

Effect of Antiretroviral Therapy on CD 4 cell count and WHO Staging among PLHIV Accessing Services at Tertiary care Hospital, Coastal Karnataka

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Abstract

Background: Human immunodeficiency virus attacks CD4 cells primarily. Current CD4 count is a strong predictor of the immediate risk of acquired immune deficiency syndrome or death. Antiretroviral therapy results in an improvement in immunologic status, one feature of which is an increase in the CD4 cell count.

Objectives: To study the effect of Antiretroviral therapy on CD4 cell count & WHO staging among people living with HIV/AIDS.

Methodology: A retrospective cross-sectional descriptive study was conducted using data available from Antiretroviral therapy centre attached to Teaching Hospital of Karwar Institute of Medical Sciences, Karwar.

Conclusion: Antiretroviral therapy among People Living with HIV was significantly associated with the increase in their CD4 cell count. The mean difference of the CD4 count increase in patients obtained was of 451 and is statistically significant ($P < 0.01$). There is improvement in the WHO staging of the disease after the start of Antiretroviral therapy.

Key words: PLHIV, Anti Retroviral Therapy, CD4 cell count, WHO staging

Introduction

India has a low HIV prevalence of 0.22%. Even with this low prevalence, in terms of absolute numbers, India has the third highest burden of HIV in the world.¹ Human immunodeficiency virus (HIV) attacks CD4 T cells primarily and

the CD4 count decreases. Current CD4 count is a strong predictor of the immediate risk of acquired immunodeficiency syndrome (AIDS) or death than HIV RNA level.² Antiretroviral therapy has reduced HIV/AIDS morbidity and mortality significantly and has improved the prognosis for people living with HIV/AIDS (PLHIV).³ Government of India has

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launched free ART for PLHIV was since 2004.⁴ CD4 cell counts are commonly used markers of HIV disease progression and for starting and monitoring antiretroviral treatment in the absence of viral load.⁵ Sustained increase in the CD4 cell response to highly active antiretroviral therapy (HAART) and suppression of HIV load were both associated with greater increases in CD4 cell counts.⁵ HAART results in an improvement in immunologic status, one feature of which is an increase in the CD4 cell count.⁶ Inhibitory of HIV duplication is generally associated with a steady increase in the CD4 cell count and results in improved clinical outcomes. This increases the chances of survival for HIV infected patients.⁷

Objectives

To evaluate the effect of Antiretroviral therapy on CD 4 cell count & WHO staging among people living with HIV/AIDS accessing services at tertiary care hospital in Karwar, coastal Karnataka.

Methodology

Retrospective cross-sectional descriptive study was conducted using data available from Antiretroviral Therapy Centre attached to Teaching Hospital of Karwar Institute of Medical Sciences, Karwar where Antiretroviral therapy is provided free of cost under National AIDS Control Organization.

Study population:

People Living with HIV/AIDS, who were accessing services at ART Centre attached to Teaching Hospital of Karwar Institute of Medical Sciences, Karwar and who were on first line Antiretroviral Therapy for at least past 6 months were included in the study.

Sample size and data collection:

This study was carried out as a part of study which aimed at assessing the level of adherence to Antiretroviral therapy and its determinants among People Living With HIV/AIDS utilising services of Anti retroviral Therapy Centre attached to Teaching Hospital of Karwar Institute of Medical Sciences, Karwar. Hence the sample size calculation was derived accordingly.

The sample size was calculated based on expected proportion of adherence to ART among PLHIV based on previous studies⁸ using the formula $n=4pq/d^2$ with a relative precision of 15%. Accordingly, a sample size of 110 was derived.

The data of those who were interviewed was collected. Data related to the CD4 cell count and WHO staging of disease before starting ART and at the time of study was collected from the patient records maintained at ART centre.

Statistical analysis:

Data collected was entered into excel sheet and analyzed using SPSS version 16 statistical software. Frequency, percentage and means were used to present the data. Relevant data was analysed by calculating standard error of mean, standard deviation, paired t tests & Chi square test. For all the tests, p-value of < 0.05 was considered for statistical significance. Binary Logistic Regression was applied to know the association.

Ethical clearance:

Ethical clearance was obtained from Institutional Ethical Committee of Karwar Institute of Medical Sciences, Karwar.

