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SCHOOL OF GRADUATE STUDIES

Lost opportunities to complete CD4+ T cell testing among HIV positive patients attending selected health centers in Afar region Northeast Ethiopia, 2014.

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List of acronyms and abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
CD4	Cluster of differentiation Four
DRERC	Departmental Research and Ethics Review Committee
EPHI	Ethiopian Public Health Institute
HIV	Human Immunodeficiency Virus
I-TECH	International Training and Education Center for Health
LTFU	Loss to Follow up
OI	Opportunistic Infection
PEPFAR	President's Emergency Plan for AIDS Relief
PIHCT	Provider Initiated HIV Counseling and Testing
PMTCT	Prevention of Mother to Child Transmission
POC	Point of Care
RNA	Ribonucleic Acid
STI	Sexually Transmitted Infection
TAT	Turnaround Time
TB	Tuberculosis
VCT	Voluntary Counseling and Testing
WHO	World Health Organization

Abstract

Background: In resource limited settings CD4+ T cell count (CD4 testing) facility is not available in peripheral areas and often either patients need to travel long distances or the samples need to be transported to the centers where the facility for CD4 testing is available. These results in delays in the completion of CD4 testing, and hence further delays occur in obtaining appropriate care and treatment.

Objective: To estimate rates of completion of CD4+ T cell count within 12 weeks of testing positive for human immunodeficiency virus (HIV) as well as predictors for completion at ART clinics in Afar region of Northeast Ethiopia.

Methods: The study was conducted in three most accessible selected Health centers with CD4 sample referring and ART services found in Afar Region of Northeast Ethiopia. Monthly report of HIV Positive patients was used to identify individuals with HIV positive results. Routine data was used separately to calculate the number and proportion of patients passing through PICHT, VCT, PMTCT, TB clinic. Of the total 1299 positive individuals at each entry point, 931 were linked to clinic patient card and ART data base. CD4 testing was considered complete once a patient had retrieved the test results. To determine the rate of CD4 testing completion, records of patient were reviewed. Predictors for completion were identified through multivariate logistic regression. SPSS version 16 was used for data cleaning and analysis. P values less than 0.05 were taken as statistically significant.

Result: Between September 1, 2007 and June, 2013, a total of 1299 patients consisted of 492(37.88%), 387(29.79%), and 420(32.33%) at Gewane, Werer and Semera health centers, respectively were tested positive for HIV. Patients who initiated CD4 testing after they tested positive for HIV and enrolled to ART clinic had a median CD4 cell count of 172/μl (interquartile range, IQR: 88–261). Majority 326 (59.8% of 545) had a CD4 cell count ≤ 200/μl and were already eligible for ART. The other 219 (40.2% of 545) had a CD4 cell count > 200/μl and were thus eligible for pre-ART medical care.

Of the 931 patients who were included in the study, 58.5% initiated CD4 testing within the 12 weeks study timeframe. Of these patients, 59.8% were immediately eligible for antiretroviral therapy (ART) because of a CD4 cell count ≤ 200/μl, but only 42.9% of the patients in this

category completed CD4 testing within 12 weeks of HIV testing. Among those not immediately eligible for ART (CD4 cells > 200/µl), only 31.5% completed CD4 testing within 12 weeks. Overall, of HIV+ patients who initiated CD4 testing, 61.65% did not complete it within 12 weeks of diagnosis. Among the predicting factors, the higher the baseline CD4 cell count, the lower the odds of completing CD4 testing within 12 weeks ($P<0.05$).

Conclusion: Majority of patients were already eligible for ART at the time of HIV diagnosis even under the restrictive threshold of 200 CD4 cells/µl that prevailed at the time of the study. But most did not complete CD4 testing within 12 weeks of diagnosis. Proper linkage of patient tested positive at any testing center and provision of immediate baseline CD4 cell count has indispensible role in reducing delayed treatment of patient with low CD4 cell count and maintaining patient enrolled at ART clinic.

1. INTRODUCTION

1.1. Background

Infection with human immunodeficiency virus (HIV) leads to the development of acquired immunodeficiency syndrome (AIDS), which is characterized by the loss of CD4+ T cells that are required for proper functioning of a person's immune system (1,2). Without treatment, the vast majority of HIV-infected individuals will eventually develop progressive immune suppression characterized by CD4+ T cell count (CD4 count) depletion, leading to AIDS-defining illnesses and premature death. The primary goal of antiretroviral therapy (ART) is to prevent HIV-associated morbidity and mortality. This goal is best accomplished by using effective ART to maximally inhibit HIV replication so that plasma HIV RNA levels remain below detection limit. Durable viral suppression improves immune function and quality of life, lowers the risk of both AIDS-defining and non- AIDS-defining complications, and prolongs life (2).

The CD4 count serves as a major laboratory indicator of immune function in patients who have HIV infection. It is one of the key factors in determining both the urgency of ART initiation and the need for prophylaxis for opportunistic infections. It is also the strongest predictor of subsequent disease progression and survival according to findings from clinical trials and cohort studies. The World Health Organization (WHO) has recommended using CD4 counts for initiation and monitoring of ART in HIV infected individuals in resource limited settings. CD4 testing is recommended at multiple points during the course of patient care. After a positive HIV diagnosis, a CD4 count is used to stage the disease so as to help determine whether the patient is eligible for ART; once on ART, the count is useful for monitoring of responses.(2).

Starting care and treatment for HIV infection and AIDS in patients with a low CD4 cell count imposes unnecessary costs on patients and society. Costs to patients include additional morbidity and mortality from HIV- and AIDS-related illnesses and a worse prognosis after initiating ART. Numerous studies have shown that a low CD4 cell count (≤ 100 cells/µl) and WHO Stage IV at the start of treatment are major predictors of mortality. Immune system recovery after 3 years on ART is also positively correlated with a patient's CD4 cell count when ART is begun. Access to care and treatment among patients with very low CD4 cell counts is associated with additional health care utilization costs to society through outpatient and inpatient services for opportunistic

infections and AIDS-related illnesses. A portion of these costs could be avoided through earlier access to HIV care and treatment, since a substantial share of health care is paid for by the government (3).

An estimated 0.8% of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. Sub-Saharan Africa bears the lion's share of the global HIV burden, with 23.5 million infected people, which constitutes 69% of the global total (4).

According to the Ethiopian HIV related estimates and projections for the year 2013, there are 734,048 People living with HIV/AIDS in Ethiopia which is 1.3% of the national adult HIV prevalence. Of these, 420,167 need ART. Ethiopia introduced a fee based Anti-Retroviral Treatment (ART) program in 2003. Since 2005, much progress has been made in starting and scaling up free ART to a large number of Ethiopians (5). The routine data supplied to the national HIV/AIDS prevention and control office (HAPCO) indicate that many patients have dropped out of chronic care. By the end of June 2008, there were only 110,611 patients (75%) who were alive and on ART out of the 150,136 patients who had been started on ART since 2003 (6).

The scaling up of the public ART programmes increased the demand for CD4 counts globally. In a resource limited setting CD4 count facility is not available in peripheral areas and often the patients need to travel long distances or the samples need to be transported to the centers where the facility for CD4 count estimation is available**.** This could be a barrier for expansion and decentralization of the ART programme and adherence to treatment (7).

On the other side, expanding access to HIV ART is hampered by high patient loss to follow up and delays in ART initiation. These challenges are partly due to limitations in access to CD4 testing. To facilitate easy access, CD4 testing should be done as close to the patient as possible, ideally at the primary health care level or with a dedicated specimen referral system that is dependable and timely (8).

1.2. Statement of the Problem

HIV testing services have expanded rapidly in many developing countries in order to reach ambitious targets for ART coverage. However, the potential for testing services to act as a

gateway to HIV treatment can be met only if individuals diagnosed with HIV are subsequently linked to onward care and treatment services in a timely manner. Delays in registering at HIV treatment clinic services following an HIV diagnosis can lead to late initiation of prophylactic treatment against opportunistic infections or ART, potentially resulting in poorer prognoses for patients and an additional clinical burden on overstretched health services (9).

