ADDIS ABABA UNIVERSITYCOLLEGE OF NATURAL AND COMPUTATIONAL SCIENCES DEPARTMENT OF ZOOLOGICAL SCIENCES

HEALTH STATUS IN ADOLESCENT AND ADULT HIV/AIDS CASES ON ANTIRETROVIRAL THERAPY AT ALEMBANK HEALTH CENTER, WEST ADDIS ABABA

THESIS SUBMITTED TO DEPARTMENT OF ZOOLOGICAL SCIENCES, SCHOOL OF GRADUATE STUDIES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN BIOLOGY

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DECLARATION

This is to certify that the thesis prepared by -Nefissa Seid, entitled: health status in adolescent and Adult HIV/AIDS cases on ART at Alembank Health Center, Addis Ababa, and submitted in partial fulfillment of the requirements for the degree of Master of Science in Biology complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Thesis title health status in adolescent and adult HIV/AIDS cases on ART at Alembank Health Center, West Addis Ababa.

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ACRONYMS

3TC	Lamivudine
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
AZT	Zidovudine,
cART	combination Antiretroviral therapy
CD4	Cluster Designation four
CDC	Center of Disease Control and Prevention
COP/ROP	Ethiopia Country/Regional Operational Plan
CSA	Central Statistical Agency
DHHS	Department of Health and Human Services
EFV	Efavirenz
EPHI	Ethiopian Public Health Institute
FMOH	Federal Ministry of Health
HAART	Highly Active Antiretroviral Treatment
HAPCO	HIV Control and Prevention Office.
Hb	Hemoglobin
HC	Health Center
HCT	HIV Care and Treatment Services
HIV	Human Immunodeficiency Virus
LTFU	Lost to follow-up
NNRTIs	Non-Nucleoside Reverse Transcriptase Inhibitors
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
NVP	Nevarapine
PITC	Provider Initiated Testing and Counseling
PLHIV	People living with HIV
PMTCT	Prevention of Mother-to-Child transmission
SPSS	Statistical Package for Social Sciences
TDF	Tenovudine
UNAIDS	United Nations Programme on HIV/AIDS
VCT	Voluntary Counseling and Testing
WHO	World Health Organization

Abstract

Although the human immunodeficiency virus (HIV) which is the cause of acquired immunodeficiency syndrome (AIDS) continues to be a major global public health problem, with the introduction of antiretroviral therapy (ART) a major breakthrough is achieved. However, the success rate of the ART service is variable from setting to setting influenced by multiple factors. The present study assessed the health status ofpeople living with HIV/AIDS attending ART service at Alembank Health Center, southwestern Addis Ababa. It is a retrospective cohort study that examinedthe records of participants on ART for a minimum of six months and a maximum of fiveyears.Baseline and post-ART initiation socio-demographic as well as clinical data such asCD4 count, body mass index, hemoglobin level, functional status and WHO HIV-stagingwereorganized the central outcome variable being CD4 count. Data were analyzed using SPSS version 16.0 and Microsoft Excel statistical software. Paired t-test and correlation (Pearson bivariate) were performed to test change in mean CD4 count after ART initiation and the association between the socio-demographic and clinical factors.Statistically significance of the associations was set at $p \leq 0.05$.The records of 388participants (64.9% female and 35.1% male) were complete and analyzed. The mean and median CD4 count increments, respectively,were 180.3(61.1%)and 183.5(72.2%)cells/µl from the baseline.Adherence was significantlycorrelated withincrease in CD4 count ($p=0.044$) and functional status ($p=0.018$) indicating thatwith good adherence CD4 count increases and performance improves. Also, asignificant relationshipwas observed between the WHO HIV-staging and nutritional status ($p=0.008$), with better nutritional status there is improvement in HIV clinical stage.Overall, there was significant increase in the mean of CD4 count, improvement in performance status and WHO clinical staging (from III&IV to I&II) compared to the baseline demonstrating the betterment of health status of the cohort. Hence, the study confirms that ART therapy with good adherence is effective in improving the health status of people living with HIV/AIDS.

Keywords/Phrases:ART,CD4 count, Factional status, Hemoglobin, HIV/AIDS, WHOclinical stage.

1. Introduction

1.1 Global Situation of HIV/AIDS

Acquired immunodeficiency syndrome (AIDS) was first recognized among homosexual men in the United States in 1981. Later the etiological agent, human immunodeficiency virus (HIV), was identified. Since then AIDS has become one of the world's most serious health and development challenges. At the end of 2017, there were an estimated 36.9 million people living with HIV/AIDS and 940,000 HIV-related deaths with two-thirds of people living with HIV (PLHIV) residing in sub-Saharan Africa (UNAIDS 2018a).

1.2 HIV transmission and progression to AIDS

HIV can be transmitted via the exchange of a variety of body fluids from infected individuals, such as blood, breast milk, semen and vaginal secretions. Studies showed that higher levels of viremia increase the risk for HIV transmission (Simon et al. 2006). It is established, however, individuals cannot become infected through ordinary day-to-day contact such as kissing, hugging, shaking hands, or sharing personal objects, food or water (CDC 2015).

Primary HIV infection is not easily recognized, because symptoms are nonspecific, consisting fever, malaise, generalized lymphadenopathy, pharyngitis, diarrhea and rash. Following primary infection, most persons have mild or no symptoms for several years (Palmisano et al. 2011). Over time, infection with the virus results in the progressive deterioration of the immune system, leading to immunodeficiency. A healthy, uninfected person usually has 500-1500 CD4+ T-cells per cubic millimeter of blood. During HIV infection, the number of these cells which are the main targets of the virus falls progressively.

HIV infection progresses through the increasing degrees of immune weakness. The clinical staging method is a standardized way to describe the condition having 4 distinct stages. The end-stage (stage 4) of the disease is full-fledged AIDS which is defined by varieties of opportunistic illnesses such as cryptococcal meningitis, severe bacterial infections and cancers like lymphomas and Kaposi's sarcoma. These illnesses are considered AIDS-related because they generally are uncommon in people with normally functioning immune systems (HHS-CDC, GAP 2009).

2. Antiretroviral therapy

Before the discovery of the first antiretroviral therapy (ART) and without specific treatment, HIV-infected persons progressed through all of the clinical stages. People usually died within a few years being diagnosed with AIDS. Although ART does not clear HIV infection it effectively suppresses viral replication and allows an individual's immune system to strengthen and regain the capacity to fight off infections. HIV can be suppressed by combination of ART consisting of three or more ARV (antiretroviral) drugs. ARV therapy is potent, convenient and usually well-tolerated, capable of reducing HIV blood concentration to undetectable values within a few weeks from treatment initiation and of inducing a vigorous and sustained CD4 T-cell gain (Mocroft et al. 2007, Kaufmann et al. 2003).

