J Med Allied Sci 2016; 6 (2): 68-71
www.jmas.in
Print ISSN: 2231 1696 Online ISSN: 2231 170X
Journal of Medical & Allied Sciences

Original article

CD4 lymphocyte response following anti-retroviral therapy in HIV/AIDS patients - A study in Osmania General Hospital

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Article history

Received 13 January 2016
Revised 25 March 2016
Accepted 22 April 2016
Early online 29 May 2016
Print 31 July 2016

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Abstract

The present study aimed at serial three year assessment of CD4 cell response after initiation of anti-retroviral therapy (ART) in patients with HIV/AIDS attending to Osmania General Hospital. It was a retrospective hospital based observational study. Data was collected over a period of 3 years from 2005 to 2007 in the ART Centre, Department of Medicine, Osmania General Hospital. We included 110 HIV/AIDS who were on ART. Serial monitoring of CD4 count was done and assessed. All patients were on ART as per National Aids Control Organisation (NACO) guidelines. Investigations included complete blood picture, serum creatinine, blood urea, serum electrolytes, liver function tests, sputum for acid fast bacilli, chest radiography, CD4 cell count and if required fine needle aspiration and biopsy, magnetic resonance imaging, computerized tomography, colonoscopy were also performed. The result of the present study shows increase in mean CD4 count by 128.78 cells/mm^3 after 6 months of initiation of ART, 24.77 cells/mm^3 after 1 year, 67.53 cells/mm^3 after 2 years and 5.59 cells/mm^3 after 3 years from the base line CD4 cell count. It certainly reveals the improvement in the CD4 count after ART initiation. Improvement in CD4 count was almost equal in both male and female and in all age groups. Mean CD4 cell count improved by 240.31 cells/mm^3 in females and 220.54 cells/mm^3 in males from the baseline after 3 years of treatment with ART. The present study clearly shows definite improvement in CD4 cell count after ART of more than 100% irrespective of age and sex. Regular intake of drugs will improve immunologic response. Therefore, strict adherence to ART and regular counselling sessions at ART centres should be stressed upon.

Key words: Anti-retroviral therapy, CD4 count, HIV, National Aids Control Organisation

DOI: 10.5455/jmas.215189

The development of effective anti-retroviral therapy (ART) for human immunodeficiency virus (HIV) infection is one of the most notable achievements in modern medicine. The first cases of acquired immunodeficiency syndrome (AIDS) were reported from Los Angeles in 1981. In the early to mid – 1980s, without any available antiretroviral treatment, the life expectancy of an

individual diagnosed with AIDS was only approximately 6 to 12 months. The first anti-retroviral drug, Zidovudine (Azidothymidine, AZT) was approved by the US Food and Drug administration (FDA) in 1987 on the basis of a short term survival benefit. Triple drug therapy was first introduced in the mid-1990s and resulted in a two thirds decrease in HIV related deaths within 2 years in developed countries. Presently there are a total of 28 antiretroviral drugs that are approved by the FDA and three drug combination regimens are the standard of care. The benefits of ART were extended to developing countries, and an estimated over 14 million people currently are taking ART worldwide. The life expectancy of an HIV-infected individual appropriately treated with ART is now estimated to be nearly that of the general population, both in developed and developing countries[1-3.]

As of the end of 2010, the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that 34 million (31.6–35.2 million)[4] people were living with human immunodeficiency virus (HIV)infection, globally. HIV infection can be diagnosed with a rapid point-of-care blood test, but only half of all persons living with HIV worldwide are aware of their infection[5-7]. During 2010, an estimated 2.7 million (2.4–2.9 million) new infections occurred worldwide, including an estimated 3,90,000 among children, and approximately 1.8 million (1.6–1.9 million) people died of AIDS-related causes[6,7]. Furthermore, there has been increasing awareness that early initiation of ART may significantly decrease HIV transmission and have a societal prevention benefit additional to individual clinical benefit[2,8-11]. With continuing advances in HIV drug development, the goal of antiretroviral therapy for all patients is to achieve an undetectable viral load in the blood using an ultrasensitive assay. Effective antiretroviral therapy should also result in restoration of at least partial cell-mediated immunity with successful treatment resulting in a rise of CD4 lymphocyte cells (CD4 cells) of 50 to 100 cells/mm^3 at the end of 1 year[12].

