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Research Article

Pattern of dyslipidaemia in human immunodeficiency virus infected patients- a study from rural tertiary care hospital in central India

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ABSTRACT

Background: HIV/AIDS is a major health problem affecting the whole globe. With introduction of highly active antiretroviral therapy longevity of HIV patient have increased and they are subjected to high cardiovascular risk as age increases due to various risk factors. Of these dyslipidaemia is one of important risk factor and HIV patients have different degree of deranged lipid profile. Various studies have shown different lipid derangement in these patients but most of them were conducted in urban areas, so this study was conducted to look for lipid profile in HIV patients who are resident of rural areas.
Methods: This study was conducted on 66 HIV infected or AIDS cases. Each case was subjected to history taking, through clinical examination and fasting lipid levels. Dyslipidaemia was a classified using NCEP/ATP III guideline.
Results: Of total 66 cases, there were 39 male and 27 female with average age of 37 years. Hypercholesterolemia was present in 50% of patients, hypertriglyceridemia in 36.4%. LDL and VLDL were raised in 37.9% and 36.4% respectably while HDL was found below 40 mg/dl in 37.9% of the patients. S. total cholesterol, HDL and LDL was found to have positive correlation while S. TG and VLDL have no significant correlation with CD4 count.
Conclusions: Present studies have shown high prevalence of dyslipidaemia in different WHO clinical stage with variable correlation with CD4 count.

Keywords: CD4 count, Dyslipidaemia, HIV/AIDS, Rural

INTRODUCTION

AIDS (acquired immunodeficiency syndrome) is a global pandemic caused by HIV virus and cases are being reported from all countries across the world.[1] According to WHO total number of HIV/AIDS cases reported in 2014 were 36.9 million of which 2 million were reported in year 2014.[1,2]

According to National AIDS Control Organisation (NACO) total number of people living with HIV/AIDS was estimated to around 21.17 lakh in year 2015.[3] In June 1981 Centre for Disease Control and Prevention (CDC) published cases of rare lung infection among male homosexual in Los Angelis giving first report of existence of immunodeficiency but it was September 24,1982 when CDC used the term AIDS(acquired immune deficiency syndrome) for the first time, and released the first case definition of AIDS.[4,5] The mortality among the HIV/AIDS was very high in comparison to general population.[6]

With the introduction of Highly active antiretroviral therapy (HAART) in mid to late 1990s, mortality and morbidity associated with HIV/AIDS have significantly reduced and longevity has increased.[7] With the effective treatment option as HAART the incidence of opportunistic infections has decreased and with increasing longevity there emerged the major concern regarding cardiovascular risk in these patients.[8] HIV

patients are subjected to dyslipidaemia and other complications secondary to HAART are often referred as HIV metabolic syndrome.[9] Studies even before HAART have also shown a variety of lipid abnormalities.[10,11] Various studies have shown different prevalence and pattern of dyslipidaemia.[10-13]

Infection can increase serum triglyceride (TG) level by decreasing the clearance of circulating lipoprotein, which thought to be due to reduced lipoprotein lipase or by stimulating lipid synthesis in liver through increase in either hepatic fatty acid synthesis or re-esterification of fatty acid derived from lipolysis.[14]

Multiple pathogenic mechanisms by which HIV virus leads to dyslipidaemia have been hypothesized but they are still controversial.[14-19] Patient of HIV have two fold increased risk of MI compared with those without HIV infection and this is attributed to the metabolic alteration due to HIV itself, dyslipidaemia and increasing age due to increased longevity.[20]

There were several studies done for the prevalence and pattern of dyslipidaemia in HIV patient but most of them were conducted in urban setting and there was no study done from central India in rural set up to show the lipid profile in HIV patient, therefore this study was undertaken to find out lipid profile in HIV patient across different stages of HIV/AIDS.

METHODS

A cross sectional study was carried out at U.P. University of medical sciences, Etawah, U.P. Total 66 cases of HIV infected/ AIDS patients who attended Anti-Retroviral Therapy(ART) centre, department of medicine, UPUMS, Etawah, were included in the study.

