Immunological response among HIV/AIDS patients before and after ART therapy at Zewuditu Hospital Addis Ababa, Ethiopia

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Abstract

Background: HIV is isolated in 1983, human immunodeficiency Virus (HIV), the agent that causes acquired immune deficiency syndrome (AIDS), is classified as members of the lentivirus subfamily of retroviruses. Although HAART is known to profoundly suppress viral replication, it increases CD4 cell count and delays disease progression and death; patients on Highly Active Antiretroviral Therapy (HAART) commonly suffer from side effects of the drug. Each antiretroviral drug is associated with specific adverse effects.

Objective: The aim of this retrospective cohort study was to describe immunological response among HIV-infected individuals receiving highly active antiretroviral therapy (HAART) with long-term follow-up.

Method: A Cohort retrospective study design was conducted to assess immunological (the CD_4^+ recovery) among HIV-infected individuals receiving highly active antiretroviral therapy (HAART) with long-term follow-up. ART-naive patients with symptomatic HIV disease at baseline (before ART) and after 6 and 9 and 12 months of ART was collected from records.

Result: A total of 887 HIV positive patients involved in this research; Out of these 472 (53.2%) were female and 415 (46.8%) male patients. None of them have any opportunistic infection during the time of follow up. The mean age of the study group was 36.76 (17-76). The mean baseline $CD4^+$ count was 81.40; the mean CD4 count at the 6^{th}, 9^{th} and 12^{th} month was 191.65, 284 and 331 respectively. There was a good immune recovery at the 6^{th} month of therapy from the baseline mean CD_4^+ T cell count of 81 cells/µl to 191.65 cells /µl, which was statistically significant ($p<0.0001$). This first remarkable rise was continued in the achieving in the mean

$CD4^+$ count of 284 cells/µl at the 9^{th} month of visit. Followed by relatively steady lower increase and approaching stable CD4+ T cell count and 12^{th} months of visit.

Conclusion: In this study, 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. As there is poor recovery of CD4 cell when the start <200 than when they start ART at CD4 count >200 CD4 cell therefore, interventions need to be designed to promote early HIV testing and early enrollment of HIV infected individuals into ART services. ART has considerably improved the immune recovery. We strongly recommend the need of ART in HIV infected patients for immune reconstitution should be started as early as possible. The differential recovery rate between those with base line CD4+ T cell count below 50cells/µl and above 500cells/µl needs further investigation.

Keywords: Immunological response, CD^+_4 HIV/AIDS, HAART

{**Citation:** Moges Derbe, DP Monga and Deresse Daka. Immunological response among HIV/AIDS patients before and after ART therapy at Zewuditu Hospital Addis Ababa, Ethiopia. American Journal of Research Communication, 2013, 1(1): 103-115} www.usa-journals.com, ISSN: 2325-4076.

Introduction

Human immunodeficiency Virus (HIV), the agent that causes acquired immune deficiency syndrome (AIDS), is classified as members of the lentivirus subfamily of retroviruses. It is isolated in 1983. There are two main types of HIV: HIV type 1(HIV-1): the most prevalent throughout the world. HIV type 2 (HIV-2) is prevalent in West Africa. They both cause ADIS and the routes of transmission are the same. However, HIV-2 causes AIDS much more slowly than HIV-1 [1].

Acquired Immunodeficiency Syndrome (AIDS) is one of the most destructive epidemics in the history of mankind. In Ethiopia the adult prevalence of HIV was estimated to be 1.5% in 2011. The total number of People Living with HIV/AIDS (PLHIV) in the same period was estimated to

be 1,037,267 adults and 68,136 of them were children. Furthermore the number of deaths due to AIDS for the same period was estimated to be 58,290 for adults and 9,284 among children [2].

The goals of treatment with antiretroviral drugs are to inhibit viral replication while minimizing toxicities and side effects associated with the available drugs. The inhibition of virus replication permits restoration of the immune system (suppression of HIV replication, as reflected in plasma HIV concentration, to as low as possible and for as long as possible, the preservation or enhancement of the immune function (CD4 restoration), thereby preventing or delaying the clinical progression of HIV disease. Viral eradication from the host genome is not achievable, thus a cure for HIV is not yet possible. By using HAART, it is possible to promote growth in children and prolong the survival of all HIV infected patients, reduce their morbidity and improve their quality of life [3].