Materials and methods

It was a retrospective hospital based observational study. We included 110 HIV/AIDS who were on ART. Data was collected over a period of 3 years from 2005 to 2007 in the ART centre, Upgraded Department of Medicine, Osmania General Hospital. Data collected was assessed for mean CD4 cell count, trends, age and sex wise distribution. All patients were on ART as per NACO guide lines.

Investigations: Complete blood picture, serum creatinine, blood urea, serum electrolytes, liver function tests, sputum for acid fast bacilli, chest radiography, CD4 cell count were done in all patients. If required fine needle aspiration and biopsy, magnetic resonance imaging, computerized tomography and colonoscopy were also performed.

Results

Out of 110 patients, 64 were male and 46 were female and mostly in the age groups of 21-40 years. Out of 64 male patients, only 1 patient was less than 20 years of age, 53 patients were in the age group of 21-40 years and 10 were in the age group greater than 40 yrs (Table1 and Fig 1). In male patients, mean CD4 cell count at baseline was 215.66 cells/mm^3, after six months of ART was 340.64 cells/mm^3, after twelve months was 343.70 cells/mm^3 after 2 years was 410.91 cells/mm^3 and after 3 years was 435.08 cells/mm^3 respectively.

Table 1: Age and sex distribution

Age (years)	Male	Female	Total
<20	01	02	03
21-40	53	39	106
>40	10	5	14
Total	64	46	110

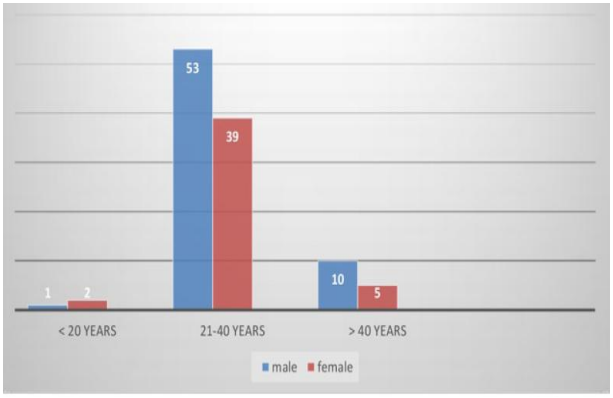

Fig 1. Age distribution

Out of 46 females, only 2 were in the age group of less than 20 years; 39 were in the age group of 21-40 years and 5 were in age group greater than 40 years. In females mean CD4 count at baseline was 225.54 cells/mm^3, after six months of ART was 362.02 cells/mm^3, after twelve months was 408.37 cells/mm^3, after 2 years was 478.22 cells/mm^3 and after 3 years 465.72 cells/mm^3.

Mean CD4 count in male patients at baseline was 215.66 cells/mm^3, after 3 years of ART was 435.08 cells/mm^3 with improvement by 220.54 cells/mm^3. Mean CD4 count in female patients at baseline was

225 cells/mm^3, after 3 years of ART was 465.72 cells/mm^3 with improvement by 240.22 cells/mm^3 (Table 2, Fig 2).

Table 2: Mean CD4 lymphocyte cell response – Gender wise distribution

Gender	Mean CD4 cell count				
	Baseline	6 months	1 year	2 years	3 years
Female	225.54	362.02	408.37	478.22	465.22
Male	215.66	340.64	343.70	410.91	435.08
Total	220.55	351.33	376.03	444.56	450.15

