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Monitoring of CD4 Response Over a Period of Thirty Six Months in Patients of HIV/AIDS on ART:A Study in Osmania General Hospital

KEYWORDS: Human Immunodeficiency Virus(HIV), Acquired Immunodeficiency Syndrome(AIDS), CD4 cell count, Anti retroviral therapy(ART).

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ABSTRACT *Aim:The present study aims to assess the progression of CD4 cell count after initiation of ART in patients with HIV/AIDS with different mean CD4 cell counts at the time of presentation.*

MATERIAL AND METHODS:It was a retrospective hospital based observational study. Data was collected over a period of 4 years from 2005 to 2009 in the ART CENTRE, Department of Medicine, Osmania General Hospital. We included 182 HIV/AIDS who were on ART. CD4 cell count data was collected and assessed for changes in mean CD4 cell count after ART initiation. 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 to all patients , Fine needle aspiration and biopsy(if necessary), Magnetic Resonance imaging (if necessary), Computerized Tomography(if necessary), Colonoscopy(if necessary).

RESULTS:Out of 182 patients, 100 were male and 82 were female which were categorised into 4 groups as per base line mean CD4 cell count . Group 1 includes CD4 cell count < 50 n= 10; group 2 with CD4 cell count between 51 to < 100 n= 30; group 3 with CD4 cell count between 101 to 200 n= 83 and group 4 with CD4 cell count 201-250 n= 59. In group 1, base line mean CD4 cell count of 31.08 cells/mm3 improved to 307.90 cells/mm3 ,in group 2 CD4 cell count improved from baseline of 80.30 cells/mm3 to 337.27 cells/mm3 , in group 3 with baseline CD4 cell count of 160.08 cells/mm3 improved to 422.99 cells/mm3 and in group 4 CD4 cell count baseline of 222.95 increased to 423.44 cells/mm3 after 36 months of ART. CD4 cell counts improvement is more in younger patients (age < 20 years[n = 4]) with baseline count of 142.52 to 639.50 cells/mm3(468.98) compared to patients with age > 40 years age (n= 39) with baseline mean CD4 cell count 153.31 to 419.19 cells/mm3(265.88) .

Conclusion:This study shows definite improvement in the CD4 cell count after initiation of ART. Regular intake of ART will improve immunologic response and improve CD4 cell counts irrespective of base line CD4 cell count. Most of the patients are falling in age group between 21-40 years n=139. CD4 cell counts improvement is maximum in first six months post ART initiation and more in younger age groups.

Introduction:

AIDS was first recognized in 1981 following clusters of PCP (Pneumocystis carnii pneumonia) in young gay and drug-using men in California and New York [1, 2, 3]. Worldwide, it is estimated that 30.6 million patients are living with HIV and 90% of these are in developing countries[4].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. As a result, there is a significant fall in CD4 cells and viral levels may be as high as 10^6-10^7 viral copies/ml [5]. CD4 cell count in peripheral blood is used as an indicator of immune function. In active phase of infection, CD4+ loss can be up to 2 million cells per day.[6]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)[7].

Effective ART that durably suppresses HIV replication results in rapid and sustained rises in absolute CD4 counts. Typically, a 2-phase increase in CD4 cells occurs after effective ART is initiated: a rapid initial rise in the first few months, primarily due to increases in memory T cells, followed by a slow, steady increase in naive T-cell counts that can continue for years with sustained suppressive ART.[8,9] The majority of patients,whose plasma HIV RNA levels remain below the level of detection, on ART eventually achieve absolute CD4 counts that are in the normal range. However, several recent long-term follow-up studies have reported that up to one third of patients with long term ART suppression of HIV RNA do not achieve absolute CD4 counts >500 cells/μL.[10,11]

RESULTS:

Out of 182 patients, 100 were male and 82 were female. They were categorised into 4 groups as per base line mean CD4 cell count : Group 1 includes CD4 count < 50 n= 10 (male n=6,female n= 4) with baseline mean CD4 cell count of 31.08 cells/mm^3 , group 2 CD4 cell count between 51 to 100 n= 30 (male n=18,female n=12) with baseline mean CD4 cell count of 80.30 cells/mm^3 , group 3 CD4 cell count between 101 to 200 n= 83 (male n=49,female n=34) with baseline mean CD4 cell count of 160.13 cells/mm^3, group 4 CD4 cell count 201-250 n= 59 (male n=27,female n=32), with baseline mean CD4 cell count of 222.95 cells/mm^3. In group 1 base line mean CD4 cell count improved to 171.20 cells/mm^3 after

