

Original Article

Prevalence of dyslipidemias in human immunodeficiency virus-infected patients with and without antiretroviral therapy.

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Abstract

Background: Disturbances in the lipid profile and dyslipidemia are prevalent among human immunodeficiency virus (HIV) patients. Furthermore, long-term use of antiretroviral therapy (ART) exacerbates the condition. Data on lipid profile abnormalities among patients receiving highly active antiretroviral treatment in Pakistan are very limited. The present study aims to assess the frequency of dyslipidemia and lipid concentrations among HIV-infected patients receiving active art in comparison to those not receiving any treatment.

Methodology: A cross-sectional study was carried out at the HIV clinic of Pakistan Institute of Medical Sciences, Islamabad, from January to July 2018. A total of 100 HIV-infected patients aged 13 to 60 years who gave consent and fulfilled the inclusion criteria were enrolled in the study via non-probability consecutive sampling. All patients who had positive HIV antibodies via the Elisa process were considered positive. Samples were examined for fasting lipids by using standard laboratory procedures.

Results: The patients' mean age was 32.7 ± 13.4 ranging between 13-60 years. The total patient population consisted of 71% males and 29% females with a mean BMI of 21.1 ± 3.4 kg/m². Out of 100, 38% of the study patients had dyslipidemia. The observed prevalence rate of hypertriglyceridemia, hypercholesterolemia, low HDL-C, and high LDL-C were 21%, 30%, 20%, and 16%, respectively. None of the factors were found in significant association with abnormal lipid parameters except the older patients (41-60 years) were at higher risk of hypercholesterolemia [aOR 0.15 (95% CI 0.02-0.92); p=0.04] than the counterpart.

Conclusion: The study has demonstrated that a higher percentage of HIV-infected patients have concomitant dyslipidemia with or without art treatment.

Keywords

Human Immunodeficiency Virus, Dyslipidemia, Antiretroviral Therapy, Cholesterol.



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Introduction

Dyslipidemia, a detrimental cause of arteriosclerosis and cardiovascular disease (CVD), is common in patients infected with the human immunodeficiency virus (HIV). It is characterized by increased serum LDL, elevated serum total cholesterol, serum triglycerides, and decreased serum HDL. HIV-associated dyslipidemia can be caused by impaired reverse cholesterol transport (RCT) by the HIV nef protein, which leads to the degradation of adenosine triphosphate (ATP) binding cassette subfamily A member 1 (ABCA1)¹. Increased serum triglyceride is caused by impaired peripheral trapping of free fatty acids (FFAs) in adipose tissue and into the blood, which results in abnormal modulation mediated by strong inflammatory cytokines affecting removal of triglyceride from the blood due to diminished lipase activity².

Furthermore, the risk of cardiovascular events and myocardial infarction, in particular, is significantly increased in patients with HIV infection. Up to 6.5-15% of the mortality rate with reference to HIV has been attributable to cardiovascular disease³. HIV infection associates itself with a number of protein and lipid compositional changes in HDL particles. Moreover, HIV infection also affects the cholesterol efflux function of HDL, thus contributing to an increased risk of atherosclerosis in this patient population⁴. Aged HIV-infected men have shown a reduced oxidative enzyme activity and increased oxidative stress compared to age-matched controls⁵⁻⁷.

Due to the widespread use of antiretroviral drugs (ARVs), the global prevalence of dyslipidemia in HIV-infected patients has accelerated. As patients are required to take ARVs for the rest of their lives, hyperlipidemia is becoming a real concern, putting them in a condition of ongoing lipid derangement, which further leads to cardiovascular disease and atherosclerosis^{8,9}. In Uganda, 58% of patients on first-line Active ART had metabolic syndrome, observed more in women than men¹⁰. Peripheral lipoatrophy, dyslipidemia, dysglycemia, and increased cardiovascular risk have been significant concerns with long-term ART. Participants on ART

had higher triglycerides, total cholesterol, LDL-cholesterol, and HDL cholesterol than the ART-naïve group, according to a study done in South Africa¹¹. There are several studies conducted to find the mechanism involved in the association between HIV, CVD, and dyslipidemia, the findings are yet uncertain, but it is proven that these three conditions are strongly linked together¹²⁻¹⁷.

This study aimed to evaluate how HIV infection affects lipid concentrations, determining the frequency of dyslipidemia among these patients. Furthermore, the effect of ARV medicines on lipid profiles would be determined by comparing the serum lipid profiles of HIV-positive ART-naïve individuals with those currently on ART. This would not only provide local population statistics, but it would also increase existing research on lipid metabolism and its negative effects on HIV patients' health. As a result, cholesterol surveillance may provide additional benefits in terms of lowering morbidity and mortality in HIV patients.

