

Lipid Profile among Art Treated and Untreated Patients in HIV Positive Cases

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Abstract

HAART treated or untreated HIV Seropositive cases have dyslipidaemia. In untreated HIV infection, most of the ATP is used in the reverse transcription process in attaining morphism of the host cell. The aim of the study was to find the lipid profile pattern in treated HIV patients after shorter period of time with ART (First line of treatment i.e. zidovudine, lamuvudine and Nevirapine) and comparing them against HIV infected untreated individuals and controls within our locality. Subject field of HIV Seropositive cases (n=84) and age and sex matched healthy non-HIV cases as controls (n=47). Comparison between the HIV infected (n=42), HIV infected ART treated (n=42) and controls were significant (p 0.000) for fasting cholesterol, triacylglycerols (p 0.000) and HDLc (p 0.000) and LDLc (p 0.000). Insignificant when TAG compared controls to HIV infected ART untreated subjects. Statistical significance in between sexes within untreated patients' lipid profile in HDLc (35 ± 3.8 against 37.4 ± 3.5) and LDLc (48.0 ± 8.3 against 38.0 ± 7.2). Patients infected with HIV, constantly screened for lipid abnormalities when ART treated or untreated and carefully prescribe an anti retroviral treatment regime which will undeniably support in supervision of dyslipidaemia in HIV seropositive patients in future.

Keywords: HIV, Dyslipidaemia, HAART

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Introduction

Human Immunodeficiency Virus (HIV) is a pandemic disease. In 1986, the first case of HIV was diagnosed in India [1]. The disease has shown its full blow since then, affecting people all around the country. The government of India estimates 2.4 million Indians are living with HIV infection. The percentage distribution of HIV infection by age is estimated at 4.4% among children under the age of 15 years, 82.4% among adults aged 15-49 years and the remaining 13.2% among persons above over 50 years of age. Of all HIV infections, 0.8 million are among women. Approximately 500,000 HIV infected people are in the state of Andhra Pradesh in India [2]. Testing positive for HIV in Andhra Pradesh districts with the highest and the lowest prevalence were Guntur district (26.6%) and Medak district (0.4%) [3]. About 0.1 million were dead according to the report of national AIDS control organization (NACO) due to acquired immunodeficiency syndrome (AIDS) related complications in the 2011-12 report in India [2].

Immune cells during HIV infection, release number of inflammatory mediators (cytokines) which hamper the T- cell

proliferation, suppress the cell mediated immune function and deplete the cluster of differentiation -4 (CD4) cells [4,5] which is a characteristic feature of the disease.

Various studies were performed on HIV infection vis-à-vis the lipid profile across the globe in ART untreated HIV Seropositive subjects and proclaim dyslipidemia [5-10]. Grunfeld et al. reported hepatic citrate levels are increased due to cytokines like TNF, IL-1, and IL-6, an allosteric activator of acetyl CoA carboxylase which is a rate limiting enzyme in fatty acid synthesis [11].

The introduction of antiretroviral therapy (ART) regime which consists of combination of nucleoside reverse transcriptase inhibitors (NRTI), non nucleoside reverse transcriptase inhibitors (NNRTI) and Protease inhibitors (PIs) delayed the progression of the disease, increased the life expectancy of HIV Seropositive cases. Dyslipidaemia in HIV patients receiving ART treatment is more obvious [5,12,13]. It has been the confounding factor during the treatment or before the treatment and is more prone to cardiac disease risks and reduced quality of life [4,13-15].

The aim of this study was to find the lipid profile pattern in

treated HIV patients after shorter period of time with ART (First line of treatment i.e. zidovudine, lamivudine and Nevirapine) and comparing them against HIV infected untreated individuals and controls within our locality. Once infected with HIV the subject should be constantly screened either under treatment or without treatment whether in developed or developing country.

Clinical Material and Methods

Study population and criteria

Integrated counseling testing center (ICTC) outpatient departments were introduced to help, control and prevent the spread of HIV infection in the nation under the guidelines of the NACO program [16] of the country. This center in Mamata medical colleges and general hospital, Khammam, India provides HIV care and treatment to the HIV infected individuals. The total OPD strength was over one thousand patients per year with an average of 500 new cases. The study was conducted between March to July, 2010. The Study was divided into HIV seropositive cases (n=84) along with age and gender matched healthy non-HIV cases as controls (n=47). Study group patients were positive for HIV in serum (positivity was determined by ELISA) and included in the written report.

