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Original Research Article

A Comparitive Study of Lipid Profile in Human Immunodeficiency Virus (HIV) Patients with and Without Haart Therapy. A Hospital Based Study in Govt General Hospital, Kadapa, YSR District, Andhra Pradesh.

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Abstract

Background: Acquired immune deficiency (AIDS) is retroviral disease caused by human immunodeficiency virus (HIV). AIDS is seen in all continents of the word. There were approximately 39 million people across the globe with HIV in 2022. Of these 37.5 million were adults, and 1.5 million were children (<15years). Antiretroviral drugs also have side effects like dyslipidemia of order of severity. Between 33 to 75% of patients with HIV infection receiving highly active antiretroviral therapy(HAART) develop a syndrome often referred to as lipodystrophy, consisting of elevations in plasma triglycerides(TGs), Total cholesterol(TC) and apoipoprote in B. HAART causes increase in low density lipoprotein(LDL). However, with protease inhibitors(PIs)-based therapies, HDL levels remain low and hypertriglyceridemia may be seen, giving rise to a distinctly atherogenic lipid profile.

Aim: The aim of our study is to see the Dyslipidemia in HIV patients with and without HAART therapy.

Material and Methods: A total of 150 subjects taken for study. The study was divided in to 3groups.Group-1: Healthy controls, Group-2: 50 newly diagnosed HIV patients and Group-3: HIV patients on ART. The age group of the subjects varied from 25-50 years.

Sample Collection: Blood samples were collected in ART centre at Government General Hospital, GGH, Kadapa, Andhra Pradesh.5ml of venous blood sample was collected in plane tube in the morning after an overnight fast. After collection, the sample was centrifuged and serum was analyzed for estimation of Total cholesterol, Triglycerides, High density lipoprotein(HDL) by using Semi-auto analyzer (Erba). Serum LDL cholesterol was estimated by using Friedewalds formula.

Statical Analysis: Data was entered in MS excel .The data was analyzed and consolidated as mean and standard deviation (SD). To analyze the statistical significance, we are using SPSS 23 software. The test probability of less than 0.05($P<0.05$) was considered as statistically significant.

Results: In the present study the mean serum value of Total cholesterol, LDL-cholesterol, Triglycerides are high in Group-2 compared to Group-1($P<0.0001$) and mean serum value of HDL-cholesterol is low in Group-2 compared to Group-1($P<0.0001$). The mean serum total cholesterol, LDL-cholesterol, Triglyceride value is high in Group-3 compared to Group-1 and the mean value of serum HDL-cholesterol is low in group-3 compared to Group-1 ($P<0.0001$). The mean value of serum Total cholesterol, LDL-cholesterol, Triglycerides significantly high in Group-3 compared to Group-2($p<0.0001$).The mean value of serum HDL-cholesterol is significantly low in Group-3 compared to Group-2.

Conclusion: We concluded that lipid profile can be a good index of disease progression in HIV infection. Significant dyslipidemia is present in HIV patients on antiretroviral therapy.

Keywords: Human immunodeficiency virus (HIV), Highly active antiretroviral therapy (HAART), Dyslipidemia, Cardiovascular risk

Introduction

Acquired immune deficiency (AIDS) is retroviral disease caused by human immunodeficiency virus(HIV).Two different forms of HIV, namely HIV-1 and HIV-2 have been isolated from AIDS patients.HIV-1 is more common, being found in AIDS patients of USA, Canada, Europe and Central Africa while HIV-2 is mainly found in West Africa. Transmission of AIDS essentially requires the exchange of body fluids (semen, vaginal secretions, blood, milk)containing the virus or virus-infected cells. There are three major routes of HIV transmission-sexual contact, parenteral inoculation, and from infected mothers to their newborns. The distribution of risk factors for AIDS transmission are as follows. Sex between men (homosexuals)-60%, Sex between men and women-15%, Intravenous drug abusers-15%, Transfusion of blood and blood products-6%. All others-4% [1].

