Original Article

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Immunological Response of Human Immunodeficiency Virus Positive Patients after Initiation of Highly Active Antiretroviral Therapy

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Abstract

Background: Effective care for people living with human immunodeficiency virus (PLHIV) requires highly active antiretroviral therapy (HAART). HAART mainly acts on suppression of viral replication and allows the recovery of patient's immune system protecting him/her from the development of AIDS and death.

Objective: The study aims to document the experience of immunological response among PLHIV on HAART comparing different categories of patients.

Methods: This is a retrospective analytical quantitative study with a sample size of 224 patients who were started with HAART. A total of three CD4 counts were measured pre-therapy, 1st post therapy, and 2nd post therapy at 6 monthly intervals to determine the change in CD4 counts. The rates of CD4 change were also compared among the different categories of patients.

Results: Men had higher CD4 count (mean of 96.4 cells) with mean age of participants being 37 years at baseline. The CD4 count increased from a mean baseline of 86.2 cells to 372.2, 390.0, respectively, at 6, 12, months of treatment ($P < 0.001$ at each time point). There was no gender ($P = 0.46$) and age ($P = 0.96$) differences in treatment response. There was no much difference ($P = 0.18$) in treatment response comparing those with CD4 <200 and those with CD4 count >200 at baseline although patients with baseline CD4 count <200 cells showed larger increases after 12 months of treatment. The patients with pre-therapy CD4 count <200 cells, 127 (81.4%) patients out of 156 were adherent, and 29 (18.6%) were non-adherents.

Conclusion: Adherent patients with base line CD4 <200 achieved greater improvement in their CD4 cell counts. A high level of adherence to HAART is required to achieve a significant improvement in CD4 cell counts (immunological improvement) among PLHIV.

Key words: Human immunodeficiency virus, Immunological, Patient, Therapy

INTRODUCTION

Since its discovery in 1981 by Centers for Disease Control in the US, human immunodeficiency virus (HIV) became an emerging disease and became a global pandemic. Approximately, 35.3 million people have HIV world wide[1] with 2.3 million people infected newly in 2012 and are down from 3.1 million new infections in 2001. It resulted in 1.34 million deaths in 2013, down from a peak of 2.2 million in 2005.[2] In India, as of 2013 estimates 2.1 million people living with HIV (PLHIV). As per NACO report 1.16 lakh new infections in 2011 and PLHIV is estimated as 2.1 million and AIDS-related deaths being 1.48 lakhs.[3]

Effective care for PLHIV requires highly active antiretroviral therapy (HAART) for those who are eligible for treatment.[4] Mortality and morbidity rates in HIV-infected individuals in countries with widespread access to HAART have been decreased. HAART mainly acts on suppression of viral replication and allows the recovery of patient's immune system protecting him/her from the development of AIDS and death. In developing countries, viral load is not done due to several limitations and initiation of ART depends on clinical and immunological assessment.[5]

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The immunological response of PLHIV initiated on HAART in our region is not well documented, but there is documentary evidence on immunological response to HAART is well documented.[5,6,7] The study objective, therefore, was to document the experience of immunological response among PLHIV on HAART in our region comparing different categories of patients.

METHODS

The study was conducted between January 2014 and December 2014. HAART was initiated in population with baseline CD4 <350 cells. These patients were stratified into two CD4 categories: The patients with CD4 cell count <200 cells and those CD4 cell count >200 cells. HAART regimen consists of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-NRTIs.[6] "Adherent" was defined as patients with >95% drug intake without interruptions while "non-adherent" was defined as patients who defaulted in treatment during the study period. Adherence was monitored using pharma fill cards.[8,9]

The study population composed of HIV-positive patients, who were treatment naïve. These patients had enrolled at the Rajiv Gandhi Institute of Medical Sciences and were due to start HAART treatment. The patients' demographic data and clinical data collected from their clinic files. The total sample size was 224. Three CD4 count measurements were taken at 6 monthly intervals. These were pre-therapy, 1st post therapy, and 2nd post therapy counts.

