Original article

ART-naive HIV patients at Feleg-Hiwot Referral Hospital Northwest, Ethiopia

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Abstract

Objectives: To determine socio-demographic and immunological status of anti-retroviral treatment (ART)-naïve HIV-positive patients.

Methods: This was a longitudinal survey of HIV-positive patients treated with ART at Felege-Hiwot Hospital. CD4 cell counts were enumerated at baseline and after 6 months of treatment using FACS count (Becton Dickinson). Socio-economic data were collected using pre tested questionnaires.

Results: Three hundred sixty eight (62% female), with median age 30 years were enrolled. Of these, 207 (56.5%) were uneducated and 233 (66.8%) had monthly income ≤ 250 birr. Three hundred fifteen (85.6%) started ART within 6 months of HIV diagnosis. The mean (95% CI) CD4 cell count at baseline was 153 (139-167); 156 (137-175) for females and 122 cells/µl (105-139) for males ($p<0.01$). At baseline, 280 (76.3%) and 134 (36.4%) patients had CD4 cell count <200 and ≤ 100 cells/µl, respectively. Six months follow-up CD4 counts were enumerated for 225 (61%) patients and their mean CD4 cells increased from 143-261 cells/µl ($p < 0.05$) with a mean cell gain of 117 cells/µl. Of the 166 follow-up patients withCD4 count <200 cells/µl at baseline, 130 (78%) attained a higher CD4 cells count after treatment compared to 50 (85.6%) of the 59 with CD4 cell >200 cells/µl ($p=0.21$).

Conclusion: In this setting, HIV patients started ART with lower mean CD4 cell counts of 153 cells/µl and most patients with low baseline CD4 cells (<200 cells/µl) counts didn't achieve an increase in the number of CD4 cells after treatment. The majority of ART-naïve HIV patients were from low levels of education and with minimum monthly income. Appropriate interventions should be implemented to promote and enable HIV positive individuals to enter into ART programs as early as possible [*Ethiop. J. Health Dev* 2010;24(1):3-8].

Introduction

An estimated 31 million adults worldwide were living with HIV and of these 2.3 million were newly infected with the virus and 1.7 million died of HIV/AIDS in 2008 (1). Sixty seven percent of HIV infection worldwide, 68% new cases among adults with 72% of AIDS related deaths were estimated in sub-Saharan Africa in 2008. According to the World Health Organization (WHO) estimation, nearly 3 million people living in low and middle-income countries (LMIC) were receiving Antiretroviral Therapy (ART) at the end of 2007 (2). According to the UNIAIDS/WHO update data the number of AIDS-related deaths has declined by over 10% over the past five years due to antiretroviral treatment (1).

In Ethiopia, approximately one million people are living with HIV which has become the leading cause of mortality among 15-49 years of age, that accounts for about 43% of all population in 2008 (3). ART was started in the country in 2003 and free ART was launched in 2005. In 2009, 93 public hospitals, 47 private hospitals, 12 military hospitals and 292 health centers and 3 non-governmental organization clinics were providing HIV care and treatment services in all regions of the country (4). The prevalence of HIV infection is the highest in Amhara regional state where this study was based compared to other parts of Ethiopia. In the region, more than 97,588 cases needed ART and only 38,067 (39%) were able to be treated in 17 hospitals and 62 selected health centers (5).

HIV infection causes progressive depletion of CD4 cells, which leads to immunodeficiency syndrome with a wide range of opportunistic infections and malignancies that eventually leads to death. Several studies indicated that proper use of antiretroviral treatment substantially reduces morbidity, mortality and prolongs life expectancy of HIV/AIDS patients (1,6-8). However, there are numerous factors that could limit its effectiveness especially in resource limited settings. Studies indicated that the response of ART varies among population due to differences in viral subtype, host factors, co-infections, such as tuberculosis (TB), other bacterial diseases or socioeconomic status and environment (9-11).

