



ASSESSMENT OF ANTIRETROVIRAL THERAPY (ART) OUTCOMES VERSUS CD₄ CELL COUNT THRESHOLD AMONG HIV/AIDS PATIENTS IN RAS DESTA HOSPITAL, ADDIS ABABA, ETHIOPIA

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ABSTRACT

The initiation of ART is best based on CD₄ cell count, a marker of immune status, rather than on viral load, a marker of virologic replication. For patients with advanced symptoms, treatment should be started regardless of CD₄ count. However, the point during the course of HIV infection at which antiretroviral therapy (ART) is best initiated in asymptomatic patients remains unclear. The objective of this study is to assess ART treatment outcomes versus CD₄ count threshold among HIV/AIDS patients in Ras Desta hospital. This was a periodic retrospective cross sectional study of HIV positive patient's ART treatment outcomes in relation to CD₄ count threshold in Ras Desta hospital. From all HIV positive patients who had registered for ART from September 2009- February 2011 at Ras Desta hospital, 636 patients had met the criteria of the study and they were selected. Out of the 636 patients chosen for the study, 372 (58.5 %) were females while 264 (41.5 %) were males. For the whole sample under study, the median age was 36 years. Out of 636 patients 504 patients had a CD₄ count less than 200 cells/mm³, 120 had a CD₄ count greater than 200 and less than 350 cells/μl. Lastly, a total of 12 patients had a CD₄ count greater than 350 cells/mm³ at the initiation of ART. Other findings show that for all patients in the study receiving ART, median weight was 53 Kg (range 27 kg to 93 kg). Four hundred eighty (75.5 %) patients were alive, twenty one (3.3 %) patients had transferred out, 67 (10.5 %) were lost to follow-up and 68 (10.7 %) had died during two year period of ART use. A further observations of the deaths revealed that 53 (78 %) were CD₄ count less than 200 cells/μl, 14 (20.5 %) patients were CD₄ count > 200 and < 350 cells/μl, while only 1 (1.5 %) of the patient were died whose CD₄ count > 350 cells/μl. This study show that early initiation of ART at CD₄ levels higher than 200 cells/μl reduces mortality, immune-depression and weight loss and also improve outcome of ART treatment in asymptomatic, ART-naive, HIV-infected people. Practitioners and policy-makers may consider initiating ART at levels > 200 cells/μl.

Keywords: HIV/AIDS, CD₄⁺ cell count, ART Regimen, Epidemiology, Ethiopia

INTRODUCTION

HIV/AIDS and CD₄ count

AIDS (Acquired Immune Deficiency Syndrome) is caused by a virus, HIV (Human Immunodeficiency Virus) which was first isolated in 1983. It has been identified in over 200 countries and territories worldwide and is spreading rapidly in many affected populations, particularly in developing countries. HIV begins its infection of a susceptible host by binding to the CD₄ receptor on the host cell. CD₄ is present on the surface of many lymphocytes, which are a critical part of the body's immune system. Recent evidence indicates that a co-receptor is needed for HIV to enter the cell. CD₄ cell counts should rise following the initiation of therapy in most patients. This trend may continue for many years although the rise may be less rapid if the baseline CD₄ count was very low¹. The primary goals of antiretroviral therapy (ART) are to reduce HIV-related morbidity, prolong survival, improve quality of life, restore and preserve immunologic function and prevent HIV transmission². The guidelines from the earliest versions have emphasized that any adult with symptomatic HIV infection (e.g. unexplained fevers, weight loss and diarrhea) should initiate ART as soon as possible as these patients are at increased risk for progression to AIDS-related complications. Similarly, patients with CD₄ counts of < 200 cells/μl have been recommended to start ART for more than a decade given data from clinical cohorts and clinical trials that consistently demonstrate reduction in AIDS-related morbidity and mortality. Debate, however, continues as to the optimal timing for ART in asymptomatic adults with CD₄ counts above 200 cells/μl. Current guidelines recommend ART when CD₄ counts drop below 350 cells/μl but recent studies and improving treatment options have suggested to many experts that earlier starting times with CD₄

counts up to 500 cells/μl might be appropriate at least for some patients³. Also in July 2010, the World Health Organization (WHO) published new recommendations on providing antiretroviral therapy (ART) to adults and adolescents in resource-limited settings that revised the guidelines previously published in 2006. The new recommendation encourage starting ART earlier, usually at a CD₄ count of 350 cells/μl or lower, specifies regimens for first and second line therapies and contains other recommendations regarding laboratory monitoring and other elements⁴. Recommendations on the timing for ART initiation differ based on availability of resources, leading to confusion amongst clinicians and policy-makers in determining the most favorable point to begin treatment⁵. The objective of this study is to assess the evidence for the optimal time to initiate ART for obtaining better treatment outcomes in HIV-infected adults who have received therapy in Ras Desta hospital.

Statement of Problem

Every day, over 6800 people become infected with HIV and over 5700 persons die from AIDS, mostly because of inadequate access to HIV prevention and treatment services. The HIV pandemic remains the most serious of infectious disease challenges to public health. Sub-Saharan Africa is the most seriously affected region. The estimated number of deaths due to AIDS in 2007 was 2.1 million [1.9–2.4 million] worldwide of which 76 % occurred in sub-Saharan Africa⁶. Ethiopia populations will probably continue growing by more than 2 percent annually through 2025. With 45 percent of people living below the poverty line, this expected increase will continue to strain limited resources and likely result in higher levels of poverty. Chronic and widespread poverty makes it especially difficult for Ethiopians to cope with HIV. Poor people

have less access to information, prevention tools, care, support, and treatment. They are also more likely to be involved in transactional sexual behavior⁷. According to the 2007 Single Point Estimate, 336,160 PLHIV were in need of ART in 2009, out of which 20,522 were children below the age of 15 years⁸. This indicates that, Ethiopia is one of the seriously affected countries in sub Saharan Africa. Chinsebu (2009) reports; that poverty in Africa still plays a major role in the dynamics of the HIV/AIDS⁹. There are concerns that free public sector ART programs are not sustainable due to their heavy reliance on donor funding. Besides funding, access to treatment still has many shortcomings, including lack of confidentiality, lack of bed space, lack of transport to hospitals, shortages of qualified health workers, the criterion of treatment supporter, and serious side-effects now causing new forms of stigma and also globally the point during the course of HIV infection at which ART is best initiated in asymptomatic patients' remains unclear and unanswered question for people infected with HIV, clinicians and policy-makers⁹. Guidelines issued by various agencies provide different initiation recommendations according to resource availability. This can be confusing for clinicians and policy-makers when they are determining the best time to initiate therapy⁵. After looking many studies, World Health Organization (WHO) published new recommendations on providing antiretroviral therapy (ART) to adults and adolescents in resource-limited settings that revised the guidelines previously published in 2006. The new recommendations encourage starting ART earlier, usually at a CD₄ count of 350 or lower⁴, but Ethiopia still used the 2006 ART guideline and states that ART should be initiated based on CD₄ count until it becomes below 200 cells/ μ l and with WHO clinical stage III and IV with TB-co-morbidity and pregnancy⁷, but at this CD₄ count, that means 200 cells/ μ l which is only 15 % of the natural immune system initiating ART have an associated risk which can reduce the therapeutic outcomes of ARV drugs and patient life expectancy because of possible risk of irreversible immune system depletion, difficulty in suppressing viral replication, increase risk of viral Transmission and increased adverse drug reaction¹⁰.