Of particular concern are the poor retention rates observed between HIV diagnosis and treatment initiation (10), resulting in patients accessing ART at a later, more advanced stage of disease. Much of this attrition occurs between HIV diagnosis and assessment for ART eligibility (11, 12) indicating that many HIV-positive patients leave care without the knowledge of their need for treatment (13).

One of the major challenges for the delivery of CD4 services is ensuring that testing is accessible to all eligible patients. CD4 capacity is typically developed first in urban centers to service higher testing demands. The need for CD4 counts is expanding to sites with fewer patients and low test volumes and often having no CD4 machine or no laboratory (7).

Low retention of patients undermines efforts to scale up antiretroviral therapy. Up to 45% of patients (median 22%) are reported to be lost to follow-up in the first year after initiation of treatment (13-19). The rate of loss between diagnosis of HIV infection and initiation of treatment is much higher than the first-year rate—up to 80%; losses are associated with distance travelled to the clinic, weak referral linkages, and high death rates. To find patients who are lost to follow-up can be difficult, costly, and ineffective, which highlights the need to prevent losses. Most losses happen between HIV diagnosis and CD4 cell staging, but few interventions have been reported. Pre-ART loss to follow-up is a common but less clearly defined challenge in settings with limited resources (20).

Access to CD4 testing remains a barrier to providing effective HIV patient care and treatment in Ethiopia. Only 24% of health facilities providing ART in Ethiopia had conventional CD4 diagnostic machines by mid-2011 and only these facilities can provide same day results; even with specimen referral networks, this limits patient access to CD4 testing. Most health centers providing HIV care do not conduct CD4 testing, most refer specimens to a conventional laboratory for testing. In the sample referral system, there are more than 500 health facilities that

refer samples to higher-level facilities for CD4 monitoring on conventional CD4 machines. This often requires complex logistics and transport conditions that may compromise specimen quality in addition to the usually long turn-around-times (TATs). If specimens can only be referred on certain days, this limits access to testing. Patients must return to the facility multiple times to receive CD4 results. This places a high burden on patients, and it can adversely affect effective management of patients on treatment and delay in initiation of treatment and cause patient loss-to-follow-up (21).

As far as our knowledge goes, in Ethiopia there are no published studies that assess the magnitude of loss of patient in sample referring Health institutions. In this study, the proportion of patient loss to complete CD4 testing among HIV positive patient attending selected sample referring Health centers in Afar region will be assessed based on routine patient data.

2. SIGNIFICANCE OF THE STUDY

CD4 count is an important qualifying test for antiretroviral treatment in HIV-positive individuals and is also used to monitor treatment efficacy. The scale up of public ART programs globally has led to an increased demand for CD4 counting, especially to assess treatment eligibility. Despite expansion of laboratory infrastructure and services, access to CD4 testing remains a bottleneck to ART scale-up (22).

Growing recognition of the benefits of timely treatment and the consequences of losing pre-ART eligible patients is leading to increased awareness of the importance of regular CD4 and clinical monitoring before treatment eligibility (9).

Immediate and accurate CD4 testing is crucial at the primary level of the health system, where approximately 80% of patients in need are referred. In pregnant women, where clinical staging performs poorly, timely access to CD4 results for ART eligibility is crucial as emphasized in the preventing mother-to-child transmission (PMTCT) guideline for low and middle income countries released by the World Health Organization in 2009 (23).

In Ethiopia, the volume of patients in chronic HIV care is high with almost 300,000 currently on antiretroviral therapy. The number of HIV positive persons enrolled into ART care in Ethiopia is nearly 3,000 patients per month; however, CD4 testing services that are critical for treatment monitoring and initiation of therapy are not easily accessible. The Ethiopian Public Health Institute (EPHI) conducts approximately 650,000 CD4 test per annum; however, the need for CD4 testing is much greater. In addition to EPHI, many regional hospitals and laboratories have conventional CD4 testing machines. Though the laboratory network in Ethiopia is extensive and sample referral networks established, the total need for CD4 testing is unfortunately not being met due particularly to challenges with specimen transportation logistics (21).

In this study, the proportion of patient loss to complete CD4 testing among HIV positive patient in selected sample referring Health centers found in Afar region was assessed based on routine patient data. By conducting this study proportion of loss and complete CD4 count was assessed which help decision makers on at what stage of HIV care need intensive intervention. A first step

in solving the problem of post HIV diagnosis loss to initiation of appropriate HIV care and treatment is to obtain accurate estimates of the magnitude of the problem in public-health facilities that serve most Ethiopian patients. Because patients who test positive for HIV infection need to complete CD4 testing to enroll in an appropriate care or treatment programme. The study also helps to identify the magnitude of loss to follow up CD4 testing after initiating ART and design appropriate intervention for action.

The results in this study contribute to a growing literature that explores the problem of post-HIV Test loss to initiation of HIV/AIDS care and treatment in Ethiopia and other sub-Saharan countries

3. LITERATURE REVIEW

A growing body of studies from resource limited settings documented poor patient retention in HIV care after HIV counseling and testing. Nevertheless comparing retention in pre-antiretroviral care across sites and countries is complicated by varying definitions and methods of measurement. This was quoted by Larson BA *et al* (2010) that a large percentage of people testing HIV-positive at HIV counseling and testing sites do not return to collect CD4 test results, do not return on schedule for pre-ART monitoring and care, and/or do not initiate ART as soon as they become eligible (3).

As discussed by Geng EH, *et al* and Peter T *et a*l, rapid expansion of access to antiretroviral therapy (ART) to nearly 4 million patients in sub-Saharan Africa has been a major accomplishment of HIV care and treatment programs (24), although loss to clinic of patients enrolled in HIV care is a persistent challenge (23). Prior studies attribute large numbers of loss to clinic of ART patients to early mortality, but the study done by Faal *et al* (2011) showed that, patients who are not yet eligible for ART are less likely to have died (11). However, as clearly stated by Larson *et al* (2010) from South Africa, patients who loss for follow up remain at risk of late ART initiation and, consequently, increased risk of early mortality after starting ART (25). Furthermore, as quoted by Larson BA *et al* (2010), pre-ART patients who are neither engaged in care nor on ART are more likely to transmit HIV to sex partners than those who engage in care and initiate early ART (3). Growing recognition of the benefits of timely treatment and the consequences of losing pre-ART eligible patients is leading to increased awareness of the importance of regular CD4 and clinical monitoring before treatment eligibility (26, 27).

The availability of CD4 counts in selected centers required either long distance travel for the patient or transport of the sample to the laboratory. This resulted in missed visits of the patients and hence problems in patient management. Providing CD4 count result for patients on the day of diagnosis for HIV contributes largely in reduction of lost to follow-up occurred between HIV diagnosis and CD4 cell staging. Jani I, *et al* (2011) in their observational cohort study conducted on data of patient extracted retrospectively from patients' records at four primary health clinics providing HIV treatment and point-of-care CD4 services in Mozambique showed that loss to follow-up between enrolment and antiretroviral therapy initiation was 64%. The study mentioned that large effect was due mainly to loss to follow-up before completion of CD4 staging, which

was 57%; the median time from enrolment to antiretroviral treatment initiation which was 48 days; the median time between enrolment and completion of CD4 staging which was 32 days; to have samples drawn and CD4 tests completed at the laboratory took a median of 10 days after enrolment. The staging visit, in which the patient received the test result, took an additional 17.5 days. For this reason to obtain a CD4 result involved several steps each with delays. The study concluded that reduced visits and waiting time for patients before they can initiate ART can help reduce patient loss and reduce the patient burden of time and travel to receive care (20).

Jani *et al* (2010) in the conference abstract presented on XVIII International AIDS Conference that a study done in Mozambique Motola district health center, the lost-to-follow up rate was 37.3%. The average CD4 TAT was 27 days, consisting of 12 days from ART clinic enrollment to CD4 requisition, 3 days from CD4 requisition to test performed and 12 days from test performed to CD4 result returned to patient file (28).

As clearly stated by Rituparna *et al* (2013) in the study done on routinely collected service delivery data on HIV infected adult patients (>15 years old) enrolled at 23 free HIV care and treatment clinics across Mozambique showed that, 39% of patients not yet known to be ART eligible did not have a documented CD4 count within three months of their first visit. The proportion of 12-month loss to clinic among those with >1 clinical care visit was 41-48%. Out of 37,352 patients, the proportion of those who were not yet known to be eligible for ART at enrolment and continued in care until ART initiation during the study period was 23%, with an additional 25% remaining in care at the site where they initially enrolled until the end of follow-up. The study magnified large number of pre-ART attrition was due to the large portion of patients who were lost after just one clinic visit (19,783, or 34.5% of 57,880 pre- ART patients) (29).

