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Comparison of Prevalence of Dyslipidemia and Carotid Atherosclerosis among Newly Diagnosed HIV Reactive Patients and Those on ART.

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ABSTRACT

Background: Since the availability of highly potent anti-retro viral drugs, the management of the human immunodeficiency virus infection has significantly improved and has increased the patient's survival rate. This increased longevity has unmasked many complications like dyslipidaemias which place them at higher risk of developing atherosclerotic vascular disease. The present study was conducted to compare the prevalence of Dyslipidaemia and Carotid Atherosclerosis among newly diagnosed HIV Reactive patients and Those on ART for 6 months. **Methods:** This descriptive-cross sectional study was conducted among 200 subjects who attended Medicine OPD, ART Centre and admitted in various medical Wards of Rajindra Hospital, Patiala over a period of 2 years from November 2014 to October 2016. 100 newly diagnosed HIV reactive subjects as per NACO guidelines but not on ART of age 20 years and above were included in Group A while 100 subjects of similar age group on ART for 6 months included in group B. The subjects having thyroid disease, Diabetes Mellitus, Hypertension and those on hypolipidemic drugs were excluded from the study. Lipid profile was estimated biochemically and CIMT was measured using high resolution B mode ultrasonography system. Data generated from the study was analyzed according to standard statistical methods. Non normaldistribution variables were applied Mann-Whitney rank sum testand normal distributed variables by't' test. Pearson product-moment correlation coefficient was applied to measure the correlation between two variables. **Result:** The study observed a significant higher levels of Serum Total Cholestrol (TC) (182.13+24.88 mg/dl Vs 160.69+18.49 mg/dl), Triglycerides (TG) (162.70+26.15 mg/dl vs 141.23+22.99 mg/dl), Low density lipoprotein cholesterol (LDL¬-c) (110.72+22.76 mg/dl vs 94.30+16.89 mg/dl), Very low density lipoprotein(VLDL-c)(32.54+5.23 mg/dl vs 28.21+4.62 mg/dl), High density lipoprotein cholesterol (HDL¬-c)(39.66+3.36 mg/dl vs 38.18+3.83 mg/dl) and CIMT(0.93+0.145 mm vs 0.85+0.138 mm) among subjects on ARTas compared to newly diagnosed HIV reactive subjects. **Conclusion:** It is evident from our study that there was significantly greater prevalence of dyslipidemia in HIV reactive patients on ART as compared to newly diagnosed HIV reactive patients though it was there in both. Our study also suggested the role of HAART in the development of carotid atherosclerosis in HIV patients. HAART has dramatically reduced the morbidity and the mortality in HIV infected patients but we should not overlook these possible complications related to dyslipidemia and carotid atherosclerosis. Hence, a periodical screening and long term follow up of all the HIV patients who are on ART should be done to assess and timely detect risks associated with them.

Keywords: Carotid Atherosclerosis, Dyslipidemia, HIV.

INTRODUCTION

The hallmark of HIV disease is a profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as helper T cells occurring in a setting of polyclonal immune activation.[1]

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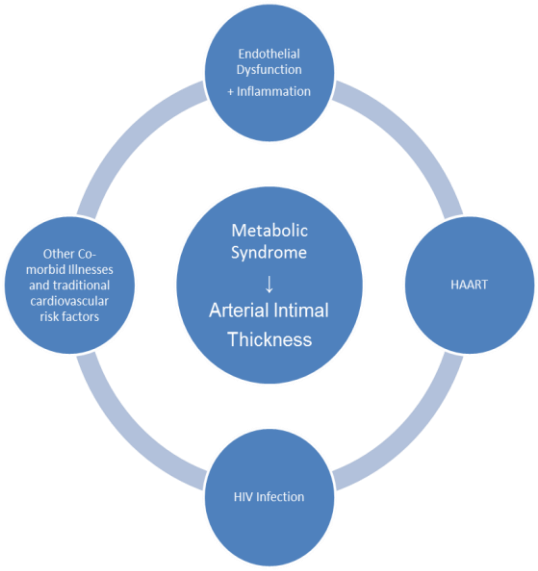
Activation of the immune system and variable degrees of inflammation are essential components of any appropriate immune response to a foreign antigen. However, immune activation and

inflammation, which can be considered aberrant in HIV-infected individuals, play a critical role in the pathogenesis of HIV disease and other chronic conditions associated with HIV disease.[1] It has become clear as the survival of HIV-infected individuals has increased that a number of previously unrecognized medical complications are associated with HIV disease and that these complications relate to chronic immune activation and inflammation. Of particular note are endothelial cell dysfunction and its relationship to cardiovascular disease.[1]