Univariate analysis was done to determine the association between treatment response and age of the patient. For all comparisons, P - value was taken as $P < 0.05$ for establishing statistical significance.

RESULTS

The geometric mean of CD4 counts was taken. Of the 224 patients in the study, 198 (88.3%) were adherents. Of these 198 patients, 127 (56.6%) patients had their baseline CD4 cell count <200. Remaining 26 (13.5%) patients were non-adherents. The main baseline characteristics are shown below in Table 1. The following table shows the age, gender distribution of population, their level of education and economic status.

The patients were divided into three groups based on their age. 156 adherent patients with their baseline CD4 cell count of <200 were evaluated for immune response to HAART after 6, 12 months of treatment (Table 2). The mean pre-therapy CD4 cell count was 86.22 cells. A significant response to treatment occurred after 6 months of therapy with a mean CD4 increase to 372 cells ($P < 0.001$). Subsequently, a slower steady increase in CD4 counts is observed as shown in Figure 1. The immunological response to HAART was very much significant in the first 6 months of treatment (from 86.22 to 372 cells) with $P < 0.001$.

In all, there were 156 patients who started therapy with baseline CD4 count of <200 cells. Of this, 127 (81.4%) and 29 (18.6%) were adherents and non-adherents respectively

Table 1: Baseline characteristics

Characteristics	*n* (%)
Gender	
Women	101 (45.1)
Men	123 (54.9)
Employment status	
Unemployed	20 (8.9)
Self-employed	106 (47.3)
Workers	58 (25.8)
Missing data	40 (17.8)
Level of education	
Non-educated	36 (13.7)
Primary/JSS	127 (48.5)
Secondary	36 (13.7)
Tertiary	15 (5.8)
Missing data	48 (18.3)
Age group (years)	
<12	4 (0.1)
12-60	208 (92.8)
>60	12 (5.3)

Table 2: Age-wise and gender-wise distribution with their geometric mean of baseline CD4

Characteristics	Baseline CD4 (cells/$l)
Age (years)	
<12	68.7
12-60	87.6
>60	86.9
Sex	
Women	89.6
Men	96.4

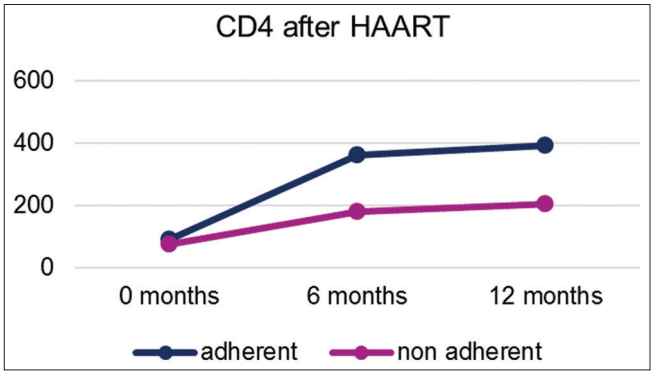

Figure 1: Rate of CD4 increases showing immunological response of 156 patients who commenced therapy with baseline count of <200 cells

The immune responses of these both adherents and non-adherents (both of which had baseline CD4 count <200 cells) were compared. The mean pre-therapy CD4 count for adherent patients was 89 which were slightly higher than non-adherent patients (89 cells) as shown in Figure 2. After 6 months of treatment, CD4 count had increased to 362 ($P < 0.001$) and 180 cells ($P = 0.21$) for adherents and non-adherents, respectively.

Among the adherent patients in the study, there were a higher proportion of men (65.2) than women (34.8). Men exhibited higher CD4 count values (84.6 cells) than women (67.8 cells) before therapy. The rise in CD4 count for men and women were 360.8 and 374.2 cells at 6 months, and 384.2 and 402.6 at 12 months. A univariate analysis was done for the patient's counts, and it showed significant improvement in CD4 for both men and women, respectively. However, no significant gender difference in treatment response ($P = 0.35$) after 12 months was found.