2.1 HIV lifecycle and ART inhibition

2.1.1 HIV lifecycle

Following HIV's entry into a host's system through a mucosal membrane or directly bloodstream it binds to dendritic cells or macrophages, which transport the virus to the lymphoid organs where resident cells having CD4 receptors allow HIV to gain access to the cell (Pope et al. 2003). Upon fusion with the target cell the virus uncoated, this only allows the core of HIV to enter into the cell cytoplasm. In the cytoplasm, the viral RNA is reverse transcribed into double stranded cDNA by HIV reverse transcriptase (Chinen 2002) then reverse transcription results in the HIV pre-integration complex (PIC). This large complex crosses into the nucleus to deposit the viral cDNA.

The viral cDNA is integrated into host's genome. Here the viral DNA can either be immediately transcribed into viral RNA or the virus can enter latency. Latency is when the viral cDNA remains silent in the host cell (Zheng et al. 2005). The cDNA is transcribed into multiple segments of viral RNA. The segments are assembled and released from the host cell and start searching for a new host (Sierra et al. 2005).

2.1.2 Classes of ART drugs and their mechanisms of action

The different stages of the replication cycle of HIV (fig. 1) correspond to the different classes of ART medications (Palmisano and Vella 2011). Drugs that can stop viral fusion with host cell and

entry are called fusion/entry inhibitors (FIs) and chemokine receptor antagonists (CRAs) (Rathbun et al. 2012). Chemokine receptor antagonists inhibit the entry of HIV into the host cell. Two chemokine receptors, CXCR4 and CCR5, are necessary for the virus to enter the cell, so by inhibiting these chemokine receptors the disease can be slowed (https://www.drugs.com/drug-class/chemokine-receptor-antagonist.html).The drugs that inhibit HIV genome integration with host cell and its reverse transcription are respectively called integrase inhibitors (IIs) and nucleoside reverse transcriptase inhibitors (NRTIs). HIV protein synthesis, processing and assembly, virion maturation, budding off and release from host cell are stopped by ART drug classes termed protease inhibitors (PIs) and maturation inhibitors (MIs).

The first class of antiretroviral are the Nucleoside Reverse Transcriptase Inhibiter (NRTIs) which have been in use since 1987, in the early nineties, the non-nucleoside reverse transcriptase inhibitors (NNRTIs), a second class of antiretroviral, became available. But because of the development of viral resistance the use of NNRTI's was limited (Iris et al. 2013). PIs are third class of antiretroviral introduced in 1996. For the treatment of people with HIV infection, the standard combination of ART recommended worldwide consists of three or more ART drugs of separate classes and become more effective (WHO 2012). These combinations are known as highly active antiretroviral therapy (HAART). HAART was important in the history of HIV treatment that turns HIV infection from fatal condition into chronic manageable disease (Paterson et al. 2000). Nowadays, just ART means HAART. In summary, so far there are six classes of antiretroviral drugs that are NRTIs, NNRTIs, PIs, IIs, FIs, and CRAs (Rathbun et al. 2012).

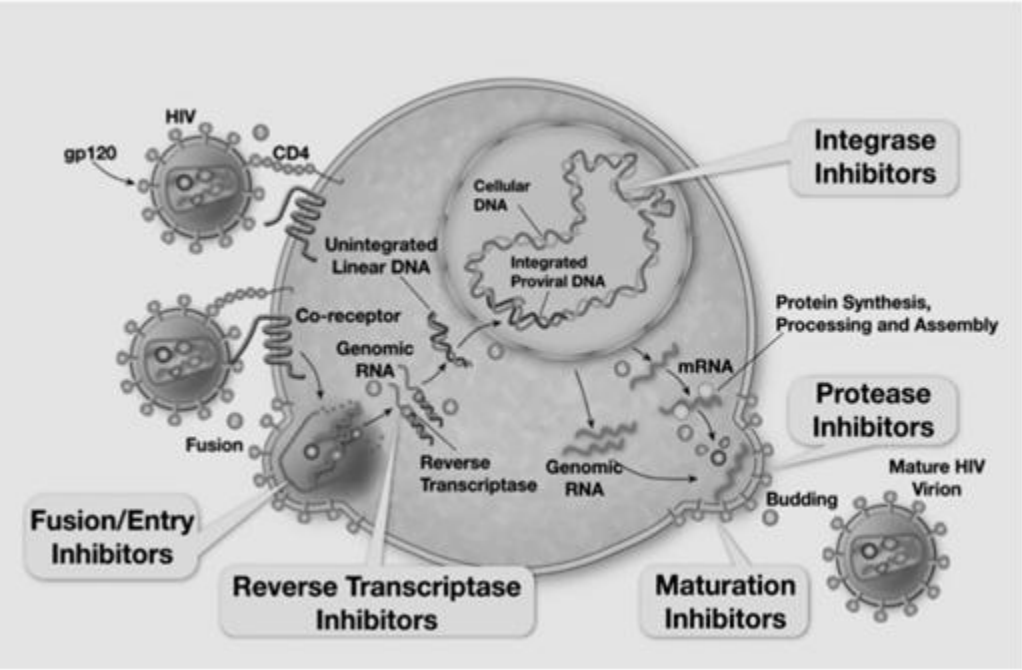

Figure 1 Targets of antiretroviral drugs in the HIV lifecycle (Source: Palmisano and Vella 2011)

2.2 Global ART coverage and impact

Following widespread deployment and implementation of ART service, new infection dropped by 47% globally since the peak in 1996 (UNAIDS 2017). In 2017, only 1.8 million new infections compared to 3.4 million in 1996. Since 2010, new HIV infections among adults declined by an estimated 16%, from 1.9 million to 1.6 million in 2017. AIDS-related deaths have been decreased by more than 51% since the peak 2004. In 2017, about 940 000 people died from AIDS-related illnesses worldwide, compared to 1.9 million in 2010 (WHO 2018). The decline reflects the increased availability of ART as well as care and support to people living with HIV, particularly in low and middle-income countries.