The chronic inflammation and immune activation associated with HIV-infection and the dyslipidemia associated with Antiretroviral Therapy (ART) contribute to increased risk of atherosclerotic vascular disease among HIV-infected adults relative to the general population.[2]

HIV is associated with dyslipidemia, namely, hypocholesterolemia, hypertriglyceridemia, and low levels of both low density lipoproteins (LDL) and high density lipoproteins (HDL).In addition, ART is associated with dyslipidemia, which tends to be worse with many protease inhibitor (PI) -containing regimens.[2]



Extensive functional and structural arterial changes have been observed in the HIV positive patients. It has been documented that these vascular changes are closely associated to the Highly Active Antiretroviral Therapy (HAART) induced metabolic syndrome and to the HIV infection itself. The sub-clinical carotid lesions have a highly significant association with all the cardiovascular risk predictors Thus, the recognition and assessment of the carotid intimal thickness would further help in predicting the risk of the cardiovascular events among these patients and addressing these factors as well as the therapy optimization with lipid lowering agents and a antiretroviral therapy modification will improve the outcome.[3]

However, in India Dyslipidemia and CIMT in HIV reactive patients and patients on HAART has not been studied in detail, and data regarding lipid abnormalities and CIMT in treatment naïve and HIV reactive patients in India are limited. So, the study was conducted to compare the prevalence of Dyslipidemia and Carotid Atherosclerosis among newly diagnosed HIV Reactive patients and Those on ART in Rajindra Hospital, Patiala, Punjab.

MATERIALS AND METHODS

This descriptive-cross sectional study was conducted among 200 subjects who attended Medicine OPD, ART Centre and admitted in various medical Wards of Rajindra Hospital, Patiala over a period of 2 years from November 2014 to October 2016. 100 newly diagnosed HIV reactive subjects as per NACO guidelines but not on ART of age 20 years and above were included in Group A while 100 subjects of similar age group on ART for 6 months included in group B. The subjects having thyroid disease, Diabetes Mellitus, Hypertension and those on hypolipidemic drugs were excluded from the study. Purpose of study was explained and Informed consent was taken from patients and family in their vernacular language. A detailed history, clinical examination was done and lipid profile was estimated biochemically and CIMT was measured radiographically. For dyslipidemia, present study was referred to NCEP-ATP III Guidelines. According to these standard guidelines, hypercholesterolemia is defined as TC >200mg/dl, LDL-C as >100mg/dl, hypertriglyceridemia as TG >150mg/dl and HDL-C <40mg/dl. Dyslipidemia is defined by presence of one or more than one abnormal serum lipid concentration.[4,5] Carotid Atherosclerosis was determined by measuring Carotid Intima media thickness by using high resolution B mode ultrasonography system Philips Whole Body Color MC15601 Doppler machine with multi transducer system; done by trained ultrasonologist in the department of Radiodiagnos is, Govt. Medical College, Patiala. Data generated from study was analyzed according to standard statistical methods. Non normal distribution variables were applied Mann-Whitney rank sum test and normal distributed variables by 't' test. Pearson product-moment correlation coefficient was applied to measure the correlation between two variables.

RESULTS

The mean age of patients in group A was 41.93+8.26 years while 42.49+8.55 years in group B. Ratio of male to female was 68:32 in both groups. [Table 1] shows the pattern of lipid profile and CIMT in group

A (Newly diagnosed HIV reactive patients as per NACO guidelines but ART Naïve of age 20 years and above) and group B (HIV reactive patients on ART for 6 months of age 20 years and above). The study observed a significantly increased levels of Serum TC, TGs, LDL-c, HDL-C, VLDL-c, CIMT and Carotid plaques in patients on ART than HIV reactive ART naïve patients.

Table 1: Lipid Profile and CIMT in ART-Naïve and ART Patients.