Enumeration of CD_4^+ T cell count has been useful to initiate and monitor therapy in HIV infected individuals taking potent ART. The CD_4^+ T cell count recovery shows high variability among patients [4]. The CD4 cell count response to ART varies widely, but a poor CD4 response is rarely an indication for modifying a virologically suppressive ARV regimen [4].

The guiding principles of good ART include: not to start ART too soon (when CD4 cell count is close to normal) or too late (when the immune system is irreversibly damaged) [5].

Antiretroviral therapy in the developed world has resulted in substantial reductions in HIV-associated morbidity and mortality, changing an HIV diagnosis from a likely death sentence into a manageable chronic infection [3].

The effects of HAART on its Immunological response rate and hematological disorders among sub-Saharan Africans, for whom access to antiretroviral therapy is expanding, remain largely unknown [1, 6].

Highly active antiretroviral therapy confers several benefits, including reduction in viral load and longevity in HIV positive patients. However, metabolic and morphological complications have

been increasingly reported among patients in the advanced industrialized countries receiving chronic HAART up to 10-20 years [1, 6].

A research carried on 1281 HIV-infected patients initiating HAART were enrolled in the Anti PROtease (APROCO) cohort to investigated determinants of increase in CD4 count using longitudinal mixed models in patients who maintained a plasma HIV RNA <500 HIV-1 RNA copies/mL. Mean estimated increases in CD4 count in patients with persistent virological response were 29.9 cells/µL/ month before month 4, 64 cells/µl/month between months 4 and 36 [7].

As study conducted by Jesus De et al., (2004) indicated that a positive correlation between adherence and virologic and immunologic responses [8].

As the report of FMOH, Ethiopia ART was started at the end of February, 2007 [9]. Regardless of the fact that Ethiopians' normal immunohematologic profile is known to be lower than the white population by 2 to 3% [10]. Therefore, using the western cut of point may not guaranty to suggest clinical cases in Ethiopia. AZT-based HAART is one of the first line regimens in the guideline [11].

Methodology

Study area

The study was carried out in the Zewditu Hospital Addis Ababa Capital City of Ethiopia. The hospital as a teaching referral hospital has a referral status and is located in the Addis Ababa, Ethiopia. Zewditu referral hospital provides HIV/AIDS interventions including free diagnosis, treatment and monitoring. The centre diagnoses new cases and monitors those on therapy. Also structured HIV/AIDS data were available at this referral Hospital. Of these data 2006-2010 were used for this study.

Study design

A retrospective cohort study design was conducted to assess the immunological response mainly of their $CD^{+}4$ count before and after ART initiation. All patients, ART-naive patients with

symptomatic HIV disease at baseline (before ART) and exactly at 6th, 9th and 12th months of ART which were free from any infection were included. And their initial their CD^+4 were collected from records and after start ART in the Zewuditu Hospital, Addis Ababa, Ethiopia. In this study a patient with incomplete information and having any other infection during the study time was not included. Also a patient whose CD4+ count are not monitored at beginning, 6th, 9th and 12th months were not included. The study was conducted at Zewuditu Hospital, Addis Ababa, Ethiopia.

Study population

A total of 887 HIV/AIDS patients data were recruited for this study. The patient's secondary data consisted of 887 (415 males and 472 females) HIV/AIDS patients on HAART were selected for this study purpose. The age range of the patients was 15–61 years with a mean of 36.76 ± 17.76 years. In Zewditu referral hospital the HAART regimen for HIV patients on HAART consist of zidovudine, stavudine and nevirapine.

Determination of CD4+ T-cells

The CD4+T-cell count of patients in Zewditu referral Hospital laboratory determined using an auto analyzer–Sysmex KX-21 [12].

In this study CD4+ cell responses was evaluated as the following ways: i) whether patients failed to attain mean CD4+ cell count increase from baseline of at different interval months (defined as immunological non-response); ii) whether patients achieved an absolute CD4+ count of 200 cells/µl at the 12th months visit; iii) and whether patients had achieved an absolute CD4+ cell count of 500 cells/µl at 12 months (super-responders). Mean and the median were compared using normally distributed therefore; the mean was used in the evaluation of the response. Baseline CD4 cell counts were categorised as follows: <50, 50–99, 100–149 and >150 cells/µl. Also the mean CD4+ cell counts during three intervals (from baseline to 6 months of ART, 6 to 9 months, and 9 to 12 months)

Statistical analysis

SPSS version 17 was used for statistical computation. Pearson's Chi (χ^2) square and Fishers exact tests, paired *T*-tests were done. The data were arranged in a 2x2 contingency table before manual analysis. For example, the HIV patients were grouped as HAART naïve and on HAART, at beginning, 6th month 9th month and 12th month

Results

A total of 887 HIV positive patients in this research; Out of these 472 (53.2%) were female and 415 (46.8%) male patients. None of them have any opportunistic infection during the time of follow up. The mean age of the study group was 36.76 (17-76).