Starting ART using simplified, less toxic and more convenient regimens as fixed-dose combinations is recommended for first-line ART, once-daily regimens comprising two from NRTI and one from NNRTI. When ART is given to the infected partner at a higher CD4 count the risk of transmission is decreased by 96% when compared with those who started ART at CD4 counts <350cells/mm^3 (FMoH 2014a). Further, a study in China showed that immediate ART is associated with a 63% reduction in overall mortality among PLHIV with CD4 counts >500cells/mm^3 than delayed treatment (initiation after 30 days of diagnosis) which reduced

mortality only by 26% (Carter 2017). In general, early treatment initiation is associated with clinical and HIV prevention benefits, improving survival and reducing the incidence of HIV infection at the community level.

Since 2015, the World Health Organization (WHO) has recommended that all PLHIV should take ART regardless of CD4 cell count. Consequently; in 2017, about 21.7(59%) million PLHIV were accessing ART which was an increase of 2.3 million since 2016 (UNAIDS 2018a).

2.3 ART monitoring and indicators of effectiveness

Viral load (copies of HIV RNA) and CD4 cell count are the two important indicators of initial and sustained response to ART. It is recommended that these should be measured in all PLHIV at entry into care, at initiation of therapy, and on a regular basis repeatedly (http:// www. aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf). Repeated measurement of CD4 count is most important in patients who initiate ART with more advanced disease and require opportunistic infection (OI) prophylaxis or treatment. In these patients, the magnitude and duration of CD4 count increase can be used to determine whether to discontinue OI prophylaxis and/or treatment as recommended in the guidelines for treatment and prophylaxis of OI. The value of a patient's pre-ART viral load decline after initiation of ART provides prognostic information about the probability of disease progression (Mellors et al. 1997). Furthermore, high plasma HIV-1 RNA is a major risk factor for HIV transmission, and effective ART can reduce viremia and transmission of HIV to sexual partners by more than 96% (Quinn et al. 2000).

2.4 Adherence, drug resistance and treatment failure

The risk of drug resistance resulting in treatment failure always remains a concern. The most common underlying cause for drug resistance and virological failure is incomplete adherence to treatment (Mathes et al. 2013). For the success of ART medication, treatment adherence is very important. It is defined as the extent to which a person currently takes prescribed medication. It is widely agreed that in order to achieve an undetectable viral load and prevent the development of drug resistance, a person on antiretroviral drugs needs to take at least 95% of the prescribed doses on time (Chesney 2006).

Adherence to ART was evaluated by the percentage of missed doses documented by the ART physician and was ranked as good (if <5% (<2 doses of 30 doses or <3 dose of 60 doses missed), poor (if >15% (>6 doses of 30 doses or >9 dose of 60 dose missed) as documented by ART physician. The patient must correctly take the drug everyday, if incase s/he forgets to take the dose s/he should take the missed dose as soon as it is remembered. If 2 hours is left to take the next dose, the next dose can be taken at the usual time and continued with the normal schedule. But if it is less than 2 hours until the next dose, after taking the missed dose, the next dose can be omitted and then continued with the normal schedule (FMoH/HAPCO 2008).

Inadequate adherence to ART results increase risk of viral resistance. Thus the association between clinical variables and ART adherence indicates that adherence is associated with lower viral load, higher CD4 count, asymptomatic stage, and less experience of adverse events of antiretroviral medication (Al-Dakkak et al. 2001).

3. HIV/AIDS in Ethiopia

The first case of HIV in Ethiopia was reported in 1986. Although there was a declining trend nationally in the post-ART era, the virus has affected the lives of so many people and has left behind hundreds of thousands of orphans since its first report. In 2011 it was estimated that the national prevalence was 1.5% (DHS 2011) and 1.1% in 2015 (FMoH 2014b).

Although control efforts are in place recent estimates show that about 769,500 Ethiopians are living with the virus with 367000 being on ART in 2014 (FMoH 2014a) There is prevalence variation by Region from Gambella (6.6%) to 0.7% in Southern Nations, Nationalities and Peoples' Region. In terms of residence; 3.8% urban and 0.6% rural, and gender 1.9% female versus 1.0 male in 2011 (COP/ROP 2016). In Ethiopia there is expansion of HIV care and treatment services (HCT) and notable results have been achieved. Over the last five years on average per year more than 10 million people have been tested for HIV, with 27% HIV testing counseling coverage among adult population in 2014. About 20,000(65%) of HIV-positive pregnant women have received ART to prevent the transmission of HIV from mother-to-child in 2014. The number of HIV-positive mothers receiving treatment has increased from less than 7,000 in 2001 to 19,813 in 2014 (WHO 2015).

4. Problem statement

Although ART service is rapidly expanding in Ethiopia and the health status of PLHIV is improving substantially, treatment outcomes are variable depending on several factors. For instance, adherence which is aforementioned as a key factor for the success of ART is a complex behavior that is influenced by a wide range of sociodemographic, clinical and health system related factors. Lack of clear information or instruction on medication, limited knowledge on the course of HIV infection and treatment and adverse effects can all be barriers to adherence to ART making its effectiveness variable from setting to setting and/or patient to patient. Thus this study aimed at assessing the health status of PLHIV and getting service in a public health center in southwestern Addis Ababa, Ethiopia.

5. Objectives

5.1 General objective

To assess the health status of PLHIV attending ART clinic at Alembank Health Center, southwest Addis Ababa.

5.2 Specific objectives

The study had the following specific objectives:

5.2.1 Comparing CD_4 count at the start of ART and at least 6 months post-ART start.

5.2.2 Assessing the body-mass-index (BMI) of the participants before and after ART initiation.

5.2.3 Comparing the hemoglobin (Hb) level of the participants at ART initiation and at least 6 months post-ART start.

5.2.4 Determining the health status of the participants in relation to CD4 count, Hb level, BMI and adherence.

6. Materials and Methods

6.1 Study area

The study was conducted in Addis Ababa (AA) city government. In 2017, the population of AA was estimated 6.6 million as projected from the 3,384,569 in 2007 population census (CSA 2007). The city is divided into 10 sub-cities and 210 *woredas* (districts). Kolfe-K'eranyo sub-city

which is one of the ten sub-cities in AA with a population of 546,219 people had 12 health centers at the time of this study.

Alembank Health Center (AHC) in *woreda* 4 of Kolfe-K'eranyo sub-city was where this study specifically conducted. The sub-city, the *woreda* and the health center were selected because of convenience. Further, AHC had relatively large number of PLHIV sero-positive cases in the *woreda*. AHC which was established in 2010 is situated in the southwest of AA covering an area of 8,000 square meters (fig. 2). The health center had a catchment population of 64,976 people and 99 health professionals and 69 management workers during the study period.

