

**Study of the Effect of HAART on Lipid Profile in HIV Positive Patients**Dr. Chandraprakash<sup>1</sup>, Dr. Anil Sejwar<sup>2\*</sup>, Dr. Gopal Krishna<sup>3</sup><sup>1</sup>Senior Resident, Dept. of Medicine, GMC Bhopal, Madhya Pradesh, India<sup>2</sup>Asst. Proff, Dept. of Medicine, GMC Bhopal, Madhya Pradesh, India<sup>3</sup>Senior Resident, Dept. of Medicine, GMC Bhopal, Madhya Pradesh, India**Original Research Article****\*Corresponding author**

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**Abstract:** Human immunodeficiency Virus (HIV) infection is pandemic worldwide). Patients with HIV infection were reported to have hypocholesterolemia with or without hypertriglyceridemia however the mechanism of decrease in cholesterol levels is not known. Infections can increase serum triglycerides levels by decreasing clearance of circulating lipoprotein levels as process seems to inhibit the lipoprotein lipase activity or stimulating hepatic lipid synthesis through increase in either hepatic fatty acid synthesis or esterification of fatty acids derived from lipolysis. Keeping in view of the various biochemical abnormalities associated with lipid metabolism, our research was inclined to assess the lipid profile in HIV positive cases, with an attempt to further elucidate more features of HIV disease which erupts as acquired immunodeficiency syndrome (AIDS) linking any possible involvement of lipid profile in disease progression of AIDS. A hospital based descriptive cross-sectional study. Conducted at ART centre, Department of Medicine, Hamidia Hospital, Gandhi Medical College, and Bhopal. Study participants were between age group 20 to 50 years those who newly diagnosed cases of HIV/AIDS in whom decision about ART was yet to be taken and patients on HAART whose initial lipid profile is available in records. Patients participating in study were thoroughly examined with standard clinical methods and assigned WHO clinical staging and subjected to various laboratory investigations. Mean age being ( $\pm$ SEM)  $34.85 \pm 2.46$  years. Highest number of the patients was of stage III disease with number of 102(51%). Out of all 200 patients 51 registered patients were HAART naïve and never started ART during study. Patients on HAART shows statistically significant ( $p < 0.05$ ) for Total Cholesterol (TC) which increased upto  $242.6 \pm 1.42$  (Mean $\pm$ SEM) from its baseline value of  $240.3 \pm 1.09$ . Serum Triglycerides also shown significant ( $p < 0.05$ ) rise from  $137.5 \pm 2.22$  to  $140.7 \pm 2.88$  (Mean $\pm$ SEM). In lipid profile parameters all parameters raised from HAART to patients on HAART group but significant increase was seen for TC in HAART naïve group ( $p < 0.05$ ), for TC, S.TG ( $p < 0.05$ ) in Regimen I treated patients, same for the Regimen II treated patients, TC ( $p < 0.005$ ), S.TG ( $p < 0.0001$ ), HDLc ( $p < 0.05$ ) in Regimen II treated Patients and for TC, S.TG, HDLc, LDL and VLDL ( $p < 0.005$ ,  $p < 0.005$ ,  $p < 0.05$ ,  $p < 0.005$ ,  $p < 0.05$ .) in Regiment III treated patients.

**Keywords:** Serum Triglycerides, Human immunodeficiency Virus (HIV), lipid metabolism.

**INTRODUCTION**

Human immunodeficiency Virus (HIV) infection is pandemic worldwide [1]. Worldwide around 33.3 million people are living with HIV, 30.8 million are adults. In 2009, an estimated 2.6 million new HIV cases occurred. The estimated number of AIDS related deaths in 2009 was estimated to be 1.8 million with adults being 1.6 million [2]. Among Indians currently there are about 3.7 million HIV positive cases which are further predicted to rise in future if successful prevention programs are not implemented [3].

Human immunodeficiency virus patients are often associated with aberration of biochemical parameters like renal profile, liver profile, thyroid profile, thrombocytopenia and severe anemia with high erythrocyte sedimentation rate (ESR). Patients with HIV infection were reported to have hypocholesterolemia with or without hypertriglyceridemia however the mechanism of decrease in cholesterol levels is not known [4].

In developed countries, the life expectancy of HIV-infected individuals has increased substantially through the implementation of highly active

antiretroviral therapy (HAART) in the management of HIV infection [5-7]. The effectiveness of HAART lies in the co administration of different classes of antiretroviral drugs. These therapies target specific mechanisms within the HIV life cycle and provide a means for simultaneous inhibition of diverse viral processes providing tighter control of HIV replication than could be achieved with single therapy [5]. The three major classes of HIV drugs currently employed in HAART are the non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside/nucleotide analogue reverse transcriptase inhibitors (NRTI and NtRTI) and HIV protease inhibitors (PIs) [8].