An inclusion criterion for HIV infected ART treated subjects (<350cells/ cu mm, n=42) was a minimum of four months on ART medication. ART untreated patients (>350cells/ cu mm, n=42) were newly diagnosed. On the other hand, control group was composed of healthy HIV Seronegative, non smokers recruited from the student population and college staff. The subjects with diabetes mellitus, hypertension, obesity and alcohol abusers, smokers along with patients on multivitamin, antioxidant supplements and hyperlipidemic drugs were excluded.

Methodology

Blood was collected after a 12 hrs fast; 5 ml blood was taken through venipuncture in the plain, K₃ EDTA and fluoride containing test tubes. These were allowed for one hour to settle down and centrifuged for ten minutes at 3000 RPM. Analysis of serum for lipid profile, plasma for CD4 count and FPG were done on the day of collection. Fasting plasma glucose was checked by the GOD / POD

method. TC, TAG and HDL cholesterol were quantified by CHOD/PAP, GPO/PAP, and PEG-precipitation methods respectively. Kits were obtained from Transasia Biomedicals, Malpur, Solan (HP), India in collaboration with ERBA Mannheim, Germany. Friedwalds formula was used to estimate LDLc [17].

Ethical clearance & statistical data analysis

Ethical clearance was obtained from the institutional ethical committee. Participation was voluntary and informed written consent was obtained from each study subject. Non normal distribution variables were applied Mann-Whitney rank sum test and normal distributed variables by 't' test. One way ANOVA test was applied when three or more groups' means were compared. Test of significance was <0.05.

Results

The **Table 1** show altered total cholesterol, TAG, HDL cholesterol, LDL cholesterol were significant when compared controls against HIV infected and controls against HIV infected ART treated subjects (<0.0001). Insignificant decrease was found in TAG when HIV infected subject compared with HIV infected ART treated subjects. Correlation of TC, HDLc and TAG as the CD4 count lowered in untreated HIV infected subjects with pearson's coefficient of 0.955, 0.877 and -0.907. Between the sexes (**Table 2**) in group HIV infected subjects when compared within HDLc (p=0.043) and LDLc (P=0.0002) were significant, insignificant in the rest of variables and between the sexes within the variables of HIV infected ART treated subjects.

Discussion

The study consisted of 47 HIV Seronegative age and sex matched controls, 42 HIV infected ART untreated subjects and 42 HIV infected ART treated subjects. The mean CD4 count in the HIV ART untreated subjects was 170.88 ± 70.18 and after four months of treatment the mean CD4 count was 262 ± 32.12. We observed low cholesterol, HDLc, LDLc and an increase in TAG as the CD4 count decreased in HIV infected subjects (ART untreated) when compared against controls. Males have higher cholesterol, TAG, LDLc and lower HDL cholesterol than females when the values between sexes compared in HIV infected subjects (ART untreated).

Table 1 Lipid profile of controls and HIV seropositive cases.

Variable	Controls (n=47)	HIV infected ART untreated (n=42), >350 CD4 cells/mm ³	HIV infected ART treated (n=42), <350 CD4 cells/mm ³	P Value (ANOVA)
Total cholesterol (mg/dl)	137.8 ± 7.0	113.5.1 ± 18.01	149.9 ± 14.7	0.000
Triacylglycerols (mg/dl)	121.1 ± 13.9	163.7 ± 28.5	148.2 ± 32.1	0.000
HDL cholesterol (mg/dl)	42.0 ± 1.7	36.0 ± 3.8	40.9 ± 1.9	0.000
LDL cholesterol (mg/dl)	73.4 ± 7.8	65.4 ± 22.8	124.3 ± 31.8	0.000

Table 2 Lipid profile between sexes of HIV seropositive groups.