Adherent patients were divided into two categories: Baseline CD4 count of <200 and baseline CD4 count between >200. Mean pre-therapy CD4 count was 57.8 and 303.4 cells. CD4 counts came as 238.1 cells and 308.6 cells at 6 and 12 months, respectively, for those with CD4 <200, and 339.8 cells and 408.6 cells for CD4 >200. Figure 3 shows the relation between the baseline CD4 and treatment response.

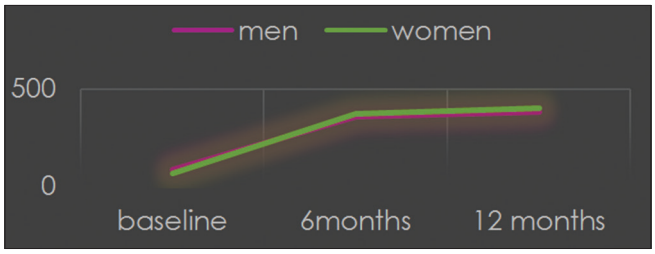

Figure 2: The relation between men and women with their CD4 differences

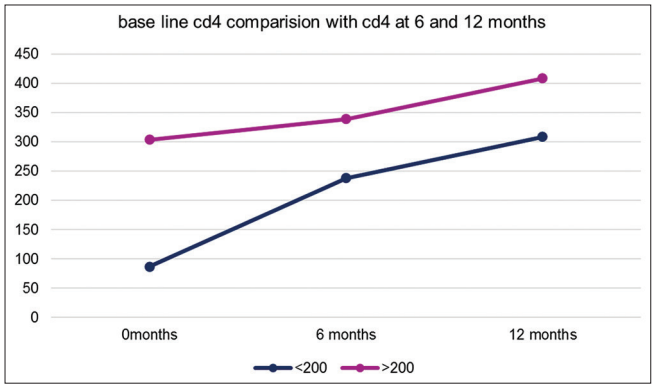

Figure 3: The relation between the baseline CD4 and treatment response

DISCUSSION

This study showed immunological recovery in two phases. A rapid phase of improvement within 6 months of therapy with a mean of 372 cells followed by more gradual second phase improvement with a mean of 390 cells at 12 months. The rapid early rise in CD4 counts in the first 6 months after HAART therapy is due to reconstitution and redistribution of CD4T cells into circulation from the lymph nodes where they were sequestered.[10] Touloumi *et al.*[11] described that slower increase in the second phase is due to the production of new CD4 cells which takes a long time.

A high level of adherence is observed in most patients in our study. Similar adherence rates were observed in a study in Cambodia where as high as 95% patients were seen.[12] Non-adherent patients were started treatment with a slightly higher baseline CD4 count than adherent patients. However, adherent patients showed a significant rise in CD4 ($P < 0.01$), whereas non-adherent patients recorded insignificant rise in CD4 ($P = 0.21$ and 0.48 at 6 and 12 months, respectively). Rougemont *et al.*[13] credits adherence as a major key for attaining good immunological improvement.

Higher proportion of men demonstrating higher CD4 count (96.4 cells) than woman (89.6 cells) at baseline. Good immunological recovery was observed during therapy in both sexes. No gender difference was found in treatment response ($P = 0.46$). The study showed that better response was observed in younger and middle-aged patients. This is attributed to preserved thymic function in young people. The slower immune response in older age is due to the gradual deterioration of the immune system as a result of the functional decline of T cells with age. Age of patient at the start of HAART therapy could influence CD4 cell recovery. The study depicted that patients with lower CD4 counts showed significant rise at 6 and 12 months, respectively. Many studies reported greater CD4 increases among highly advanced adherent patients as in our study. A study[14] in Botswana reported significant increase after 4 weeks of treatment in patients with <200 cells. The study results cannot be generalized as small study population makes a major limitation.

CONCLUSION

Significant immunological recovery is seen among PLHIV on HAART with a high level of treatment adherence. Significant CD4 improvement is seen with in the first 6 months of treatment in patients started on HAART therapy with baseline CD4 count <200. Adherence can

be used as an indicator for HIV drug resistance and monitoring

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