S. No.	Characteristic	Group A (Mean ± SD)	Group B (Mean ± SD)	P value	Significance
1.	Serum Total CHOLESTEROL	160.69 ± 18.49	182.13 ± 24.88	<0.001	HS
2.	SERUM TRIGLYCERIDES	141.23 ± 22.99	162.7 ± 26.15	<0.001	HS
3.	SERUM LDL-c	94.3 ± 16.89	110.72 ± 22.76	<0.001	HS
4.	SERUM HDL-c	38.18 ± 3.83	39.66 ± 3.36	0.001	HS
5.	SERUM VLDL-c	28.21 ± 4.62	32.54 ± 5.23	<0.001	HS
6.	CIMT	0.85±0.138	0.93±0.144	<0.001	HS
7.	Presence of Plaque in carotids(no. of patients)	2	21	<0.001	HS

HS: Highly Significant

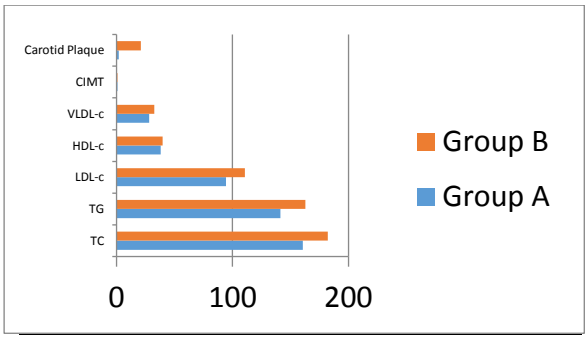


Figure 1: Showing mean values of Serum TC, TGs, LDL-c, HDL-C, VLDL-c, CIMT and Carotid plaques of patients of both groups.

Table 2: General Profile of patients in Group A and B.

S. No.	Characteristic	Group A	Group B	P value	Significance
1	Age (years)	41.93+8.26	42.49+8.55	0.6382	Non-significant
2	Sex ratio(Male: Female)	68:32	68:32	0.5	Non-significant
3	CD4 count(cells per mm^3	303.02+118.21	393.49+129.00	<0.001	HS

HS: Highly Significant

The lipid profile and CIMT measurement in patients on TLE regimen (Tenofovir Didoproxil Fumarate 300 mg +Lamivudine 300 mg +Efavirenz 600 mg) once a day were compared to those on ZLN regimen (Zidovudine 300 mg + Lamivudine 150 mg + Nevirapine 200 mg) twice a day and is shown in Table no. 3 below. [Figure 2] shows mean values of various parameters of lipid profile and CIMT of patients on above said regimens.

Table 3: Lipid Profile and CIMT Comparison between TLE and ZLN Regimen.

	Groups	Mean	S.D	P value	Significance
Serum Total Cholestrol	TLE	183.05	24.894	0.611	NS
	ZLN	179.04	25.133		
Serum Triglycerides	TLE	163.17	26.526	0.984	NS
	ZLN	161.13	25.334		
LDL-c	TLE	111.81	22.646	0.617	NS
	ZLN	107.09	23.263		
HDL-c	TLE	39.610	3.277	0.689	NS
	ZLN	39.826	3.688		
VLDL-c	TLE	32.662	5.290	0.776	NS
	ZLN	32.130	5.137		
CIMT	TLE	0.937	0.151	0.964	NS
	ZLN	0.929	0.122		

NS: Not Significant

Correlation between lipid profile and CIMT was analysed and it was observed that with increase in Total Cholesterol, Triglycerides and LDL, CIMT increases while HDL has inverse relationship; thus, CIMT increases with decrease in HDL.

Table 4: Correlation between LIPID PROFILE and CIMT.

Parameter	R value	P value
LDL	0.550	<0.001
HDL	-0.317	<0.001
VLDL	0.468	<0.001
Total Cholesterol	0.534	<0.001
Triglycerides	0.469	<0.001

DISCUSSION

Study revealed that Sex ratio (Male: Female) was 68:32 in both groups A and B. Mean age in group A was 41.93+8.26 years while 42.49+8.55 years in group B. Two groups were statistically similar in their age [p= 0.6382 i.e. (p > 0.05)] and sex distribution as [p =0.5 i.e. (p>0.05)] which is Non-significant. Mean CD4 count was higher in group B than group A; 393.49+129.00 per mm^{3}versus 303.02+118.21 per mm^3 which is statistically significant between two groups; p<0.001. The serum

