Effect of anti-retroviral therapy on cd4count in treatment naive HIV infected patients attending anti retro viral therapy centre in north Karnataka

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Abstract

Background: ART treatment has resulted in a marked decrease in the mortality and morbidity associated with HIV infection. Follow-up and monitoring is essential in patients initiated on ART to track clinical progress and monitor wellbeing.
Objectives: 1. To determine the effect of Anti-retroviral Therapy (ART) on CD4 Count in treatment-naïve HIV/AIDS patients. 2. To determine the effect of ART on Weight gain and haemoglobin percentage in treatment-naïve HIV/AIDS patients.
Materials & Methods: Longitudinal study was conducted at the ART centre, North Karnataka for a period of 1 year among 242 HIV infected patients. CD4 count, haemoglobin, weight, etc were measured at the time of initiation of ART and at the end of 6 months of ART.
Statistical analysis: Data analysed using Epi-Info 6 software. Tests used were mean, proportions, Chi square test and Paired T test.
Results: 54(22.3%) were in the age group of 25-29 years, 133(55%) were females and 109(45%) were males. Male to female ratio is 1:1.2. CD4 counts >200 cells/mm^3 at the initiation of ART were in 82 (33.9%) patients and at the end of 6 months were in 187 (85%) of patients. Increase in the CD4 counts was noticed in 206 (95.8%) patients after 6 months of ART. Significant increase in the mean CD4 count by 165.7182 cells/mm^3, mean CD4 percentage by 7.3591% & weight by 2.4727 kg were noted.
Conclusions & Recommendations: CD4 counts and CD4 percentage in HIV patients increase substantially with proper ART. Initiation of ART at an earlier stage has significant better results than wait for the counts to lower.

Key Words: Anti-Retroviral Therapy, CD4 Count, HIV infection.

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Introduction

Since the beginning of the human immunodeficiency virus (HIV) epidemic, more than 71 million people have been infected globally and as on December 2014, nearly 36.9 million people were living with HIV/AIDS worldwide. An estimated 0.8% of adults aged 15–49 years worldwide are living with HIV.[1]Over the past decade; there has been a tremendous increase in our understanding of molecular biology and the viral structure and pathogenesis of the disease. This knowledge has led to the development of a number of new anti-retroviral drugs and treatment protocols.[2]

By the end of 2013, the World Health Organization estimated that around 11.7 million people receiving antiretroviral therapy (ART) in low-income and middle-income countries, representing 36% of the 32.6 million estimated to need it.[1] In September 2003, WHO declared the lack of access to antiretroviral (ARV) treatment for HIV/AIDS a "global health emergency".

An emergency plan was announced to scale up access to ARV treatment in order to cover at least three million people by the end of 2005. This joint WHO/ UNAIDS announcement popularly came to be known as the **"3 by 5" initiative**. Since then the number of people receiving ART has more than tripled.[2]

Antiretroviral therapy (ART) does not cure HIV/AIDS, but effective antiretroviral regimens inhibit the efficient replication of the HIV virus, and reduce viraemia to the undetectable levels. This leads to slowing of disease progression and fewer opportunistic infections and helps people lead more productive lives, with perceptibly reduced stigma and discrimination. Success achieved by ART in terms of delaying the onset of AIDS has transformed the common perception about HIV from being a "virtual death sentence" to a chronic manageable illness. ART treatment has resulted in a marked decrease in the mortality and morbidity associated with the disease.[2]

The free ART initiative in India was launched on 1st April 2004. The technical guidelines were modified from "WHO guidelines for ART in resource constraints settings". The guidelines have again being modified in view of revised WHO 2006 ART guidelines. ART has been provided free of cost to the HIV infected persons under National AIDS Control Program (NACP).[3]

The initiation of ART is based on the clinical stage, and the CD4 count is used to guide treatment and follow-up[4]. Patients should start ART before the CD4

count drops below 200 cells/mm³. In most patients, CD4 cell counts rise with the initiation of therapy and immune recovery. This may continue for many years into effective therapy, although this may be blunted if the baseline CD4 count is very low.

Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Manipur and Nagaland are the six high-prevalence states in India. Karnataka is one of four large states in South India with a relatively advanced HIV epidemic, with the adult HIV prevalence in some districts exceeding 1% (HIV Sentinel Surveillance). [3]
In Karnataka, HIV prevalence in the general population according to third National Family Health Survey (NFHS-3) during 2005-06 was 0.69% of adults aged 15-49 years and the prevalence being somewhat lower among women than men (0.54% versus 0.85%). The prevalence was somewhat higher in rural than urban areas (0.79% versus 0.54%).[5]In 2005, HIV prevalence rates in Karnataka was 13.6 in STD clinics and 1.25 in ANC clinics.[6] There are many factors like practice of devadasi system, poor socio-economic status, illiteracy, etc responsible for more cases in north Karnataka.

According to WHO ART guidelines 2006, following fixed-dose drug combinations are given to the patients in the study. The selection of first-line regimens is determined on the basis of a number of considerations, such as potency, profile of side-effects, ability to keep future treatment options open, ease of adherence, cost, risk during pregnancy and potential of the development of resistant viral strains. The current global recommendation in all circumstances is a triple drug regimen.[2]
The first-line regimen was used in the given study. The first-line regimen was selected using the following principle:
1. Choose 3TC (Lamivudine) in all regimens
2. Choose one NRTI to combine with 3TC {Zidovudine (AZT) or Stavudine (d4T)}
3. Choose one NNRTI {Nevirapine (NVP) or Efavirenz (EFV)}

Follow-up and monitoring is essential in patients initiated on ART to track clinical progress and monitor well being[4,7]. The routine monitoring and follow-up for patients on ART under the national programme includes clinical and adherence counselling, Weight, Hb, Random blood sugar, CD4 count, Urinalysis, Lipid profile, HBV and HCV screening, syphilis screening, Plasma viral load. The effect of ART is measured by CD4 counts and Viral loads[4]. The CD4 counts increase by least 50 cells/μl at 4 to 8 weeks after starting therapy followed by an increase of 50–100 cells/μl per year until a threshold is reached[4]. If the CD4 counts fall is higher than 30% from peak or return to below the pre-therapy baseline values it is considered as immunologic failure.[4]

The present study was conducted among HIV patients at the ART centre Hubli a premier institute of North Karnataka to determine the effect of Anti-retroviral Therapy (ART).

Objectives
1. To determine the effect of Anti-retroviral Therapy (ART) on CD4 Count in treatment-naïve HIV/AIDS patients.
2. To determine the effect of ART on Weight gain and haemoglobin percentage in treatment-naïve HIV/AIDS patients.

Materials & Methods
It was a longitudinal (Prospective) study done at the antiretroviral therapy centre (ART) centre of in premier institute at Hubli, North Karnataka for a period of one year.

The prevalence rate of HIV positive cases in Karnataka, among the adults in the age group of 15-49 is about 0.69%.[5] Considering 95% confidence limits and 6% permissible error, the[6] sample size works out to be 230(applying the formula L=1.96√pq/n). To compensate sample attrition, 5% of sample was added (12). Total sample size works out to be 242.

A total of 242 HIV infected patients freshly started on ART were selected randomly for the study. HIV/AIDS treatment patients in the age group 15 to 49 years and who gave consent to participate in the study were included in the study. HIV/AIDS patients with already existing co-morbid conditions like tuberculosis, cancers, cardiac disease or any other opportunistic infections were excluded as it may separately affect the CD4 counts. NACO & WHO guidelines were followed by the centre for initiation of ART treatment. Each patient was followed for 6 months. The study was approved by the institutional ethical committee and written informed consent was obtained from all participants before enrolment into the study.