It has comprehensive HIV/AIDS related services including voluntary counseling and testing (VCT), provider initiated testing and counseling (PITC), prevention of mother-to-child transmission (PMTCT) and ART program. PLHIV were regularly attending the health center's ART service since September 2012. The center provides only first-line ART regimen**.** In addition, AHC provides various types of health services including child delivery, ante-natal and postnatal care, family planning, male circumcision, expanded program on immunization (EPI), laboratory and Tuberculosis/HIV collaborative care services.

6.2 Source population

The source population was all PLHIV who were attendants of the health center's ART service center. The cohort had different categories. People who missed their follow-up visits or missed any clinical or drug pick-up appointment for one month were counted as ‘lost’ (temporarily lost). Those who were transferred to another ART facility for a number of reasons were recorded as ‘transferred-out’ cases. Those categorized as ‘drop/default’ or lost from follow up (LTFU) dropped their drug pick-up for 3 months or longer and those who died from all causes related to HIV/AIDS during the study period were considered ‘dead’. Participants with complete follow-up record data until July 2017 were grouped as 'alive' or ‘the study cohort’.

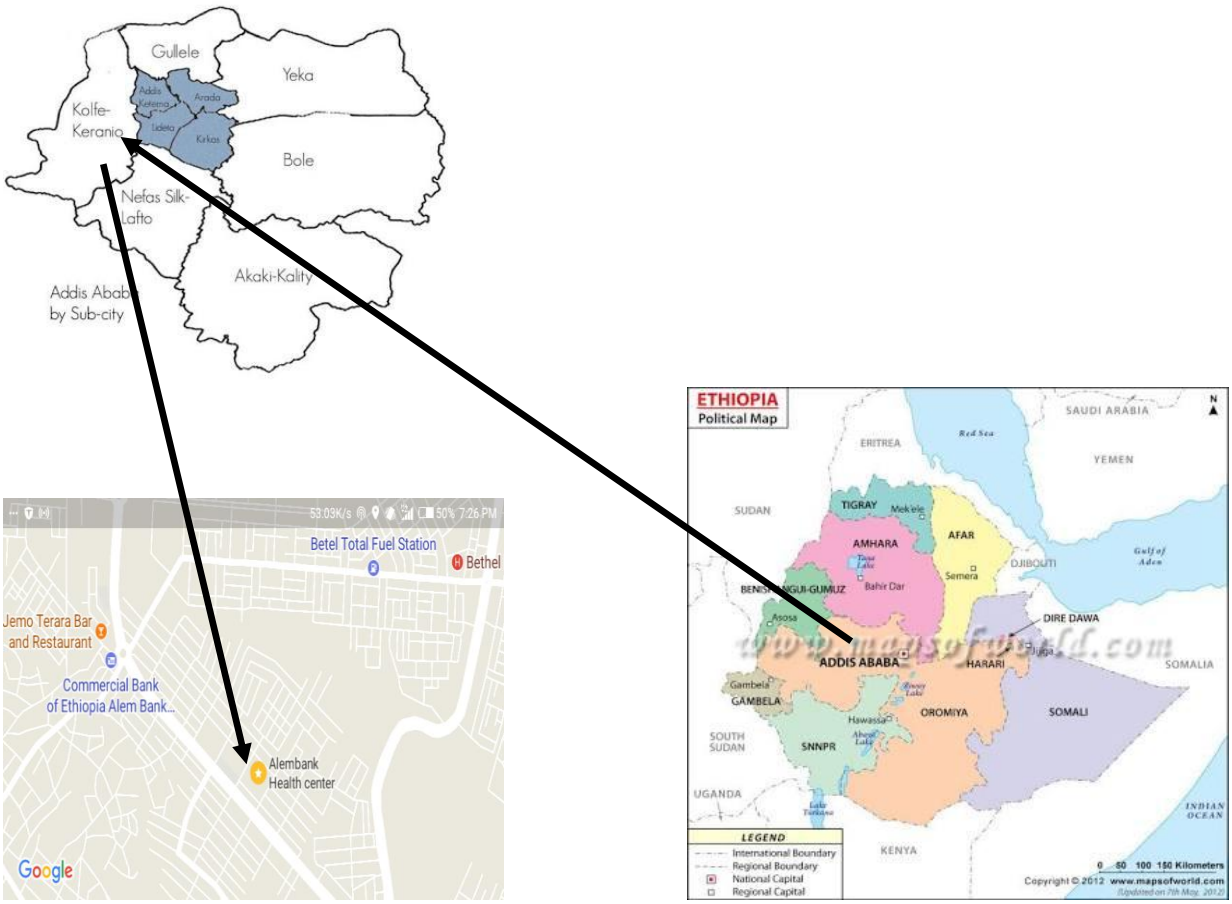

Figure 2 Map of the study area (ethiopia=source.www.mapsoftheworld.com.. Addis Ababa &AHC=source google Map)

6.3 Study population: Inclusion/exclusion criteria

The design of the study was retrospective cohort covering the period between September 2012 and July 2017. Adolescents (10-19 years) and adults (>19 years) who were receiving ART and had a follow-up history for at least six months (in July 2017), and with essential data on variables such as CD4 count, BMI, viral load (VL), Hb, etc. in their records formed the study population. While BMI and Hb level were used as indicators of patient nutritional status CD4 count was used as one of the main indicators for treatment outcome. A minimum of six-month attendance time was chosen as data on health status need long term follow-up. The records of children (<10 years), 'lost', 'dead', 'transferred-out', LTFU, below six-month follow-up period, missing essential data or those could not reach until July 2017 were excluded from analysis.

6.4 Data collection

To extract the required information data collection form was adopted from the national ART intake and follow-up forms. The data were collected by reviewing ART intake, laboratory request and follow-up forms from the health center's ART center. Baseline and follow-up records of the study population were examined and recorded.

6.5 Variables and data analysis

Data cleaned, organized and analyzed using SPSS version 16.0 (IBM SPSS, USA) and Microsoft Excel. Socio-demographic data, year on and adherence to ART, mean and median changes in CD4 count, VL (viremia), Hb, BMI, opportunistic infections and other health problems, WHO clinical stage, functional status and health status (treatment outcome) were the variables considered. Frequency, percentages, means (±standard deviation), medians (interquartile range (IQR) calculated. Paired t-test and Pearson bivariate correlation tests were used to test any association between the independent and dependent variables. $P \leq 0.05$ was considered statistically significant.