Literature Review

AIDS (Acquired Immune Deficiency Syndrome) is caused by a virus, HIV (Human Immunodeficiency Virus) which was first isolated in 1983. It has been identified in over 200 countries and territories worldwide and is spreading rapidly in many affected populations, particularly in developing countries. HIV begins its infection of a susceptible host by binding to the CD₄ receptor on the host cell. CD₄ is present on the surface of many lymphocytes, which are a critical part of the body's immune system. Recent evidence indicates that a co-receptor is needed for HIV to enter the cell. CD₄ cell counts should rise following the initiation of therapy in most patients. This trend may continue for many years although the rise may be less rapid if the baseline CD₄ count was very low¹. While many viruses can be controlled by the immune system, HIV targets and infects the same immune system cells that are supposed to protect as from illnesses. These are a type of white blood cell called CD₄ cells. HIV takes over CD₄ cells and turns them into virus factories that produce thousands of viral copies. As the virus grows, it damages or kills CD₄ cells to weaken the immune system and it make HIV/AIDS acute, it is characterized by the continuous loss of CD₄ T cells, leading to immunodeficiency, and death. A clear inverse relation exists between the number of CD₄ cells in peripheral blood and the risk of HIV associated diseases¹¹. Hence, CD₄ cell count in peripheral blood represents the principal surrogate marker for clinical symptoms and AIDS-defining illnesses¹². Antiretroviral therapy (ART) has been shown to be effective in slowing down the progression of AIDS and in reducing HIV-related illnesses and death. Traditionally, therapy is administered based on a patient's CD₄ cell count, where the number of CD₄ cells reflects the body's immune (defense) system. An HIV-infected individual with a CD₄ cell count of 500 cells/ μ l is considered healthy enough not to need ART. When a patient's cell count reaches 200 cells/ μ l, however,

the immune system is severely weakened and ART is necessary. A patient with advanced symptoms receives treatment regardless of CD₄ count; however, the point during the course of HIV infection at which ART is best initiated in asymptomatic patients' remains unclear and unanswered question for people infected with HIV, clinicians, and policy-makers. Guidelines issued by various agencies provide different initiation recommendations according to resource availability. This can be confusing for clinicians and policy-makers when they are determining the best time to initiate therapy⁵.

Criteria to initiate treatment of HIV/AIDS

In resource-limited settings, initiation of ART is predominantly dependent on clinical assessment, despite increasing availability of CD₄ testing as a guide to ART decisions. With the decentralization of HIV care to health centers, there will be even more use of clinical criteria to decide initiation. WHO recommends clinical decision-making where CD₄ counts are unavailable in order to increase access to ART. The lab networking and sample transportation must be established and strengthened to make CD₄ testing available for providers at health centers. The most important purpose of clinical assessment to initiate treatment is to stage a patient according to WHO criteria. Before the process of clinical or immunological assessment however, the HIV positive status of the patient must be confirmed⁷. The decision to initiate ART in adults and adolescents is guided by clinical, immunological assessment and viral load. In situation where immunological assessment and viral load is unavailable it is recommended to initiate ART on clinical grounds with total lymphocytes count when applicable. ART initial demands thorough assessment of patient readiness and commitment. The patient must understand that treatment is life-long and its implications (possible adverse effects, 100 % adherence, etc). Access to nutrition, psychosocial and basic social supports are important when deciding to start ART in patients. In resource-limited settings, initiation of ART is predominantly dependent on clinical, despite increasing availability of CD₄ guiding to art decisions. Immunological assessment using the CD₄ count identifies the disease progression and determines initiation of treatment. CD₄ testing can monitor the ART response as well. A patient with a CD₄ count below 200 cells/ μ l is at increased risk of developing life threatening OIs. To ensure patient safety, treatment must not be delayed until CD₄ count falls below 200 cells/ μ l. The optimum time to initiate ART is when a patient's CD₄ count is 200-300 cells/ μ l. CD₄ count levels do not determine treatment initiation in stage IV patients; regardless of CD₄ count, stage IV patients are promptly started on ART, once readiness is assured. Stages I and II, immunological assessment is important initiate ART, in stage IV patients are promptly started on ART, once readiness is assured. In stages I and II, immunological assessment is important to initiate ART in stage III, treatment can be consider under certain clinical conditions with CD₄ count of 350 and below are recommended for initiation of ART to avoid confusion with advanced and early stage III. Varies factors require consideration when interpreting CD₄ results. The test itself has an inherent variation of +/- 30 %. It is important to consider all factors in making decision to start or change treatment based on CD₄ counts¹¹.

Optimal time for initiation of antiretroviral therapy

The primary goals of antiretroviral therapy (ART) are to reduce HIV-related morbidity, prolong survival, improve quality of life, restore and preserve immunologic function and prevent HIV transmission². The guidelines from the earliest versions have emphasized that any adult with symptomatic HIV infection (e.g. unexplained fevers, weight loss, and diarrhea) should initiate ART as soon as possible as these patients are at increased risk for progression to AIDS-related complications. Similarly, patients with CD₄ counts of < 200 cells/ μ l have been recommended to start ART for more than a decade given data from clinical cohorts and clinical trials that consistently demonstrate reduction in AIDS-related

morbidity and mortality. Debate, however, continues as to the optimal timing for ART in asymptomatic adults with CD₄ counts above 200 cells/μl. Current guidelines recommend ART when CD₄ counts drop below 350 cells/ μl but recent studies and improving treatment options have suggested to many experts that earlier starting times with CD₄ counts up to 500 cells/ μl might be appropriate at least for some patients³. Study conducted by Seigfried, *et al* reveal that there is evidence of moderate quality that initiating ART at CD₄ levels higher than 200 or 250 cells/μL reduces mortality rates in asymptomatic, ART-naive, HIV-infected people⁵. Practitioners and policy makers may consider initiating ART at levels ≤ 350 cells/μL for patients who present to health services and are diagnosed with HIV early in the infection⁵. In 2008, the United States Panel of the International AIDS Society recommended that ART in adults with HIV infection should not be initiated before CD₄ cell count declines to less than 350 cell/ μL. In patients with 350 CD₄ cells/μL or more, the decision to begin therapy should be individualized based on the presence of co-morbidities, risk factors for progression to AIDS and non-AIDS defining disease^{13,14}. Also in July 2010, the World Health Organization (WHO) published new recommendations on providing antiretroviral therapy (ART) to adults and adolescents in resource-limited settings that revised the guidelines previously published in 2006. The new recommendations encourage starting ART earlier, usually at a CD₄ count of 350 or lower, specify regimens for first and second line therapies, and contain other recommendations regarding laboratory monitoring and other elements⁴. Recommendations on the timing for ART initiation differ based on availability of resources, leading to confusion amongst clinicians and policy-makers in determining the most favorable point to begin treatment⁵. At least all international guidelines agree that all symptomatic patients as well as patients with CD₄ count less than 200 cells/μl should be treated. Since 2007 or 2008, most guidelines have determined a CD₄ T cell count of < 350 CD₄/ μl as a threshold for initiation ART^{13,14}.