Results

In the present study, 110 PLHIV on ART were included. Among them 54.5% were males & 45.5% were females. More than half of the participants i.e. 54.5% of them were in the age group of 40-59 years. Table 1 Shows that before starting ART, 80% of the participants had CD4 cell count below 500 cells/cmm and only 20% had CD4 cell count above 500 cells/cmm, whereas at the time of study, it was observed that only 33.6% were having CD4 cell count below 500 cells/cmm and 66.4% had CD4 cell count above 500 cells/cmm. After the start of ART, there was significant decrease in number of patients with CD4 cell count below 200 and between 200-350. Also, there was significant increase in number of patients with CD4 cell count between 350-500 and above 500.

In this study when CD 4 cell count before starting ART & at the time of study were compared, it was observed that the mean CD4 cell count before starting

ART was 311.92 ± 257.24 . At the time of study, the mean value of CD4 count increased to 672.82 ± 357.28 . It was observed that the mean increase in CD4 cell count was 360.6 and this difference between the mean CD4 cell count was statistically significant ($P < 0.01$). (Table 2)

In our study when change in CD4 cell count after starting ART was compared with duration on ART, it was observed that mean decrease in CD4 cell count was 172 Cells/cmm with SD 140 Cells/cmm and mean increase in CD4 cell count was 451 Cells/cmm with SD 324 Cells/cmm. Significant association was observed between duration on ART & change in CD4 cell count of PLHIV after starting ART.

Binary logistic regression analysis of change in CD4 cell count after starting ART with different

Table 1: CD 4 cell count before starting ART & at the time of study

CD4 Cells/cmm	Before starting ART	At the time of study	Z-test for difference in Proportions (p-value)
	n(%)	n(%)	
< 200	41 (37.3)	6 (5.4)	-5.76 ($p < 0.00001^*$)
200-350	38 (34.5)	11 (10.0)	-4.38 ($p < 0.00001^*$)
350-500	9 (8.2)	20 (18.2)	2.19 ($p=0.029^*$)
> 500	22 (20.0)	73 (66.4)	6.94 ($p < 0.00001^*$)

* Significant Difference

Table 2: Comparison of CD 4 cell count before starting ART & at the time of study

CD 4 cell count(Cells/cmm)	Mean	N	Std. Deviation	Std. Error Mean	t	p
Before starting ART	311.92	110	257.24	24.53	-10.115	<0.001*
At the time of study	672.86	110	357.28	33.07		

* Statistically significant

Table 3: Binary Logistic Regression Analysis

Variable		Change in CD4 count after the start of ART		Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
		Decrease (19) n(%)	Increase (91) n(%) Ref				
Age group (Years)	18-20	0 (0)	1 (1.1)	1		1	
	21-40	6 (31.6)	20 (21.9)	-	-	-	1.000
	41-60	11 (57.9)	63 (69.3)	-	-	-	1.000
	>60	2 (10.5)	7 (7.7)	-	-	-	1.000

variables like age group, gender, adherence (three months), duration on ART and WHO Stage at the time of study, it was found that PLHIV who were on ART for more than 5years had 11.242 times more chances (Adjusted OR= 11.24 with $p=0.001$) of increase in CD4 cell count as compared to those who were on ART for less than 5years. (Table 3)

Table 4 Shows that, before starting ART 30.9%, 25.5%, 31.8% & 11.8% of the PLHIV were in the WHO stage I, II, III and IV respectively, while at the time of study 99.1% were in the WHO stage I, while 0.9% were in WHO stage II. None of them were in WHO stage III and IV at the time of study. It was observed that, significant number of PLHIV who were in WHO stage II, III & IV before starting ART were now in WHO stage I due to effect of ART.

Variable		Change in CD4 count after the start of ART		Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
		Decrease (19) n(%)	Increase (91) n(%) Ref				
Gender	Female	10 (52.6)	40 (44.0)	1		1	
	Male	9 (47.4)	51 (56.0)	1.42 (0.53 - 3.82)	0.49	1.634 (0.46 - 5.78)	0.446
Adherence	≤ 95%	4 (21.1)	8 (8.8)	1		1	
	>95%	15 (78.9)	83 (91.2)	2.77 (0.74-10.36)	0.13	1.343 (0.21-8.56)	0.755
ART duration	≤ 5 Yrs	15 (78.9)	28 (30.8)	1		1	
	>5 Yrs	4 (21.1)	63 (69.2)	8.44 (2.57-27.72)	0.0004*	11.242 (2.73-46.22)	0.001*
WHO Stage at the time of study	Stage I	16 (84.2)	90 (98.9)	1		1	
	Stage II	1 (5.3)	0 (0)	0.06	0.09	-	1.000
Constant						6.54*10 ⁷	1.000
*Significant							
Cox & Snell R ² = 0.172 Nagelkerke R ² = 0.295							
Omnibus tests of model coefficients was significant with p = 0.01 and According to Hosmer & Lemeshow test, the model was a good fit with P = 0.615							