Structured questionnaire was used to obtain the data like demographic factors. Weight was recorded for each patient. Haemoglobin values were also recorded from the patient records. CD4 count was measured at the time of initiation of ART. Each patient was followed for 6 months to take the CD4 counts, CD4 percentages, Hemoglobin percentages, Adherence (which was another objective). The CD4 counts and percentages (at initiation and end of 6 months) were taken from the individual patient records. They were matched with the laboratory records for any discrepancies.

Two types of ART regimen were followed. Regimen 1consists ofZidovudine + Lamivudine + Nevirapine and Regimen 2 with Stavudine + Lamivudine + Nevirapine.13 patients died during study period. 9 patients missed ART doses completely & were not available for the CD4 count testing at 6 months. Hence CD4 values were analysed for 220 HIV patients in the study.

Statistical analysis: Data was entered in the MS Excel and analysed using Epi-Info version 6 (CDC). Results were presented in the form of tables and charts with mean and proportions. Chi-square test and Paired T-test were used for statistical analysis. P< 0.05 was considered as statistically significant.

Results

The analysis was done on 242 HIV/AIDS patients, 54 (22.3%) were in the age group of 25-29 years, mean age was 35 years (Standard deviation =7.826, with ranging from 20 years to 49 years). 109(45%) were males and 133(55%) were females. Male to female ratio was 1: 1.2. In the present study among the 109 males, majority 81 (74.3%) were married, but among 133 female HIV/AIDS patients majority 68 (51.1%) were married & none were unmarried. Widow rates 52 (39.1%) was higher than the widower rates 9 (8.3%). (Table 1)

160(66.1%) patients had CD4 counts <200 cells/mm^3 at the initiation of ART. CD4 counts at the initiation of ART were 201-250 cells/mm^3 in 46 (19%) of patients and > 251 in 36 (14.9%).

Of the total 242 patient at the initiation, 13 died during the duration of study, 9 missed the doses completely. 22 patients were not available for the CD4 count testing at 6 months. CD4 counts and percentages at the end of 6 months were done only on 220 patients.

CD4 counts at the end of 6 months of ART were >250 cells/mm^3 in 149 (67.7%) patients & none had < 50 counts. Majority 187(85%) had CD4 counts > 200 cells/mm^3. Increase was noticed in the CD4 counts range after 6 months ART. This was statistically highly significant. (χ^2=155.32, p<0.0001 highly Significant. DF=4 after merging rows 1 & 2). (Table 2)

The increase in CD4 counts was significantly higher in > 80% of patients with initiation counts >150 cells/mm^3. It was further higher as the initiation counts increased. 100% (35 patients) had higher counts in those with initiation counts > 251 counts. (Table 3).

112 (77.2%) patients with CD4 below 200 at initiation had CD4 counts above 201 after 6 months. 33 (22.8%) had below 200 after 6 months. All the patients with CD4 count above 201 (75 patients) at initiation had CD4 above 201 at end. There is significant improvement of CD4 counts in those with higher counts at the initiation than with lower counts. It was statistically significant. Initiation of ART at an earlier stage of HIV (with higher CD4 counts> 200 at initiation) has better results than with those with lower counts. (Fischer exact test. P< 0.001 Highly significant) (Table 4)

There is a significant increase in the mean CD4 count of 165.7182 cells/mm^3 after 6 months of ART which was statistically significant (P<0.001). Similarly statistically significant increase in the mean CD4 percentage of 7.3591% was noted (P<0.001). Significant weight gain of 2.4727 kg was noted after 6 months ART (P<0.001). There was no significant increase in Hemoglobin percentage (0.1032) after ART. This may be due to anemia itself being a side effect of ART (Zidovudine based regimen) (P>0.05).(Table 5).