Global and National Epidemiology of HIV/AIDS

Global epidemiology of HIV/AIDS

In 2008, an estimated 2.7 million new HIV infections occurred worldwide; this was 30 % lower than the 3.5 million new infections at the peak of the epidemic in 1996¹⁵. Sub-Saharan Africa remains the most heavily affected region, accounting for about 71 % of all new HIV infections in 2008. There are two related but distinct types of HIV: HIV-1 and HIV-2¹⁶. HIV-1 is the most pathogenic and causes over 99 % of HIV infections¹⁷. HIV-2 is also known to cause AIDS but is much less prevalent, being present in fewer and isolated geographic locations such as West Africa. Therefore, most research is done on HIV-1¹⁸. AIDS-related diseases remain one of the leading causes of death globally. According to UNAIDS, the number of people living with HIV/AIDS worldwide was estimated at 33.4 million in 2008; > 20 % higher than the number in 2000. It was estimated that 2 million deaths due to AIDS-related illnesses occurred worldwide in 2008; this was ~10 % lower than in 2004. The declines in new infections and AIDS-deaths may be attributed to the scale-up of antiretroviral therapy (ART) programmes, especially in the developing world. As of December 2008, approximately 4 million people in low- and middle-income countries were on ART, representing a 10-fold increase over five years. In eastern and southern Africa, ART coverage rose from 7 % in 2003 to 48 % in 2008¹⁵.

Epidemiology of HIV/AIDS in Ethiopia

The HIV pandemic created unprecedented burden on the economies and health care systems of affected countries, particularly in sub-Saharan Africa, where prevalence is highest. In Ethiopia, the total number of people who have died due to HIV/AIDS in 2006 alone was 88,997; and in 2007, it is estimated that, 71,902 people will die.

In 2007, there are an estimated 898,350 children have lost one or both parents to the epidemic (AIDS orphans). According to the calibrated single point estimate (from 2005 sentinel surveillance and EDHS data), prevalence of adult infection is 2.1 % (urban 7.7 %, rural 0.9 %). In 2007, the estimated number of people living with HIV is 977,394, including 64,813 children. The current estimate of people requiring antiretroviral therapy is 258,264 and of these 6 % (15,716) are children⁷.

Ethiopia response to the HIV/AIDS epidemic

The Government of Ethiopia is making tremendous efforts towards containing the epidemic. As part of this endeavor, the Government put in place a national HIV/AIDS policy in 1998 to create an enabling environment to fight the pandemic. Overall, support and commitment in relation to HIV and AIDS has increased over the years, and progress has been made in the development of specific HIV/AIDS related legislation and revising the HIV policy to promote and protect human rights. Moreover, there have been some encouraging efforts to enforce the existing policies, laws and regulations. Civil society involvement in the process of planning, monitoring and evaluation of HIV/AIDS responses at various levels are improving. According to the 2007 Single Point Estimate, 336,160 PLHIV were in need of ART in 2009, out of which 20,522 were children below the age of 15 years. The number of AIDS cases ever started on ART has grown to 241,759 as of December 2009, among which 176,632 were currently on treatment coverage of 53 % of those in need. In 2009 alone, 43,130 new HIV patients were started on ART. Likewise the total number of people ever enrolled to chronic HIV care reached to 435,150 by the end of 2009. Out of all ART clients 58 % (102,379) were female, a reflection of the higher number of women living with HIV. The vast majority of the patients (80.1 %) initiated ART below 200 CD₄ count at entry. ART has also improved the functional status of patients with the rate of change of working patients increased positively by 42 % within six months duration of treatment while the rate of change of ambulatory and bedridden patients declined considerably. Adherence rate declines as the duration of treatment increases, 88 % at the first six months and 84 % at 12 months. The highest levels of death and lost to follow up are observed in the first six months of ART treatment, where about 14.5 % dropped out from the program. The most cited reasons for drop out are economic problems, seeking religious treatment, fear of drug side effects and poor patient handling. Furthermore, the overall death rate was 6.5 % at six months. Both death and lost to follow up rates have declined at 12 and 24 months of treatment⁸. Current ART guideline for PLWHA of adult patients by FMOH of Ethiopia decided to initiate ART to asymptomatic patients with a CD₄ + count < 200 cells/ μl, to patients in WHO stage 3 with a CD₄ + cell count < 350 cells/ml and patients in WHO stage 4 regardless of CD₄ + count. If CD₄ count is not available ART initiate based on TLC total lymphocyte count⁷.

The study conducted in Ethiopia: - Oromia region, Shashemene and Assela a total of 290 patients were initiated with ART in both facilities during the study period. Data available for analysis include 272 ART patients from a total of 409 that follow-up the treatment. The demographic characteristics of the cohorts showed that 70 % were under the age of 24, 47.4 % were aged 25-44 and 16.9 % were above 45 at the time of treatment initiation. The median age of patients at the start of treatment was 33 years ranging from 19 up to 68. The majority of the patient was women (57 %) and the rest were men, 59 % of the patients have a base line weight less than 50 kg and the median base line weight was 49 kg. The clinical parameters of the patients are 71 % of patients had CD₄ count of < 200 cells per μl, this indicating that the majority had advanced HIV disease at the initiation of ART. The median CD₄ count of the patients at the time of the treatment initiation was 103 cells/ μl and 82 % of the patient started ART based on the Cd₄ - 200 cells/ μl criterion and the rest for clinical or combined reasons¹⁹.

Recovery of CD₄ cells after initiation of antiretroviral therapy

Antiretroviral therapy usually results in a biphasic increase in CD₄ cell count. The initial increase in CD₄ cell count is very rapid and is usually observed in the first 3–6 months and a second phase of slower increase follows. More than 95 % of successfully treated individuals with well-controlled HIV-1 viraemia reach a CD₄ cell count of more than 200 cells per μ L. However, one-third of successfully treated patients appear not to reach a normal CD₄ cell count within 5 years. This observation raises concerns for the long term prognosis of these patients and suggests that antiretroviral therapy should be initiated before CD₄ cell counts fall below a certain threshold. With adequate monitoring, CD₄ cell counts can be maintained above pre-specified levels during scheduled treatment interruptions. However, a lower CD₄ cell count may expose patients to an increased risk of clinical events. This risk needs to be carefully balanced against the potential benefits associated with decreased exposure to antiretroviral drugs²⁰.