Mtapuri-Zinyowera *et al* (2010) showed in their study done in VCT clinic of Zimbabwe that, delays in CD4 testing can occur for 2–3 weeks on average. There is substantial loss-to-follow-up of patients between HIV diagnosis and registration at the OI clinics and delays in CD4 testing can result in further loss of patients who do not return or who die before initiating treatment. The study added that situation is exacerbated in rural areas where more limited CD4 access creates a significant bottleneck to the scale up of ART (22).

By using systematic literature review of patient retention in sub-Saharan Africa Rosen and Fox (2011) estimated that fewer than one-third of patients remain continuously in care between testing HIV-positive and starting ART. Specifically, a median of 45% (range 5-58%) of patients were lost to care after enrolment. Based on finding they concluded that the possible interventions to maximize retention in care are making point-of-care CD4 cell counts available at HIV testing facilities to minimize losses between HIV diagnosis, CD4 count and pick-up of the result, reduce the number of required visits before ART initiation and thus the financial burden on patients (10).

Bekker *et al* (2006) discussed in their study conducted in South Africa on Linkage to HIV and ART care in a random sample of 47% of individuals tested HIV positive through ANC, STI and VCT services and 100% of individuals tested through TB services indicated that only 62.6% of clients attended for a CD4 count measurement within 6 months of testing HIV positive and 26.3% did not have any recorded CD4 count test. In this study the proportion of individuals attending for a CD4 count measurement within 6 months was highest among individuals tested through ANC (81.3%) and STI (84.1%) services and lowest among those who learnt of their status via VCT (53.5%). Adding to this in individuals with a delayed first CD4 count measurements, the mean time between HIV diagnosis and first CD4 count was 490 days. Among patients with delayed first CD4 count measurements, 33.2% had a CD4 count of < 200 cells/μL and 26.2% had a CD4 count of 201–350 cells/μL (19). Another study by Katharina K. *et al* (2010) states that Pre-Treatment Loss to Care after HIV Diagnosis in South Africa was 15% (36 patients) who had a CD4 count within 8 weeks did not return for the results of that CD4 count (30).

Patten *et al* (2013) conducted a study on Impact on ART initiation of point-of-care CD4 testing at HIV diagnosis among HIV-positive youth in South Africa using routinely collected data. For those with a recorded CD4 count, the median number of days from HIV test to receiving a CD4 count result was 14 days (range 2-404 days) so that point of care POC CD4 testing improved ART eligibility assessment, optimized the opportunity to provide a prognosis to the patient at HIV diagnosis and reduced attrition between HIV-testing and ART eligibility (13).

The study done on lost opportunities to complete CD4+ lymphocyte testing among patients who tested positive for HIV by Larson BA *et al* (2010) in large academic hospital in Johannesburg,

South Africa showed that expansion of testing has not translated into earlier treatment initiation. Among such patients in this study, 85% did not complete CD4 testing within 12 weeks of being diagnosed as HIV+. These patients are likely to return for HIV care and treatment at a later date with substantially lower CD4 cell counts. They discussed that, the likely reason for this is people who test positive do not always complete CD4 testing after their HIV test. Whereas waiting for 1, 2 or 3 weeks to complete CD4 testing have negative consequences for their health; a delay of several months or more could involve substantial risks to patients who already have very low CD4 cell counts. In their study CD4 cell counts are available within 1 week and patients are requested to return 1 week after their HIV test to collect their CD4 cell count results and complete CD4 cell testing, therefore, because of delays in the completion of CD4 testing, further delays occur in obtaining appropriate care and treatment (3).

Geng *et al* (2010) quoted in their article that distance to clinic and transportation are major barriers to retention in care in a wide variety of settings in Africa and Asia. In rural Uganda, among 111 patients lost to follow-up, the most common reasons for absence were lack of transportation in 50% and excessive distance in 42% (31). In rural Malawi, 35% of patients who were lost and traced cited the high cost of transport to the clinic as the reason for absence (32). The International Center for AIDS Care and Treatment (ICAP) performed a multisite analysis in Western, Eastern, and Southern Africa using a 6-month absence as the outcome. The study found that if travel time to clinic exceeded 2 hours, the risk of non-retention was doubled (33).

In Cambodia, among 6688 patients studied by Raguenaud et al of whom 4150 were on ART, living out of province was the only risk factor for failure to return to clinic (34). In Rajasthan, India, among 106 patients who failed to return for 3 or more months, 20% cited distance and lack of transportation (35). In pre-ART patients in Jinja, Uganda, 44% of patients who were eligible for ART but did not start cited transportation as the major reason for failure to initiate (36). In Western Kenya, one study found that among pre-ART patients, travel time was only significantly associated with failure of retention among women (OR = 1.07; 95% CI = 1.00–1.16) (37).

Micek *et al* (2009) discussed on their study of retrospective cohort of people testing for HIV that among those who were identified as HIV-positive, arrived to the HIV clinic, and underwent CD4 testing within the defined time-periods for these steps, less than 50% of ART-eligible patients

started treatment, and less than 33% started treatment within 90 days after CD4 testing. Loss was most pronounced among women tested for HIV at PMTCT centers (38).

Ismael Ahmed *et al* (2013) in the case–control study using chart review of HIV patients conducted in Gondar University Hospital showed that, the majority of patients in study started care after reaching compromised immune system. This was shown by the high proportion of patients that had baseline CD4 count of ≤ 200 cells/µl and WHO stage III and IV. A higher proportion of loss to follow up (LTFU) patients (42.2%) had a CD4 count >350 cell/µl when compared to those who were in care (9.1%). Similarly, higher proportions of LTFU patients (34%) were in WHO stage I compared to those who were in care (19.1%). Individuals who were in care (97.8%) were more likely to have their next appointment date recorded than those that were LTFU (20.4%). Concerning the length of follow-up time in HIV chronic care, most (61.7%) of the patients had less than one month follow-up during their pre-ART period. The median length of time in the pre-ART period was less than one month, ranging from less than one up to 37 months. Out of a total of 363 pre-ART LTFU cases, 86% had less than one month of follow-up, 10.4% had between one and six months of follow up, and 3.6% had more than seven months of follow-up time in the clinic. They examined the time of LTFU of the 363 pre-ART LTFU patients that, 84.8% of LTFU patients failed to return since their first clinic visit or did not show up after the date of enrollment (39).

Mulissa Z *et al (*2010) in the study conducted in District Hospital of Southern Ethiopia suggested that the median time between HIV diagnosis and pre-ART enrolment was 1 day with 49% of the patients being enrolled within same day of testing (40).

The above two studies are hospital based data from our country and no study addresses the situation in sample referral sites having no CD4 testing facility.

4. OBJECTIVE OF THE STUDY

4.1. General objective

To estimate rates of completion of CD4 cell count (CD4 testing) within 12 weeks of testing positive for human immunodeficiency virus (HIV) and associated clinical and demographic predictors for completion at ART clinics in Afar region of Ethiopia.

4.2. Specific objectives

- To estimate the proportion of pre-ART loss to initiation of CD4 testing (those who knew their HIV status but disappeared for CD4 counting and follow up)
- To estimate the proportion of loss to completion of CD4 testing after initiating ART
- To analyze the baseline demographic factors associated with completing CD4 testing.

5. MATERIALS AND METHODS

5.1. Study Setting

The study was conducted in three most accessible selected Health centers with CD4 sample referring ART services found in Afar Region of Ethiopia, about 620 kilometers North East of the capital city Addis Ababa. Primarily four health centers were selected, that is, Gewane, Semara, Logia and Werer Health centers for the study while one of the four (Logia Health Center) was found with insufficient data concerning the testing and enrollment to ART clinic. The selected heath centers for this study started providing ART service and CD4 sample referring in 2007 prior to the other remaining health centers. The region has one Referral, four District Hospital and 61 Health centers. Currently of total Health centers, only 10 health centers provide CD4 sample referral supported by PEPFAR via I-TECH-Ethiopia to the facility with CD4 machine.