WHO reported that as of December 2008, approximately 4 million people in low- and middle income countries were receiving antiretroviral therapy? Between 2003 and 2008, access to antiretroviral drugs in low- and middle-income countries rose 10-fold [2].

It is estimated that the scale up of free Anti-Retroviral Treatment (ART) since 2004 has saved over 1.5 lakh lives till 2011 by averting deaths due to AIDS-related causes in India. Wider access to ART has led to 29% reduction in estimated annual AIDS-related deaths from 2.07 lakh in 2007 to 1.48 lakh in 2011 highlighting the impact of scale up of free ART services in india[9].

Studies have been observed when HIV patients are treated with protease inhibitors they tend to exhibit hyperlipidaemia with increase in total cholesterol, triglycerides, low-density lipoproteins and concomitant decrease in high-density cholesterol[10].

Infections can increase serum triglycerides levels by decreasing clearance of circulating lipoprotein levels as process seems to inhibit the lipoprotein lipase activity or stimulating hepatic lipid synthesis through increase in either hepatic fatty acid synthesis or reesterification of fatty acids derived from lipolysis.

Keeping in view of the various biochemical abnormalities associated with lipid metabolism, our research was inclined to assess the lipid profile in HIV positive cases, with an attempt to further elucidate more features of HIV disease which erupts as acquired immunodeficiency syndrome (AIDS) linking any

possible involvement of lipid profile in disease progression of AIDS.

The current study is an attempt to examine whether any changes in lipid profile do take in HIV positive patients and those who are taking ART, and whether those changes which are involved could be linked to the development of clinical AIDS with HIV infection. Thus the current study was undertaken to address whether HIV infection and HAART can affect lipid profile status in patients.

**METHODS**

This was a hospital based descriptive cross-sectional study. This study was conducted between November 2013 to November 2014. At ART centre, Department of Medicine, Hamidia Hospital, Gandhi Medical College, Bhopal. The patients attend the clinic once in a month for clinical evaluation and refill of ARV. Study participants were between age group 20 to 50 years those who newly diagnosed cases of HIV/AIDS in whom decision about ART was yet to be taken and patients on HAART whose initial lipid profile is available in records. Patients who were on HAART more than six months or on HAART less than six months but no baseline lipid profile record available for them and who were on lipid lowering drugs and pregnant and with long standing illness like diabetes and obesity were excluded. Patients participating in study were thoroughly examined with standard clinical methods and assigned WHO clinical staging and subjected to various laboratory investigations. Data collection was done with hospital records and use of a questionnaire.

Statistical analysis was done using a computer program SPSS version 15.0. Subgroups were compared using student's *t* test. Multiple regressions were done to determine the independent predictors of different Dyslipidemia. Differences were considered significant if p-value were less than 0.05.

**ETHICAL CONSIDERATION**

Study is approved by Institutional ethical committee, Gandhi Medical College & Associated Hamidia Hospital, Bhopal (M.P.)

**OBSERVATIONS**

**Table-1: Sex Ratio of Patients participated in study**

	Male	Female
Sex	162	38

**Table-2: Age Distribution among the patients included in study**

Age Group	Number of Patients (%)
20-25	37
26-30	31
31-35	39
36-40	30
41-45	37
46-50	26

**Table-3: Showing number of patients according to their category on the basis of WHO Clinical classification**

WHO Category	Number of Patients (%)
Stage I	19
Stage II	51
Stage III	102
Stage IV	28

**Table-4: Different HAART Regimes used for treatment of patient along with distribution of patients among HAART Naïve and HAART treated patient with respective regimes**

	HAART NAÏVE (%)	PATIENTS ON HAART (%)			
		Category I	Category Ia	Category II	Category III
REGIME	51(25.5%)	21(10.5%)	10(5%)	114(57%)	4(2%)

**Table-5: Evaluation of Lipid profile for Baseline (0 month) and Follow up values (6 month) in HAART Naïve patients (n=51)**

HAART naïve		
Lipid Parameters	Baseline	6 month
TC	223.82 ± 1.79	224.84 ± 1.77*
S.TG	136.06 ± 1.55	136.76 ± 1.51
HDLC	51.67 ± 0.51	48.88 ± 0.69
LDL	105.06 ± 0.9	106.1 ± 0.98
VLDL	26.67 ± 0.96	27.35 ± 1.01

n=51, All values are presented as Mean±SEM, paired students t-test was applied and p<0.05 considered statistical significant (\*= p<0.05).

