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A Prospective Study to Evaluate the Impact Of Highly Active Antiretroviral Therapy On CD4 T Cell Count

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Abstract

Human Immunodeficiency Virus, the cause of AIDS, continues to spread, being described as a global health emergency by the world health organization. HIV type 1 is the etiologic agent of most cases of AIDS. India has the Third highest HIV / AIDS burden in the world next to South Africa and Nigeria. It is a disease that is acquired, for which no permanent cure has been found till date, and consequently has a great impact on the quality of life of a patient. HIV/AIDS infection results in a wide range of clinical consequences from asymptomatic carriage to life threatening opportunistic diseases. The present study was to evaluate the impact of highly active antiretroviral therapy on CD4 T cell count.

Aims & Objectives: The aim of the study which was conducted on patients attending antiretroviral therapy centre (ART Centre) of Govt. Siddhartha Medical College Hospital was to evaluate the impact of highly active antiretroviral therapy on CD4 T cell count.

Patients And Methods: Patients who are confirmed to have HIV/AIDS and attending the ART CLINIC were taken up for the study in the period between December 2011 to September2013. Only adults above the age of 12 years among both males and females were selected. Total of 120number of patients were analyzed.

Inclusion Criteria: All confirmed HIV/AIDS patients whose CD4 cell count was less than 350/µl were only taken up for highly active antiretroviral therapy.

Patient above the age of 12 years.

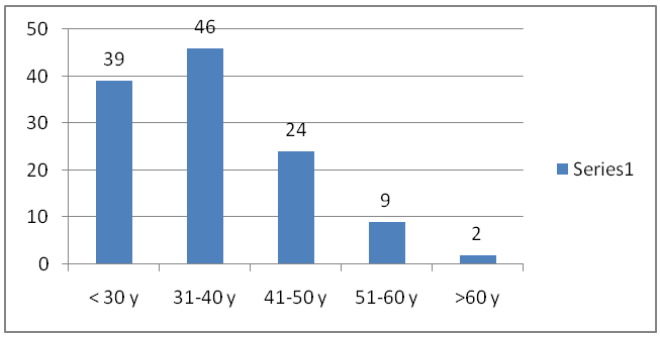
Exclusion Criteria: Patients who were confirmed as HIV/AIDS positive patients whose CD4 cell count was more than 350 / µl were excluded from the study.

Patient who was in the pediatric age group of less than 12 years was also excluded.

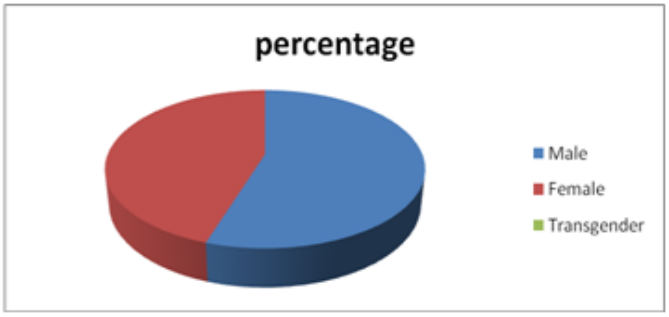
In this study, patients irrespective of the clinical stage, whose CD4 count was less than 350 / µl were started on HAART.

Results: Total number of 120patients were analyzed. Both the initial CD4 count and CD4 count after 6 months of highly active antiretroviral therapy were obtained as follows:

Age Distribution – Analysis: Among the 120 patients studied the age incidence was highest in the 31-40 year age group (38.33%). This was followed by 32.5% in under 30, 20% in age group between 4 1-50 years ,7.5% in age group 51-60 years and 1.66% above 60 years.



Sex Distribution – Analysis: Among the 120patients studied the males where more commonly affected (55%) when compared to females 45% and transgender of (0%).



Mode of Spread

Mode	No of Cases	%
Heterosexual (1)	115	95.83
Intravenous Drug abuse (2)	0	0
Commercial sex workers (3)	5	4.16
Men having sex with men (4)	0	0
Total	120	100

Among the 120 patients analysed it is the heterosexual transmission that is most common mode of transmission (95.83%), With men having sex with men constituting 0% and intravenous drug abuse constituting 0% and commercial sex workers constituting 4.16%.

Alcoholism – Correlation to Sexual Behaviour

History of Alcohol Intake	No of Cases	%
Yes	48	40
No	72	60

Smoking - Correlation to Sexual Behaviour

History of Smoking	No of Cases	%
Yes	55	45.8
No	65	54.2

Among the 120 patients studied 48 cases (40%) have history of Alcohol intake and 55(45.8%) cases have history of smoking. Overall 40 patients out of 120 patients were both alcoholic and smoker. So it seems that smoking and alcohol influence sexual behaviour.

