting form

Jimma University College of Public Health and Medical sciences

Data retrieving form for assessment of gender disparities in enrollment to HIV/AIDS care and survival among patients on anti retroviral therapy in Arba Minch town Gamo Gofa, Ethiopia.

Form identification number_____

ART unique .ID no----------__/__/___/_____

Patient's Card No ----------_/__/___/____

Name of Data Collector_____ Signature----------

Name of Supervisor _____Signature----------

Health facility Name_____Date of retrieval_____/_____/2014

Part-I SOCIO DEMOGRAPHIC CHARACTERISTICS **(**HIV Care/ART clinic intake form **A** patient registration form**)**

No	Question	Possible response	Answer	Remark
101	Age at enrollment to ART	In year ----------		
102	Sex	0. Female 1. Male		
103	Marital Status	1. Never married 2. Married 3. Separated 4. Divorced 5. Widow		
104	Level of Education	1. No education 2. Primary 3. Secondary 4. Tertiary		

105	Religion	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 5. Other		
106	Occupation	1. Housewife 2. Private employ 3. Driver 4. Governmental employ 5. Teachers 6. Merchant 7. Military(police/ solder) 8. Other		
107	Ethnicity	1. Gamo 2. wolayta 3. konso 4. Amhara 5. Goffa 6. Other, specify--------		
108	Address	1. Urban 2. Rural		
109	Dependent children at home (children age <5)	1. Yes 2. No		
Part-II Base line clinical, laboratory and ART information				
110	Past TB test (a year before initiation of ART)	1. No 2. Negative 3. Positive 4. Not determined		If 110 is 1 skip to 113
111	When positive		_____month	
112	Past TB treatment	1. No 2.2SRHZ/6EH 3.2HRZES/1HRZE/5HRE 4.2HRZE/6HE		
113	Past medications	1. No 2. Cotrimoxazole 3. INH 4. Other specify----------		

114	Past Opportunistic infection	1. No 2. Yes		If 114 is 1 skip to 116
115	Opportunistic infection	1. CMV 2. PCP 3. PGL 4. PML 5. EPTB 6.Candidiasis 7. Diarrhea 8. Pneumonia 9. Herpes simplex 10. Kaposi sarcoma 11.Toxoplasmosis 12.Encephalopathy 13.Wastingsyndrome 14.Herpes zoster 15. Other specify-------		Look for specific diagnosis code at the end of this form *more than 1 ans. is possible
116	CD4 count at base line		-------cell/l date__/___/__	
117	Hgb count at base line		----------	
118	TLC count at base line		----------	
119	Weight at base line		---------- K.G	
120	Height at base line		---------- CM	
121	Pregnancy status at base line (for females)	1. Pregnant 2. Non- pregnant		
122	Functional status at base line	1. Working 2. Ambulatory 3. Bed ridden		
Part-III ART treatment				
124	ART eligibility criteria	1. CD4<200 2. WHO stage IV 3. WHO stage II and III with TLC<1200		

125	OI prophylaxis given	1. Not given 2. Cotrimoxazole 3. INH 4. Fluconazole 5. Others specify----------		
126	Starting regiment	1. 1a(30)=d4t(30)-3TC-NVP 2. 1a(40)=d4t(40)-3TC-NVP 3. 1b(30)=d4t(30)-3TC-EFV 4. 1b(40)=d4t(40)-3TC-EFV 5. 1c=AZT-3TC-NVP 6. 1d=AZT-3TC-EFV		
Part-IV patient follow up information (filled from ART follow up form) recent results				
127	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		
128	Date of confirmed HIV+	Date/Month/year	__/___/_____ __	
129	Eligible date	Date/Month/year	__/___/_____ __	
130	Last follow up date	Date/Month/year	__/___/_____ __	
131	Duration since initiation of ART		----------month	
132	Recent weight		----------kg	
133	Recent Functional status	1. Working 2. Ambulatory 3. Bed ridden		
134	Recent WHO clinical staging of HIV	1. Stage II 2. Stage III 3. Stage IV		

135	INH given	1. No 2. Yes		If 134 is 1 skip to 136
136	Date of INH start	Date/Month/year	____/___/____	
137	Recent TB Screened	1. No 2. Negative 3. Positive		If 136 is 1,2 go to 138
138	When positive		_____month	
139	TB treatment	1. No 2.2SRHZ/6EH 3.2HRZES/1HRZE/5HRE 4.2HRZE/6HE		
140	Recent Opportunistic infection	1. No 2. Yes		If 139is 1 go to 141
141	Recent Opportunistic infection	1. CMV 2. PCP 3. PGL 4. PML 5. EPTB 6.Candidiasis 7. Diarrhea 8. Pneumonia 9. Herpes simplex 10. Kaposi sarcoma 11.Toxoplasmosis 12.Encephalopathy 13.Wastingsyndrome 14.Herpes zoster 15. Other specify-------		Look for specific diagnosis code at the end of this form *more than 1 ans. is possible
142	Cotrimoxazole	1. Given 2. Not given		If 141 is 1 skip to 143
143	Date of Cotrimoxazole (CTX) start	Date/Month/year	____/___/____	

144	Recent ARV adherence	1. Good 2. Poor		If 143 is 1 skip to 145
145	Reason for 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----------		
146	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----------		
147	Starting regiment	1. 1a(30)=d4t(30)-3TC-NVP 2. 1a(40)=d4t(40)-3TC-NVP 3. 1b(30)=d4t(30)-3TC-EFV 4. 1b(40)=d4t(40)-3TC-EFV 5. 1c=AZT-3TC-NVP 6. 1d=AZT-3TC-EFV		
148	Any regimen change	1. No 2. Yes		If 147 is 1 skip to 149
149	If yes to what regimen	1. 1a(30)=d4t(30)-3TC-NVP 2. 1a(40)=d4t(40)-3TC-NVP 3. 1b(30)=d4t(30)-3TC-		

		EFV 4. 1b(40)=d4t(40)-3TC-EFV 5. 1c=AZT-3TC-NVP 6. 1d=AZT-3TC-EFV		
150	Reason for regimen change	1. Toxicity/SE 2. Pregnancy 3. Risk of pregnancy 4. New drug available 5. Drug out of stoke 6. Clinical failure 7. New TB 8. Other specify----------		
151	Is regimen stopped	1. No 2. Yes		
152	Reason for stopping regimen	1. Pregnancy 2. toxicity/SE 3. Treatment failure 4. Poor adherence 5. Drug out of stock 6. Lack of finance 7. Other patient decision 8. Planned treatment interruption 9. Other specify----------		
153	Recent CD4 count		_____cell/µl Date----/----/---	
154	Recent TLC count		--------- Date----/----/---	
155	Recent Hgb count			
156	Current status	1.Alive 2. Dead	date__/___/___	