total cholesterol, serum triglycerides, LDL-c, VLDL-c, HDL-c levels were higher in group B patients than group A patients and this difference was statistically significant; 182.13±24.88 mg/dl Vs 160.69±18.49 mg/dl, 162.70±26.15 mg/dl vs 141.23±22.99 mg/dl, 110.72±22.76 mg/dl vs 94.30±16.89 mg/dl, 32.54±5.23 mg/dl vs 28.21±4.62 mg/dl, 39.66±3.36 mg/dl vs 38.18±3.83 mg/dlrespectively; (p<=0.001). There were greater number of patients i.e. 40% patients in group B had total serum cholesterol >200mg/dl as compared to 11% patients in group A, 48% patients in group B had serum Triglyceride levels >150mg/dl as compared to 28% patients in group A, 48% patients in group B had serum LDL-c levels of >100mg/dl as compared to 11% in group A, 16% patients in group A had serum VLDL-c levels >40 mg/dl as compared to 5% in group A. There were lesser number of patients i.e. 56% patients in group B had total serum HDL levels <40mg/dl as compared to 64% in group A. Overall, dyslipidemia was present in 70% of patients in group B (HIV Reactive on ART for 6 months) patients as compared to 64% in group A (Newly diagnosed HIV Reactive ART Naive) patients. The mean value of the carotid initial thickness was higher in group B patients than group A patients and this difference was statistically significant; 0.93±0.145 mm vs 0.85±0.138 mm (p<0.001). 21% showed presence of plaques on Doppler study of carotids in group B as compared to 2% in group A and this difference was statistically significant; (p<0.001). In group B, 77% patients were on TLE regimen (Tenofovir+ Lamivudine+ Efaverinz) while 23% patients were on ZLN regimen Zidovudine + Lamivudine + Nevirapine) as TLE regimen was most commonly used in our centre as per NACO guideliens. The lipid profile and CIMT of patients on TLE regimen were compared to those on ZLN regimen and there was no significant difference between these two different ART regimen subgroups; (p>0.05). Correlation between lipid profile and CIMT was analysed and there was found positive correlation between Serum Total cholesterol, Triglycerides, LDL-c, VLDL-c and CIMT while negative correlation between Serum HDL-c and CIMT. The results of the study were in correlation with studies conducted by Calza et al in 2009,[6] PNS et al in 2013,[7] V I et al in 2014,[8], Bekolo et al in 2014,[9] Limas et al in 2014.[10]

Previous reports have demonstrated that HIV-infected patients exhibit multiple abnormalities in lipid metabolism parameters both in pre-HAART and post-HAART eras, especially with the use of protease inhibitors (PIs). Several mechanisms have been proposed to explain the dyslipidemia seen with both HIV infection and exposure to ART.[11]

HAART induces raised levels of TC, LDL and TG, and variables effects on HDL levels. The pathogenesis of HAART associated dyslipidemia is complex, and several factors are involved, including direct effects of HAART on lipid metabolism, endothelial and adipocyte cell function and mitochondrial dysfunction. Cytokines, especially TNFα, interleukin1 and interleukin6, which mediate the host acute phase response to infection and inflammation, also mediate changes in lipid metabolism and HAART leads to activation of these proinflammatorycytokines. Overall, the dysfunctions observed with HIV infection and ART suggest a scenario where excess systemic cholesterol availability and reduced clearance of cholesterol from both the circulation and M/M produce a specific dyslipidemia that may contribute to accelerated atherosclerosis and increased CVD risk, particularly in an aging cohort.[12-14]

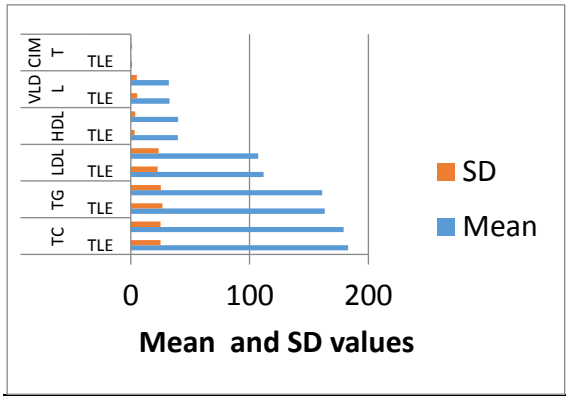


Figure 2: showing mean values of various parameters of lipid profile and CIMT of patients on both regimens.

Many studies have shown an increased prevalence of subclinical atherosclerosis in the patients who were on ART.[7] In accordance to our results, Calza L et al., also reported a higher prevalence of carotid atherosclerosis in the treatment experienced patients than in the treatment naïve patients.[6] Results of our study should be interpreted in light of some limitations. Limitation of our study was that PIs were not used in any patient because our center provides only first line ART according to NACO guidelines. Our study included the cross sectional design in which it is difficult to draw a causality. The sample size also was smaller to make a valid conclusion.