Factor affecting the effectiveness of ART

Malnutrition

Malnutrition at the time of starting ART was significantly associated with decreased survival, but the effect appeared not to be mediated by impaired immune reconstitution. Given the increasing access to ART in developing countries and the high frequency of HIV-associated wasting, studies of nutritional therapy as an adjunct to the initiation of HAART are urgently needed. However, no previous study has specifically examined the impact upon survival of malnutrition at the time of starting ART. It is possible that malnutrition may impair the immune response to ART, prolonging the period during which patients are at risk of opportunistic infection and directly or indirectly increasing the risk of death. Malnutrition may therefore represent a potentially reversible cause of increased mortality in patients who are initiating ART. The study performed the analysis using data from a retrospective observational cohort study in order to examine the associations of malnutrition with survival and with CD₄ count response in patients commencing ART²¹.

ART adherence

The study conducted by Ross-Degnan *et al* shows that adherence and attendance indicators measured using routine data that exist in typical African HIV/AIDS care settings were significantly associated with key clinical outcomes during the early treatment period. Consistency of clinic visits and dispensing-based adherence indicators were both moderately to highly associated with weight gain during the first nine months after ART initiation. In addition, both dispensing-based adherence measures and self-reported adherence were predictive of improvements in CD₄ counts in that period²¹. Adherence to ART is well recognized to be an essential component of individual and programmatic treatment success. Higher levels of adherence are associated with improved virological and clinical outcome. Correct medication taking is desirable in order to maximize the benefit of ART. This means taking the correct dose of drugs at the right times and observing any dietary restrictions, but anything without this leads to the development of viral resistance and hence to much earlier treatment failure. Many patients who are on ART regimens may lead to non-adherence due to different contributing factors like: socio-cultural factors (negative attitude or perceptions, poor social support, lack of family, community and employer support, stigma, religion and preference to traditional medicine). Patients/ provider relationship (lack of trust and confidence). Non adherence to ART clinical setting and service delivery (poorly motivated, unfriendly, unsupportive, judgmental staff, lack of confidentiality, inadequate counseling, inconvenient appointments, non-functional laboratories), disease characteristics

and type of ARV drugs (prior OIs and their management, pill burden, food or fluid restriction, side effect and adverse drug reactions), patient variables (sex, age, unemployment, insufficient nutrition, lack of education, alcohol, depression etc.)²³.

Current status and challenges of antiretroviral research and therapy

The impact of antiretroviral therapy on human medicine is often compared to that of antibiotics and rightfully so, since both types of drugs are saving millions of lives worldwide. However, the challenges of the current HAART regimens are incomparably more complex than those encountered by modern antibiotics. HAART faces a persistent enemy with great evolutionary potential in a long battle that cannot be won using currently available drugs. Although the goals of antiretroviral therapy are the same around the world, the conditions, resources, and outcomes of HIV treatment are deeply affected by economic, political and geographic factors. Much has been done to narrow the gap between resource abundant and resource-constrained regions, but the process of reversing the course of the HIV pandemic has barely begun. In some areas, progress is being held back by the elementary failure of state or clerical officials to acknowledge the problem. However, it is one of the fortunate traits of the human race that persistent challenges continue to stimulate and inspire the search for new solutions, strategies and resources. Above all, however, this issue is meant as a tribute to the hard work and dedication of countless researchers, physicians, medical workers, activists, drug developers, and regulatory officials over the course of 25 years, who have changed a deadly disease into a manageable illness and given us hope that one day the success of HIV control will be compared to that of polio and smallpox²⁴.

Objective

General objective

To assess ART treatment outcomes versus CD₄ count threshold among HIV/AIDS patients in Ras Desta hospital.

Specific objective

- To assess the improvement of patient CD₄ count at different threshold.
- To describe the mortality rate in relation to CD₄ count threshold.
- To assess the improvement of weight and current outcomes of the patients.

MATERIALS AND METHODS

Study Setting

This survey was conducted in Ras Desta hospital, located in Gulele sub-city, Addis-Ababa administration. Ras Desta hospital is one of the oldest hospitals in Ethiopia; it was established in 1932 and named with the name of Ras Desta Damtew. Now this hospital is administered under Addis Ababa regional health bureau. The hospital has 92 beds and serves for more than 180 patients per day in both inpatient and outpatient medical wards. Concerning staffs the hospital has pharmacy, nurse, lab technician, midwife, medical doctors, health officers, ophthalmologist, anesthetic nurse, ray technician etc giving service in its different departments including surgical referral OPD, medical referral OPD (internal medicine department), orthopedic referral OPD, dental clinic, eye clinic department of Pharmacy, Radiology and Laboratory. ART clinic is one of the medical referral clinics given services for around 4892 peoples in the study year and the services given at the center include diagnosis, treatment of HIV/AIDS and co-infection, ARV drug dispensing and counseling and voluntary counseling testing (VCT).

Study Design

This was a retrospective cohort study of HIV positive patient's ART treatment outcomes in relation to CD₄ count threshold in Ras Desta hospital. From all HIV positive patients who had registered for ART from September 2001-2003 at Ras Desta hospital, 636 patients had met the criteria of the study and they were selected. Data of interest was abstracted on to data collection tool (Appendix 1). This data of interest at initiation of ART included socio-demographic details like sex, age, examination results of weight, height, patient current status and laboratory results of CD₄ cell count. On follow up care, data was collected on weight and CD₄ counts at 6, 12, and 24 months. Finally patient outcome was recorded during the 24 months period of ART use in order to check whether the patient was still alive or dead and whether had defaulted treatment or else had transferred out to other facilities. All patients that fulfilled the above criteria were included in the study.

Data Quality assurance

Before starting the study pre-test was conducted in the hospital ART center by the principal investigator and little modification was made accordingly.

Study Population

All HIV infected patients that started ART at Ras Desta Hospital between September 2009 and February 2011 and had complete data on socio-demographic details, examinations of weight, laboratory findings of CD₄ values on initial and follow up and their outcomes were included in the study. At this Ras Desta Hospital patients were initially followed up every month for first two months thereafter it was every six months using both clinical assessment and laboratory monitoring of CD₄ count in order to assess response to treatment intervention. Inclusion criteria was for all patients presenting at Ras Desta hospital ARV clinic who had complete data on socio-demographic details, examinations of weight, current patient outcome records and CD₄ checked at the starting of ART and follow up. The study included those patients living, dead or dropped out from treatment. An exclusion criterion was for all patients who started ART prior to commencement of ART at Ras Desta hospitals including those patients who were transferred in from other health facilities and patient that lack important data.

Data Collection and Analysis

Information was collected by using a data abstraction format from computer data base by hospital investigator and specific checklist by principal investigator. The checklists included the following variables: age, sex, initial and follow up weight, CD₄ count results and current outcomes. Patients were not identified by name. Data was collected using special code numbers which were already being used at this hospital. This collected data was analyzed manually and using Excel software and presented to present in the form of tables, graphs and charts.