5.2. Study design and period

A retrospective study was conducted based on data of patients who were tested HIV positive between September 2007 and June 2013 at three selected health centers. Four HIV testing center was identified as provider initiated counseling and testing (PICT), voluntary counseling and testing (VCT), prevention of mother to child transmission (PMTCT) and tuberculosis (TB) clinic and monthly report of people tested positive were collected and their respective ART linkage code was used to access linked (enrolled) individual on ART database which was stored centrally in ART clinic with secured pass word. Patient intake registration form and ART data base were used, and the corresponding full information of the patient was collected. Their demographic data, dates of HIV diagnosis and dates patient returned for their CD4 result, baseline CD4 cells count, at 12 months, current status of patient, WHO stage attached to patient ART log book, and patient TB history were collected. Data was collected starting from April-May, 2014.

5.3. Source population

Source population was all patients tested for HIV in the selected Health centers.

5.4. Study population

Patients with positive HIV diagnosed in one of HIV care entry point (PICT, VCT, PMTCT and TB clinic) between September 2007 and June 2013 were the study population.

5.5. Sample size determination:

All patients diagnosed HIV positive between September 2007 and June 2013 were included in the study based on the inclusion criteria.

5.6. Inclusion criteria

HIV-positive patients with complete records of HIV diagnosis were included in the study.

5.7. Exclusion criteria

Patients younger than 18 months , were excluded initially throughout, because HIV rapid test is not a criterion for diagnosis in this age group, according to the WHO pediatric treatment guidelines. Of the total 1299 tested positive at selected Health center, 1011 were enrolled to ART clinic while 288 were lost before enrollment to ART clinic. There is no complete information about these patients to predict for reason of their loss and were excluded from the study. Among enrolled patients 41 patients were transferred out, 21 died before baseline CD4 count and 184 had incomplete information. These patients were also excluded from the study.

5.8. Study variable

Independent variable: demographic data like Age, sex, marital status, level of education, religion, TB history, WHO stage, date of HIV diagnosis, actual visit date for CD4 count was the explanatory variable,

Dependent variable: follow up status, CD4 test at baseline; weeks of completing CD4 testing was the dependent variable.

5.9. Data collection procedures

Routine data was used separately to calculate the number and proportion of patient passing through each program. The procedure for calculating flow through each of these three steps includes:-

Step 1. Test for HIV—we determined the monthly number of patients tested for HIV, and HIV-positive, at each types of HIV testing sites between September 2007 and June 2013: provider initiated Counseling and testing (PICT), voluntary counseling and testing (VCT), prevention of mother-to-child transmission (PMTCT), and TB clinic (Figure 1).

PICT provided HIV testing for patients who came to the health center for other medical condition by initiation through health care provider. VCT centers primarily served people wishing to know their status on their own initiative, although they also provided testing for outpatients referred by health care provider. PMTCT centers offered "targeted" testing for pregnant women. While PMTCT centers also provided testing to infants and male partners of pregnant women, we included all patients tested. TB clinic provided HIV testing for those on TB treatment or newly diagnosed of active pulmonary tuberculosis. All testing centers performed pre-and post-test counseling by trained counselors, and used rapid HIV tests (KHB, Stat pack and Unigold for confirmation) with results given the same day. The number of HIV positive at each testing center were collected from monthly reports including numbers of people testing, and testing positive, for HIV, at each selected health center.

Step 2. Enrolled for care at the ART clinic—HIV-positive persons identified at testing sites included in this study should have been referred by testing counselors to the ART clinic, as they were the separated center offering free HIV treatment services in the respective health centers. Total monthly HIV positive at each testing centers were taken and checked for enrollment at ART clinic based on the database and intake form which was centrally stored for those enrolled to the clinic. The number and proportion of HIV-positive adults who enrolled for care within 30 days after their HIV test was used as a measure of successful referral to the ART clinic. Days between being HIV positive and enrollment to ART clinic were calculated by subtracting date HIV positive at each testing centers from date enrolled to ART clinic. While the HIV testing center and ART clinic databases were theoretically linked by an HIV test code, this linking was necessary for our capture of enrolled patient to ART clinic for care in analysis of this data.

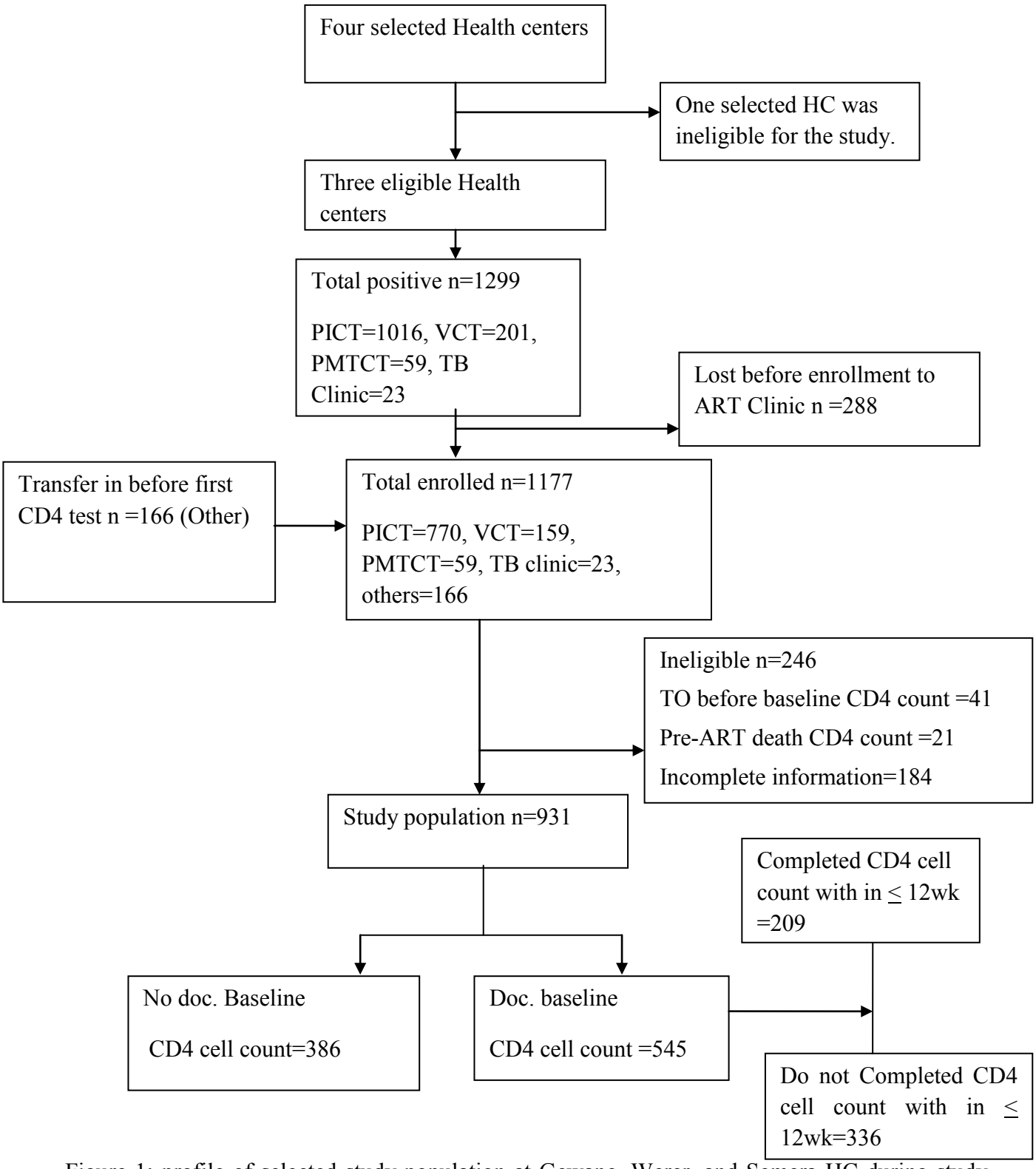

Figure 1: profile of selected study population at Gewane, Werer, and Semera HC during study period (from September 2007- June 2013)

5.10. Data quality assurance

Records with implausible errors, for example impossible dates, miswritten referral code, were corrected in consultation with the ART database manager or excluded from specific analyses. The first three month data was collected twice by different collector and cross checked for consistency. In addition, patient card and ART database were used in parallel with patient card for consistency of patient information.