CONCLUSION

To conclude, it is evident from our study that there was greater prevalence of dyslipidemia in ART patients as compared to Newly diagnosed HIV reactive patients though it was there in both. Our study also suggested the role of HAART in the development of carotid atherosclerosis in HIV patients. HAART has dramatically reduced the morbidity and the mortality in HIV infected patients, which clearly outweigh the possible adverse effects which are associated with ART. But we should not overlook these possible complications related to dyslipidemia and carotid atherosclerosis. Hence, a periodical screening and long term follow up of all

the HIV patients who are on ART should be done to assess and timely detect risks associated with them. However, further larger studies are required to validate the results and to decide if any therapeutic intervention required along with.

REFERENCES

1. Fauci AS and Lane HC. Human Immunodeficiency Virus Disease: AIDS and Related Disorders. In: Harrison's Principals of Internal Medicine (18thedn.) Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. (Eds.). McGraw Hill 2012; 1506-27.
2. Ssinabulya I, Kayima J, Longenecker C, Luwedde M, Semitala F, Kambugu A et al. Subclinical Atherosclerosis among HIV-Infected Adults Attending HIV/AIDS Care at Two Large Ambulatory HIV Clinics in Uganda. PLoS ONE 2014;9(2):e89537.
3. PN S, Achappa B, B U, Madi D, Chowta MN, Ramapuram JT et al. The Evaluation of Carotid Atherosclerosis in Patients with the HIV-1 Infection: The Role of the Antiretroviral Therapy. J ClinDiagn Res. 2013;7(2):261-4.
4. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [special communication]. JAMA 2001;285:2486-947.
5. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report [special communication]. Circulation 2002;106: 3143-421.
6. Calza L, Verucchi G, Pocaterra D, Pavoni M, Alfieri A, Cicognani A, Manfredi R, Serra C, Chiodo F. Cardiovascular risk factors and ultrasound evaluation of carotid atherosclerosis in patients with HIV-1 infection. Int J STD AIDS. 2009Oct;20(10):683-9.
7. P N S, Achappa B, B U, Madi D, Chowta MN, Ramapuram JT, Rao S, MahalingamS.The Evaluation of Carotid Atherosclerosis in Patients with the HIV-1 Infection:The Role of the Antiretroviral Therapy. J ClinDiagn Res. 2013 Feb;7(2):261-4.
8. V I, V V, Shekhanawar MS, Rajeshwari, M A, D S. Comparison of Serum Lipid Profile in HIV Positive Patients on ART with ART Naïve Patients. J ClinDiagn Res. 2014 Oct;8(10):CC06-9.
9. Bekolo CE, Nguena MB, Ewane L, Bekoule PS, Kollo B. The lipid profile of HIV-infected patients receiving antiretroviral therapy in a rural Cameroonian population. BMC Public Health. 2014 Mar 7;14:236.
10. Limas TG, Pinto Gde A, Marcato LM, Coelho DR. Analysis of the prevalence of dyslipidemia in individuals with HIV and its association with antiretroviral therapy. Rev Soc Bras Med Trop. 2014 Sep-Oct;47(5):547-51.
11. Cotter AG, Satchell CS, O'Halloran JA, Feeney ER, Sabin CA, Mallon PW. High-density lipoprotein levels and 10-year cardiovascular risk in HIV-1-infected patients. AIDS 2011;25(6):867–9.
12. Zhou H, Gurley EC, Jarujaron S, Ding H, Fang Y, Xu Z et al. HIV protease inhibitors activate the unfolded protein response and disrupt lipid metabolism in primary hepatocytes. Am. J. Physiol. 2006;291(6):G1071-80.
13. Liang JS, Distler O, Cooper DA, Jamil H, Deckelbaum RJ, Ginsberg HN et al. HIV protease inhibitors protect apolipoprotein B from degradation by the proteasome: a potential mechanism for protease inhibitor-induced hyperlipidemia. Nat. Med. 2001;7(12):1327–31.
14. Den Boer MA, Berbee JF, Reiss P, van der Valk M, Voshol PJ, Kuipers F et al. Ritonavir impairs lipoprotein lipase-mediated lipolysis and decreases uptake of fatty acids in adipose tissue. Atheroscler. Thromb. Vasc. Biol. 2006;26(1):124–9.

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