**Table-6: Evaluation of Lipid profile for Baseline (0 month) and Follow up values (6 month) in treatment Category I patients (n=21)**

Category I		
Lipid Parameters	Baseline	6 month
TC	236.81 ± 1.52	252.43 ± 1.68*
S.TG	143.67 ± 1.95	167.95 ± 2.2*
HDLC	45.48 ± 1.35	44 ± 1.41
LDL	110.05 ± 1.29	111.24 ± 1.3
VLDL	31.05 ± 1.16	31.86 ± 1.23

n=21, All values are presented as Mean±SEM, paired students t-test was applied and p<0.05 considered statistical significant (\*=p<0.05).

**Table-7: Evaluation of Lipid profile for Baseline (0 month) and Follow up values (6 month) in treatment Category Ia patients (n=10)**

Category Ia		
Lipid Parameters	Baseline	6 month
TC	240.3 ± 1.09	242.6 ± 1.42*
S.TG	137.5 ± 2.22	140.7 ± 2.88*
HDLC	45.1 ± 1.93	44 ± 2.57
LDL	110.5 ± 2.34	113.3 ± 2.74
VLDL	32.8 ± 1.76	34.3 ± 2.03

n=10, All values are in mg/dl presented as Mean±SEM, paired *students t-test* was applied and p<0.05 considered statistical significant (\*=p<0.05).

**Table-8: Evaluation of Lipid profile for Baseline (0 month) and Follow up values (6 month) in treatment Category II patients (n=114)**

Category II		
Lipid Parameters	Baseline	6 month
TC	235.92 ± 0.64	236.73 ± 0.64**
S.TG	141.81 ± 0.66	167.12 ± 0.72***
HDLC	46.32 ± 0.52	45.73 ± 0.6*
LDL	109.38 ± 0.57	109.39 ± 0.75
VLDL	31.76 ± 0.51	32.17 ± 0.5

n=114, All values are presented as Mean±SEM, paired students t-test was applied and p<0.05 considered statistical significant (\*=p<0.05, \*\*=p<0.005, \*\*\*=p<0.0001).

**Table-9: Evaluation of Lipid profile for Baseline (0 month) and Follow up values (6 month) in treatment Category III patients (n=4)**

Category III		
Lipid Parameters	Baseline	6 month
TC	242.75 ± 2.56	260.5 ± 3.75**
S.TG	145.25 ± 3.07	170.75 ± 3.22**
HDLC	52.5 ± 1.26	48.75 ± 2.14*
LDL	109 ± 3.34	124.5 ± 2.9**
VLDL	31.91 ± 1.73	35.5 ± 1.85*

n=4, All values are presented as Mean±SEM, paired students t-test was applied and p<0.05 considered statistical significant (\*=p<0.05, \*\*=p<0.005).

**Table-10: Association between Parameters of lipid profile and CD4 count**

Lipid Parameters	Standard Error	R Square	p Value
TC	0.9155	0.2382	p<0.0001
S.TG	0.9833	0.1057	p>0.05
HDL	1.5056	0.0969	p<0.0005
LDL	1.2936	0.0382	p<0.001
VLDL	1.443	0.1601	p>0.05

Multivariate Regression Analysis where n=200 in each variable group, and CD4 count as independent variable taking TC, S.TG, HDL, LDL and VLDL being dependent variable.

On multivariate analysis correlation between CD4 count and Total Cholesterol, HDL and LDL was established with R<sup>2</sup> being 0.2382(p<0.0001), 0.0969(p<0.0005) and 0.0382 (p<0.001).

## RESULTS

Total 200 patients included in study out of with number of males were 162(81%) while rest 38(19%) patients were female. Age of patients ranges from 20 to 50 years with mean age being (±SEM) 34.85±2.46 years. Highest number of patients (39) belonged to 31-35 years of age group followed by 20-25 and 41-45 years age group, 26-30(31 patients) and 46-50 (26 patients). Highest number of the patients were of stage III disease with number of 102(51%) followed by stage II with 51(25.5%) patients, stage IV with 28(14%) patients and stage I with 19 (9.5%) patients constituted smallest number of patient in this group. Out of all 200 patients 51 registered patients were HAART naïve and never started ART during study. While total 149 patients were kept on different categories of HAART with highest number of patients in Category II (114 patients), followed by Category I (21 patients), Category Ia (with 10 patients) and Category III with smallest 4 number of patients. In HAART naïve patients showed deterioration in all parameters of lipid profile but not statistically significant except the increase in Total Cholesterol (TC), which was found to be statistically significant increase 224.84 ± 1.77 against the baseline value of 223.82±1.79 (Mean±SEM)? In treatment category-I lipid profile showed deterioration in all parameters which was statistically in Total Cholesterol(TC), which was found to be significantly increase 252.43 ± 1.68 against the baseline value of 236.81 ± 1.52 (Mean±SEM). Similarly Serum Triglycerides (S.TG) increased significantly against its baseline value of 143.67 ± 1.95