Study variable

Independent variable

- Age
- Sex
- Base CD₄ count
- Base weight
- Height

Dependent variable

Patient treatment outcomes (CD₄ count and weight improvement, death rate)

Sampling and sample size

Purposive sampling technique was used to choose Ras Desta hospital. This was because the hospital has its own data base registration for CD₄ count and other necessary information. Out of a total of 4892 eligible patients' case notes, a purposive sampling of every alternate file was pulled aside for the research such that by the end of the exercise, a sample size of 636 was arrived at for the study because these groups of patients fulfilled the criteria of the study.

Operational definition

- Early initiation of ARV: initiating ARV drugs at CD₄ count greater than or equal to 350 cells/ μ l.
- Delayed initiation of ARV: initiating ARV drugs late after CD₄ count less than or equal to 200 cells/ μ l
- CD₄ cell count: it measures the number of immune system cells that have CD₄ receptor, count is determined by a blood test measured by the number of CD₄ cell/ μ l.
- A treatment outcomes measure defines as the following ways according to this study:
 - ✓ Clinical occurrence of new HIV-related events (death or AIDS-defining illness)
 - ✓ Immunologic response (changes in mean CD₄ cell count or mean absolute change compared with baseline).
 - ✓ Weight improvement (proportion of patients maintaining the weight change in (mean relative change (percent) or mean absolute change, compared with baseline)

Ethical Considerations

The study approved by school of pharmacy AAU, cooperation letter was written by the department of pharmaceuticals to Addis Ababa health bureau ethical committee. Then the health bureau wrote a permission letter which address to Ras Desta hospital to do my study in the behalf of the hospital medical director and ART center team members so as to available and accessible all information to be collected from patient records by the hospital investigator and the principal investigator and confidentiality of data extracted from patient card was maintained by excluding identifier during analysis and data presentation. The collected data was kept in my home in a closed metal box for sake of privacy.

Significance of the Study

The study will aims at providing the necessary information on the initiating of ART and treatment outcomes of the patients in related to CD₄ count, this may bearing a significant difference in prevention and treatment of HIV/AIDS which determine the appropriate measure to be taken at the time of initiating ART for maximum benefit of PLWHA with possible minimum adverse drug reaction with better adherence and compliance for treatment, as to achieve better therapeutic out come and improved patient quality of life

Limitation of the study

The study conducted only in one governmental hospital so it doesnot represent the whole sample and there is a higher data storage system problem in the ART pharmacy, since 128 (20 %), 229 (36 %), 262 (41 %) had no registered CD₄ count at 6, 12, 24 month respectively, and there is higher dropout rate as 68 (10.7 %) patients were lost to follow-up at 24 months of treatment. When patient lost to follow-up phone calls were used to contact them but we are unable to actively trace lost to follow-up cases. Due to poor registration system we cannot asses the BMI, since it is better indicator of outcome measure than weight. Furthermore, due to limited time frame it was not possible to investigate all relevant data that are used to assess the study in details.

RESULT

Socio-demographic characteristics

Out of the 636 patients chosen for the study, 372 (58.5 %) were females while 264 (41.5 %) were males. For the whole sample under study, the median age was 36 years (range 15 to 78 years). Looking at females only, the median age was 35 years (range 16 to 70 years) while as for males the median age was 40 years (range 15 to 78 years). Further findings showed that the largest group of patients belonged to those in age group 25-44 years making up 68.6 %, followed by patients in the age group 45-78 years at 23.4 % the lowest group 8 % was for patients in the age group of 15 to 24 years.

Table 1: Socio-demographic characteristics ART of HIV patients at Ras Desta hospital, Ethiopia, 2009-2011

Variable	Frequency	Percent
Sex		
Male	264	41.5
Female	372	58.5
Age in years		
15-24	51	8
25-44	436	68.6
45 and above	149	23.4

The rise of CD₄ cell counts in patient on ART

Out of 636 patients 504 patients had a CD₄ count less than 200 cells/mm³, 120 had a CD₄ count greater than 200 and less than 350 cells / μl. Lastly, a total of 12 patients had a CD₄ count greater than 350 cells/mm³ at the initiation of ART (Table 2). The initial median CD₄ count values for all 636 patients receiving ART were 134 cells / μl and 273 cells / μl in the first six month. Other findings derived from calculating the mean CD₄ counts amongst patients starting ART in CD₄ count less than 200 cells / μl had a mean CD₄ count improvement of 110 (101 to 211) cells / μl, 22 (211 to 233) cells / μl, 40 (233 to 273) cells / μl at 6, 12, 24 month respectively. While, for those patients who had CD₄ count greater than 200 and less than 350 cells / μl had median CD₄ cell count improvement of 101 (244 to 345) cells / μl, 15 (345 to 360) cells / μl, 17 (360 to 377) cells / μl at 6, 12, 24 month respectively. Lastly, for those patients who had a CD₄ count greater than 350 cells / μl had median CD₄ cell count improvement of 42 (475 to 517) cells / μl, 94 (517 to 611) cells / μl, 39 (611 to 650) cells / μl at 6, 12, 24 month respectively.

Improvement in weight at follow up CD₄ count

Findings show that for all patients in the study receiving ART, median weight was 53 Kg (range 27 kg to 93 kg). More findings reveal that at the start of ART, patients in CD₄ count < 200 cells/ μl had a mean weight of 53.4 Kg, While patients CD₄ count > 200 and < 350 cells/ μl had a mean weight of 55.4 Kg and lastly, for patients whose CD₄ count > 350 cells/ μl their mean weight was 56 Kg. Overall, for all patients in the sample, initial mean weight was 54 Kg, at 6 months mean weight was 60 Kg, at 12 months follow up, mean weight was 61 Kg. Finally, at 24 months follow up, mean weight was 61 Kg. Overall looking at individual findings reveal that at 24 months of follow up, patients receiving ART at CD₄ cell count less than 200 cells/ μl had higher improvement in their mean weight from an initial value of 54 rise of up to 61 kg and while as patients receiving ART whose CD₄ cell count > 350 cells/ μl patient had the least weight improvement from 56 kg to 59 kg.

Patient outcome by twenty-four months of ART

Four hundred eighty (75.5 %) patients were alive, twenty one (3.3 %) patients had transferred out, 67 (10.5 %), were defaulters of

treatment while as 68 (10.7 %) had died during two year period of ART use.

Death analysis

A further observations of the deaths revealed that 53 (78 %) were CD₄ count less than 200 cells/μl, 14 (20.5 %) patients were CD₄ count > 200 and < 350 cells/μl, while only 1 (1.5 %) of the patient were died whose CD₄ count > 350 cells/μl. Laboratory findings show that patients who died had a lower mean CD₄ cell count (65.6 cells/μl) at initiation of treatment.