The mean baseline CD4 was 81.40; the mean CD4 count at the 6th, 9th and 12th month was 191.65, 284 and 331 respectively. There was a good immune recovery at the 6th month of therapy from the baseline mean CD_4^+ T cell count of 81 cells /µl to 191.65 cells /µl, which was statistically highly significant ($p<0.0001$). This first remarkable rise was continued in the achieving in the mean $CD4^+$ count of 284 cells/µl at the 9th month of visit. Followed by relatively steady lower increase and approaching stable CD4+ T cell count and 12th months of visit. The pick recovery was noted in those patients having a base line CD_4^+ of >200cells/µl, while patients with a base line CD_4^+ count <200cells/µl showed less recovery rate. In general, the result indicated that the recovery was significantly in those patients who started therapy at the base line CD_4^+< 200cells/µl.

Table 1: Mean $CD4^+$ count at different time intervals of 887 HIV patients at Zewuditu Hospital from 2006-2010.

		$CD4^+$ count			
Sex		**Base line**	**After 6 month**	**After 9 month**	**After 12 month**
Female	**Mean**	87.96	207.49	304.278	344.63
	N	472	472	472	472
Male	**Mean**	73.94	173.98	260.843	315.46
	N	415	415	415	415
Total	**Mean**	81.40	191.81	283.956	330.98
	N	887	887	887	887

Table 2: **Baseline CD4$^+$ cell count among ART naïve HIV patients in different age categories at Zewuditu Hospital from 2006-2010**

Age	Base line CD4 count						
	<50	**50-99**	**100-149**	**150-199**	**200-249**	**250-299**	**Total**
	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**
<20	0 (0.0)	1 (0.6)	0(0.0)	0 (0.0)	2(7.7)	0(0.0)	3 (0.3)
20-29	86 (21.7)	25 (14.2)	25(18.5)	24(17.0)	4(15.4)	2(15.4)	166(18.7)
30-39	185 (46.7)	82 (46.6)	58(43.0)	68(48.2)	15(57.7)	8(61.5)	416(46.9)
40-49	90 (22.7)	52 (29.5)	39(28.9)	30(21.3)	3(11.5)	3(23.1)	217(24.5)
50-59	25 (6.3)	14 (8.0)	11(8.1)	16(11.3)	2(7.7)	0(0.0)	68(7.7)
>=60	10 (2.5)	2 (1.1)	2(1.5)	3(2.1)	0(0.0)	0(0.0)	17(1.9)
Total	**396**	**176**	**135**	**141**	**26**	**13**	**887**