Various studies in sub-Saharan Africa and in low income settings reported that many HIV infected patients are accessing antiretroviral treatment program after developing advanced immunodeficiency (12). This study was conducted to explore the socio-demographic characteristics and immunological status of ART-naive

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Methods

Study design and area

A longitudinal study was done from September 2008 to August 2009 at Felege Hiwot Referral Hospital, that is one of the government sponsored ART centers at Bahir Dar town; the capital of Amhara Regional State, North West Ethiopia.

Study population

All volunteer ART-naïve HIV-infected individuals age above 15 years who were initiating ART were enrolled consecutively and followed for six months. During enrolment for ART, socio-demographic data including gender, age, income and educational status were recorded by ART trained physicians using a structured and pre tested questionnaire. Participants were asked when they were first tested for HIV and the reason why they were tested.

CD4 cell counts

At initiation of ART and after 6 months of treatment, 4 ml venous blood was collected from each participant using K3 EDTA vacutainer tube. CD4 T cells and CD8 T cell counts were enumerated using FACS (Fluorescent Antibody Cell Sorter, Becton Dickinson).

Statistical analysis

Data were entered and analyzed using SPSS window version 16. Categorical variables were tested by chi-square tests and p- values <0.05 were considered to be statistically significant.

Ethical considerations

Ethical approval was secured from Research Ethics Committee of the College of Medicine and Health Science of Bahir Dar University as well as from Bahir Dar Regional Health Research Laboratory. Informed consent was obtained from each study participant.

Results

Socio-demographic characteristics

Among a total 368 patients recruited, 227 (61.6%) were females. The median age of the participants was 30 years (range 15- 65years) and 73.6% were age between 20 and 40 years. The majority of the participants 207 (56.2%) were illiterate and had low economic status 233 (66.8%) as defined by their monthly income (Table 1). Among 263(75.4%) the main reasons for being tested for HIV was related to experiencing repeated and/or persistent risky sexual behavior. The time interval between the first HIV testing (knowing their HIV status) and date of staring ART was very short. Since the majority [315 (85.6%)] of HIV patients started ART within 6 months and 14 (3.8%) between 6 months to 1 year from the date of diagnosis (Table 1).

Common Opportunistic Infections and co-morbidities

We have attempted to determine the common opportunistic infections, which are cause of morbidity and mortality among HIV-infected patients at baseline. In this study, at baseline, 327 (88.9%) HIV patients presented with common opportunistic infections. Of these, 143 (38.6%) had chronic diarrhea, 127 (34.5%) with TB, 113 (30.7%) with herpes zoster, 52 (14%) with Oro-pharyngeal candidiasis, 13 (3.5%) with pneumonia and 46 (12.5%) with other sexually transmitted infections (STI) as shown in (Table 2).

Table 1: **Socio-demographic characteristics of ART naïve HIV patients at Feleg Hiwot Hospital, Ethiopia, 2008**

Participants Characteristics	Frequency N (%)
Time interval from HIV diagnosis to commencing ART (N = 368)	
Within 6 months	315 (85.6)
6 months to 1 year	14 (3.8)
1 to 2 years	22 (6)
2-3 years	13 (3.5)
> 3 years	4 (1.4)
Education status (N = 368)	
No formal education	207 (56.2)
Primary (grade 1-6)	36 (9.7)
Secondary complete (grade 7-12)	31 (8.4)
High school complete (grade 12)	65 (17.6)
Above high school (grade 12 +)	29 (7.8)
Reason for getting HIV testing (N=349)*	
Due to repeated illness	263 (75.4)
Risk sexual behaviors	41 (11.7)
After death of spouse	11 (3.2)
Premarital testing	7 (2)
Provider initiative counseling and testing	10 (2.86)
Others	17 (4.8)
Income per month (Ethiopian birr) (N=349)*	
≤ 250	233 (66.8)
251-500	53 (15.2)
501-1000	51 (14.6)
≥1001	12 (3.4)

*Reason for testing and income was not recorded for 19 patients, N = number, ART = Anti-retroviral therapy