5.11. Operational definition

Complete CD4 testing- when a patient after giving blood sample for CD4 testing actually returned to the ART center and obtained CD4 results.

Walk-in patients- are those patients who come to the clinic of their own accord and request an HIV test.

Pre-ART care- All services provided to patients between testing positive for HIV and dispensing of the first dose of antiretrovirals.

Loss to follow up (or attrition) - Discontinuation of active engagement in pre-ART or post-ART care for any reason, including death.

Transfer out- ART Patient sent to another health facility for follow up.

Transfer in- ART patient received from another facility.

Died- ART patient who died at any time during follow up

HIV care entry point- center where HIV testing performed VCT clinic, ANC clinic, STI clinic, OPD

5.12. Data management:

Patient data from register first collected manually on A4 size paper, then entered into SPSS version16 for window and excel database was used for importing into SPSS, and backup to CD and flash disk for each facility was taken. Subsequently, the stored data was retrieved for analysis. Any error of data was checked back to the manually stored data for consistency. Manually stored data was stored in lockable shelves for security and confidentiality. Electronic files were password protected.

5.13. Data analysis:

At the study site, CD4 cell counts are available within 1 week and patients are requested to return 1 week after their HIV test to collect their CD4 cell count results and complete CD4 cell testing. To allow for an adequate period to complete CD4 cell testing, whether or not a person completed CD4 testing within 12 weeks (84 days) of testing positive for HIV infection was used. As a secondary analysis, two categories of stratified time interval was used: testing completed within 6 weeks (≤ 42 days) or between 6 and 12 weeks (43–84 days). These definitions were used to estimate the proportion of patients who completed CD4 testing within each period. Baseline demographic and clinical characteristics (sex, age, WHO stage, TB history, CD4 level) of the group of patients who returned to collect their results versus those who did not return within 12 weeks was compared by using simple proportions and medians, where appropriate. predictors of returning for CD4 cell count results were identified using binary logistic regression. All Data processing and statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software (Windows version 16.0).

5.14. Ethical consideration

The research proposal was evaluated by the research and ethics committee of Addis Ababa University, College of Health sciences, Department of Medical Laboratory Science. The department had written official letter of co-operation to Afar Health Bureau. Afar regional health bureau in turn wrote a letter of cooperation to the respective selected health centers. High degree of patient confidentiality was maintained so that name and specific ID of patient of the study participant was deleted from database. Codes assigned only for the study were used during data collection. All extracted data was dissociated from personal identifiers and remained anonymous and unlinked throughout the study.

5.15. Result dissemination

The results of this study will be submitted to Department of Medical Laboratory Sciences (DMLS) Addis Ababa University (AAU).. Reports will also be submitted to Afar Regional Health Bureau. In addition the finding will also be presented on annual conferences of

professional societies. A manuscript will be submitted to peer reviewed local or international journals for publication.

6. RESULTS

6.1. HIV Testing

Between September 1, 2007 and June, 2013, a total of 1299 (591 males and 708 females), consisted of 492(37.88%), 387(29.79%), 420(32.33%) from Gewane, Werer and Semera health centers, respectively, were tested positive for HIV. Among these, the majority of those tested positive for were from PICHT 1016 (78.21%) center followed by VCT 201 (15.47%) (Table1).

Table1: Total tested positive at Gewane, Werer, and Semera Health Centers from September 2007- June 2013, Afar Region

Testing Centers		Sex		Total
		Male (N)	Female (N)	
	PICT	472	544	**1016**
	VCT	88	113	**201**
	PMTCT	16	43	**59**
	TB clinic	15	8	**23**
Total		**591**	**708**	**1299**

Of total tested (1299) at three health centers 1011(77.83%) were enrolled to ART clinics and 22.17 %(288) were lost before enrollment to ART clinic. Since there is complete lack of patient history related to before enrollment loss, we were unable to compute the demographic and clinical predictor for loss to patient before linkage to ART clinic. Among enrolled HIV positive majority 553(42.57%) were female patients while Gewane Health center 395(30.40%) contributed majority of study population followed by Werer 320(24.63%) while Semera 296(22.78%) contributed the least. Of total enrolled to ART clinic at each selected health center, majority 770(65.42%) were PICHT, while the other were VCT 159(13.51%), PMTCT 59(5.01%), TB Clinic 23(1.95%), and individuals tested positive somewhere referred to health center for care on ART clinic before their baseline CD4 count and we labeled it as others 166(14.10%). Based on this TB clinic 23(100%) and PMTCT 59(100%) enrolled all patients tested at these centers (Table.2)**.**

Table 2: Total enrolled to ART clinic at Gewane, Werer, and Semera Health Centers from September 2007- June 2013, Afar Region

Patient Referral Information		Sex		
		Male N(%)	Female N(%)	**Total N(%)**
	PICT	352(29.90)	418(35.51)	**770(65.42)**
	VCT	75(6.37)	84(7.14)	**159(13.51)**
	PMTCT	16(1.36)	43(3.65)	**59(5.01)**
	TB clinic	15(1.27)	8(0.68)	**23(1.95)**
	Other	70(5.95)	96(8.16)	**166(14.10)**
Total		**528(44.86)**	**649(55.14)**	**1177(100)**

Among the total of 931 HIV positive patients 889 (95.5%) had documented date of enrollment into ART clinic for care while 42 patients had no documented date of enrollment. Of total 889 of HIV positive patients with documented date of enrollment, 666 (74.92%) were enrolled on the day of HIV diagnosis while 184 (20.70%) of them were enrolled between 1 and 30 day/s of HIV diagnosis (Table 3).

Table 3: Days before enrollment to ART clinic at Gewane, Werer, Semera Health Centers from September 2007- June 2013, Afar region

		Days			
		0	1-30	>30	Total
Sex	Male	306	70	16	392
	Female	360	114	23	497
HIV Testing Center	PICHT	490	108	20	618
	VCT	76	16	6	98
	PMTCT	39	4	2	45
	TB clinic	11	6	0	17
	Other	50	50	11	111

6.2. Baseline socio-demographic and clinical characteristics of the study population

Out of the 931 study subjects analyzed, 56.1% (522) were female. By the time of enrollment into HIV care, nearly half (43%; n=400) of the study subjects were between 25–34 years of age. The mean age was 31.3 years with a standard deviation of 10.234. Of the total study population, 41.2% (n=384) were married. With regards to educational status of study subjects, 49.4% (n=460) of patients were illiterate and followed by 39.8% (n=371) of patients with only primary education. Almost Half of (49.4%; n=460) study subjects were followers of orthodox Christianity followed by Muslim 48.7 % (n=453). More than half 52.2 % (n=486) were unemployed. Among 801 that had complete information about WHO staging, the majority (38.83%; n=319) of patients were stage III followed by stage I (35.45%; n=284) patients (Table 4).

Of the total 931 study population, 58.54 %(n=545) had a documented baseline CD4 count while the rest 41.46% (n=386) had no baseline CD4 count documented. Of the patients with no documented CD4 cell count 226(58.5%) were lost to follow up while it was relatively low 155 (28.44%) of the total with documented baseline CD4 cell count. Among the 545 patients who had their baseline CD4 cell count documented, 59.8% (n=326) had CD4 count ≤200 cell/µl and 12.48% (n=68) had a CD4 count >350 cell/µl. Majority of patients were already eligible for ART at the time of HIV diagnosis even under the restrictive threshold of 200 CD4 cells/µl that was prevailed at the time of the study (Table 5). Under the revised CD4 count eligibility criterion of 350, adopted in August 2011, some 87.5% of patients during the study period would have been eligible for ART at the time of their HIV test.

Out of the remaining 931 study population, 59.1% (n=550) were patients who were under active follow-up in HIV care while the rest 40.9% (n=381) were lost to follow-up; the loss before baseline CD4 count was 24.2% (n=226) and after baseline CD4 count was 16.7% (n=155). In this study, in total of 381 LTFU only 155 (40.7%) of them have baseline CD4 count (Table 5).