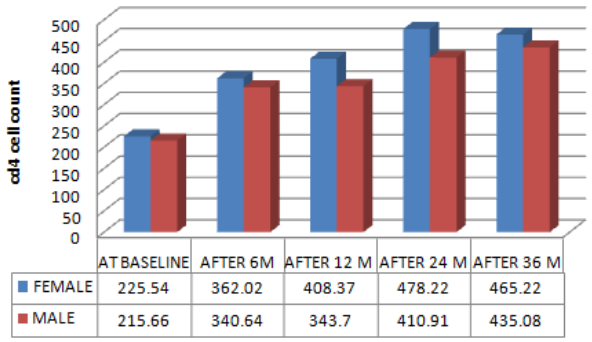

Fig 2. Mean CD4 lymphocyte cell response-Gender distribution

Discussion

A normal CD4 count in a healthy, HIV negative adult can vary but is usually between 500 and 1400 CD4 cells/mm^3 (though it may be lower in some people)[13]. HIV infection affects immune system by extirpating CD4$^+$ T cells. The principal impact of HIV infection on the immune system is destruction of the CD4 T-lymphocytes. During primary infection, HIV and HIV-infected cells reach the lymph nodes and other lymphoid tissues. The virus rapidly disseminates during this early phase of HIV infection. During early phase of HIV infection, virus spreads rapidly which results in high levels of viremia and significant dip in CD4 cell counts. As a result, there is a significant fall in CD4 cells and rise in viral levels as high as 10^6-10^7 viral copies/ml[14]. CD4 count in peripheral blood is used as an indicator of immune function. There could be CD4$^+$ cell loss of upto 2 million cells/day in active phase of infection.

Table 3: Mean CD4 lymphocyte cell count at time of initiation and post ART

Gender	At initiation of ART	Post ART	Improvement in CD4
Female	225.54	465.22	240.31
Male	215.66	435.08	220.54
Total	220.55	449.15	230.45

In HIV patients, CD4$^+$ cell count is a major indicator of immunodeficiency, a pointer for initiating ART and for monitoring treatment response.

Among those with human immunodeficiency virus (HIV) infection, the CD4$^+$ T-lymphocyte count is the major indicator of immunodeficiency, a main factor in deciding whether to initiate highly active antiretroviral therapy (HAART), and an important parameter in monitoring treatment response[15,16].

Studies of the kinetics of CD4$^+$ count response post-HAART indicate that the CD4$^+$ count increases rapidly during the first 3-6 months, in part due to release of memory T-cells from lymphoid tissue, and then increases slowly during the next 3-4 years, reflecting reconstitution of the immune system[17]. The rate of CD4$^+$ recovery depends on various factors like baseline CD4$^+$ count at HAART initiation, age of the patient, maintenance of virologic suppression.

ART initiation guidelines used in developing countries have been based on both clinical and laboratory parameters [18,19]. In the face of high AIDS mortality, initial prioritization was to rapidly expand antiretroviral access to the largest number of patients with advanced clinical disease. Late presentation is costly in terms of morbidity and mortality[10] and utilization of healthcare resources and also limits the potential for restoration of immune function[2]. Treatment of patients with earlier disease is less demanding, results in better outcomes utilizing less health resources and also decreases the proportion of the population progressing to AIDS. In 2010, the WHO changed the recommended CD4 T-cell initiation threshold from 200 to 350 cells/μL in addition to clinical stages 3 and 4. However, implementation of CD4 count criteria only has utility when there is wider access to CD4 counts integrated with voluntary counselling and at all interfaces with the healthcare system[8].The trend for earlier ART initiation is further supported by recognition of lower HIV transmission from HIV-infected partners of discordant sexual relationships with CD4 cell counts above current treatment thresholds who are receiving effective ART[9]. Furthermore, modelling exercises have proposed that universal early initiation of ART has the potential to prevent HIV transmission at a population level.

Table 4: CD4 monitoring and follow-up schedule

CD4 count	Monitoring interval
Any value and on ART	Every 6 months
350 to 500 and not on ART	Every 3 months
> 500 and not on ART	Every 6 months

In most patients, the CD4 cell count rises with the initiation of ART and immune recovery. However, this may be blunted if the baseline CD4 count is low. In general, the lower the baseline CD4 count is at the start of ART, the longer it will take for the count to increase with time. In some patients, clinical improvement may never correlate with $CD4^+$ count i.e. counts never reach 200cells/mm^3.

In those who have achieved a substantial peak response, a subsequent progressive decline in the CD4 count in the absence of inter current illness indicates an immunological failure (determined by the trend of regular six-monthly CD4 counts).

Ensuring good adherence to the treatment is imperative for the success of the national programme as well as for the prevention of drug resistance. To achieve this, counselling must start from the first contact visit by the clinical team and should include preparing the patient for treatment and providing psychosocial support through an identified guardian and through support networks. All patients should undergo at least two counselling sessions before the initiation of ART[20].

Conclusion

Present study clearly shows definite improvement in CD4 cell count after ART is more than 100% irrespective of age and sex. Therefore strict adherence to ART /regular counselling sessions at ART centres should be stressed.

Acknowledgements: ART Center staff and HIV& AIDS patients for their cooperation, Osmania General Hospital, Hyderabad.

Conflict of interest: Nil

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