Inclusion criteria

HIV positive patients who had no critical illness were included in the study.

Exclusive criteria

Critically ill patients, diabetics, hypertensive, hypothyroid, chronic smoker those with sedentary life style were excluded from the study. After informed consent from each patient, they were subjected to detailed history taking and thorough clinical examination, including anthropometric and demographic characteristics.

For diagnosis of HIV infection NACO recommendations of HIV testing i.e. three strategy testing were used and patient were divided in different clinical stages according to NACO guidelines.[21]

The serum lipid profile was estimated by the enzymatic CHOD-PAP method for Total Cholesterol, by the GPO method for Triglyceride and by the PVS/PEGME method for HDL cholesterol.[22,23] These estimations were carried out by using ERBA-XL 300 (Transasia) fully automated analyser. LDL Cholesterol and VLDL Cholesterol were calculated by Friedwald's formula LDL= T.C×HDL (TG/5).[24]

All the kits used were commercially prepared, System packs kits were used for Lipid profile estimation. Calibration was performed using Randox quality control sera. The quality control was established using Erbapath and Erbanorm. Abnormal lipids were defined as per NCEP (National Cholesterol Education Program) ATP III classification as shown in Table 1.

Table 1: NCEP (National cholesterol education program) ATP III classification of lipid levels.

Risk	S. cholesterol (mg/dl)	S. triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Very high	-	≥ 500	-	≥ 190
High	≥240	200 - 499	<40	160-189
Borderline	200-329	150 -199	40 - 59	130-159
Desirable	<200	<150	>60	100-129
optimal	-			<100

The CD 4 lymphocytes were estimated by fluorescence activated cell sorter (FACS) count system (Becton Dickinson).

Other baseline investigation included haemoglobin, total leucocyte count (TLC), liver function test (LFT), renal function test (RFT) were determined using auto analyser. HBsAg for HBV and anti-HCV for HCV was tested using rapid diagnostic kits.

Statistical analysis

Statistical analysis of data was performed using Statistical Package for Social Sciences version 21.0.

Categorical variables were expressed as absolute number and percentage and continuous variables were expressed as mean and standard deviation (SD). Correlations between different variables were calculated using

Pearson's correlation method and values were expressed as correlation coefficient(r). A p value of less than 0.05 was considered significant.

RESULTS

Demographic characteristics and baseline biochemical parameter of HIV patients are presented in Table 2.

Average ages of subjects were 37±9.8 years and average BMI were 21.28±3.3. Most of the patient were in age group of 30-39 years (N=28), most of the subject have primary education (N=30).

Most prevalent occupation among females was house wife and that of males was farmer. Most of the subject had their income between Rs 2000-10000 per month (N=51).

Table 2: Demographic and clinic-biochemical characteristics of subjects.

S.N	Characteristic		Number	S.N	Characteristic		Number
1.	Sex	Male	39	7.	CD4+ Count (Count/mm^3)	<50	2
		Female	27			50-200	10
2.	Age	20-29	11			201- 500	32
		30-39	28			>500	22
		40-49	19	8.	ART status	Pre- ART	5
		50-59	8			ART	61
3.	Education	Illiterate	10	9.	Drug Regimen	TLE	20
		Primary	30			TLN	3
		Secondary	20			ZLN	38
		Graduate	6	10.	Average weight(Kg)	52.52± 10.12 (Mean±SD)	
4.	Occupation	Driver	3		Average height(cm)	156± 9.8 (Mean±SD)	
		Farmer	12		BMI (Kg/m^2)	21.28± 3.3 (Mean±SD)	
		Housewife	26	11.	Haemoglobin (mg/dl)	11± 1.7 (Mean±SD)	
		Labourer	4		TLC(count/mm^3)	6847± 2464 (Mean±SD)	
		Business and shopkeeper	9	12.	Total Protein (mg/dl)	7.27± 1.19 (Mean±SD)	
		Security	3		S. Albumin (mg/dl)	4.03± 0.53 (Mean±SD)	
		Govt/Pvt job	6	13.	S. Urea (mg/dl)	36.76± 14.68 (Mean±SD)	
		Unemployed	3		S. Creatinine(mg/dl)	0.97± 0.21 (Mean±SD)	
5.	Family Income (INR/Months)	<2000	12	14	S. bilirubin (mg/dl)	0.38±0.21 (Mean±SD)	
		2000-5000	30		SGOT (units/dl)	39.89±14.3 (Mean±SD)	
		5000-10000	21		SGPT units/dl)	44.13±10.77 (Mean±SD)	
		>10000	3		S. ALP	152±57.7 (Mean±SD)	
6.	WHO Stage	1	51	15	ESR	26±10.63 (Mean±SD)	
		2	8				
		3	4				
		4	3	Total number of cases 66			