Disease Configuration: Among the 120 patients studied,16 patients had co-existing illness. Pulmonary tuberculosis was present in 14 patients, extra pulmonary tuberculosis in 2 patient. So tuberculosis was the most common opportunistic infection in the study population. The associated illness was diagnosed at the time of the initial diagnosis of HIV and no patient developed any opportunistic infection during HAART so it seems HAART decreases the incidence of opportunistic infections.

Disease	No of Cases	%
Pul.TB	14	87.5
Extrapul.TB	2	12.5
Jaundice	0	0
Total	16	100

Weight gain during HAART:

Time Frame	Mean (Kgs)	Standard Deviation
Pre HAART weight	52.8	10
During HAART (at 6 months Follow up)	55.5	9.1

(Paired t = 6.68; degrees of freedom = 105; p <0.001 => significant). Among 120 patients, only 106 could be followed up till 6 month into HAART. The initial mean weight was 52.8 ± 10 Kgs. The follow up mean weight was 55.5 ± 9.1 KGs, thus showed an average improvement of 2.7 KGs before and after HAART. The difference was statistically significant, when analyzed using paired t test. The p value was less than 0.001 which seems to show that there is weight gain after HAART

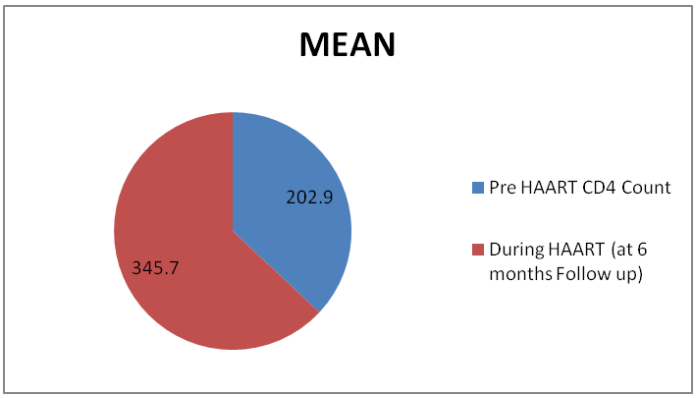
CD4 Count Analysis: Among the 120 patients, the maximum no. of patients who were started on HAART had a CD4 count between100-249 (48.33%) followed by 42 patients in Group-3 having CD4 count between 250-349(35%) followed by 20 patients in Group I having CD4 count between 0-99 (16.66%).

	Pre HAART CD4 Count	No of Patients	Percentage
Group I	0 – 99	20	16.66
Group II	100 - 249	58	48.33
Group III	250 - 349	42	35
Total		120	100

CD4 counts during HAART

Time Frame	Mean	Standard Deviation
Pre HAART CD4 Count	202.9	95
During HAART (at 6 months Follow up)	345.7	171.2

(Paired t = 10.6; degrees of freedom = 105; p <0.001 => significant). The initial mean CD_4 count was 202.9 ± 95. The follow up mean count was 345.7 ± 171.2, thus showed an average improvement of 142.8 before and after HAART. The difference was statistically significant, when analyzed using paired t test. The p value was less than 0.001 which seems to show that there is improvement in CD_4 counts after HAART.



CD4 Cell Count Comparison: Among the 120 patients analysed for the impact of HAART on CD4, the mean increase of 142 cells / mm3 was noted after six months of HAART, which was also statistically significant when analysed by paired 't' test which showed the 'P' value of 0.0000.

CD4 Cell Count	Mean ± SD
Pre HAART CD4	199.50 ± 93.70
During HAART CD4 (after 6 months follow up)	345.74± 167.80

Discussion

The first cases of HIV infection were reported in 1981 and today, more than 30 years later: there are approximately 34 million people currently living with HIV and nearly 30 million people have died of AIDS-related causes since the beginning of the epidemic.[1] It is important to view untreated HIV infection as a chronic ultimately fatal process that is punctuated by various manifestations, which are influenced by multiple factors

like route of HIV infection, size of inoculum, gender, medical intervention etc. In India it is commonly acquired through Heterosexual contact. In the study the most common mode of transmission was found to be heterosexual with 95.83% acquiring the disease through this route. Once acquiring the infection, one to 6 weeks later patients experience a nonspecific illness called as "acute retroviral syndrome". An Indian study showed that the majority of the HIV infected individuals with CD4 counts of 200-350 cells/µl had higher viral load than that suggested by the International AIDS society[2] and a cut-off CD4+ T cell count of 243 cells/µl reported in this study distinguished asymptomatic (CDC clinical category A) from symptomatic (CDC clinical category B) individuals[3]. . Recently a study conducted by Kitahata et al[4] suggested that the early initiation of the treatment might be important for better prognosis of the HIV infection. CD4 count may recover for some patients but most patients demonstrate a decrease of 100 to 200 cells in the first 6 months after sero conversion and a decline of an additional 100 cells in the next 6 months.