6.6 Data quality assurance

Quality control was associated with the reduction of error. All completed data collection forms were examined for completeness, consistency and clarity during data collection, data entry and analysis.

6.7 Ethics

A cooperation letter from Department of Zoological Sciences, Addis Ababa University, was dispatched to Alembank Health Center and the purpose of the study was explained to the health center administration. Permission was obtained and the study took off. Confidentiality was kept by avoiding individual identifiers.

7. Results

7.1 Characteristics of the source population

The total number of PLHIV who were registered and receiving ART in AHC between September 2012 and July 2017 was 748 (table 1). Out of these, 277(37%) were males and 471(63%) females. The population was overwhelmingly (721) adult and only 27 adolescents. Most of the people 214(28.6%) had follow-up time of one year, and 483(64.6%) were in the WHO clinical staging I. Majority 472(63.1%) of the population had CD4 count ≥200cells/µl.

Table 1 Sociodemographic and clinical data of PLHIV (N=748) registered for ART at AHC (Sep 2012 - July 2017)

Characteristics	**Follow-up year (year on ART)**				
	1, n(%)	2, n(%)	3, n(%)	≥4, n(%)	Total
Age (year)					
Adult (>19)	205(27.4)	178(23.8)	154(20.6)	184(24.6)	721(96.4)
Adolescent (10-19)	9(1.2)	10(1.3)	6(0.8)	2(0.3)	27(3.6)
Total	214(28.6)	188(25.1)	160(21.4)	186(24.9)	748(100)
Gender					
Male	80(10.7)	75(10.0)	49(6.6)	72(9.6)	277(37.0)
female	134(17.9)	113(15.1)	111(14.8)	114(15.3)	471(63.0)
Total	214(28.6)	188(25.1)	160(21.4)	186(24.9)	748(100)
WHO stage					
Stage I	143(19.1)	122(16.3)	101(13.5)	117(15.7)	483(64.6)
Stage II	38(5.1)	27(3.6)	34(4.5)	34(4.5)	133(17.8)
Stage III	26(3.5)	30(4.0)	20(2.8)	31(4.2)	107(14.3)
Stage IV	7(0.9)	9(1.2)	5(0.6)	4(0.5)	25(3.3)
Total	214(28.6)	188(25.1)	160(21.4)	186(24.9)	748(100)
CD4 count (cells/µl)					
<200	39(5.2)	49(6.6)	53(7.1)	79(10.6)	220(29.4)
≥200	139(18.6)	119(15.9)	107(14.3)	107(14.3)	472(63.1)
CD4 missing	36(4.8)	20(2.7)	-	-	56(7.5) *
Total	214(28.6)	188(25.1)	160(21.4)	186(24.9)	748(100)

*56 people had no CD4 count. Adolescent :10-19 years old. Adult >19 years old (WHO 2017).

7.2 Inclusions and exclusions

Nearly half (360) of the records that did not satisfy the inclusion criteria were excluded from consideration (table 2). Of these, 169(46.9%), 65 males and 104 females, were 'lost'. Almost half

(49.7%) of them were under clinical stage I and 67 of them had two-year time on ART. Those recorded dead were 19(2.5%), 13 males and 6 females, with 9(47.4%) of the deaths occurring in the patients' two-year time on ART. The rest 10 patients died in different periods of their follow-up schedule. The exact causes of the deaths were unknown because all of the patients were not inpatients. Health professionals heard their clients' deaths when they tried to reach the patients' families on phone.

Due to resident change 55 males and 92 females total of 147(19.7%) were transferred to other health facilities, 62(42.2%) of them had one-year time on ART and 89(60.5%) were under clinical stage I. Twenty-five (6.9%), 8 males and 17 females, were LTFU of these 14(56.0%) of had one-year follow-up time and 18(72.0%) were under clinical stage I.

Table 2 Exclusions from the study

Characteristics	**'Lost' n(%)**	**LTFU n(%)**	**'Dead' n(%)**	**'Transferred-out' n(%)**	**Total n(%)**
Gender					
Male	65(38.5)	8(32.0)	13(68.4)	55(37.4)	141(39.2)
Female	104(61.5)	17(68.0)	6(31.6)	92(62.6)	219(60.8)
Total	169(46.9)	25(6.9)	19(5.3)	147(40.8)	360(100)
Follow-up year					
1	52(30.8)	14(56.0)	4(21.0)	62(42.2)	132(36.7)
2	67(39.6)	3(12.0)	9(47.4)	32(21.8)	111(30.8)
3	37(21.9)	4(16.0)	3(15.8)	35(23.8)	79(21.9)
≥4	13(7.7)	4(16.0)	3(15.8)	18(12.2)	38(10.6)
Total	169(46.9)	25(6.9)	19(5.3)	147(40.8)	360(100)
WHO stage					
Stage I	84(49.7)	18(72)	3(15.8)	89(60.5)	194(53.9)
Stage II	57(33.7)	3(12)	6(31.6)	38(25.9)	104(28.9)
Stage III	24(14.2)	2(8.0)	6(31.6)	15(10.2)	47(13.1)
Stage IV	4(2.4)	2(8.0)	4(21.0)	5(3.4)	15(4.2)
Total	169(46.9)	25(6.9)	19(5.3)	147(40.8)	360(100)

7.3 The study cohort

7.3.1 Characteristics of the study cohort

7.3.2 At ART initiation (baseline)

Out of 388 patients on ART in July 2017, 64.9% were females. The lowest and highest baseline ages were 16 and 65 respectively and the mean age was 33.7±9.19 years with 97.2% adults. Regarding the marital status, a proportion were married (59.5%) followed by divorced/separated (20.4%). On other aspects, about 68.1 % of the study participants attended primary and secondary level of school, whereas 20.6% had no formal schooling. Most of the clients 370(95.4%) were new and only 18(4.6%) were transferred-in cases. The majority, 85.5% and 74.5%, had normal weight (BMI category, WHO clinical stage) and stage 1 respectively. The CD4 count of 39.9% of the population was below 200cells/µl. The mean (±SD) and median (IQR) CD4 counts were 295.2 and 254 cells/µl respectively. Half (50%) of the participants had CD4 count below the median. Furthermore, 28.9% were anemic. Most 315(81.2%) were working while the rest 73(18.8%) had ambulatory or bedridden functional status. The majority of the females were non-lactating and non-pregnant (57.2%). The sociodemographic and health status of the cohort at ART initiation and post-initiation is summarized in table 3.