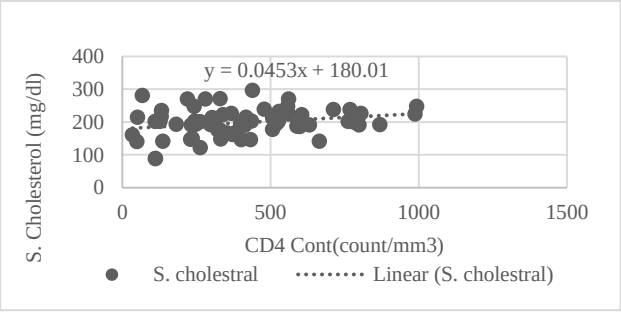

Figure 1: Distribution of S. cholesterol values against CD4 count.

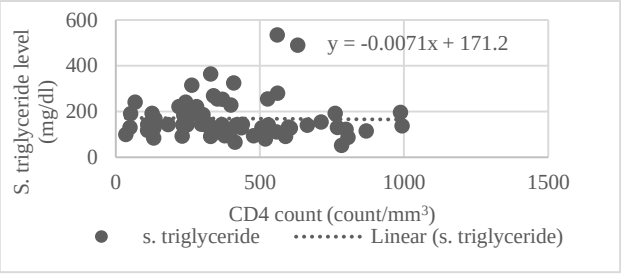

Figure 2: Scatter diagram showing no significant correlation between CD4 count and s. triglyceride level.

Maximum number of patient belong to the WHO stage 1 (N=51) and most have their CD4 count 201-500 (N=32). 5 patients were pre-ART and 61 were on antiretroviral drugs of which 20 were on TLE, 3 were on TLN and 38 were on ZLN (Table 2). Mean value with SD of different lipid parameter in different WHO stages were presented in Table 3 and that of different ranges of CD4 count is presented in Table 4.

Table 3: Lipid profile in different WHO clinical stages in HIV positive cases.

WHO stage	Mean CD4 count (number/mm^3)	S. total cholesterol	S. triglyceride	HDL	LDL	VLDL
I	445	205.15±36.82	169.2±98.97	46.5±18.70 (p 0.021)	125.5±35.99	33.9±19.70
II	315	209±36.0	171.1±38.75	42.13±10.53 (p 0.024)	132.57±36.63	34.45±7.42
III	169	115.5±31.84	133.2±10.75	45±16.69	44.05±42.09	26± 2.12
IV	310	164.6±43.01	192.6±57.29	44.4±4.17 (p 0.025)	82± 46.7	38.4±11.47

Table 4: Lipid profile in different ranges of CD4 count in HIV positive cases.

Lipid types	CD4 ranges (N); Mean lipid levels (mg/dl) Mean±SD				Correlation (R)	p- value by t test w.r.t. CD4
	<50 (2)	51-200 (10)	201-500 (32)	>500 (22)		
S. total cholesterol	150±14.14	185.6±61.96	196.88±42.38	210.8±28.95	0.247	0.045
S. triglyceride	113.5±21.92	153.8 ±44.45	173.88±74.92	171±121.96	-0.018	0.883
HDL	48±19.79	48.45±10.0	41.33±11.89	50.8± 24.23	0.243	0.049
LDL	80±38.18	107.4±61.10	118.8±38.79	129.61±34.87	0.255	0.039
VLDL	22.7±4.67	30.72±8.92	34.91±14.80	34.49±24.33	0.019	0.880

Table 5: Lipid profile in HIV cases.