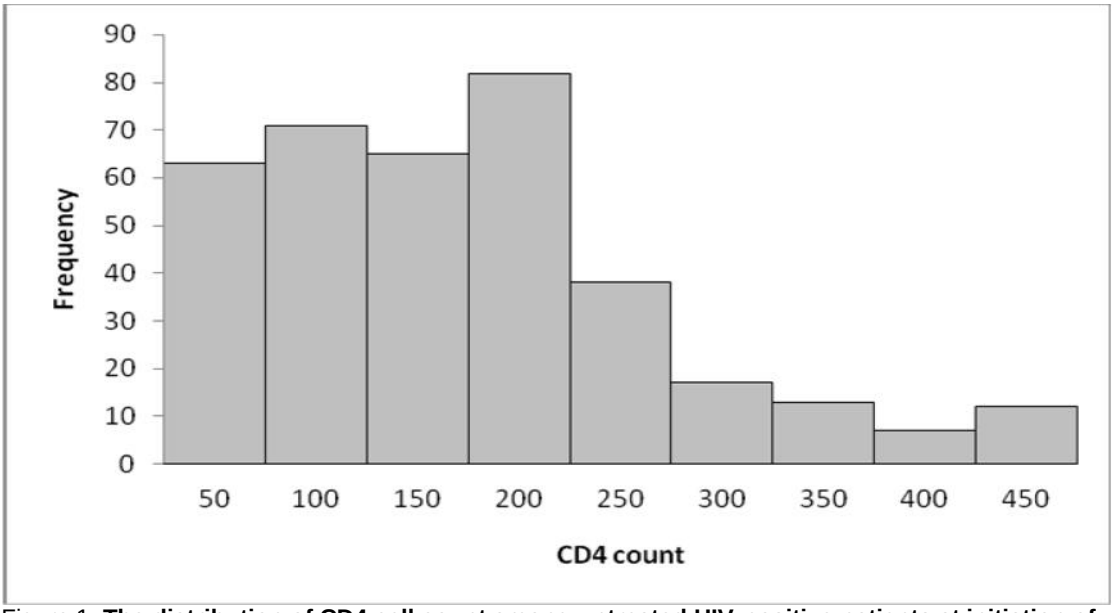

Figure 1: **The distribution of CD4 cell count among untreated HIV-positive patients at initiation of ART at Felege Hiwot Hospital, Ethiopia, 2008.**

Table 2: **Number of ART naïve HIV patients diagnosed with common opportunistic infections by sex at Felege Hiwot Hospital, Ethiopia, 2008**

Opportunistic infections N (%)	Sex			
	Male N (%)	Female N (%)	P value	Total
Tuberculosis	62 (44)	65 (28.6)	0.003	127 (34.5)
Chronic diarrhea	60 (42.5)	83 (36.6)	0.63	143 (38.6)
Herpes Zoster	41 (29)	72 (31.7)	0.24	113 (30.7)
Oro-pharyngeal Candidiasis	17 (12.5)	35 (15.4)	0.36	52 (14)
Other Sexually transmitted infections	21 (15)	25 (11)	0.27	46 (12.5)
Pneumonia	6 (4.2)	7(3)	0.76	13 (3.5)
Total	141	227		368

CD4 cell counts

At baseline, the mean CD4 cell count for both sexes was 153cells/µl (95% CI: 139-167). The mean CD4 cell count was 156 cells/µl (95% CI: 137-175) for females and 122 cells/µl (95% CI: 105-139) for males (P = 0.002). Two hundred and eighty (76.3%) of the HIV- infected patients had CD4 cell count of less than 200 cells/µl and therefore had AIDS and 134 (36.4%) had CD4 cell counts ≤ 100 cells/ µl. The overall mean CD4/ CD8 T cell ratio was 0.22. One hundred twelve (30.4%) patients had CD4/CD8 cell ratio between 0.01-0.09.