7.3.3 Post-ART (follow-up)

The mean age of the study participants was 36.5±9.5 year. The functional status of the patients was changed after initiation of ART that out of 73(18.8%) ambulated or bedridden patients only 20(5.2%) remained so. At the start of ART 112(28.9%) individual who were identified as anemic improved reducing the cases to 86(22.2%).

Table 3 Pre- and post-ART initiation socio-demographic and health characteristics of the study cohort between September 2012 and July 2017 (N = 388)

Characteristics	Baseline (Pre-ART)	Follow-up (Post-ART)
	n(%)	n(%)
Gender		
Male	136(35.1)	136(35.1)
Female	252(64.9)	252(64.9)
Age (years)		
Adolescent (10-19)	11(2.8)	8(2.1)
Adult (>19)	377(97.2)	380(97.9)
Marital status		
Never married	49(12.6)	49(12.6)
Married	231(59.5)	231(59.5)
Separated	34(8.8)	34(8.8)
Divorced	45(11.6)	45(11.6)
Widowed	29(7.5)	29(7.5)
Education		
Illiterate	80(20.6)	80(20.6)
Primary	171(44.1)	171(44.1)
Secondary	93(24.0)	93(24.0)
Tertiary	44(11.3)	44(11.3)
Functional status		
Working	315(81.2)	368(94.9)
Ambulated or bedridden	73(18.8)	20(5.2)
Hb, g/dl[b]		
Normal	276(71.1)	302(77.8)
Anemic	112(28.9)	86(22.2)
Pregnancy status (n=252)	-	
Non-pregnant and non-lactating		222(88,1)
Pregnant		17(6.7)
Lactating		13(5.2)

Stages[a] III & IV are advanced stages of HIV infection with CD4 cell count <200cells/µl (WHO 2017); [b]Hb: haemoglobin (anemia: male <13; female <12.3 (MoA and FAO 2005); BMI: body mass index

Clinical staging has also shown change, 61 people at baseline were at stage 3, of these 55(90.2%), 4(6.6%), 1(1.6%) and 1(1.6%) were stage1, 2, 3 and 4 respectively at follow up. 6(66.7%) and 3(33.3%) of stage 4 at baseline has shown improvement to stage 1and 2 respectively during the follow up time (table 4).

Table 4 Change in count and proportion of study cohort across four WHO clinical staging before and after ART at AHC between September 2012 and July 2017 (N = 388)

Base line(pre-ART) n%		Follow up(post-ART), n%			
WHO staging	**n%**	**WHO Stage 1**	**WHO Stage 2**	**WHO Stage3**	**WHO Stage4**
1	289(74.5)	244(84.4)	38(13.1)	6(2.1)	1(0.3)
2	29(7.5)	27(93.1)	1(3.4)	1(3.4)	0
3	61(15.7)	55(90.2)	4(6.6)	1(1.6)	1(1.6)
4	9(2.3)	6(66.7)	3(33.3)	0(0%)	0(0%)
Total	388(100)	332(85.5)	46(11.9)	8(2.1)	2(0.5)

The baseline mean and median CD4 count 295.2 and 254cells/µl was changed to 475.5 and 437.5 cells/µl at follow-up time. Table 5 represents change in count and proportion of the study cohort across two CD4 count categories before and after ART initiation The CD4 count, when measured after ART initiation was below 200cell/µl for only 54(13.9%) people. 106(68.4%) of the participants with below 200 CD4 count at initiation were improved to ≥200 at follow up.

Table 5 Change in count and proportion of study cohort across two CD4 count categories recorded before and after ART at AHC between September 2012 and July 2017 (N = 388)

Baseline		**Follow-up n%**	
CD4 count (cell/µl)	**n%**	<200	≥200
<200	155(40)	49(31.6)	106(68.4)
≥200	233(60)	5(2.1)	228(97.9)
Total	388	54(13.9)	334(86.1)

The table below showed change in count and proportion of study cohort across three BMI categories recorded before and after ART. At the initiation of ART 48(12.4%) and 333(85.8%) of the people were underweight (BMI<18.5kg/m2) and normal weight (BMI 18.5-25kg/m2) respectively. However, during follow-up 47(97.9%) of the underweight, improved their nutritional status to normal rang. 9%&0.6% of the normal rang at base line were changed to under and overweight respectively during follow-up (table 6).

Table 6 Change in count and proportion of study cohort across three BMI categories recorded before and after ART at AHC between September 2012 and July 2017 (N = 388)

Baseline (Pre-initiation)		**Follow up (post-initiation), n%**		
MBI, , kg/m^2	**n%**	**Underweight**	**Normal**	**Overweight**
Underweight <18.5)	48(12.4)	1(2.1)	47(97.9)	-
Normal (18.5-25)	333(85.8)	30(9)	301(90.4)	2(0.6
Overweight (>25)	7(1.8)	2(28.6)	5(71.4)	-
Total	388(100)	33(8.5)	353(91.0)	2(0,5)

7.3.4 The health performance

The mean and median CD4 count increment was by 180.3(61.1%) and 183.5(72.2%) from baseline level. The change was significant (t = 17.976, p<0.001).

In bivariate analysis significant correlations were established between adherence and increase in CD4 count (p=0.044), and adherence and functional status (p=0.018). Similarly, WHO HIV-staging and nutritional status (BMI) were significantly associated (p=0.008), but no association between adherence and BMI, and WHO HIV staging was noted (table 7). Undernutrition was more frequent among patients at clinical stages III and IV and ambulated or bedridden than those in stages I & II and having working status.

Table 7 Association among CD4 count, BMI, functional status, Hb, adherence and WHO staging in PLHIV on ART at AHC (September 2012 and July 2017)

	Bivariate analysis p-values for each pair of combination					
	BMI	CD4 count	WHO staging	Functional status	Hb	Adherence
CD4 count	0.042*	-	0.621	0.114	0.684	0.044*
WHO staging	0.008**	0.621	-	0.000**	0.746	0.721
Functional status	0.005**	0.114	0.000*	-	0.669	0.018*
BMI	-	0.042*	0.008**	0.005**	0.312	0.068
Hb	0.312	0.684	0.746	0.669	-	0.195
Adherence	0.068	0.044*	0.721	0.018*	0.195	-

*, **Significant associations at 95% (p<0.05) and 99% (p<0.01) confidence intervals; MBI: body mass index; Hb: hemoglobin

7.3.5 HIV/AID related problems

Although more than half (54.4%) of the participants were apparently healthy a significant number of participants (45.4%) reported various types of HIV/AIDS related health problems (table 8). The most notable cases were tuberculosis (9.3%), diarrheal disease (7.5%) and febrile illness (6.7%).