S. total cholesterol	Frequency (percentage)	S. triglyceride	Frequency (percentage)
<200 Desirable	33 (50%)	<150 Normal	41 (62.1%)
200-239 Borderline	24 (36.4%)	150-199 Borderline high	10 (15.2%)
≥ 240 High	9 (13.6%)	200-499 High	14 (21.2%)
HDL	**Frequency (percentage)**	≥500 Very high	1 (1.5%)
>60 High	6 (9.1%)	**LDL**	**Frequency (percentage)**
40-59 Intermediate	36 (54.5%)	<100 Optimal	18 (27.3%)
<40 low	24 (36.4%)	100-129 Near optimal	23 (34.8%)
VLDL	**Frequency (percentage)**	130-159 Borderline high	14 (21.2%)
2-30 Normal	42 (63.6%)	160-189 high	10 (15.2%)
>30 High	24 (36.4%)	≥190 Very high	1 (1.5%)

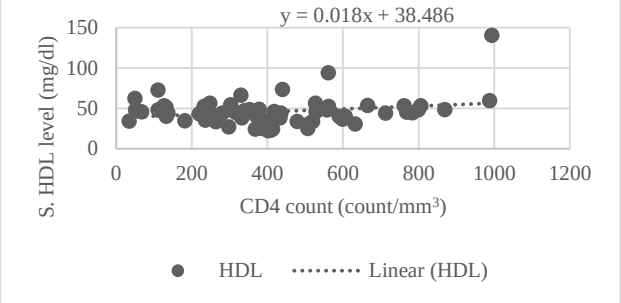

Figure 3: Positive relation between CD4 count and HDL level (r=0.243; p-value=0.049).

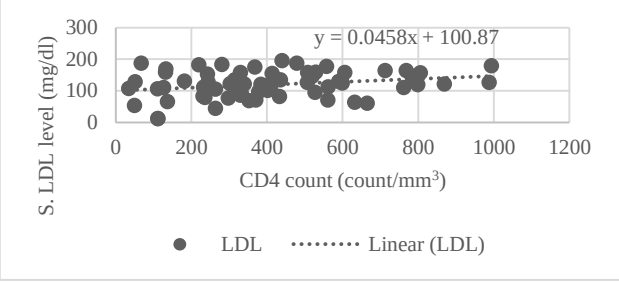

Figure 4: Positive correlation between S. LDL level and CD4 count evidenced by the positive correlation coefficient (r= 0.255; p-value=0.039).

S. cholesterol found to be highest in WHO clinical stage II (209±36.32), S. triglyceride were highest in WHO stage IV (192.6±57), HDL value were lowest in WHO stage WHO stage II (42.13±10.53 p=0.024). S. LDL was highest value in stage II (132.57±36.6) while that of VLDL was in WHO stage IV (38.4±11.47) (Table 3). S. total cholesterol has maximum value in >500 CD4 group with p value of 0.045 that is significant. S. triglyceride has maximum value in 201-500 CD4 group with R value of-0.018.

HDL has maximum value in >500 CD4 group with p value of 0.49 while LDL also have maximum value in same group with p value of 0.039 (Table 4). Frequency of cases in different risk categories of NACP/ATP III are given in table 5. S. cholesterol was raised in 33 (50%), S. triglyceride was raised in 25 (37.9%), HDL was below 40 in 24 (36.4%). LDL was high in 25 (37.9%) while VLDL was increased in 24 (36.4%) of cases (Table 5).