DISCUSSION

The human immunodeficiency virus (HIV) has created an enormous challenge worldwide. Since its recognition, HIV has infected close to 70 million people, and more than 30 million have died due to acquired immunodeficiency syndrome (AIDS). More than 66 % of the 40 million people living with HIV/AIDS are in sub-Saharan Africa, where AIDS is the leading cause of death. Ethiopia is the second most populous and one of the seriously affected countries in sub Saharan Africa⁷. Chronic and widespread poverty makes it especially difficult for Ethiopians to cope with HIV. Poor people have less access to information, prevention tools, care, support, and treatment. HIV/AIDS is not specific to a certain age group of people. Rather it attacks any age groups that are exposed to the risk factors to transmit the virus from infected persons to non-infected one. Most of the HIV infected patients enrolled in this study were young age between 24 and 44 years old who were sexually more active and thus have a higher risk of infection compared to the other age groups²⁵. It also infects any sex group of population even if the degree of exposure is different²⁶. Findings from the study revealed that for patients accessing ART at the Ras Desta hospital, women outnumber men by a ratio of 1.75:1.25. This is what is expected if provision of ART services in Ethiopia was equitable since women bear the brunt of the HIV epidemic in the Sub-Saharan Africa. The higher percentage of HIV infection amongst females is similar to the overall findings of Ethiopia national figure which also shows that by March, 2010 out of all ART clients 58 % (102, 379) were female, a reflection of the higher number of women living with HIV⁸; this is because of biological, cultural, and economic problems. Biologically, due to more exposed surface area in the female genitals (sex organs) than in the male genitals and more semen is exchanged during sex than vaginal fluids makes them more likely to get HIV²⁷. A similar finding was also reported by Dzimmenani *et al* stated that women's in the Sub Saharan region are more at risk of getting HIV/AIDS because of sexual trade, migration, polygamy, teenage marriages and lack of emotional support, this are the exact outcome of poverty and culture in the region. Also the same study revealed that, Ethiopia has one of the highest rates of child marriage in the world. Nationwide, 60 % of girls under the age of 18 are married. Indeed, girls who marry young in Africa are mostly from poor families and have low levels of education²⁸. Results in this study show that 79 % of the patients initiated ART below 200 CD₄ count at entry, this indicating that the majority had advanced HIV disease at the initiation of ART almost a similar finding was reported by HIV/AIDS Prevention and Control Office, states that vast majority of the patients (80.1 %) initiated ART below 200 CD₄ count at entry, but a little higher result was stated by Alemu and San sabastia, it says 82 % of the patient started ART based on the CD₄ - 200 cell/ μl criterion and the rest for clinical or combined reasons^{8,19}. At baseline, the median CD₄ cell count of ART-naïve HIV infected patients was higher (134 cells /μl) than the reports from study conducted in Assela (103 cells/μl), Jimma university specialized hospital, Ethiopia and the study conducted in India, which stated that the median CD₄ count of enrolled patients was 119 cells/ μl^{19,29,36}, but lower (250 cells/μl) than the reports from other countries³⁰. This could be due to delayed presentation and/or testing, differences in educational and socio-economic levels.

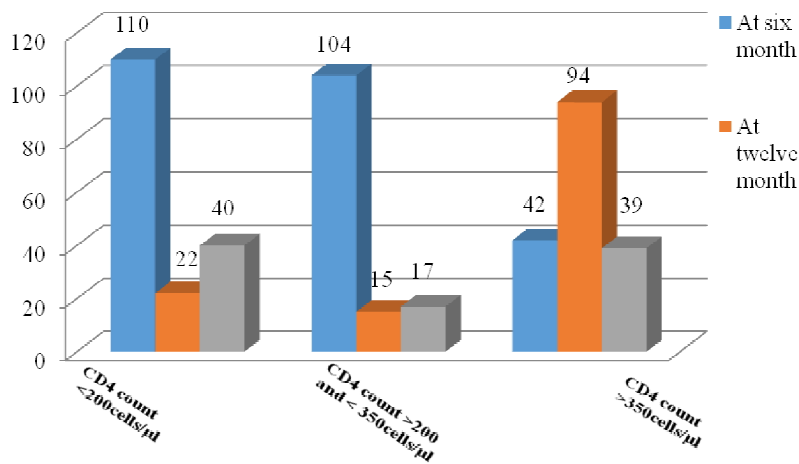


Figure 1: Average CD₄ count improvement over 24 month

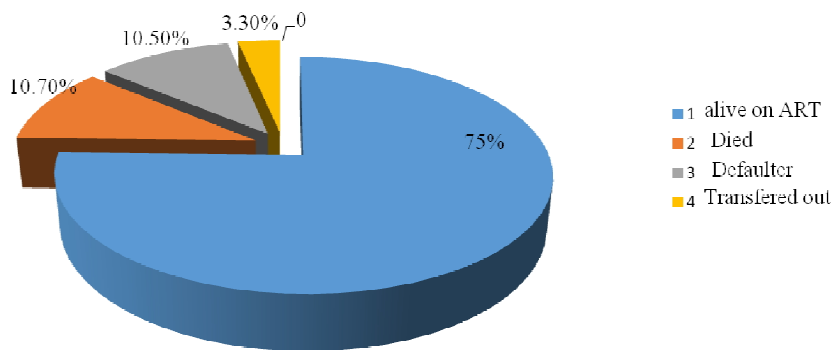


Figure 2: Patient outcome by the twenty four months

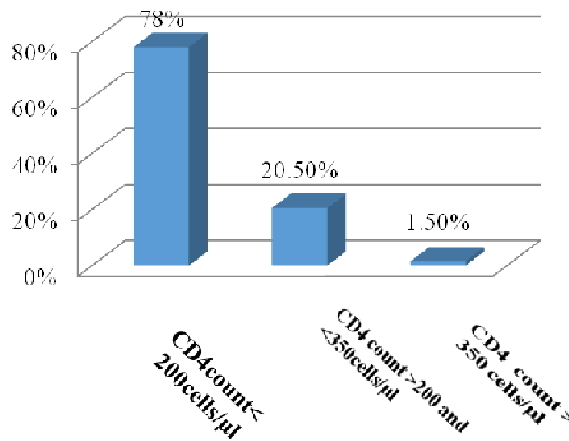


Figure 3: Death analysis at different CD₄ count threshold

The CD₄ count of most patients before starting ART is initially low (< 200). This is because of HIV affects the human immune system directly or T helper cells that representing the patient immune system for protection, whereas after initiation of ART the patient CD₄ count increased significantly (> 200) due to the initiation of drugs. After an initial rapid increase in CD₄ T lymphocyte counts within the first 3–6 months of ART, a second phase of slower increase occurs in most patients. However, considerable individual variation has been noted in this response. Several factors are associated with impaired CD₄ T cell reconstitution, including older

age, non-suppressed HIV replication, and treatment interruption. In general, the lower the CD₄ T cell count at the initiation of ART, the longer it takes to reach desired target levels. Certain investigations even suggest that CD₄ T cell recovery may level off before the physiological range is reached, particularly in individuals who begin ART when their CD₄ T cell counts are extremely low⁸. Among HIV-positive persons starting HAART, the study identified a rapid average increase of 42-110 cells / μl during which is lower than the study conducted in U.S.A, which is in six month 93-151 cells / μl³¹. In this study patient who had CD₄ count < 200 and between 200-300