Table 8 HIV/AIDS related health problems among the study population during the follow-up period

Description	Frequency	Percent
Apparently healthy	212	54.4
Hypertensive	1	0.3
Diarrheal disease	29	7.5
Febrile illness	26	6.7
Oral disease	20	5.2
Gingivitis	3	0.8
Skin disease	20	5.2
Pneumonia	11	2.8
urinary tract infection (UTI)	5	1.3
Respiratory tract infection (RTI)	10	2.6
Tuberculosis	36	9.3
Herpes zoster	4	1.0
Fungal disease	11	2.8

7.3.6 Type and duration of ART

Most of the patients (294) had duration of over 18 months on ART with median duration of 34 months. Majority of the participants 328(84.5%) were taking first-line regimen TDF+3TC+EFV (table 9) manufactured in India (Macleods Pharmaceuticals Ltd).

Table 9 Type of ART first-line regimen the study participants were on and duration (months)

Description	Sex		Age		Frequency	Percent
ART first-line regimen	Female	Male	Adolescent	Adult		
TDF+3TC+EFV	212	116	6	322	328	84.5
AZT+3TC+NVP	22	12	2	32	34	8.8
AZT+3TC+EFV	5	5	0	10	10	2.6
TDF+3TC+NVP	13	3	0	16	16	4.1
Treatment duration (months)						
6-18	68	26	6	88	94	24.2
19-36	73	41	2	112	114	29.4
37-54	81	44	0	125	125	32.2
≥55	30	25	0	55	55	14.2

3TC: Lamivudine (epivir), AZT: Zidovudine, EFV: Efaviren, NVP: Nevirapine, TDF: Tenovudine

7.3.7 Adherence and its impact on the health performance

During the follow-up period two adherence categories, good and poor, were identified for each participant. 342(88.1%) patients had'good' adherence, only 46(11.9%) were known to have 'poor' adherence. Table 10 presents the count/proportion of the participants under different classes or levels of health status indicators across the two adherence categories. Also figure 3 shows the distribution of study cohort based on adherence versus post ART CD4 count, and change in CD4 at and post initiation of ART.

Table 10 Count/proportion of study participants under different classes or levels of health status indicator across two adherence categories

Variables	**Levels/classes**	**Adherence**	
		Poor, n(%)	**Good, n(%)**
Count (%)	Total	46(11.9)	342(88.1)
BMI	Underweight	4(12.1)	29(87.9)
	Normal	40(11.3)	313(88.7)
	Obese	2(100)	0(0.0)
WHO clinical stage	I	40(12.0	292(88)
	II	5(10.9)	41(89.1)
	III	1(12.5)	7(87.5)
	IV	0(0.0)	2(100)
CD4 count (cells/µl)	<200	9(19.6)	37(80.4)
	≥200	37(10.8)	305(89.2)
Hb (g/dl)	Anemic	12(14.0)	74(86.0)
	Normal	34(11.3)	268(88.7)

Good: if adherence is >95% (if only <5% (<2 doses of 30 doses or <3 dose of 60 doses missed). Poor (if >15% (>6 doses of 30 doses or >9 dose of 60 dose missed) as documented by ART physician.

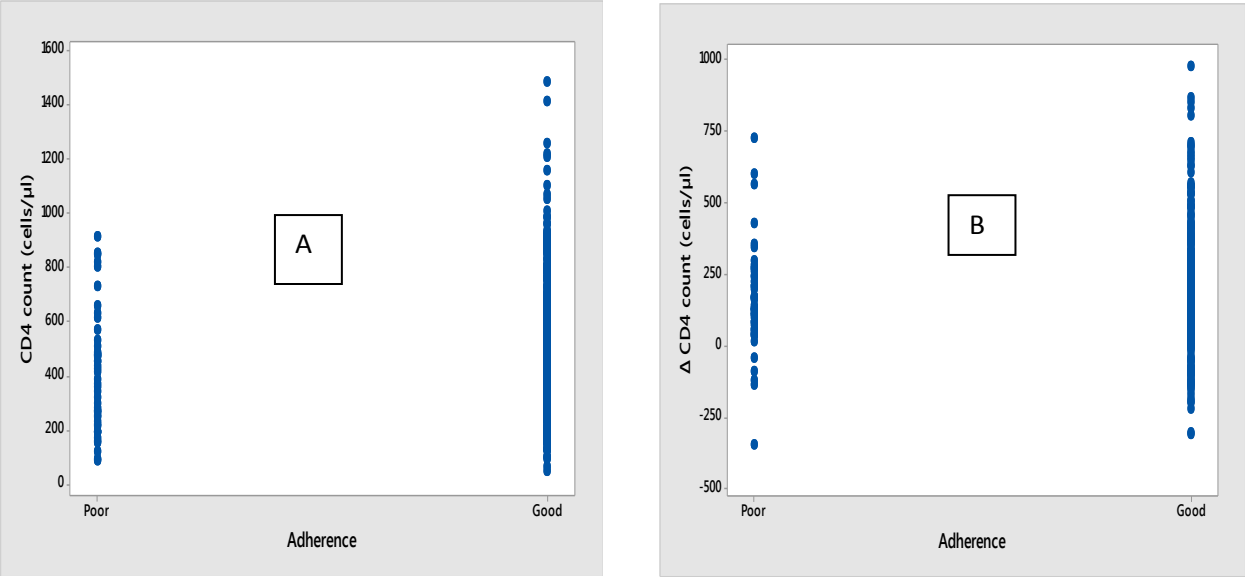

Figure 3. Scatter plot showing the distribution of patients based on adherence versus: (A) Post ART CD4 count (B) Change in CD4 count between and within adherence groups

8. Discussion

Close half (360) of the records that did not satisfy the inclusion criteria (including the transferred outs (147 people) were excluded. More than a quarter, 213(28.5%), of the population had no complete monitoring data as per the HIV care and ART guideline. Although LTFU were low (6.9%) compared to other study (26.7%) (Berhto et al. 2014), regular follow up of ART is an important part of HIV care. Cases who are LTFU affect their own health and the long-term success of ART programs. Moreover, it is difficult to achieve USAID and WHO 2020 goal that stated as 90–90–90 target, include 90% of PLHIV know their HIV status, 90% of the people who know their HIV status receiving ART, and sustained viral suppression is achieved in 90% of those receiving treatment (UNAIDS 2018b). Thus in addition to, making phone call to confirm remind 'LOST' and LTFU needs strong emphasis on patient retention mechanisms.