There was an increase in cd4 counts in 116 (96.6%) patients on Zidovudine + Lamivudine + Nevirapine regimen (Regimen 1) & among 90 (94.7%) on Stavudine + Lamivudine + Nevirapine regimen (Regimen 2). This was not statistically significant (P>0.05). Both regimens had significant increase in CD4 counts. Of the total 242 patients 13 died during the duration of study, 9 missed the doses completely & were not available for the CD4 count testing at 6 months. 1 was on the Zidovudine + Lamivudine + Efavirenz regimen, 4 on Stavudine + Lamivudine + Efavirenz regimen. These 5 patients were excluded.

Of the 215 patients, increase in Hemoglobin% was seen in 76 (80%) of those on regimen 2 (Stavudine based regimen) while only 36(30%) in the regimen 1 (Zidovudine based regimen). This was statistically highly significant(χ^2 =53.116, P< 0.0001, Highly Significant). On the contrary the Hb% decreased in 84 (70%) on regimen 1 & in 19 (20%) on regimen 2. One of the main adverse effects of Zidovudine is anemia which is also one of the reasons for switching the regimen to Stavudine based regimen.

It was observed in the present study that of the 215 patients weight increased in 69 (72.6%) patients on regimen 2 & 78 (65%) on regimen 1. There was no statistically significant difference in weight gain on the 2 regimen (P>0.005).

Table 1: Distribution of the HIV/AIDS patients according to sex and marital status

Marital status	Male (%)	Female (%)	Total (%)
Married	81 (74.3%)	68 (51.1%)	149 (61.5%)
Unmarried	12 (11%)	0	12 (5%)
Divorced	7 (6.4%)	13 (9.8%)	20 (8.3%)
Widow	NA	52 (39.1%)	52 (21.5%)
Widower	9 (8.3%)	NA	9 (3.7%)
Total	109 (100%)	133 (100%)	242 (100%)

Table 2: Distribution of HIV/AIDS patients according to CD4 counts at the time of initiation & at the end of 6 months of ART

CD4 count range Cells/mm^3	Number of patients at Initiation (%)	Number of patients at end of six months (%)
≤ 50	23(9.5)	0
51-100	43(17.8)	7(3.2)
101-150	42(17.4)	12(5.5)
151-200	52(21.5)	14(6.4)
201-250	46(19.00)	38(17.3)
$\geq$251	36(14.9)	149(67.7)
Total	242(100.0)	220(90.9)

P<0.01 highly significant

Table 3: Distribution of HIV/AIDS patients according to CD4 counts (category-wise) at the time of initiation & at the end of 6 months of ART

		Number of patients at end of six months (%)						
	CD4 count range Cells/mm^3	51-100	101-150	151-200	201–250	≥ 251	Total	Number of people Missed/Died
Number of patients at Initiation (%)	≤ 50	2(9.5%)	6(28.6%)	5(23.8%)	5(23.8%)	3(14.3%)	21(100%)	2
	51 - 100	4(10.5%)	5(13.2%)	3(7.9%)	7(18.4%)	19(50%)	38(100%)	5
	101 - 150	1(2.8%)	0(0%)	4(11.1%)	12(33.3%)	19(52.8%)	36(100%)	6
	151 - 200	0(0%)	1(2%)	2(4%)	7(14%)	40(80%)	50(100%)	2
	201 – 250	0(0%)	0(0%)	0(0%)	7(17.5%)	33(82.5%)	40(100%)	6
	≥ 251	0(0%)	0(0%)	0(0%)	0(0%)	35(100%)	35(100%)	1
	Total	7(3.2%)	12(5.5%)	14(6.4%)	38(38.3%)	149(67.7%)	220(100%)	22

Table 4: Distribution of patients according to change in CD 4 counts at the time of initiation & at the end of 6 months of ART

CD4 Counts at Initiation	CD4 Counts after 6 months		Total (%)	
	< 200 (%)	>201 (%)		
<200	33 (22.8%)	112 (77.2%)	145 (100%)	P< 0.001
>201	0	75 (100%)	75 (100%)	Highly significant
Total	33(15%)	187(85%)	220(100%)	