Patient follow-up

Follow-up CD4 cell counts were enumerated for only 225 (61%) HIV positive patients as 143 (38.8%) patients were lost to follow-up at 6 months of treatment. The mean CD4 cell count for these 225 follow-up patients increased from 143 at baseline to 261 cells/µl (95% CI: 240-282) at 6 month of treatment as shown in (Table 5). The mean number of CD4 cell gained was 117 cells/µl in 81.8% (78% from patients who had low baseline CD4 cells count or <200 cells/µl) follow-up cases. Seventy two (32%) HIV positive patients failed to attain CD4 cell count above 200 cells/µl after 6-month of treatment. Of these, 61 (84%) were from those with low baseline CD4 cell count (< 200 cells/ µl). Forty one (18.2 %) patients had a lower CD4 cell count after six month of treatment compared to the baseline count. Among 166 follow-up HIV patients who had CD4 count of <200 cells/µl at baseline, 130 (78%) showed an increment in CD4 cells count whereas, among 59 follow-up patients who had CD4 cell count of >200 cells/µl at baseline, 51 (86%) had increased CD4 cells count although the difference was not statistically significant (P=0.15).

Table 3: **CD4 cell count among ART naïve HIV patients by age at Felege Hiwot Hospital, Ethiopia, 2008**

CD4 count cells/µl At baseline	Age groups (year)						
	< 20	20-29	30-39	40-49	50-59	≥ 60	Total
< 50	3	16	27	15	2	-	63
50-99	1	24	28	10	8	-	71
100-149	1	26	27	9	2	-	65
150-199	3	30	26	14	7	2	82
200-249	-	11	13	10	4	-	38
250-299	1	6	9	-	1	-	17
300-349	-	7	5	1	-	-	13
350-399	-	3	4	-	-	-	7
≥ 400	2	5	4	1	-	-	12
Total	11	128	143	60	24	2	368

Table 4: **Mean baseline CD4 cell count of ART-naïve HIV positive patients by gender at Feleg Hiwot Hospital, Ethiopia, 2008**

	Mean CD4/CD8 cells		
Sex	**CD4 cells/µl**	**CD8 cells/µl**	**CD4/CD8 ratio**
Female (N = 227)	156	809	0.23
Male (N = 141)	122	829	0.2
P value	0.002	>0.05	
Average	153	833	0.22

Table 5: **CD4 cell counts at baseline and after six month ART of HIV patients at Felege Hiwot referral hospital, Ethiopia, 2008**

CD4 cell/µl	At baseline (N = 368) N (%)	At six month follow- up (N= 225)* N(%)	P value
<100	134 (36.4)	18 (8)	<0.001
100-200	147 (39.9)	54 (24)	<0.001
201-300	55 (14.9)	60 (26.6)	<0.001
301-400	20 (5.4)	37 (16.4)	<0.001
≥400	12 (3.3)	56 (25)	<0.001
Mean CD4 cells (95% CI)	153 (139-167)	261 (240-282)	<0.05

*143 patients were lost to follow up

Discussion

In this study, the majority of ART-naïve HIV patients were females. A similar finding was reported by Braitsein *et al*; (11) from South Africa who stated that ART-naïve patients in low-income countries were more likely to be females. This is because females are biologically and socially more vulnerable to HIV infection in the developing countries (13). Most of the HIV infected patients enrolled in our study were young age between 20 and 40 years old who were sexually more active and thus have a higher risk of infection compared to the other age groups (13). Higher proportions of ART-naïve HIV infected patients had low educational level and were from minimum income groups. These findings conform previous reports from the same study area (14) and elsewhere in Ethiopia which reported that HIV prevalence decreases significantly with increasing level of education (15).

At baseline, the mean CD4 cell count of ART-naïve HIV infected patients was lower (153 cells/µl) than the reports from other countries (16). This could be due to delayed presentation and/or testing, differences in educational and socio-economic levels. Moreover, Tsegaye *et al*; (17) reported that healthy HIV-negative Ethiopians had lower mean CD4 cell counts (775/µl) than other Africans and individuals from Western countries.