Out of 388 patients that satisfy the inclusion criteria 64.9% were females. This is similar with the report from Ethiopian Public Institute (EPHI 2017) where females were twice affected than male population. Recent global study showed that women and girls accounted for more than half (59.0%) of the total number of PLHIV in eastern and southern Africa (UNAIDS 2017). It is suggested that this might be because of women vulnerabilities created by cultural, social and economic reasons. Most of the victim women have experienced violence or rape by older male partners who can dominate the women. For example, the women's partners may control the possibility of accessing services such as condom (Marian 2000). In addition, the more delicate vaginal lining due to the biological nature of the female is believed to increase the risk of females of HIV infection.

The higher number of adult patients, compared to adolescents, on ART in the current study is in agreement with data from the Joint United Nations Program on HIV/AIDS fact sheet which shows that out of 36.7 million PLWH in 2016, 34.5 million were adults (UNAIDS 2017). This may be because of adolescent's unawareness of their HIV status or less likely to be tested for HIV. Dr Gotttfried Hirnschall, director of WHO HIV/AIDS (WHO 2013a) says "adolescents need health services and support, tailored to their needs they are less likely than adults to be tested for HIV and often need more support than adults to help them maintain care and to stick to treatment."

Majority of the study participants had BMI measurement in normal range. Possible reasons could be that they were usually assessed for any opportunistic infections and get treated. Further, as the government provides aid for PLHIV (Personal communication, AHC-ART clinic staff) this might have helped them to take care of their nutritional and other lifestyles. The results of this study also showed change in nutritional status from baseline 48(12.37%) underweight and 7(1.8%) overweight to 33(8.1%) and 2(0.5%) respectively after ART initiation; this is in line with a result from Hawassa University hospital where the prevalence of malnutrition dropped from 38% at initiation to 20% after sometime on ART (Tafese et al. 2012).

Malnutrition in this study was significantly associated with WHO clinical stage and functional status. Malnutrition was more frequent in the stages III & IV participants than I & II. This is in line with the study conducted in different Addis Ababa hospitals, poorer nutritional responses were observed in patients who were on ART with clinical stage IV illnesses and CD4<200cell/µl before ART (Bayouh 2014). However, correlation was not shown between nutritional status and adherence to ART. This is similar with the cross-sectional study in Ethiopia which reported that nutritional status showed no impact on adherence to ART. It was reported that people with good nutritional status missed ART doses more than those with poor nutritional status (Seifu 2007). In contrast, studies in Zambia (Cantrell et al. 2008) and in Uganda (Rawat et al. 2010) reported that better nutritional status improved adherence to ART. Differences in socioeconomic status between the studies may explain these results.

In Ethiopia, like other resource-limited countries, CD4 cell counts are used as a main marker of treatment response due to the fact that viral load monitoring is not easily accessible. In this study a significant (72.2%) increment in the median CD4 count was observed from baseline to follow-up. Other reports elsewhere in sub-Saharan Africa (Lawn et al. 2006) documented that patients on successful therapy will have increased CD4 cell counts after a few months.

Tuberculosis is one of the major public health problems in PLHIV in many low-income countries including Ethiopia. A previous study in Kolfe-K'eraniyo sub-city showed that TB is highly prevalent and is an important health problem among PLHIV (Mekonnen 2015). Also, in current study from different OIs in HIV patients, the common (9.3%) type was TB. Similarly, Diarrhea

and fever are the most common symptom and complications of HIV (FMoH 2014a, Murrell 2018). Also in our cases next to TB, Diarrhea and fever were common problems.

In this study 100% of the ART regimen was first-line and the majority of the participants (84.5%) were taking the combination TDF+3TC+EFV, this combination is less toxic and more convenient regimens and preferred choice in adults, adolescents and children older than ten years as mentioned in Ethiopian National Guideline for Comprehensive HIV Prevention, Care and Treatment. First-line ART should consist of two NRTIs plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI). TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART by the WHO (WHO 2013b). Once-daily fixed-dose combination of these drugs also is recommended by the WHO as first-line ART in pregnant and breastfeeding women. The few such women in this study were taking thus the correct prescription.

The current study found that 88.1% of the PLWH had good adherence to ART medications. This is lower when compared with adherence of 93.1% in a study conducted in Debre Markos Referral Hospital (Moges et al. 2014). The reason for such difference could be due to the difference in the sociodemographic characteristics and sample size difference. However, adherence was significantly associated with CD4 count and functional status. Moreover; increment in CD4 count was observed more in patients with good adherence than poor adherence (fig. 3). Similar findings were observed in a study conducted in Ethiopia showing that adherence to ART is important for suppression of viral replication and improved CD4+ cell count that in turn determines the survival PLWH on ART (Seifu 2007). Indeed, it is well-established that good adherence is effective in reducing viral load and restoring a patient's immune system.

9. Limitations of the study

As data used in this study was retrospective, there were many incomplete follow-up records. Inclusion of only patients with complete records of baseline information during data collection might have made selection bias possible. Lack of data such as viral load in successive follow-up time made more powerful analysis is another limitation. All deaths were considered as AIDS-related for lack of available records on specific causes of death**.** Furthermore, information on the date of diagnosis with HIV (date and location confirmed HIV-positive, HIV subtype) was not available. Weight at ART start and subsequent measurements were not taken. Some opportunistic diseases were misleading, their etiology were not specifically mentioned for instance, Diarrhea and Febrile illness. Demographic information was collected once at baseline no updated with changes. Reasons for poor adherence were not recorded.

10. Conclusion and recommendation

Most of the participants in the study showed a good clinical response to therapy, as indicated by significant improvement in CD4 count, clinical stage and factional status from baseline data. Therefore, this study confirms that ART with good adherence is effective in improving health status of PLHIV Although the results are based on a limited number of patients and arriving at definitive conclusions may be premature, the results draw attention to certain important constraints that an ART center would face. That is besides provision of free ART, to derive the complete benefit of ART through national program, correct and successive registration of follow up results should be properly documented. For instance, viral load and CD4 cell count are the two important indicators of initial and sustained response to ART and should be measured in all HIV-infected patients at entry into care, at initiation of therapy, and on a regular basis repeatedly. Regular follow up of ART is an important part of HIV care. Thus ‘LOST’, LTFU and death Cases needs strong emphasis on patient retention mechanisms. To reach good conclusion larger scale studies, assessing male and female patients separately, and between the age groups, are needed.

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