Table 4: WHO staging before starting ART & at the time of study

WHO Staging	Before starting ART n(%)	At the time of study n(%)	Z-test for difference in Proportions (p-value)
Stage I	34 (30.9)	109 (99.1)	10.60 (p<0.0001*)
Stage II	28 (25.5)	1 (0.9)	-5.381 (p<0.0001*)
Stage III	35 (31.8)	0 (0)	-6.45 (p<0.0001*)
Stage IV	13 (11.8)	0 (0)	-3.72 (p=0.0002*)

*Significant Difference

Discussion

In India the guidelines on when to start ART have evolved over the years towards earlier initiation of ART;CD4 count cut-off point for ART initiation moving from less than 200 cells/cmm in 2004 to less than 350 cells/cmm in 2010 and then to less than 500 cells/cmm in 2013. The current 2021 NACO guidelines recommendation is to treat all, regardless of the clinical stage or CD4 count.¹ This has a public health importance of advocating for prompt initiation of ART and management of opportunistic infections

to save PLHIV from deteriorating further. In our study, among 110 patients who were on first line anti retroviral therapy for at least past 6 months that were observed, more than half of the participants i.e. 54.5% of them were in the age group of 40-59 years. Before starting ART only 20% had CD4 cell count above 500 cells/cmm whereas at the time of study 66.4% had CD4 cell count above 500 cells/cmm. It was observed that, the starting of ART among PLHIV was significantly associated with the increase in their CD4 cell count. In a study conducted by Asfaw A et al, similar observation of improvement in CD4 cell count among patients on ART was seen during

4 years period.⁵ These findings are consistent with the retrospective longitudinal study conducted in eastern Ethiopia where the median CD4 lymphocyte count had improved over the five year period.⁹ Similarly significant improvement in CD4 cell count was observed in study conducted by Kumar et al.¹⁰

In our study the mean increase in CD4 cell count among PLHIV on ART was observed to be 451 ± 324 , and also it was statistically significant ($P < 0.01$). This shows that PLHIV are benefitted with ART. Similar observation of significant improvement in mean CD4 cell count was observed in study conducted by Kumar et al.¹⁰ In a study conducted by Mocroft et al. have reported the greatest mean increase in CD4 count of 100 cells/cmm after the first year of ART.¹¹ CASCADE Collaboration have reported that the median CD4 cell count increase at 6 months on ART was 119 cells/cmm.¹² A study conducted by Otieno CF et al observed that, absolute mean CD4+ cell counts at initiation of HAART was 141.7 ± 176.5 cells / μ l and it increased to 192.4 ± 198.5 cells/ μ l at three months. The mean CD4+ cell count at 12th month of therapy was 268.6 ± 189.9 .¹³

We observed that, before starting ART 30.9%, 25.5%, 31.8% & 11.8% of the participants were in the stage I, II, III & IV of WHO staging respectively, while at the time of study 99.1% were in the WHO stage I, while 0.9% were in WHO stage II. None of them were in stage III & IV. This shows that here is improvement in the WHO staging of the disease after the start of Antiretroviral Therapy. Similarly, in a study conducted by Kumar A et al it was observed that before starting ART 2%, 29%, 68% & 1% of the participants were in the stage I, II, III & IV of WHO staging respectively, while at the time of study 61% were in the stage I, while 30% were in stage II and 9% were in stage III.¹⁰ Binary Logistic Regression analysis shows that only the duration on ART (more than 5years) was significantly associated with increase in CD4 cell count. Kumar A et al in their have concluded that higher mean change in the CD 4 cell count and the change was significant association with duration on ART.¹⁰ Similarly study by Sarna et al and Safren SA et al also showed similar kind of results where increase in CD 4 cell count associated with duration on ART.^{14,15}

Conclusion

The starting of ART among PLHIV was significantly associated with the increase in their CD4 cell count. There was statistically significant improvement in the mean CD4 cell count among those on ART (more than 5years). There is an improvement in the WHO staging of the disease after the start of Anti Retroviral Therapy.

Limitation:

The present study was a record based study. Opportunistic infections influencing the CD4 cell count or WHO staging at the time of study were not considered during analysis.

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