Table 4: Baseline socio-demographic and clinical characteristics of HIV positive patients at three selected sample referring Health centers found in Afar Region, (September 2007 to June 2013)

Variables	Frequency	Percent
Gender(N=931)		
Male	409	43.9
Female	522	56.1
Age (N=931)		
<=14	27	2.9
15-24	180	19.3
25-34	400	43.0
35-44	207	22.2
44+	117	12.6
Marital Status (N=931)		
Never Married	242	26.0
Married	384	41.2
separated or Divorced	289	31.0
Widowed	16	1.7
Education Status (N=931)		
None	460	49.4
Completed Primary	371	39.8
Completed Secondary	73	7.8
Completed Tertiary	27	2.9
Religion (N=931)		
Orthodox	458	49.2
Protestant	20	2.1
Muslim	453	48.7
Employment Status (N=931)		
Employed	445	47.8
Unemployed	486	52.2

Patient referral information		
PICHT	362	66.4
VCT	73	13.4
PMTCT	21	3.8
TB clinic	11	2.0
Others	78	14.3
Baseline CD4 Count(N=545)		
≤200	326	59.8
201-250	65	11.9
251-300	55	10.1
3001-350	31	5.7
>350	68	12.5
WHO Stage(N=801)		
I	284	30.5
II	148	15.9
III	319	34.3
IV	50	5.4
TB History(446)		
Yes	60	13.45
No	386	86.55

Table 5. Current status of study population at three selected sample referring Health center found in Afar Region, from September 2007 to June 2013

Variables			Status of the Patient		Total
			In-care	LTFU	
Base Line CD4 Count	No	N	160	226	386
		%	29.1	71.75	41.46
	Yes	≤200	223	103	326
		200-250	45	20	65
		251-300	45	10	55
		301-350	20	11	31
		≥350	57	11	68
		Total	390	155	545
		%	70.9	28.25	58.54

6.3. Socio-demographic and clinical factors associated with pre-ART LTFU

After controlling for the effects of gender, age, marital status, educational status, history of tuberculosis, documentation for CD4 count, CD4 cell count, WHO stage, four variables were found to be associated significantly with after ART clinic enrollment LTFU (Table 6).

Separated/divorced patients had increased odds of being LTFU compared to those who were single 2.098(1.179-3.731) (Table 6).

Those patients without documented baseline CD4 count had 3.5 times odds of being LTFU compared to those with documented base line CD4 count 3.554(95% CI: 2.699-4.679) (Table 6).

Compared to patients with a baseline CD4 count 200 cells/µl, the adjusted odds ratio for being LTFU after enrollment to ART clinic was .343(95% CI:.149-787) and .347(95% CI:.151-.795) for patients with a CD4 count of 251-300 cells/µl and >350 cells/ µl respectively (Table 6).

Similarly, patients who were in WHO stage IV at baseline, had an adjusted odds ratio for LTFU after enrollment to ART clinic of 3.277(95% CI: 1.319-8.141) when compared to patients who were in WHO stage I (Table 6).

Table 6: socio-demographic and clinical factors associated with LTFU among HIV positive patients at four selected sample referring Health center found in Afar (September 2007 to June 2013)

Variables	In-care n (%)	LTFU n (%)	COR(95% CI)	P-value	AOR(95% CI)	P-value
Gender(N=931)						
Male[1]	239(58.4)	170(41.6)				
Female	311(40.4)	211(59.6)	1.048(.806-1.354)	.725	.855(.547-1.335)	.490
Age (N=931)						
<=14[1]	21(77.8)	6(22.2)				
15-24	102(56.7)	78(43.3)	.374(.144-.970)	.043	.544(.061-4.857)	.586
25-34	237(59.2)	163(40.8)	.415(.164-1.052)	.064	.516(.060-4.461)	.548
35-44	115(55.6)	92(44.4)	.357(.138-.921)	.033	.502(.057-4.417)	.534
44+	75(64.1)	42(35.9)	.510(.191-1.363)	.510	.728(.079-6.732)	.780
Marital Status (N=931)						
Never Married[1]	147(60.7)	95(39.3)				
Married	228(59.4)	156(40.6)	1.059(762-1.471)	.734	.860(.478-1.550)	.616
separated or Divorced	165(57.1)	124(42.9)	1.163(.821-1.646)	.395	2.098(1.179-3.731)	.012[2]
Widowed	10(62.5)	6(37.5)	.928(.327-2.639)	.889	.766(.133-4.404)	.766
Education Status (N=931)						
None[1]	273(59.3)	187(40.7)				
Completed Primary	218(58.8)	153(41.2)	.976(.739-1.289)	.864	.952(.594-1.524)	.837
Completed Secondary	43(58.9)	30(41.1)	.982(.594-1.622)	.943	.587(.269-1.283)	.182
Completed Tertiary	16(59.3)	11(40.7)	.996(.452-2.195)	.993	.686(.206-2.287)	.539
Employment Status (N=931)						
Employed[1]	273(61.3)	172(38.7)				
Unemployed	277(57.0)	209(43.0)	.835(.643-1.085)	.177	1.162(.744-1.815)	.509

Documented baseline CD4 count						
Yes[1]	390(71.6)	155(28.4)				
No	160(41.5)	226(58.5)	.281(.214-370)	.000	3.554(2.699-4.679)	.000[2]
Baseline CD4 Count(N=545)						
≤200[1]	223(68.4)	103(31.6)				
201-250	45(69.2)	20(30.8)	.962(.541-1.712)	.896	.937(.491-1.789)	.843
251-300	45(81.8)	10(18.2)	.481(.233-.992)	.048	.343(.149-787)	.012[2]
3001-350	20(64.5)	11(35.5)	1.191(.550-2.577)	.658	1.182(.517-2.704)	.692
>350	57(83.8)	11(16.2)	.418(.210-.830)	.013	.347(.151-.795)	.012[2]
WHO Stage(N=801)						
I [1]	183(64.4)	101(35.6)				
II	91(61.5)	57(38.5)	1.135(.753-1.711)	.546	1.174(.634-2.175)	.610
III	176(55.2)	143(44.8)	1.472(1.060-2.044)	.021	1.350(.818-2.229)	.240
IV	18(36.0)	32(64.0)	3.221(1.722-.6.027)	.000	3.277(1.319-8.141)	.011[2]
TB History(446)						
No[1]	247	178				
Yes	38	22	.848(.485-1.481)	.562	.803(.459-1.405)	.443

AOR, adjusted Odds ratio; CI, confidence Interval; COR, Crude odds ratio; LTFU, lost to follow up

[1]used as references in calculating OR

[2] significant predictor

6.4. CD4 Testing initiated

Patients who initiated CD4 testing after they tested positive for HIV and enrolled to ART clinic had a median CD4 cell count of 172/µl (interquartile range, IQR: 88–261). As shown in figure 2, majority 326 (59.8% of 545) had a CD4 cell count ≤ 200/µl and were already eligible for ART. The other 219 (40.2% of 545) had a CD4 cell count > 200/µl and were thus eligible for pre-ART medical care.

Among the 326 patients eligible for ART at the time of HIV diagnosis, 42.9% completed CD4 testing within 12 weeks and the remaining 57.05% did not (Fig. 2). Among the 219 patients not eligible for ART at the time of HIV diagnosis (CD4 cells > 200/μl), only 31.5% completed CD4 testing within 12 weeks. Among all 545 patients, only 38.35% completed CD4 testing within 12 weeks of HIV testing.