In one review of 318 seroconverters mean CD4 + cell count in the initial 12 month after seroconversion fell from 999 to 673/ mm[5]. In this study the mean initial CD4 count of all 120 patients who were started on HAART was 199 cells / mm^3 ± 53.70.

A meta-analysis of 18 cohort studies also supports counts of 350 cells/µL as a minimum threshold [6]. Optimally, the decision to institute initiation of ART at a higher CD4 threshold on a widespread level would be based upon data from controlled studies. Recent studies indicate that initiating ART earlier than the currently recommended CD4 threshold of 350cells/µL may confer benefits on survival and immune function. And the natural history of illness has been dramatically altered by HAART. The likelihood of an initial AIDS defining condition developing in an untreated person who is HIV positive average about 4 to 10 percent per year after acquisition of HIV infection.

The absolute peripheral CD4 lymphocyte count and percentage of peripheral cells that are $CD4^+$, both correlate with the likelihood of development of AIDS. Decision on initiation of ART or prophylaxis for opportunistic infections (OIs) is a critical issue in the management of HIV infected persons. It has been observed that most of the OIs like cryptosporidiosis, toxoplasmosis, herpes zoster, cryptococcal meningitis, Pneumocystis jerovici pneumonia, penicillinosis and CMV retinitis were seen in patients having CD4+ T cells <200 cells/µl. On the contrary, tuberculosis and candidiasis may be seen below the count of 400cells/µl as observed in one of the Indian studies[7].

First, HIV infection implies that unless an effective therapeutic intervention is administered the immune function inexonerably declines and infectious complication occur. Second, the monitoring of the immunologic decline primes the clinician to do the measures in anticipation of the complication. Third the immunologic state as measured by CD4 cell count provides guidance regarding the benefit of HAART. When the CD4 count falls below 350 cells /µl, effective HAART can clearly improve survival. At higher levels, HAART may improve survival. Fourth, a rise of CD4 in response to HAART predicts clinical benefit of therapeutic intervention.

During potent antiretroviral therapy, immune recovery is characterized by suppression of HIV - 1 replication and increasing $CD4^+$ T Cell count. In our study group, the CD4 cell count improved by a mean of 142 cells / mm^3.

Many people present late with advanced HIV infection via absolute CD4 count less than 350 and / or with AIDS defining illness at the time of HIV diagnosis[8]. One of the

major causes of death inspite of initiation antiretroviral therapy is late presentation. Late presenters: mostly symptomatic, fairly sick with multiple opportunistic infections / events, higher mortality rate, high chances of immune-reconstitution inflammatory syndrome (IRIS) and antiretroviral therapy must be initiated. Control of HIV - 1 replication reduces CD4 T cell loss resulting from direct cytolysis and may partially restore T cell homeostasis by promoting decreased T cell proliferation. Redistribution of T cells into peripheral circulation and improved thymic output. Although many patients continue to have CD4 T cell recovery for several years after receiving HAART, the degree of immune recovery achieved during viral suppression is highly variable. In some individuals increases in the CD4 cell count appears to plateau after the first few months of HAART[9]. This suboptimal CD4 T cell response during therapy otherwise known as 'immunologic discordance' can have detrimental clinical consequences. At present there is no validated or accepted, definition of immune discordance during HAART.

Highly active antiretroviral therapy (HAART) increases $CD4^+$ cell numbers, but its ability to correct the human immunodeficiency virus (HIV) induced immune deficiency remains unknown. A three-phase T cell reconstitution was demonstrated after HAART, with: (i) an early rise of memory $CD4^+$ cells, (ii) a reduction in T cell activation correlated to the decreasing retroviral activity together with an improved $CD4^+$ T cell reactivity to recall antigens, and (iii) a late rise of “naive” $CD4^+$ lymphocytes while $CD8^+$ T cells declined, however, without complete normalization of these parameters[10].

In general, reconstitution of CD4 T cells during viral suppression follows a biphasic pattern. During the first three months of HAART the number of CD4 T cells typically increase by 50 to 120 cells per mm^{11}. This burst is followed by a, second slower phase of T cell repopulation with an average rate of increase of 2 to 7 cells mm3 per month[12].

In our study population, the CD4 count seems to have risen to a greater degree of about 142 cells / mm^3, which could be both due to the smaller sample size but also could be because of the nutritional counselling that is given to our patients at the ART centre and also because of the supplementation of micro and macro nutrients and monthly monitoring of body weight and height.