to follow up value at six month of 167.95 ± 2.2 (Mean±SEM). LDL also showed significant increase by p<0.05. In the treatment Category Ia patients showed deterioration in the lipid profile parameters. While this change was statistically significant (p<0.05) for Total Cholesterol (TC) which increased upto 242.6 ± 1.42 (Mean±SEM) from its baseline value of 240.3 ± 1.09 Serum Triglycerides also shown significant (p<0.05) rise from 137.5 ± 2.22 to 140.7 ± 2.88 (Mean±SEM). In the patients those were treated with Category II regime it was found that Serum triglycerides shown maximum increase from 141.81 ± 13.66 to 167.12 ± 0.72 (Mean±SEM) which was statistically significant (p<0.0001) along with increase in Total cholesterol (p<0.005) and HDLC (p<0.05). LDL and VLDL also showed increase from baseline values but were not statistically significant. Only four patients in study were there with Category III of treatment all five parameter for lipid profile evaluation increased significantly from their baseline value to follow-up value with statistical significance of p<0.005, p<0.005, p<0.05, p<0.005, and p<0.05, for Total cholesterol, Serum Triglyceride, HDLC, LDL and VLDL respectively.

## DISCUSSION

This study was conducted among HIV patients at ART Centre, Department of Medicine, Gandhi Medical College & Hamidia Hospital, and Bhopal with the aim of assessing the changes in lipid profile in this population. Both patients on HAART and HAART naïve were studied.

### Prevalence of CVD risk factors

The overall prevalence of dyslipidemia of 83% found in this study was higher than a previous of Armstrong *et al.* study among HIV patients in Dares salaam in which the prevalence of dyslipidemia was

found to be 76% [16]. The difference in prevalence with the current study could be due to the fact that the previous study studied only the HAART naïve patients while the current study studied both HAART naïve and HAART experienced patients. These results are similar to those which were reported from Latin American HIV cohort of patients on HAART in which the prevalence of dyslipidemia was reported to be 80 % [19] it is postulated that the dyslipidaemia is a result of the metabolic effects of the HIV virus itself and the metabolic effects of the HAART. This increases the risk of future cardiovascular events in HIV patients [20,21].

On top of the effect of HAART and the HIV virus itself; the dyslipidemia could also be explained in part by wrong eating habits among HIV affected patients. A common practice in the local population is to encourage HIV patients to over-feed on rich foods so that they maintain their weight and improve immunity in the past Thin subjects were social stigma and still is. Thus HIV patients strive to get nutritional support and use food supplements. This may lead to overweight and dyslipidaemia,

The prevalence of hypercholesterolemia of 42% in this study is higher than that reported by Swai *et al.* in a general multiregional survey 5%-19% [22]. However the current study is from a specified group of HIV affected patients. It is possible that a factor related to HIV disease and its treatment is responsible for increased hypercholesterolemia.

The prevalence of hypercholesterolemia in the current study is much higher than the one reported by Armstrong *et al.* in Dar es salaam among HIV patients who were not on HAART 14% [16] The difference with the current study which constituted the patients who were on HAART and HAART naïve perhaps suggest an additional effect of HAART in causation of hypercholesterolemia.

Prevalence of hypertriglyceridemia in this study was (36%) with males and females almost equally affected. The pattern is similar to that which was reported in South Africa HIV patients in which more HIV males had hypertriglyceridemia than females [21]. The prevalence in the current study was higher than that reported by Armstrong *et al.* among HIV patients HAART naïve 28% [16]. However the prevalence is lower than that was reported by Anastos *et al.* In which he reported the prevalence to be 48% [24]. The difference in prevalence from the current study could be due smaller sample size in the current study as compared to Anastos *et al.* High triglycerides levels in HIV patients has been postulated to be due to inflammation with subsequent cytokines release and decreased hepatic clearance related to a role of apolipoprotein E.

Prevalence of decreased HDL in this study (50%) is comparable to the South Africa HIV cohort in which was reported to be 46% [23]. The results are also similar to the reports from developed countries in which the prevalence of hypertriglyceridemia in a Latin American HIV cohort was reported to be 46% [19]. HDL is cholesterol scavengers, picking up excess cholesterol from the blood and taking it back to the liver. The lower the HDL levels the more the risk of hypercholesterolemia and hence increased CVD risk.