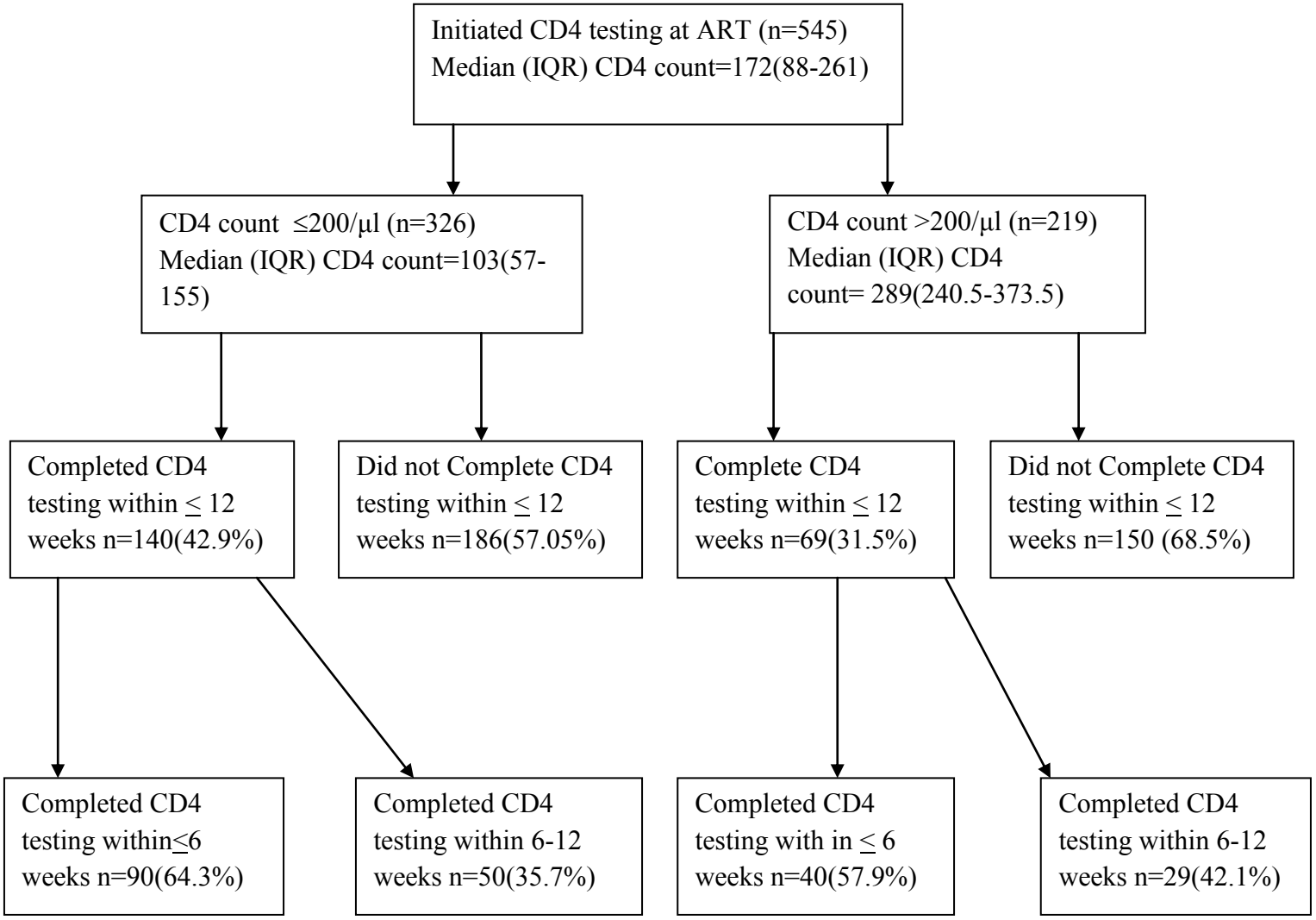

Fig. 2. Patients with high and low CD4+ lymphocyte counts who completed CD4 testing within 6 or 12 weeks of HIV testing at three selected sample referring Health centers found in Afar from September 2007 to June 2013.

There were no significant differences in basic demographic characteristics between those who returned for their CD4 cell count results within 6 weeks, those who returned within 12 weeks, and those who did not return. Most patients were women; median age ranged between 36 and 40 years, and approximately one half were married. A substantial majority of patients who completed CD4 testing within 6 weeks (69.2%) or between 6 and 12 weeks (63.3%) after HIV testing had a baseline CD4 cell count ≤ 200 cells/µl. However, 41.8% of all patients who did not complete CD4 testing were also already eligible for ART based on their CD4 cell counts. There is no significant (P>0.091) difference between baseline median CD4 cell count of 156.5 cells/µl in patients who completed CD4 testing within 6 weeks a median count of 155 cells/µl in patients who completed testing between 6 and 12 weeks. The median CD4 cell count of 184/µl in patients who did not complete testing within 12 weeks was significantly higher (P < 0.01) than in both of the groups who completed testing (Table 7).

Table 7. Baseline characteristics of patients who tested positive for HIV infection and who did or did not complete CD4 testing within the 12 ensuing weeks, at three selected sample referring Health centers found in Afar Region (September 2007 to June 2013)

Variables	Completed CD4 testing		Did not complete CD4 testing within 12 weeks	p-value		
	Within 6 weeks	After 6–12 weeks				
	Column A	Column B	Column C	A=B	B=C	A=C
Male %	44.6	40.5	46.4	>.05	>.05	>.05
Median Age in Years(IQR)	28(25-38)	32(27-40)	30(25-37)	.670	.103	.522
Married %	40.0	43.0	39.6	>.05	>.05	>.05
Employed %	50.8	51.9	48.8	>.05	>.05	>.05
WHO stage I%	33.3	28.2	32.4	>.05	>.05	>.05
Baseline CD4 count≤ 200 cells/ µl, %	69.2	63.3	55.4	>.05	>.05	>.05
Median baseline CD4 cell count cells/ µl(IQR)	156.5(84.5-218.5)	155(62-246.5)	184(94-294.75)	.091	<.001	<.001

6.5. Completion of CD4 cell count

Completion of CD4 cell count by Health center

Among the three health centers included in this study, the proportion of completion of CD4 cell count within six month was high in Semera Health center (60.6%) while it was very low in Gewane Health center (1.3%) in which 81.5% of patients with HIV test positive did not complete within 12 weeks of HIV+ test (Table 8).

Table 8: Proportion of Completing CD4 testing among selected Health centers, Afar (September 2007 to June 2013)

			CD4 completed weeks			Total
			Within 6 wk	Between6-12wk	Not completed ≤ 12wk	
Health Centers	Gewane HC	n	3	40	190	233
		%	1.3%	17.2%	81.5%	
	Werer HC	n	24	34	84	142
		%	16.9%	23.9%	59.2%	
	Semera HC	n	103	5	62	170
		%	60.6%	2.9%	36.5%	
Total		n	130	79	336	545
		%	23.9%	14.5%	61.7%	

Logistic regression analysis (Table 9) showed that the baseline CD4 cell count was negatively associated with the odds of a patient completing CD4 testing. Compared to the group with the lowest baseline CD4 cell count (0–200 cells/µl), those whose baseline CD4 cell count was between 201 and 250 cells/µl had 0.039(95% CI.005-.286) times the odds of completing their tests within 6 weeks. Those with higher CD4 cell counts (251–300 cells /µl or > 350 cells/µl) had even lower odds of completing testing. When the 12-week criterion used, the odds of patients with baseline CD4 cell counts from 201 to 250 cells/µl completing testing were .20(95% CI .003-.145) time the odds for those in the lowest CD4 cell count category (< 200 cells/µl), whereas those in the higher categories continued to be substantially less likely to complete (Table 9).

Table 9. Predictors of completing CD4 testing in patients who tested positive for HIV infection, at three selected sample referring Health centers, Afar Region, (September 2007 to June 2013)

Predictors	Completed CD4 testing			
	Within 6 weeks		Within 6–12 weeks	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Male (Versus female)	1.028	.692-1.528	1.146	.809-1.622
Tertiary(versus no Education)	1.578	.443-5.621	1.246	.454-3.420
Employed (Versus unemployed)	1.056	.712-1.567	.909	.643-1.284
Married (versus single)	.943	.571-1.558	.960	.622-1.482
CD4 cell count (cells/µl)	-	-	-	-
0-200(references)				
201-250	.039	.005-.286	.20	.003-.145
251-300	.060	.008-.471	.027	.004-.209
300-350	.036	.005-.285	.002	.002-.096
>350	**.031**	**.004-.259**	**.016**	**.002-130**

7. DISCUSSION

Every HIV-infected patient entering into care should have a complete medical history, physical examination, and laboratory evaluation and should be counseled regarding the implications of HIV infection. The goals of the initial evaluation are to confirm the diagnosis of HIV infection, obtain appropriate baseline historical and laboratory data, ensure patient understanding about HIV infection and its transmission, and to initiate care as recommended in WHO HIV primary care guidelines and guidelines for prevention and treatment of HIV associated opportunistic infections (2). In contrast to this, in our collection of patient data for the study there were many data with incomplete medical history, physical examination and laboratory evaluation improperly filled intake form and incomplete follow up information, causing large number of exclusions.