In this study there were 120 patients with CD4 cell count of less than 350 / µl, who were started on highly active antiretroviral therapy and followed up for 6 months. Of these 120 patients 20 patients had a CD4 count between 0-99, who were classified a Group I, 58 patients had a CD4 cell count between 100-249,who were classified as Group II and, 42 patients had a CD4 cell count between 250-349, who were classified as Group III. But, of these 120 patients only 106 patients could be followed up for 6 months and a repeat CD4 count could be done. These 106 patients 6 month follow up CD4 count was analyzed and it showed an improvement by a mean of 142 cells / mm^3, which was also statistically significant when analyzed by paired 't' test, that showed 'p' value of < 0.001. From the study it is clear, when HAART is started, with the CD4 count at a higher level (Group III), the improvement in CD4 count as well as the general condition improvement is better.

Conclusion

1. In this study there were120 patients with CD4 cell count of less than 350/ µl who were started on highly active antiretroviral therapy and followed up for six months. But only106 patients came back after 6 months of HAART, whose follow up CD4 count was done and

analyzed to evaluate the impact of HAART on CD4 cell count.

2. It is important to do CD4 cell count in all the patients who are confirmed as HIV/AIDS, irrespective of the clinical stage, since the clinical stage and the CD4 count do not correlate.

3. Patients were classified into three groups as per the initial CD4 cell count. (N = 106).

	Initial CD4 Cell Count	No of Patients followed up for 6 months
Group I	0-99	4
Group II	100-149	28
Group III	150-199	74
Total		106

4. These106 patients 6 month follow up CD4 count was analysed and it showed an improvement by a mean of 142 cells / mm3 which was also statistically significant when analysed by using the paired 't' test, that showed a 'p' value of < 0.001. So HAART has a significant improvement on CD4 cell count when HAART is started with the CD4 count at a higher level as in Group III.

5. HAART has improved the BMI and thereby improving the general condition and well being of the patients. This could also be attributed to the micronutrients and the macronutrients that were provided to the patients at the ART centre, new GGH,vijayawada .

6. HAART decreases the incidence of opportunistic infections.

7. Tuberculosis was the most common opportunistic infection.

8. CD4 cell count monitoring is very important and could be done every 3 months, but for resource constraints it is being done every 6 months.

9. Limitation of the study:

(a) small sample size,

(b) four combinations of HAART regimens where used in these 106 patients and the individual effect of each combination on CD4 count was not evaluated.

References

1. Global report 2012. Geneva: UNAIDS, 2012. Available online at: (http://www.unaids.org/en/resources/campaigns/20121120_ globalreport2012/globalreport/).

2. Hammer SM, Saag MS, Schechter M, Montaner Julio SG, Schooley RT, Jacobse DM, et al. Treatment for adult HIV infection: 2006 Recommendations of the International AIDS Society-USA Panel. JAMA 2006; 296: 827-43.

3. Kannangai R, Kandathil AJ, Ebenezer DL, Nithyanandam G, Samuel P, Abraham OC, et al. Evidence for lower CD4+ T cell and higher viral load in asymptomatic HIV-1 infected individuals of India: implications for therapy initiation. Indian J Med Microbiol 2008; 26: 217-21.

4. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 2009; 360 : 1815-26

5. Stein DS, Corvick JA, Vermund SH. $CD4^+$ lymphocyte cell enumeration for prediction of clinical course of HIV disease: a review. J. Infect. Dis. 1992; 165: 352.

6. When to Start Consortium. Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 19 HIV cohort studies. Lancet 2009; 373:1352-63.

7. Singh HR, Singh NG, Singh TB. Estimation of CD4+ and CD8+ T-lymphocytes in human immunodeficiency virus infection and acquired immunodeficiency syndrome patients in Manipur. Indian J Med Microbiol

2007; 25: 126-32.

8. Jurgen K Rockstorh, Jose gatell, Roland Landmen, et al.Management of late presenters patient with HIV infection. *Antiviral Therapy* 2010;15suppl1:25-30.

9. Hansjee N, Kaufmann GR, Strub C, et al. Persistent apoptosis in HIV-1 infected individuals receiving potent antiretroviral therapy is associated with poor recovery of CD4 T lymphocytes. JAcquir Immune Defic Syndr 2004; 36: 671-7.

10.B. Autran[*], G. Carcelain, T. S. Li[†], C. Blanc[†], D. Mathez, R. Tubiana, C. Katlama, P. Debré,J. Leibowitch . Positive Effects of Combined Antiretroviral Therapy on $CD4^+$ T Cell Homeostasis and Function in Advanced HIV Disease, Science 4 July 1997: Vol. 277 no. 5322 pp. 112-116 .

11. Kaufmann GR, Bloch M, Finlayson R, Zaunders J, Smith D, Cooper DA. The extent of HIV-1 related immunodeficieny and age predict the long-term CD4 T lymphocyte response to potent antiretroviral therapy. AIDS 2002; 16: 359-67.

12. Hunt PW, Deeks SG, Rodriguez B, et al. Continued CD4 cell count increases in HI V-infected adults experiencing 4 years of viral suppression on antiretroviral therapy. AIDS 2003; 17: 1907-15.