AIDS is seen in all continents of the word. There were approximately 39 million people across the globe with HIV in 2022. Of these, 37.5 million were adults, and 1.5 million were children (<15years). In addition, 53% were women and girls. The number of people living with HIV(PLHIV) are estimated at around 24 lakhs in India [2]. Annual new infection (ANI) are estimated at 66,000 in 2022 in India [3]. Lipids constitute about 15-20% of the body weight in humans. Triacylglycerols(TG) are the most abundant lipids comprising 85-90% of body lipids. Plasma cholesterol is associated with different lipoprotein fractions: Low density lipoproteins (LDL), Very low density lipoprotein (VLDL),High density lipoprotein (HDL). Lipoproteins are molecular complexes that consist of lipids and proteins(conjugated proteins). 5 major classes of lipoproteins are identified, chylomicrons, Low density lipoproteins (LDL), High density lipoproteins (HDL), Very low density lipoproteins (VLDL), Free fatty acids-albumin complex.

Chylomicrons are synthesized in intestine, and transport exogenous (dietary) triacylglycerol to various tissues. Very low density lipoproteins (VLDL) are produced in liver and intestine and are responsible for the transport of endogenously synthesized triacylglycerols. Low density lipoproteins (LDL) are synthesized from VLDL in the blood circulation. They transport cholesterol from liver to extra hepatic tissues. High density lipoproteins (HDL) are mostly synthesized in liver. Three different fractions of HDL (1,2,3) can be identified by ultracentrifugation. HDL particles transport cholesterol from peripheral tissues to liver(reverse cholesterol transport). In healthy individuals, the total plasma cholesterol is rang of 150-200 mg/dl. The women have relatively low plasma cholesterol which is attributed to the hormones-estrogens. Cholesterol level increases with increasing age (in women particularly after menopause) and also in pregnancy. Increased in plasma cholesterol (>200mg/dl) concentration is known as hypercholesterolemia [4]. Lipid abnormalities are also seen in HIV infections that could be due to acute phase response induced by infection. Cytokine (Tumor necrosis factor (TNF), Interleukins and interferons) produced in an infection result in host response that causes lipid profile changes such as increased triglycerides and low HDL-cholesterol [5].

Antiretroviral drugs also have side effects like dyslipidemia of order of severity. Between 33 to 75% of patients with HIV infection receiving highly active antiretroviral therapy(HAART) develop a syndrome often referred to as lipodystrophy, consisting of elevations in plasma triglycerides (TGs), Total cholesterol (TC) and apolipoprotein B, as well as hyperinsulinemia and hyperglycemia. HAART causes increase in low density lipoprotein (LDL). However, with protease inhibitors (PIs)-based therapies, HDL levels remain low and hypertriglyceridemia may be seen, giving rise to a distinctly atherogenic lipid profile. In contrast, initiation of nonnucleoside reverse transcriptase inhibitor(NNRTI)-based HAART regimens has been shown to result in increases in high density lipoprotein(HDL) approximately 40% with, with increase in TC, LDL, and TGs also seen, although the TG increases are usually not as severe as those seen with some PIs. Increased insulin resistance and high prevalence of diabetes is a well-known side effect of exposure to HAART in HIV-infected individuals. All of these factors likely act in combination with dyslipidemia to increase overall cardiovascular risk for those infected with HIV[6]. AIM: The aim of our study is to see the dyslipidemia in HIV patients with and without HAART therapy.

Material and Methods:

Study Design : Case-control study

Study Setting : ART centre, GGH, Kadapa

Study Subjects : A total of 150 subjects were taken for this study and divided into 3 groups. Group-1: Healthy controls.

Group-2: 50 HIV – Newly diagnosed seropositive patients.

Ents (determined by ELISA).

Group-3: 50 HIV patients who are on antiretroviral drug for minimum 6 months (on ART) (includes 25 on are on TLE (Tenofovir+ Lamivudine +Efavirenz) regimen and 25 on ZLN regimen (Zidovidine+Lamivudine+ Nevirapine).

Study Period: 6 months from the approval from IEC.

The age group included individuals from 25-50 years.

Exclusion Criteria:

- Subjects with ischemic heart disease,
- Patients who are on lipid lowering drugs,
- Hepatic failure, Renal failure,
- Diabetic patients and Hypertensive patients, pregnant women excluded from the study.

Sample Collection: Blood samples were collected in ART centre at Government General Hospital, GGH, Kadapa, Andhra Pradesh.5ml of venous blood sample was collected in plane tube in the morning after an overnight fast. After collection, the sample was centrifuged and serum was analyzed for estimation of Total cholesterol by CHOD-PAP method[7], HDL cholesterol by cholesterol HDL precipitating reagent method [8], Triglycerides by GPO-TRINDER method [9] by using Semi-auto analyzer (Erba). Serum LDL cholesterol was estimated by using Friedewalds formula (LDL cholesterol= Total cholesterol-(HDL-holesterol + TG/ 5) [4].