cells / μ l there is very rapid initial increase in CD₄ cell count observed in the first 6 months and a slower increase follows than patient who had CD₄ count > 350 cells / μ l this is a sign of severe immune-depression, developing of opportunistic infection^{13,14}. The pattern of weight gain observed appears to be consistent with previous reports, with the highest rate of weight gain occurring in the first six months after ART initiation, then stabilizing afterwards. Patients in ART programs in Vietnam observed a similar pattern of weight gain, although patients in that study continued to gain weight up to 24 months post-ART before weights stabilized. It was found that several significant predictors of weight gain, particularly in the first six months after ART initiation. Patients with more advanced HIV infection at baseline (CD₄ cell counts <200 cells/ μ l) were more likely to have positive weight changes (54 to 61 kg) in the first six months of therapy than the other, likely due to the beneficial effects of ART, which is similar to the above study³², while patients receiving ART whose CD₄ cell count > 350 cells/ μ l patient had the least weight improvement from 56 kg to 59 kg this may due to they had good immune system. The average weight gain over the 24 months was 6 kg this is higher when compared with study conducted by Ross-Degnan *et al* and BMC Health services research both research stated that patients gained an average of 3.9 kg in the first six months of treatment²². Patient outcome by twenty-four months of ART reveals that four hundred eighty (75.5 %) patients were alive, twenty one (3.3 %) patients had transferred out, 67 (10.5 %) were lost to follow-up and 68 (10.7 %) died, when this result compared with study conducted in India there is higher value of alive on ART and lower level of dead and lost to follow up, the study stated that over 2 years, 71 % were alive, 13 % died, 16 % were lost to follow up²⁹. Furthermore, according to national figure about 14.5 % lost to follow up from the program which higher than this study and 6.5 % died which is lower. The most cited reasons for drop out are economic problems, seeking religious treatment, fear of drug side effects and poor patient handling and the study setting used phone calls to contact patients and it noted that the reasons for the failure to follow-up were serious illness and deteriorating health situation, change in address, undocumented transfer out to other hospitals, lack of support, seek of religious treatment, financial reasons or death⁸. The study reveals that sixty-eight (10.7 %) of patients had died within the 24 months period of ART use. This is higher compared to the National figure which states that by 2010, 6.5 % of patients on ART had died and lower than the study conducted in India^{8,29}. Many other cohort studies have found a clear association between CD₄ T cells at ART initiation and mortality rates^{33,5}. The lower the CD₄ T cells the higher the risks over the following period what I observed in this study, patients who had CD₄ count < 200 cells/ μ l accounts 78 % of the death, whereas 22 % was that of patient > than 200 cells/ μ l this is evidence of moderate quality that initiating ART at CD₄ levels higher than 200 or 250 cells/ μ l reduces mortality rates in asymptomatic, ART-naive, HIV-infected people. Since 2007 or 2008, most guidelines have determined a CD₄ T cell count of < 350 CD₄/ μ l as a threshold for initiation ART^{13,14} and also in July 2010, the World Health Organization (WHO) published new recommendations on providing antiretroviral therapy (ART) to adults and adolescents in resource-limited settings that revised the guidelines previously published in 2006. The new recommendation encourage starting ART earlier, usually at a CD₄ count of 350 cells/ μ l or lower, specifies regimens for first and second line therapies and contains other recommendations regarding laboratory monitoring and other elements, but our countries still uses the 2006 guidelines⁴. Studies conducted in Ethiopia and Tanzania reported that neither of the guideline development processes fully satisfies minimal requirements of procedural fairness. There is a lack of transparency. The reasons for decisions are rarely given and are not publicly available. This reduces the opportunity for public questioning, debate and revisions. The guidelines were based on expert opinion and consensus. Recommendations from the WHO were copied without much discussion, disagreement or adjustment, so it seeks revision³⁴. Initiating therapy at 200–350/ μ l and above 350/ μ l was

more effective, but requires more resources than deferring therapy to CD₄ cell count < 200/ μ l³⁵.

CONCLUSION

Early initiation of ART at CD₄ levels higher than 200 cells/ μ l reduces mortality, immune-depression, and weight loss and also improve outcome of ART treatment in asymptomatic, ART-naive, HIV-infected people.

Recommendations

With all the study findings and discussions above, the following recommendations are made; Practitioners and policy-makers may consider initiating ART at levels > 200 cells/ μ l for patients who present to health services and are diagnosed with HIV early in the infection. There is need for policy makers in poor resource setting like Ethiopia need to consider and advocate effective CD₄ count threshold for initiation of ART. There is need to increase availability of Counseling and Testing (CT) services to enable individuals know their HIV status early enough and if positive, the knowledge of their HIV status would allow them to better protect themselves, their partners, plan their future well, access early care, support and ARV therapy. The data registration system would be checked continuously by separate individual other than the data recorder to obtain appropriate patient data this may be an important issue to increase the outcomes of ART. This study indicated that loss to follow-up would be an important issue in ART program in resource limited countries and shouldn't be overlooked during the initiation and expansion of the ART program to obtain better outcome.

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REFERENCES

1. National AIDS and STI Control Program Ministry of Health and Social Welfare Republic of Liberia: Integrated Guidelines for Prevention, Testing, Care and Treatment of HIV/AIDS in Liberia second Edition; 2007. p. 15.
2. Hammer S, Eron J, Reiss P, Schooley R, Thompson M, Walmsley S, Cahn P, Fischl M, Gatell J, Hirsch M, Jacobsen D, Montaner J, Richman D, Yeni P, Volberding P. Antiretroviral treatment of adult HIV infection: recommendations of the International AIDS Society-USA panel. *The Journal of the American Medical Association* 2008; 300: 555–570. <http://dx.doi.org/10.1001/jama.300.5.555>
3. Kitahata M, Gange S, Abraham A. Effect of early versus deferred antiretroviral therapy for HIV on survival. *N. Engl. J. Med* 2009; 360: 1815–1826. <http://dx.doi.org/10.1056/NEJMoa0807252>
4. Stover J, Bollinger L and Avil C. Estimating the Impact and Cost of the WHO 2010 recommendations for Antiretroviral Therapy. *AIDS Research and Treatment*; 2010. p. 1-7.
5. Siegfried N, Uthman OA, Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naive adults (Review). *Intervention Review* 2010; 3: 2-18.
6. Melusi N. Strengthening the capacity of traditional health practitioners to respond to HIV/AIDS and TB in KwaZulu Natal, South Africa; 2009.
7. Federal HIV/AIDS Prevention and Control Office /Federal Ministry of Health). Guidelines for management of OIs and ART in adolescents and adults in Ethiopia; 2007.

