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Impact of BMI and CD_4^+ count on lipid profile among newly diagnosed HIV patients: A hospital-based study in a medical college from India

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Abstract
The relationship between lipid profile, BMI and CD_4^+ count is not well understood among HIV infected male and female individuals. The purpose of this study was to understand the lipid profile parameters along with the BMI and CD_4^+ cell count of HIV infected participants and also to find the impact of sexual dimorphism in it. The present cross-sectional study assessed the lipid profile, BMI and CD_4^+ status of 100 HIV-infected and 100 HIV-non-infected individuals from the Jangalmahal areas and adjacent areas of three districts of West Bengal attending the Midnapore Medical College and Hospital. The changes in serum TC, TG, HDL, VLDL were insignificant when compared between HIV^+ and HIV^- cases. Significantly higher levels of LDL among female positive participants were observed. A negative correlation between BMI and LDL was established among infected females. LDL level was increased proportional to the increase in CD_4^+ cells particularly for female individuals. The changes in lipid-profile may be a good marker of disease progression in HIV infected females.

Keywords: lipid profile, CD_4^+cell count, HIV positive patients, AIDS, antiretroviral therapy

Introduction
Human immunodeficiency virus (HIV) and the syndrome of opportunistic illnesses generally characterize late-stage HIV disease, i.e. immunodeficiency syndrome (AIDS). HIV/AIDS is responsible for 35 million deaths so far [1]. Recent reports revealed that nearly 36.7 million people are living with HIV infection and nearly 1.8 million people have been newly infected in 2016 throughout the globe [1]. Thus, it has become a serious public health issues all over the world [2]. Hypocholesterolaemia with or without hypertriglyceridaemia were reported in HIV infected males [3-5]. BMI is reflected as an important predictor of HIV/AIDS. Low body mass index (defined as BMI<18.5) may reflect both HIV/AIDS disease progression and under nutrition. Low BMI strongly predicts mortality independent of CD_4^+-lymphocyte counts at the time of diagnosis and enrollment [6-7]. Depression is a key factor, it has been shown to be associated with reduced dietary intake in adults living with HIV [8]. A critical association was established between HIV/AIDS disease progression, health-related outcomes, and BMI for understanding the factors associated with low BMI at enrollment into HIV care. During the course of HIV infection, the endocrinal, metabolic and nutritional disturbances are common. A greater number of HIV population are affected by multiple metabolic abnormalities dominated by dyslipidaemia, lipodystrophy and insulin resistance [9]. Insulin is recognized to impede lipolysis in adipose tissue by inhibiting hormone sensitive lipase. Thus, HIV patients with insulin resistance have a higher degree of adipose tissue lipolysis with an increase in free plasma fatty acid, cholesterol and triglycerides. Reduced numbers of CD_4^+ lymphocyte in HIV infection have been accompanied with low insulin levels and evidence of insulin resistance. Metabolic disturbances are common factors in the HIV-infected patients and are incriminated to be risk factors of accelerated atherosclerosis and cardiovascular diseases and altered lipid metabolism. These are known to have adverse effect on immune processes [10]. Foulkes *et al*. observed a racial variations of serum lipid levels in HIV affected individuals [11].
A study by Crook *et al*. showed that hypercholesterolemia, hypertriglyceridaemia and low plasma HDL-cholesterol are the common consequences of HIV infection [12]. But another study argued about the absence of a significant difference in low-density lipoprotein and total cholesterol between HIV-infected and non-infected healthy women. Keeping in view of the various biochemical abnormalities associated with lipid metabolism the present study is an attempt to examine whether any change in lipid profile exists in HIV positive patients of both sexes and also to find the impact of nutritional status, disease progression on lipid profile in the varied HIV state.

Methods
Study Area: This hospital based cross sectional study was conducted at the Department of Biochemistry of the Midnapore Medical College and Hospital, Midnapore, West Bengal, India during August 2014 to September 2015. However, the suspected individuals came from Jangalmahal areas and adjacent areas of West Medinipur, Bankura and Purulia districts of West Bengal for medical treatment in this hospital as a first point of contact.

Human Participants: The randomly selected sample size for this study was 200; of which 100 individuals were under the category of HIV positive group and the rest of the 100 participants were in the HIV negative group.

Ethical issue and inclusion criteria: Institutional Ethical permission was obtained prior to the study. Confidentiality was assured to all participants. The participants, who consented to participate in the study following the explanation of the objectives of the study were enrolled for blood sample collection. The participants who had an indeterminate HIV test result, with incomplete evaluation and whose age was less than 15 years or greater than 50 years were excluded from the study.