Accumulated evidences showed that reduced visits and waiting time for patients before they can initiate ART can help reduce patient loss and reduce the patient burden of time and travel to receive care. They showed the availability of CD4 counts in selected centers required either long distance travel for the patient or transport of the sample to the laboratory. This resulted in missed visits of the patients and problems in patient management. Providing CD4 cell result for patients on the day of diagnosis for HIV contributes largely in reduction of lost to follow-up occurred between HIV diagnosis and CD4 cell staging as supported by a number of studies from sub Saharan Africa (13,20,22,28). In our study, proportion of patients who did not complete CD4 cell count within 6 and 12 week of HIV positive test was high (P<001) between Semera (36.5%) and the other two health centers (Gewane 81.1%, Werer=59%); this was because of distance to which they transfer CD4 sample. In this case sample travel more than 150km and 30km for Gewane and Werer respectively while it was only 10km for Semera health centers so that sample collected once a week which resulted in additional patient visit and delay in results.

Existing study on Linkage of HIV and ART care in South Africa showed that the proportion of individuals attending for a CD4 count measurement within 6 months was highest among individuals tested through ANC (81.3%) and STI (84.1%) services and lowest among those who learnt of their status via VCT (53.5%). Adding to this in individuals with a delayed first CD4 count measurements, the mean time between HIV diagnosis and first CD4 count was 490 days;

among patients with delayed first CD4 count measurements, 33.2% had a CD4 count <200 cells/ml and 26.2% had a CD4 count of 201–350 cells/ml (19). In our study, of the total 931 HIV positive patients the proportion of individuals completed CD4 cell count within 12 weeks was relatively high in individuals tested through TB clinic (63.7%) followed by VCT (54.1%).

In this study four factors associated with Pre-ART LTFU were identified using logistic regression; marital status, WHO stage, CD4 cell count document, CD4 cell count.

Having documented baseline CD4 cell count had strong association with being staying in-care when compared to those patients with no CD4 cell count document i.e. those patients without documented baseline CD4 count had 3.5 times odds of being LTFU compared to those with documented base line CD4 count 3.554(95% CI: 2.699-4.679). In addition 41.46% of patients enrolled into ART clinic for care did not have a documented CD4 count during the study period and of 381 LTFU only 155 (40.7%) of them have baseline CD4 count. This showed us that providing immediate CD4 cell count and documenting on the patients chart can reduce the challenging large number of LTFU occurring at pre- ART stage of patient care. One study done on routinely collected service delivery data on HIV infected adult patients (>15 years old) enrolled at 23 free HIV care and treatment clinics across Mozambique showed that, 39% of patients not yet known to be ART eligible did not have a documented CD4 count within three months of their first visit (29). According to WHO recommend, there must be baseline CD4 count for patients newly diagnosed and linked to ART, since CD4 T-cell count (CD4 count) serves as the major laboratory indicator of immune function in patients who have HIV infection. It is one of the key factors in determining both the urgency of antiretroviral therapy (ART) initiation and the need for prophylaxis for opportunistic infections. It is also the strongest predictor of subsequent disease progression and survival according to findings from clinical trials and cohort studies (2).

To increase substantially the proportion of patients who initiate ART as soon as they are eligible, a large proportion of patients need to complete CD4 testing before they become eligible (i.e. while CD4 cells are still > 200/µl). Among such patients in our study, however, 68.5% did not complete CD4 testing within 12 weeks of being diagnosed as HIV+. Under current conditions, these patients are likely to return for HIV care and treatment at a later date with substantially lower CD4 cell counts. This may also increases the cost of medical and over usage health care

services which is the major concern for resource limited setting. The proportion of patients who did not complete CD4 test when their CD4 cell count is ≤ 200 cells/µl is higher (58.05%) when we compared with the study conducted in South Africa with a report of small proportion of patients who did not complete CD4 cell count (48.7%). While this was even higher in patients with CD4 cell count ≥ 200 cells/µl.

A case–control study using chart review of HIV patients conducted in Gondar University Hospital showed that, the majority of patients in study started care after reaching compromised immune system. This was shown by the high proportion of patients that had baseline CD4 count of ≤ 200 cells/µl and WHO stage III and IV (39). This was observed also in our study that 59.8% had baseline CD4 cell count ≤ 200 cells/µl at enrollment and 46% of them was at advanced disease stage (WHO stage III and IV).

A higher proportion of LTFU patients (42.2%) had a CD4 count >350 cell/µl when compared to those who were in care (9.1%) had seen (39). In contrast to this, in our study low CD4 cell count and advanced disease stage was predictor of loss to follow up; compared to patients with a baseline CD4 count 200 cells/µl, the adjusted odds ratio for being LTFU after enrollment to ART clinic was .343(95% CI:.149-787) and .347(95% CI:.151-.795) for patients with a CD4 count of 251-300 cells/µl and >350 cells/ µl respectively. Similarly, patients who were in WHO stage IV at baseline, had an adjusted odds ratio for LTFU after enrollment to ART clinic of 3.277(95% CI: 1.319-8.141) when compared to patients who were in WHO stage I. This may be as the result of high death rate due low baseline at enrollment and difference in time and study design.

Having high CD4 cell count was shown to be the predictor of incomplete CD4 testing (3). This was observed also in our current study that patient with Higher CD4 count (>350 /µl) had low completion rate of CD4 cell count within six week (OR.(95% CI) .031(.004-.259) and within 12 weeks (OR.(95% CI) .016(.002-.130)).

8. STRENGTH AND LIMITATION OF THE STUDY

Strength of the study

- The study was performed in the most untouched and remote area of Ethiopia so that it initiates appropriate intervention needed for the area.
- Three Health facility was assessed which may reduce biases from study of a single health facility with high or low completion of CD4 cell count in generalizing for the other similar areas.

Limitation of the study

- The study was confined to only health centers with sample referral and cautions must be taken in generalizing for Health centers with CD4 count machine and performing CD4 cell count in their own facility.
- The study was retrospective that it cannot assess causes for not completing CD4 testing in relation to Laboratory TAT system and patient factors.
- There was also limitation of references to which this study can be compared conducted in our country.
- Since CD4 cell count was not performed in center where patient tested positive the quality of sample handling and reliability of results was unknown.

9. CONCLUSION AND RECOMMENDATIONS

Conclusion

Linking of patients who tested HIV positive at different testing center to ART care was the major problem identified in this finding that more than 22% of patients tested positive at PICTH, VCT, PMTCT were lost before enrollment to ART clinic.

Positive part of the selected Health centers was 95% of patients linked to ART were linked within 30 days of HIV diagnosis that was the time assumed as successful linkage.

In other way it is important to note that, majority of patients were already eligible for ART at the time of HIV diagnosis even under the restrictive threshold of 200 CD4 cells/µl that prevailed at the time of the study. Under the revised CD4 count eligibility criterion of 350, adopted in August 2011, some 87.5% of patients during the study period would have been eligible for ART at the time of their HIV test.

Loss to follow up was high in patients with no documented (71.75%) baseline CD4 cell count when compared to patients with documented baseline CD4 count (28.25%). The higher the baseline CD4 cell count, the lower the odds of completing CD4 testing within 12 weeks.

Finally, proper linkage of patient tested positive at any testing center and provision of immediate baseline CD4 cell count has indispensible role in reducing delayed treatment of patients with low CD4 cell count and maintaining patients enrolled at ART clinic.

Recommendations

- Improved referral systems with a more structured process of patient tracking are needed in all stages of HIV testing, (i.e. CD4 testing and enrolment in care to initiation of ART).
- Health care providers working in the area of ART should have to fill all information needed in the intake form of HIV tested patients and enrolled into ART clinic since large number of incomplete documents were observed in this study.
- Immediate intervention is in need to provide immediate CD4+ T cell count for patients tested HIV positive.

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Annex I. Declaration

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

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