Methodology

A cross-sectional study was conducted at the General Medicine Ward and HIV clinic of PIMS, Islamabad, from January to July 2018. The sample size of 100 was calculated using the WHO standard sample size calculator, keeping the population proportion of dyslipidemia in HIV (+ve) patients = 0.85¹¹, precision = 10%, level of significance = 5%.

All included participants were HIV (+ve) and between 13 to 60 years of age. While smokers (current or who have stopped it <10 years ago), BMI > 30 kg/m², known case of dyslipidemia before HIV diagnosis, those with positive family history for early coronary artery disease (<50 years) and/or lipid abnormalities were excluded from the study.

The HIV (+ve) status was considered only if found with positive antibodies through ELISA. Venous sample from HIV (+ve) patients for fasting lipid profile was drawn from peripheral veins. The participant was divided into ART and treatment naïve groups based on the therapeutic approach. Total serum Cholesterol, LDL-C, and HDL-C were assayed by Beckman Coulter AU680. Dyslipidemia

was defined as TC of more than or equal to 200 mg/dl, HDL-C of less than 40 mg/dl in men and less than 50 mg/dl in women, and LDL-C of more than 190 mg/dl.

All the related data, including patient demographic characteristics and lipid concentrations, were recorded using a structured questionnaire designed for the study purpose. The collected data were statistically analyzed using SPSS version 17.0. Quantitative variables like age, BMI, and fasting lipids levels were presented as means with standard deviation. While qualitative variables like age group, BMI categories, and gender, etc., were described as frequency and percentages. Independent sample T-test was used to compare the lipid profile of treatment naïve and ART group,

where $p < 0.05$ was considered statistically significant.

The study was approved by the ethical review committee of Shaheed Zulfiqar Ali Bhutto Medical University (Ref no: F.1-1/2017/ERB/SZABMU/325; Dated 18th December 2017). Written informed consent was obtained from all included patients.

Results

Two groups of patients were studied, the first group was HIV-infected patients receiving antiretroviral therapy, and the other one was the treatment naïve group. The baseline characteristics of the patients of both groups are given in table 1.

Table 1: Baseline characteristics of the patients of treatment naïve and ART group.

Variable	Treatment Naïve Group (n=50)	ART treatment Group (n=50)
	Mean ± SD	31.26±12.86
Age	13-19 years	9
	20-40 years	28
	41-60 years	13
Gender	Male	34
	Female	16
	Mean ± SD	21.45±3.37
BMI	≤ 25 kg/m ²	43
	> 25 kg/m ²	7
Type of ART	NRTI + NNRTI	-
	NRTI + PI	-
	NRTI + II	-
Duration of ART	3-6 months	-
	6-12 months	-
	> 12 months	-

Values are given as frequency and mean ± SD.

NRTI-Zidovudine, Abacavir, Lamivudine, Emtricitabine, and Tenofovir. NNRTI-Nevirapine and Efavirenz, Etravirine and Rilpivirine. PI-Protease Inhibitors (Lopinavir, Indinavir, Nelfinavir, Amprenavir and Ritonavir Darunavir and Alazanavir. II-Integrase Inhibitors – Raltegravir, Elvitegravir and Dolutegravir

There was no significant difference in the mean TC, TG, and HDL-C among the patients of the treatment naïve and ART group ($p > 0.05$). While the mean LDL-C was significantly high among the patients in the treatment naïve group than those receiving ART treatment, i.e., 88.24 ± 26.48 mg/dl vs. 78.80 ± 20.50 mg/dl ($p=0.049$). Eighteen HIV-infected patients of the ART-treated group and 20 of the treatment naïve group were diagnosed with dyslipidemia.

Table 2: Lipid Concentrations among patients of ART and treatment naïve group.

Lipid Profile	Total	Treatment Naïve	ART treatment	p-value
		Group	Group	
(Mean±SD)				
TC	174.7±52.1	167.76±62.61	181.80±38.25	0.179
≥ 200 mg/dl	30(30.0)	16(32.0)	14(28.0)	0.663
< 200 mg/dl	70(70.0)	34(68.0)	36(72.0)	
TG	130.05±25.74	131.10±24.94	129.00±26.74	0.686
> 150 mg/dl	21(21.0)	11(22.0)	10(20.0)	0.806
< 150 mg/dl	79(79.0)	39(78.0)	40(80.0)	
HDL-C	42.2±5.8	42.14±6.16	42.42±5.57	0.812
< 40 mg/dl	20(20.0)	11(22.0)	9(18.0)	0.619
≥ 40 mg/dl	80(80.0)	39(78.0)	41(82.0)	
LDL-C	83.5±24.0	88.24±26.48	78.80±20.50	0.049*
< 130 mg/dl	84(84.0)	39(78.0)	45(90.0)	0.102
≥ 130 mg/dl	16(16.0)	11(22.0)	5(10.0)	

TC-Total Cholesterol. HDL-C-High-Density Lipoprotein Cholesterol. LDL-C-Low-Density Lipoprotein Cholesterol.