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six months, 292.70 cells/mm^3 after twelve months, 271.30 cells/mm^3 after twenty four months, and 307.90 cells/mm^3 by the end of thirty six months. In group 2 ,base line mean CD4 cell count improved to 254.63 cells/mm^3 after six months, 284.87 cells/mm^3 after twelve months,279.43 cells/mm^3 after twenty four months 2nd year 337.27 cells/mm^3 by the end of thirty six months. In group 3, base line mean CD4 cell count improved to 363.60 cells/mm^3 after six months, 335.00 cells/mm^3 after twelve months,389.14 cells/mm^3 after twenty four months, 422.99 cells/mm^3 by the end of thirty six months. In group 4,base line mean CD4 cell count improved to 339.08 cells/mm^3 after six months, 338.92 cells/mm^3 after twelve months,493.46 cells/mm^3 after twenty four months, 423.44 cells/mm^3 by the end of thirty six months.(Table 1,Figures 1 and 2).

When grouped according to age, patients with age < 20 years n=4 had improvement in CD4 count from base line of 142.52 cells/mm^3 to 639.50 cells/mm^3(486.98 cells/mm^3) , in age group 21-40 years n=139 with baseline mean CD4 count of 162.76 cells/mm^3 to 419.0 cells/mm^3 (266.88 cells/mm^3), age group > 40 years n= 39 with baseline mean CD4 count 153.31 cells/mm^3 to 419.19 cells/mm^3 (265.88 cells/mm^3). Improvement is more in younger age group(age <20 years).(Table 2 and Figure 3).

Table1: IMPROVEMENT OF MEAN CD4 COUNT AFTER INITIATION OF ART

No. of patients	CD4 count	Base line mean CD4	After six months	After twelve-months	After twenty-four months	After thirty six months
10	<50	31.08	171.20	292.70	271.30	307.90
30	51 TO100	80.30	254.63	284.87	279.43	357.27
83	101TO 200	160.13	363.60	335.00	389.14	422.99
59	201-250	222.95	339.08	338.92	493.46	477.73
182		160.29	327.13	341.89	398.40	423.44

Figure 1 : CD4 TRENDS IN RESPONSE TO ART

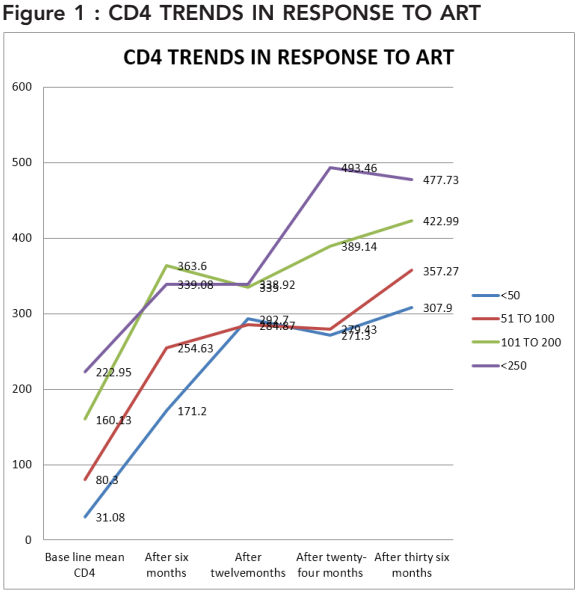


Figure 2 : Distribution of patients according to CD4 counts.