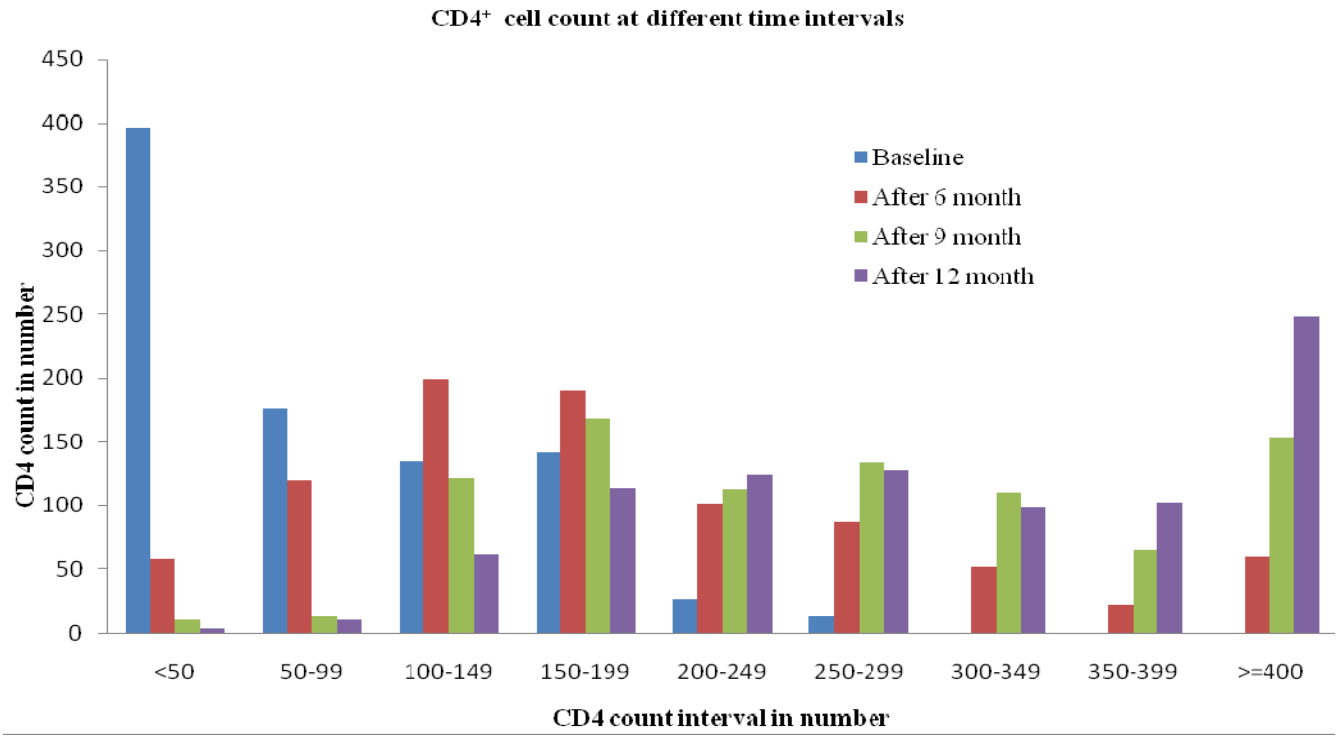

fig 1

Discussions

In this study, the majority of ART-naïve HIV patients were female. A similar finding was reported by Braitsein*et al*; [12] 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]. These findings could conform as previous reports from elsewhere in Ethiopia which reported that HIV prevalence decreases significantly to increasing level of education as well as their socio economic status [14].

At baseline, the mean CD4 cell count of ART-naïve HIV infected patients was lower 153 cells/µl than the reports from other countries [15]. This could be due to delayed presentation and/or testing, differences in educational and socio-economic levels. Moreover, Tsegaye*et al*; [16] 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*; [17] report from India. This difference could be due to several Bibliography on HIV/AIDS in Ethiopia and Ethiopians in the Diaspora: The 2009 Update 7 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*; [16]. 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 (95.6%) 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 [18-20].

Therefore, in the study hospital, delayed enrollment in ART program could be attributed by several factors. 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 [21] further compromising the utilization of the counseling and testing and ART services. A similar observation was made among South Africans where patients stared ART program with advanced immunodeficiency status [22]. 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 no socio economic status as well as educational level was included because of improper registration in the log books. The mean CD4 cell count for 887 follow-up cases increased from 81.4 to 191.8 cells/ µl (95% CI) after 6 month of treatment, from 81.4 to 284. Cells/ µl at 9^{th} month and from 81.4 to 331 cells/ µl (95% CI) on the 12^{th} month follow up.

However, among treatment-naïve HIV patients, 566 (63.8%) 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 patients whose CD4 cell count remained < 200 cells/µl at 6 month were from those groups 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. 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 [23-24]. None of the patients showed exaggerated immunological response which could lead to autoimmune disorder.

Conclusions and Recommendations

In conclusion, in our study, 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. As there is poor recovery of CD4 cell when the start >200 than when they start ART at CD4 count >200 CD4 cell.

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.

ART has considerably improved the immune recovery. We strongly recommend underline the need of anti-retroviral therapy in HIV infected patients for immune reconstitution. The differential recovery rate between those with base line CD4+ T cell count below 50cells/μl and above 500cells/μl needs further investigation

Ethical considerations

The Ethical Committee of the Addis Ababa University approved the protocol for this study. Letter of approval were given to the HIV/AIDS clinics and agreement were signed with researcher and college research office.

Acknowledgements

First, we would like to thank the staff members of Zewuditu Hospital for their constant insight, encouragement, and in providing as necessary materials, references in implementing this research. I would like to extend our thanks Hawassa University College of Medicine and Health Sciences for their valuable support. Also we appreciate all study participants.

Competing interests

The authors declare that they have no competing interests.

Author's contributions

MD developed a proposal, collect data and analyzing of the results, DD finalizing whole manuscript for publication, DM, read and correct the manuscript. All authors read the manuscript.

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