*p<0.05 is considered statistically significant

Table 3: Factors associated with dyslipidemia.

Variable	TC ≥ 200	TG > 150	HDL-C < 40	LDL-C > 100	
	mg/dl	mg/dl	mg/dl	mg/dl	
Adjusted OR (95%CI)					
Gender	Male	1	1	1	
	Female	0.74(0.29-1.87)	1.29(0.37-4.48)	1.71(0.47-6.12)	0.33(0.09-1.21)
Age	13-19 years	1	1	1	
	20-40 years	0.27(0.062-1.20)	2.23(0.42-11.63)	4.04(0.63-25.77)	0.38(0.06-2.15)
	41-60 years	0.15(0.02-0.92)*	0.68(0.10-4.68)	6.34(0.86-46.62)	1.52(0.23-9.99)

*p<0.05 is considered significant.

Discussion

The therapeutic approach in relation to HIV has come a long way. By lowering acute episodes, improving patients' quality of life, and minimizing deaths, highly active ART has changed the infection trajectory. This heralded the start of a new era of HIV treatment and indicated a significant shift in the way HIV infection was previously managed¹⁸.

Combination antiretroviral therapy, widely used in clinical practice, has profoundly reduced HIV-associated morbidity and mortality rate and has turned HIV infection into a manageable chronic

disease¹⁹. Though, increased metabolic abnormalities, cardiovascular diseases, and associated mortalities have been reported among these patients^{18,20,21} but individualized approaches that incorporate quality-of-life issues and the assessment of potential cardiovascular risks are known to play an effective role in HIV management²².

Almost 38% of patients were diagnosed with dyslipidemia in this study, which is comparatively low than a similar study reporting dyslipidemia among 50% of HIV patients²³. While other studies from rural Cameroon, urban Southern Ethiopia,

and Tanzania reported a much higher frequency of dyslipidemia among these patients, i.e., 70.2%, 82.3%, and 76%, respectively²⁴⁻²⁶. Furthermore, the prevalence rate of hypertriglyceridemia, hypercholesterolemia, low HDL-C, and high LDL-C were 21%, 30%, 20%, and 16%, respectively. A similar Southern Ethiopian and Cameroonian study reported a comparatively higher frequency of hypertriglyceridemia (55.8% and 43.5%) and high LDL-C (33.6% and 46.4%)^{25,27}. Another Cameroonian study reported hypercholesterolemia in 29.8% HIV patients, hypertriglyceridemia (51.8%), low HDL-C (18.4%), and high LDL-C (33.3%)²⁸.

None of the studied factors were associated with increased risk of disturbances in the lipid profile, except patients aged 41-60 years had 0.15 times high risk of TC \geq 200 mg/dl than their counterparts ($p < 0.05$). It is known that the pro-atherogenic lipid concentrations increase with increasing age²⁶. Furthermore, a study reported that women are more likely to experience ART-induced metabolic adverse events as compared to men²⁹, but we found no significant association between gender and lipid disturbances.

Although differences exist between individuals of different demographic characteristics, lifestyles, and regions, the prevalence of dyslipidemia universally has been found to increase with aging and ART use. Dyslipidemia has been linked to HIV infection as well as the usage of antiretroviral drugs in HIV patients²⁵. Patients on ART shown to have an increased risk of developing metabolic abnormalities, such as raised TG and LDL values and lower HDL levels^{30,31}, that are in line with the present study results.

The present study also had certain limitations that need consideration; among them the major one was the sample size which was very small, affecting the precision of the odds ratios. Furthermore, the study's cross-sectional design made it impossible to assume any causality.

Conclusion

It is concluded from the study results that dyslipidemia is common among HIV-positive patients, characterized by high TG and low HDL, high total cholesterol, and elevated LDL. Screening for dyslipidemia in HIV-positive individuals, regardless of age, before and after starting HIV treatment should be considered routine. Further large-scale studies are required to determine the influence of various lipid abnormalities on the prognosis and quality of life of HIV/AIDS patients.

Conflicts of Interest

The authors have declared that no competing interests exist.

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