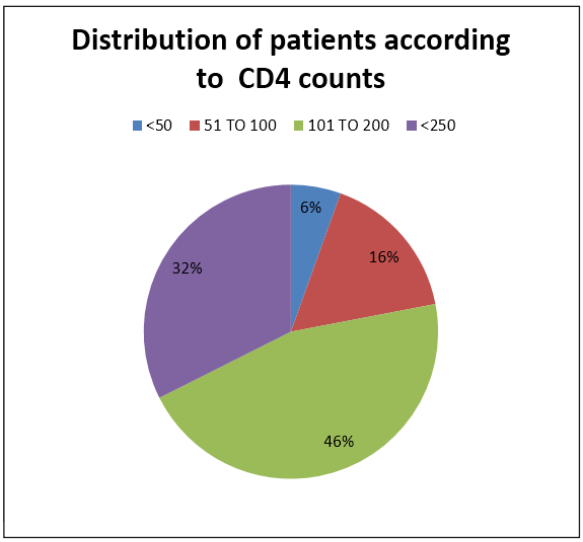
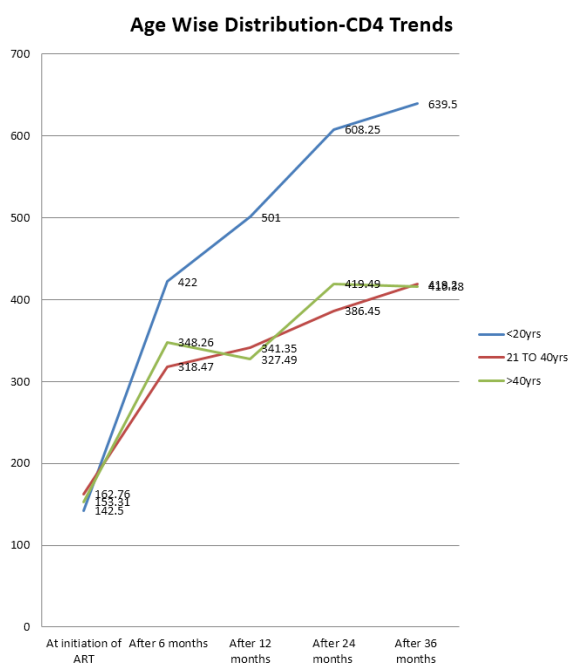


Table2:Age wise - Improvement of mean CD4 cell count over a period of 3years with ART

Age	No of patients	at initiation of ART	After 6 months	After 12 months	After twenty four-months	After thirty six months
<20yrs	04	142.50	422.00	501.00	608.25	639.50
21TO 40yrs	139	162.76	318.47	341.35	386.45	419.20
>40yrs	39	153.31	348.26	327.49	419.49	416.38
Grand total	182	160.29	327.13	341.89	398.40	423.44

Figure 3 : Age Wise Distribution-CD4 Trends



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Discussion:

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 [12,13 ,14] . 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 [15-19]. The magnitude of CD4+ recovery may depend on a variety of factors, including maintenance of virologic suppression, age, and CD4+ count at HAART initiation.[12] 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-positive cells of 50 to 100 cells/mm^3 at the end of 1 year. [20] In present study, rise of CD4 cell count was 181.60 cells/mm^3 at the end first year,266.15 cells/mm^3 at the end of thirty six months from baseline of 160.29 cells/mm^3. All India's response to HIV is guided the by National AIDS Control Programme (NACP)which was launched in 1992. An autonomous body, National AIDS Control Organization (NACO), was set up in 1992 to implement Phase 1 of this project. [21] There are 512 ART centres that are functional in the country as of July 31, 2015. These include 54 ART Plus centres. The main objective of ART centre is to provide comprehensive package of care, support, and treatment services to persons living with HIV / AIDS (PLHA) with specific objectives[22].

To minimize the travel needs and related cost, to the patients stable on ART, Link ART centres (LAC) and LAC plus centres scheme was introduced in 2008. [23] 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.[24] CD4 monitoring and follow-up schedule includes CD4 of any value and on ART every 6 months, CD4 between 350 and 500 cells/mm^3 and not on ART repeat every 3 months , CD4 > 500 cells/mm^3 and not on ART repeat 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, the count may never exceed 200 cells/mm^3 even with clinical improvement . In those who have achieved a substantial peak response, a subsequent progressive decline in the CD4 count in the absence of intercurrent illness indicates an immunological failure (determined by the trend of regular six-monthly CD4 counts) [25]. HIV infections may not disappear in the foreseeable future, but the AIDS epidemic can be ended as a global health threat. To achieve this by 2030, the number of new HIV infections and AIDS – related deaths will need to decline by 90% compared to 2010[26].

Conclusion: Present study clearly shows there is definite improvement along with maximal improvement in mean CD4 cell counts irrespective of base line CD4 cell count in the initial six months and steady progression of CD4 count with ART. Improvement is more in younger age group.

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