In our study, female HIV patients had higher mean CD4 cell counts than male ($p < 0.002$) before ART was initiated. This is consistent with Kumarasamy *et al*; (18) report from India. This difference could be due to several

reasons; HIV associated TB could be the contributing factor for the low CD4 count in males as the proportion of patients having TB was significantly higher in male HIV positive patients than females (p=0.003). In addition, it may be due to a sex-related difference in the overall CD4 counts among males and females as reported by Tsegay *et al*; (17). HIV sero-negative Ethiopian females had relatively higher CD4 cell counts than HIV sero-negative males.

Our data indicates that the majority of HIV patients started antiretroviral treatment with more advanced immunodeficiency status. Since the majority (76.3%) of HIV patients had AIDS as defined by their CD4 cell counts < 200 cells/µl, as shown in indicating advanced immune suppression at initiation of ART. This was significantly higher when compared to the studies conducted in Nigeria, south eastern United States and Thailand which reported a lower rate of AIDS at the initiation of ART (19-21).

Therefore, in the study hospital, delayed enrollment in ART program could be attributed by several factors. Moreover, Kiflie *et al*; (22) in the same hospital reported that more than 28.8% of HIV infected patients who were eligible to be on ART but never started ART, might be related to poor quality of HIV testing services in the existing delivery sites. The other possible factor may be due to fear of stigma. In Ethiopia, only one third of HIV infected persons disclosed their HIV status to their partner (23) further compromising the utilization of the counseling and testing and ART services. Moreover, it was noted that most (75.4%) of HIV infected patients seeking medical care when they had debilitating conditions and recurrent illnesses and the majority of them have started ART within 6 months of diagnosis. A similar observation was made among South Africans where patients stared ART program with advanced immunodeficiency status (24). These findings indicate urgent need to promote early and enhanced HIV testing to enable HIV/AIDS patients to benefit from the expanding ART services.

The limitation of this study was a higher dropout rate as 143 (38.8%) patients were lost to follow-up at 6 months of treatment. However, in the same hospital, about 36% patients were failed to follow-up because of multiple factors which were documented (25). Phone calls were used to contact patients but we were unable to actively trace lost to follow-up cases. Some of 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, financial reasons or death. Several studies reported that the proportion of patients on ART lost to follow-up varied in different settings ranging from 19% to 44% (11, 19). Our data 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. Tracing patients using only phone calls may not be feasible option in such areas where the majority of patients frequently change their addresses due to several reasons including stigma, socio-economic stress and luck of support.

The mean CD4 cell count for 225 follow-up cases increased from 143 to 261 cells/ µl (95% CI: 240-282) after 6 month of treatment. This was comparable with report of Gautam *et al*; (26) in India. However, among treatment-naïve HIV patients, 72 (32%) failed to attain CD4 cell count above 200 cells/µl at 6 months. Lower CD4 cell counts (< 200 cell/µl) before staring ART had significantly associated with failure to attain CD4 cell count recovery as the majority of the 61 (84%) of patients whose CD4 cell count remained < 200 cells/µl at 6 month were from those group with low baseline CD4 cell count. A higher proportion of patients with baseline CD4 count > 200 cells/µl had increased CD4 cells count after 6 months of treatment than those with a lower baseline CD4 counts. Actually the difference was not significant. Lower baseline CD4 cell counts therefore may correlate with poor immune responses and thus determine the degree of morbidity and mortality related to HIV/AIDS as reported by other studies too (27-28).

In conclusion, in our setting, although good CD4 cells recovery in response to ART was documented in more than 81% of follow-up cases, HIV-positive patients were enrolled in ART program at decreased CD4 cells levels. Therefore, interventions need to be designed to promote early HIV testing and early enrollment of HIV infected individuals into ART services. As socio-demographic factors and lack of awareness about ART services, fear of stigma and discrimination compromise the utilization of ART program, improving public awareness by advocacy and social mobilization should be included in the ART service.

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