Statistical Analysis: Data was entered in MS excel. The data was analyzed and consolidated as mean and standard deviation(SD). To analyze the statistical significance, we are using SPSS 23 software. The test probability of less than 0.05 ($P<0.05$) was considered as statistically significant. Results: In the present study ,the age group of the subjects varied from 25 -50 years. The mean age of healthy controls (group-1) was 37.3 And mean age of HIV patients (group-2) is 36.9 and mean age of HIV patients on ART (TLE regimen and ZLN regimen)(Group-3) is 38.3.

Table 1: Base line characteristics of study population

Characteristics	Group-1	Group-2	Group-3
Number of participants	50	50	50
Age(years)Mean ±SD	37.3±5.4	36.9±5.2	38.3±6.6
Sex(male/female)	28/22	28/22	28/22

In the present study the mean serum value of Total cholesterol, LDL-cholesterol, Triglycerides are high in Group-2 compared to Group-1 and mean serum value of HDL-cholesterol is low in Group-2 compared to Group-1 as shown in table-2.

Table 2: Revealed the lipid profile parameters among healthy controls (Group-1) and HIV patients(Group-2)

Parameters	Group-1	Group-2	t-value	p-value
Total cholesterol(mg/dl)	174.2±12.3	184.7±10.7		
HDL-cholesterol(mg/dl)	39.3±4.9	30.8±2.7	10.743	<0.0001 ESS
LDL-cholesterol(mg/dl)	107.8±12.2	119.2±11.0	4.9072	<0.0001 ESS
Triglycerides(mg/dl)	127.5±13.7	176.8±13.7	17.99	<0.000 ESS

ESS: Extremely statistically significant

The mean serum total cholesterol, LDL-cholesterol, Triglyceride value is high in Group-3 compared to Group-1 and the mean value of serum HDL-cholesterol is low in group-3 compared to Group-1 as shown in table-3.

Table 3: Revealed the lipid profile parameters among healthy controls (group-1) and HIV patients on TLE regimen(group-3)(in Mean ±Standard deviation)

Parameters	Group-1	Group-3	t-value	p-value
Total cholesterol(mg/dl)	174.2±12.3	184.7±10.7	6.482	<0.0001 ESS
HDL-cholesterol(mg/dl)	39.3±4.9	28.1±1.6	15.3641	<0.0001 ESS
LDL-cholesterol(mg/dl)	107.8±12.2	126.5±16.2	6.5202	<0.0001 ESS
Triglycerides(mg/dl)	127.5±13.7	189.4±10.3	25.536	<0.0001 ESS

ESS: Extremely statistically significant

The mean serum total cholesterol, Triglycerides, LDL-cholesterol value is high in Group-3 compared to Group-2 and mean serum HDL-cholesterol is low in Group-3 compared to Group-2 as shown in table-4.

Table 4: Revealed the lipid profile parameters among HIV patients (Group-2)and HIV patients on ART (group-3)

Parameters	Group-2	Group-3	t-value	p-value
Total cholesterol(mg/dl)	184.7±10.7	189.7±11.6	2.688	P=0.0084 SS
HDL-cholesterol(mg/dl)	30.8±2.7	28.1±1.6	6.0832	<0.0001 ESS
LDL-cholesterol(mg/dl)	119.2±11.0	126.5±16.2	2.6361	<0.0098 SS
Triglycerides(mg/dl)	176.8±13.7	189.4±10.3	25.536	<0.0081 SS

ESS: Extremely statistically significant; SS: Statistically significant

Discussion

The human immunodeficiency virus (HIV) pandemic has led to unprecedented consequences in global health statistics in the past three decades [10].

In the present study ,there is a significant increase of Total cholesterol, LDL-cholesterol, Triglycerides values in HIV patients (Group-2) compared to healthy controls (Group-1). Our study findings consistent with previous studies by Meena shivaji pawar et al [12], Jagjeet singh et al [6]. Hypertriglyceridemia is thus an indicator of advanced disease and severe immune impairment. It is associated with wasting syndrome, immune impairment and secondary infection. Cytokines such as IL-6,interferon-α and tumor necrosis factor (TNF) mediate acute phase response which causes an increase in VLDL and consequently a rise in triglycerides.