Elevated LDL occurred in 53% of the study subjects being significantly higher in females than in males. The prevalence is lower than that which was reported by Armstrong *et al.* in urban Dar es Salaam among HIV patients who are not on HAART (67%) [16]. The results are lower than that which was reported in Latin American study in which it was found to be 25% [19]. The results from all these studies call for a need for intervention to prevent premature CVD among HIV patients.

#### Dyslipidemia and HAART status

The prevalence hypercholesterolemia, hypertriglyceridemia, and high LDL were found to be more prevalent among HIV patients on HAART than HAART naïve patients. Even after adjusting for age and sex HAART use remained to be an independent predictor for hypercholesterolemia and hypertriglyceridemia. The similar pattern has been observed among HIV patients in Kenya [12] and in Cameroon [25]. The difference observed among HAART users and HAART naïve patients indicate that HAART use has an additive effect to that attributed by the HIV virus itself in causation of hypercholesterolemia, hypertriglyceridemia, and high LDL.

The prevalence of decreased HDL was significantly higher among HAART naïve patients than patients on HAART. The similar pattern was observed in Kenya; in which decreased HDL levels were found in 51.3% of HAART naïve patients and in 14.6% among HAART users [12]. And a study by Armstrong *et al.* suggested a higher prevalence than the current study 67% [16]. The finding in all these studies shows decreased HDL to be more prevalent among HAART naïve than HAART users. Longitudinal assessment of patients with HIV seroconversion suggests that there are decreasing HDL and low-density lipoprotein (LDL) cholesterol at the time of infection, before treatment. With the initiation of HAART, total and LDL cholesterol increase to reinfection levels, but low HDL levels persist [23].

#### Dyslipidemia and ARV types

In this study it was found that the prevalence of dyslipidemia was more prevalent among patients who were on Protease inhibitors (Treatment Category

III) as compared to other regimens that did not contain PIs. These results are in keeping with the major trial, the DAD study [14] which had reported earlier the high prevalence of dyslipidemia and dyglycaemia among HIV patients on PI. Ritonavir, a PI common in use has been found to be the most notorious cause of dyslipidemia, dyglycaemia and obesity. Ritonavir is the only PI used in the ART center as the second line treatment according to NACO HIV treatment guideline [11]. Even after adjusting for other factors PI use remain to be independent predictors of hypercholesterolemia, hypertriglyceridemia, high LDL, LDL and low HDL among patients on HAART.

In this study gradual decrease in CD4 count in patient shows negative correlation with increase in lipid profile parameters while positive correlation with decrement in HDL. This correlation was significant for Total cholesterol, HDL and LDL. Although a similar study by Njoroge does not showed any correlation. Reason for such deference may be because; analysis was analyzed for CD4 counts below and above 350 cell/microL not by using multivariate analysis method [26].

## CONCLUSION

Present study conducted at ART centre of Department of Medicine, Gandhi Medical College & Associated Hospitals, Bhopal with the aim of assessing the changes in lipid profile in this population. Both patients on HAART and HAART naïve were studied. Total number of 200 patients recruited from ART centre .It was found that:

- i) Percentage of male and female included in study was 81% and 19% respectively.
- ii) In 200 patients 51 (25.5%) was not given HAART, 21 (10.5%) was on Regimen I treatment, 10 (5%) was on Regimen Ia treatment, 114 (57%) was on Regimen II of treatment and only 4 (2%) patients were on Regimen of NACO ART regimen 2012 guidelines.
- iii) In lipid profile parameters all parameters raised from HAART to patients on HAART group but significant increase was seen for TC in HAART naïve group( $p<0.05$ ), for TC, S.TG ( $p<0.05$ ) in Regimen I treated patients, same for the Regimen II treated patients, TC ( $p<0.005$ ), S.TG ( $p<0.0001$ ), HDLC ( $p<0.05$ ) in Regimen II treated Patients and for TC, S.TG, HDLc, LDL and VLDL ( $p<0.005$ ,  $p<0.005$ ,  $p<0.05$ ,  $p<0.005$ ,  $p<0.05$ ), in Regiment III treated patients.
- iv) On Correlation multivariate analysis CD4 count was found to have significant correlation with changes in TC ( $p<0.0001$ ), HDLc (0.0005) and LDL (0.001) respectively.

Thus it can be concluded that HIV infection and ART both derange Lipid profile and increase risk for cardiovascular disease and CD4 count can be used

to as parameter for possible Dyslipidemic changes. Patients living with HIV and taking ART should be evaluated and monitored. Further well structure study in more number of patients is need to consolidate results of this study.

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