Table 5: Table showing effect of ART on CD4 Count, CD4 Percentage, Weight, & Hemoglobin percentage

Study Characteristic	Time period	Mean	Standard error	Standard Deviation	Paired t test t value	P value
CD4 COUNT (N=220) Cells/mm^3	at ART Initiation	166.17	6.270	93.005	20.181	<0.001
	at End of 6th m	331.89	10.362	153.691		
	Increase	165.7182	8.21151	121.79638		
CD4 % (N=220)	at ART Initiation	11.15	0.399	5.916	21.920	<0.001
	at End of 6th m	18.51	0.451	6.688		
	Increase	7.3591	0.33573	4.97970		
HB % (Gram %) (N=220)	at ART Initiation	10.270	0.0802	1.1900	1.135	0.258
	at End of 6th m	10.36	0.074	1.104		
	Increase	0.1032	0.08343	1.23752		
WEIGHT (N=220) Kgs	at ART initiation	47.66	0.605	8.972	9.636	<0.001
	at End of 6th m	50.13	0.613	9.093		
	Increase	2.4727	0.25662	3.80629		

Discussion

ART has a significant effect on the CD4 counts and percentages. There is a substantial increase in the CD4 counts and percentages in the present study at the end of 6 months ART.

Though the counts increased after 6 months, in both the group of HIV patients (higher and lower counts at initiation), it was more substantial in those with higher counts at initiation. Both the regimens had significant increase in CD4 counts and there was no difference between the regimens.

Significant weight gain was also noted. Hemoglobin percentage rise was not significant as one of the side effects of Zidovudine is anemia.

In the study by A Wanchu et al[8] of the 153patients on ART, the CD4 counts were less than 50 in 24 (15.7%) patients, between 50 and 200 in 63(41.2%), between 200 and 500 in 60 (39.2%) and more than 500 in six (3.9%) similar to that in our study. In the study in Manipur by Chitra Y[9] et al, of the 624 patients, 67.46% were males and 32.53% were females unlike to our study. Out of the 624 patients on ART, 95.35% (595/624) showed an increase in CD4 count while 4.64% (29/624) showed a decrease in CD4 count. The mean CD4 counts at the time of initiation were 184.5 cells/mm^3 in the study by Yengkokpam Chitra et al[9] and 105.97 cells/mm^3 in the Ortega et al[10] study. The mean CD4 counts at the end of 6 months were 292.28 cells/mm^3 in the study by Yengkokpam Chitra et al[9] and 330.29 cells/mm^3 in the Ortega et al[10] study, similar to the present study.

According to the study by Olawumi HO et al[11] in Nigeria in 2008, the HAART regimen is associated with increase in CD4 Count and weight gain similar to this study.

In the Naveet Wig et al study[12] the mean Hb% was 11.26 ± 2.38 mg/dl (Range 5-16) similar to the present study. A study by M. W. Mutugi et al[13] in Kenya observed that there was 69% increase of CD4 cell count in the first 3 months and 86% in 9 months. In the SK Sharma et al[14] study among those who were anemic, 17 (21.8%) patients were on Zidovudine implicating it in causing anemia, similar to the present study. A study by M. W. Mutugi et al[13] in Kenya observed that there was increase in weight of the patients in the first 3 months, similar to present study.

Limitations of the study

Due to paucity of time the patients were followed for only for 6 months.

Conclusions & Recommendations

CD4 counts and CD4 percentage in HIV patients increase substantially with proper ART. Initiation of ART at an earlier stage (even in those with higher counts) has significant better results than wait for the counts to lower. This helps to improve the immunity in the HIV patients and reduce many opportunistic infections in them. Thus ART helps HIV patients to improve quality of life and expectancy of life. ART treatment in HIV patients helps to increase the body weight and haemoglobin percentage.

ART treatment should be accessible and available to all HIV patients in the country at free of cost. ART treatment has resulted in a marked decrease in the mortality and morbidity associated with the HIV infection and AIDS.

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