Reduced activity of lipoprotein lipase resulting in delayed clearance of lipoprotein as well as increased hepatic lipogenesis ,either by increased acid synthesis of fatty acid, re-esterification has shown to contribute to hypertriglyceridemia [5]. Most HIV infected patients develop multiple metabolic abnormalities including Insulin resistance, lipodystropy. Insulin is known to inhibit lipolysis in adipose tissue by inhibiting hormone sensitive lipase. Thus Insulin resistance that occurs in HIV infection will lead to increased lipolysis in adipose tissue and consequently an increase in free fatty acids, Triglycerides and Cholesterol in plasma. Hypercholesterolemia is usually associated with elevated levels of cytokines [12]. There is significant decrease in mean serum value of HDL-cholesterol in HIV patients (Group-2) compared to healthy controls (Group-1)($p<0.0001$).

The obtained results was consistent with that reported by Jajeet Singh et al [6], Meena shivaji pawar et al [12]. HDL is a good marker of disease progression. This could be due increase cholesterol ester transfer protein(CETP) activity resulting in increased transfer of cholesterol esters from HDL increase, apo-B containing lipoproteins. Consequently, HDL particle become less protective against atherosclerosis [5]. Specifically ,the reduction of HDL likely occurs as result of an activation of the immune system in early HIV-infection, which promotes an increase in lipid peroxidation, inflammatory cytokine production ,and alterations in the reverse cholesterol transport. This process promotes an imbalance in the antioxidant system, a decrease in the production of anti-inflammatory cytokines, which increase the chance of developing atherosclerotic disease. As a result of the inflammatory process initiated by viral infection, the stimulation of endothelial lipase and phospholipaseA2 occurs, which in turn can reduce HDL concentration [13]. Further reduction in HDL –cholesterol could be impair prostaglandin I stabilization and thus increase the risk of Thrombotic events[5].

Dyslipidemia is responsible for more than half of the global ischemic heart disease(IHD) and more than 4 million deaths annually. Assessing the prevalence of dyslipidemia can be crucial in predicting the future disease development and possible intervention strategies. Dyslipidemia is an imbalance of blood lipids associated with elevated concentrations of Total cholesterol, LDL-cholesterol, Triglycerides and low HDL-cholesterol [14].

The prevalence of Dyslipidemia patients on antiretroviral therapy is very high [15]. In the present study, the mean serum Total cholesterol, LDL-cholesterol, Triglycerides value is high in HIV patients compared to ART patients. Our study findings consistent with previous studies by Jajeet singh et al.[6], Indumathi V et al.[11]

Hypertriglyceridemia in patients on antiretroviral therapy is common among patients taking protease inhibitors as they increase the hepatic triglyceride synthesis by increased expression of key enzymes involved in its synthesis. There is impaired uptake of triglycerides in the adipocytes which leads to increase in their levels. Antiretroviral drugs are responsible for reduced expression of LDL receptors, thus reducing fat storage and increasing free fatty acid plasma levels. Nucleoside reverse transcriptase inhibitors(NRTIs)class of drugs is associated with a worst lipid profile parameters. They cause increases in Total cholesterol, Triglycerides and LDL [15]. The non-nucleoside reverse transcriptase inhibitors(NNRTs) –based HAART, Zidovudine, Stavudine or Lamividine, have become associated with the occurrence of dyslipidemia [13].

The mean value of serum HDL-cholesterol was significantly low in HIV patients on ART(Group-3) compared to HIV patients (Group-2) (P <0.0001). Our study finding consistent with previous studies by Jagjeet Singh et al.[6], Manoj Kumar et al [16]. Protease inhibitors, particularly indinavir and lopinavir, were commonly associated with reduced HDL-cholesterol [17].

The presence of an atherogenic lipid profile in HIV patients on antiretroviral therapy makes these patients more susceptible to cardiovascular events. A longer duration ART is associated with greater chances coronary artery stenosis due to dyslipidemia and due to the metabolic effects of HIV infection. This has lead to increased concerns of myocardial infarction in HIV patients [15]

Conclusion:

HIV infected patient exhibits multiple abnormalities in lipid metabolism. Highly active antiretroviral therapy (HAART) regimens have shown to cause a metabolic syndrome such as lipodystrophy therapy, lipoatrophy and dyslipidemia in a high proportion of HIV infected patients. In the present study the mean serum total cholesterol, LDL-cholesterol, Triglyceride levels are high in HIV patients on ART(HAART) compared to HIV patients. Lipid profile results can therefore be good index for disease progression, intervention and management of HIV patients.

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