Figure 1 showing distribution of S. Cholesterol values against CD4 count. There is gradual increase of S. cholesterol level as CD4 count increases, strong correlation was shown by positive R value and the overall p-value 0.045(statistically significant).

Figure 2 is a scatter diagram showing no significant correlation between CD4 count and S. triglyceride level. In figure 3 there is positive relation between CD4 count and HDL level (r=0.243; p-value=0.049).

Figure 4 shows the positive correlation between S. LDL level and CD4 count evidenced by the positive correlation coefficient (r= 0.255; p-value=0.039). Figure 5 showing distribution of VLDL in relation to CD4 count and there is no significant correlation between them.

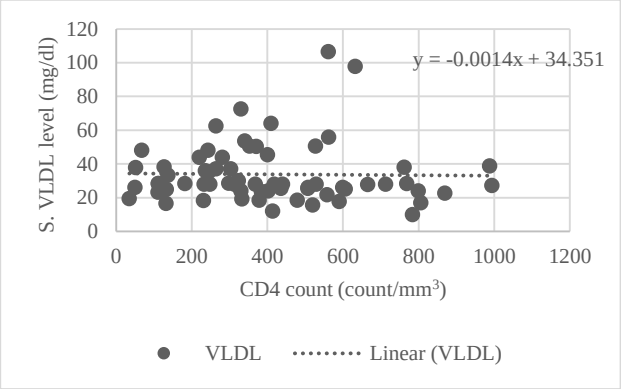

Figure 5: Distribution of VLDL in relation to CD4 count and there is no significant correlation between them.

DISCUSSION

In present study lipid levels were altered in HIV infected patients and there were varied relationship between different lipid levels WHO clinical stage and CD4 categories. Out of total 66 cases, most of the cases have lipid level above optimal between one and other lipid. In our study we have found increase in total cholesterol, triglyceride, LDL, VLDL which is consistent with previous study done by Buchacz et al.[13] Mondy et al has reported increased level of triglyceride which is consistent with our finding but they reported low levels of total cholesterol and LDL.[12]

In present study HDL was low and this is consistent with other studies by Pariad et al, Buchacz et al, Khiangte et al, Mondy et al and G Shor Posner et al.[10-13,25] Khiangte et al showed deranged lipid profile in their HIV patients and in them LDL levels decreased as CD4 count decreased which is consistent with our observation. However LDL decreases while triglyceride and VLDL increases with decrease in CD4 count in their study.[25]

In our study we have found with decrease in CD4 count there was decrease in mean levels of S. cholesterol and LDL which is not consistent with observation of Rogowska et al Ducobu et al and Crook et al which may be due to small sample size.[25-27] G Shor Posner et al demonstrated low levels of total cholesterol, HDL, LDL in HIV patients. These low levels were associated with elevated levels of β2 microglobulin.[29]

Kereveur et al stated that decreased cholesterol level observed in early and increased triglyceride levels in later stages of disease and this derangement of lipids is due to the cytokines which effects different enzymes of lipid metabolism.[30] Grunfeld et al had reported that HIV infection has high prevalence of hypertriglyceridemia and hypo-cholestrolemia along with elevated level of cytokines.[14]

Same authors reported strong correlation between S. interferon α levels and triglyceride clearance time and decrease in cholesterol and cholesterol containing lipoprotein in both AIDS and HIV patient precede the appearance of hypertriglyceridemia and are not related to IFN α or triglyceride levels.[15] Matsuyama et al high lightened the effect of HIV virus on cytokine production and the most potent cytokine expressed were TNF-α, IL-1 and IL-6.[31]

CONCLUSION

In conclusion, dyslipidemia is highly prevalent in HIV patients from rural population, characterized by increased levels of total cholesterol LDL, TG, VLDL and decreased level of HDL.

In view of young age of most of the patients and increased longevity due to HAART therapy, these patients are going to be at high risk for atherosclerosis and ischemic heart disease as they grow older. So, it is advisable to identify dyslipidemia in these patients as early institution of lifestyle modification and/or pharmacotherapy may reduce cardiovascular risk.

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