8. Federal HIV/AIDS Prevention and Control Office. Report on progress towards implementation of the UN Declaration of Commitment on HIV/AIDS Federal Democratic Republic of Ethiopia; 2010.
9. Chinsebu KC. Model and experiences of initiating collaboration with traditional healers in validation of ethno-medicines for HIV/AIDS in Namibia. *J. Ethnobiol. Ethnomed* 2009; 1186: 1746-4269.
10. Hart E. National review of first treatment change after starting HAART in naïve patients. *British HIV association on HIV management* 2007; 8: 186-187.
11. CDC. Guidelines for prevention and treatment of opportunistic infection in HIV infected adults and adolescents; morbidity and mortality weekly report; 2009.
12. Bategay M, Nüesch R, Hirschel B, Kaufmann GR. Immunological recovery and antiretroviral therapy in HIV-1 infection: Division of Infectious Diseases and Hospital Epidemiology the *Lancet Infect Dis* 2006; 6: 280–87. [http://dx.doi.org/10.1016/S1473-3099\(06\)70463-7](http://dx.doi.org/10.1016/S1473-3099(06)70463-7)
13. DHHS: US Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents; 2008.
14. European AIDS Clinical Society (EACS). Guidelines for the clinical management and treatment of HIV-infected adults in Europe; 2008.
15. UNAIDS. The regional workshop on adopting minimum standards of practice for theta evaluation team. Participatory evaluation report. Innovation or reawakening? Roles of traditional healers in the management and prevention of HIV/AIDS in Uganda. Geneva: UNAIDS; 2009.
16. Fletcher CV, Kakuda TN, Collier AC. Bone and joint infections. In: JT Dipiro, RL Talbert, GC Yee, GR Matzke, BG Wells, LM Posey (eds) *Pharmacotherapy- a pathophysiologic approach*. Mcgraw Hill Medical Publishing Division, United States of America, 5th edition; 2002. p. 2151–2174.
17. Cos P, Maes L, Berghe DV, Hermans N, Pieters L, Vlietinck A. Plant substances as anti- HIV agents selected according to their putative mechanism of action. *J. Nat. Prod* 2004; 67(2): 284–293. <http://dx.doi.org/10.1021/np034016p>
18. Klos M, van de Venter M, Milne PJ, Traore HN, Meyer D, Oosthuizen V. *In vitro* anti- HIV activity of five selected South African medicinal plant extracts. *J. Ethnopharmacol* 2009; 124: 182-188. <http://dx.doi.org/10.1016/j.jep.2009.04.043>
19. Alemu AW, San Sebastia. Determinants of survival in adult HIV patient therapy in oromia: - shashemene and assela hospital, Ethiopia. *Global Health Action* 2010; 3: 5398-5407. <http://dx.doi.org/10.3402/gha.v3i0.5398>
20. Bategay M, Nüesch R, Hirschel B, Kaufmann GR. Immunological recovery and antiretroviral therapy in HIV-1 infection: Division of Infectious Diseases and Hospital Epidemiology the *Lancet Infect Dis* 2006; 6: 280–87. [http://dx.doi.org/10.1016/S1473-3099\(06\)70463-7](http://dx.doi.org/10.1016/S1473-3099(06)70463-7)
21. Paton NI, Sangeetha S, Earnest A and Bellamy R. The impact of malnutrition on survival and the CD₄ count response in HIV-infected patients starting antiretroviral therapy. *British HIV Association* 2006; 7: 323–330.
22. Ross Degnan D, Pierre Jacques M, Zhang F, Tadege H, Gitau L, Ntaganira J, Balikuddembe R, Chalker J, Wagner AK, Inrud I. Measuring adherence to antiretroviral treatment in resource-poor settings: The clinical validity of key indicators. *BMC Health Services Research* 2010; 10: 4-7. <http://dx.doi.org/10.1186/1472-6963-10-42>
23. Wanjoy N. Factor that influence non-adherence to ART among HIV/AIDS patients in central province Kenya. *Epidemiology and disease control* 2009; 1: 22-24.
24. José AE, Cihlarb T. Current status and challenges of antiretroviral research and therapy. *Antiviral Research* 2010; 85: 25–33. <http://dx.doi.org/10.1016/j.antiviral.2009.10.007>
25. Rangel M, Gavin L, Reed C, Fowler M, Lee L. Epidemiology of HIV/AIDS among Adolescents and young adults in the USA. *Adolescenthealth* 2006; 39: 156-163.
26. Brewé D, Potterat J, Brody S. Male and Female circumcision associated with prevalent HIV infection in virgins and adolescents in Kenya, Lesotho and Tanzania. *Annals of Epidemiology* 2007; 17: 212-217.
27. National Women's Health information Center. U.S. Department of Health and Human services office on Women's health; 2009.
28. Mbirimtengerenji ND. Is HIV/AIDS Epidemic Outcome of Poverty in Sub-Saharan Africa? *Croat Med Jr* 2007; 48(5): 605–617.
29. Bachani D, Garg R, Rewari B, Hegg L, Rajasekaran S, Deshpande KV, Emanuel V, Chank P, Sujatha RK. Two-year treatment outcomes of patients enrolled in India's national first-line antiretroviral therapy programme. *The National Medical Journal* 2010; 23: 7-12.
30. *Lancet*. Prognostic importance of initial response in HIV-1 infected patients starting potent antiretroviral therapy: analysis of prospective studies. *The Antiretroviral Therapy (ART) Cohort Collaboration* 2003; 362: 679–86.
31. Lifson AR, Krantz EM, Eberly LE, Dolan MJ, Marconi VC, Weintrob AC, Crum Cianflone NF, Ganesan A, Grambsch PL, Agan BK. Long-term CD₄⁺ lymphocyte response following HAART initiation in a U.S. Military prospective cohort. *AIDS Research and Therapy* 2011; 8: 7. <http://dx.doi.org/10.1186/1742-6405-8-2>
32. Tang AM, Sheehan HB, Jordan MR, Dang Van Duong MPH, Terrin N, Dong K, Trinh Thi Minh Lien RD, Vu Trung N, Wanke CA, Duc Hien N. Predictors of Weight Change in Male HIV-positive Injection Drug Users Initiating Antiretroviral Therapy in Hanoi, Vietnam; 2010.
33. Lawn SD, Harries AD, Anglaret X, Myer L and Wooda R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. *Editorial review* 2008; 22: 1903-1905.
34. Johansson KA, Jerene D, Norheim OF. National HIV treatment guidelines in Tanzania and Ethiopia: are they legitimate rationing tools? *J Med Ethics* 2008; 34: 478–483. <http://dx.doi.org/10.1136/jme.2007.021329>
35. Badri M, Cleary S, Maartens G, J Pitt J, Bekker LG, Orrell C and Wood R. When to initiate highly active antiretroviral therapy in sub Saharan Africa? A South African cost-effectiveness study. *Inter Med Press* 2006; 11: 63-72.
36. Alemayehu Lelisa Degu, Gizat Molla Kassie, Boressa Adugna Horsa. Comparative study of the effects of antiretroviral therapy (ART) on CD₄ cell count in Jimma University specialized hospital, Jimma town, Oromia region, Ethiopia. *J Pharm Sci Innov* 2014; 3(4): 310-314. <http://dx.doi.org/10.7897/2277-4572.034162>

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