Variable	HIV infected ART untreated		HIV infected ART treated	
	Male N=25	Female N=17	Male N=24	Female N=18
Total cholesterol (mg/dl)	118.2 ± 17.7	112.6 ± 18.7	150.0 ± 13.9	149.5 ± 16.5
Triacylglycerols (mg/dl)	169.8 ± 30.3	155.7 ± 24.5	149.9 ± 30.7	147.1 ± 35.3
HDL cholesterol (mg/dl)	35 ± 3.8	37.4 ± 3.5	40.7 ± 2.0	41.1 ± 1.8
LDL cholesterol (mg/dl)	48.0 ± 8.3	38.0 ± 7.2	129.2 ± 16.2	121.1 ± 13.1

A study [10] observed no change in TC, HDLc and significant increase in TAG and LDL-c as the CD4 count decreased in HIV infected ART untreated subjects compared to controls. These findings are opposite to that of our study except in TAG levels as we observed decreased total cholesterol, HDL cholesterol, LDL cholesterol as CD4 count decreased in HIV infected ART untreated subjects. Our observations are in agreement with other studies in which significant decrease in TC, HDLc and LDLc in HIV/ AIDS cases when compared against controls [5,6]. In a study conducted in Ghana [8] on serum lipid profiling in highly active retroviral therapy naaive HIV positive patients, showed similar significant increase in TAG, decrease in TC, HDL-c and LDL-c when compared to control [7]. But the studies [9,18] found higher levels of LDL-c in HIV infected ART untreated subjects when compared to controls.

Our study observed increase in TC, TAG, significant increase in LDLc and decrease in HDLc when compared between the sexes within HIV infected ART untreated subjects, which were similar to the findings of a study on effect of highly active anti-retroviral therapy on lipid profile in a human immunodeficiency virus infected Nigerian population [19]. The finding of our study in TC in male sex is opposite to that of Shor- Posner et al., where hypocholesterolemia was found in male than female.

The possible explanation for low levels of TC, HDLc and LDLc in HIV infected ART untreated subjects have been associated with β -2 microglobulin. Some studies attributed the increase in TAG to improper clearance of lipoproteins, increase in IFN- α and altered plasma HDL-C levels [20,21]. A variation in LDL-c is due to the fact of degree of immunosuppression which has been observed in some studies stating that HIV infection affect the TC first, then HDLc, followed by LDLc and later TAG [18].

On the contrary our findings show significant increase in TC, HDLc, LDLc and decrease in TG in HIV infected ART treated subjects when compared against HIV infected ART untreated subjects. Not a significant increase was seen between sexes when compared in the group ART treated HIV infected subjects. ART treated males had significantly higher serum TAG and lower serum HDL-c levels than females A similar pattern was seen to that of a study conducted by Calza et al. [22]. Further study by Khiangte et al. [23] observed significant higher TC, TAG and HDLc in HAART group when compared to no-HAART group. A study on effect of antiretroviral therapy on lipid profile in HIV patients in Nigeria

observed significant lower levels of HDLc in HIV infected patients on ART when compared to controls [24]. In another study on HIV infection receiving protease inhibitors for a median period of 22.1 months showed higher TC, TAG, LDLc and lower HDLc level when compared to controls [25]. This finding was opposite to our observation. However HIV infected ART treated subjects in our study did not receive any PIs and were on first line of treatment as mentioned in the introduction for a period of four months. Nevirapine is considered as less atherogenic [26] and increases the HDLc which assists in reverse cholesterol transport to the liver by ingress of extrahepatic cholesterol into the HDL₂ through ATP binding cassette (ABC-1) protein transporter from the tissues than PI regime.

Though our study includes the data of HIV positive infected who were receiving ART treatment for four months period. The observations in our study are in agreement with the other countries studies and hold a good conjunction with altered lipid profile in HIV Infected subjects whether on ART or not on ART. The dyslipidaemia in ART untreated or in ART treated HIV infected individuals is an important factor in cardiovascular disease risk factors in HIV infected individuals. Health care professionals must provide utmost care in continuing a drug regime of whatever kind if patient is subjected on ART with or without PIs and should constantly watch the lipid status of HIV infected individual whether he is on treatment or not on treatment. ART treated or untreated in HIV Seropositive subjects showed altered lipid profile when compared to apparently healthy controls in our report. As a result, polyunsaturated fatty acids are more prone to be attacked by ROS, making them fit for peroxidation which may result in more oxidative cellular damage. Nevirapine (NNTRI) can be used, and is known to shield against peroxidation. Such studies could be used in ensuing supervision by providing appropriate therapy which would help in bringing down the death rate due to dyslipidaemia in HIV seropositive patients in future.

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Conflict of Interest

Our team does not possess any conflict of interest to disclose.

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