Anthropometric Measurements: All anthropometric measurements were performed by trained investigators using the standard techniques [13]. All the equipments were checked regularly to minimize random errors. Height was measured to the nearest 0.1 cm using Martin's anthropometer. Body weight of lightly-clothed subjects was recorded to the nearest 0.1 kg on a digital weighing scale. Body mass index (BMI) was computed using the following standard equations (Park 2014), BMI (kg/m^2) = Weight (kg) / $height^2$ (m^2). Nutritional status was evaluated using internationally accepted World Health Organization BMI (kg/m^2) guidelines (WHO 1995). The following cut-off points were used: Underweight: BMI< 18.5; Normal: BMI = 18.5 - 24.9; Overweight: BMI > 25.0. Chest circumference (CC) was measured following standard method.

Blood Sample collection and test procedure: Blood samples were collected in two sets of sterile test tubes from the participants in Dept. of Biochemistry, Midnapore Medical College and Hospital. The obtained serum sample from one set of test tube was used for HIV diagnosis by ELISA rapid test. The lipid profile was analyzed by the standard procedure from the serum sample. Total cholesterol (TC), triglycerides (TG) and high-density lipoprotein-cholesterol (HDL-C) were analyzed enzymatically using kits obtained from Randox Laboratories Limited. Low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) were calculated by the following formula**:**

VLDL=TG/5

LDL = total cholesterol – (triglycerides/5) – HDL

The remaining blood from other set of test tubes was used for CD_4^+-lymphocyte count, by Fluorescence Activated Cell Sorter (FACS) system.

Statistical Analysis

The data were analyzed using Statistical Package (SPSS, version 17), Data were presented as number (percentage) or mean ± SD as appropriate. The differences in means of various parameters between negative and positive groups were compared using independent sample t- test. The level of significance was determined at 5 percent ($p<0.05$).

Results

This study included data on 100 HIV positive and 100 HIV negative participants. The mean age of female and male HIV-negative participants was 27.26±4.81 and 28.56±5.60 respectively, that of HIV-positive female and male were 31.92±9.73 and 36.52±7.68 years respectively. The highest number of HIV-positive individuals (male 58% and female 36%) were found in the group of >35 years of both sexes (Table 1).

Table 1: Age wise distribution of the participants

Age (years)	Female		Male	
	HIV Negative	HIV Positive	HIV Negative	HIV Positive
<25	22(44.00)	14(28.00)	20(40.00)	4(8.00)
25-35	26(52.00)	18(36.00)	26(52.00)	17(34.00)
>35	2(4.00)	18(36.00)	4(8.00)	29(58.00)
Total	50 (100.00)	50 (100.00)	50 (100.00)	50 (100.00)
χ^2test	χ^2=16.032; P<0.001		χ^2=31.490; P<0.001	

In this present study the CD_4^+ lymphocyte count ranged from zero to 1274 cells/mm^3 and was significantly different in both male and female subjects of both the groups ($P<0.05$). It was noted that the TC, TGL, LDL and VLDL were reduced among the HIV positive female participants than that of the HIV negative female, although the significant reduction was observed only in case of LDL level. But, while comparing the male HIV positive and negative participants, reduction of all lipids in the serum viz.TC, TGL, HDL, VLDL were noticed except LDL level. Here the LDL level was elevated (Table 2).

Table 2: Anthropometric and Biochemical parameters among HIV positive and negative participants

Parameters	Female		Male	
	HIV Negative	HIV Positive	HIV Negative	HIV Positive
Height (cm)	146.67±10.66	147.62±11.09	164.13±5.30	165.85±11.88
Weight (kg)	45.20±3.49	41.26±7.17***	56.04±6.37	51.64±8.87**
BMI (kg/m^2)	21.36±3.79	19.01±3.29***	20.84±2.52	18.76±2.34***
CC(cm)	83.26±3.45	80.98±7.14*	91.90±4.41	88.34±5.16***
CD_4^+ (µ/l)	995.32±101.62	381.66±191.14***	936.82±116.99	343.34±188.10***
TC (mg/dl)	162.42±32.68	150.86±36	156.76±38.86	153.58±31.97
TGL (mg/dl)	157.38±44.44	139.00±49.49	169.52±64.40	154.74±40.47
HDL (mg/dl)	35.64±8.43	39.12±13.13	44.62±9.66	43.88±10.89
LDL (mg/dl)	95.30±30.99	82.18±34.47*	78.27±35.37	78.79±32.82
VLDL (mg/dl)	31.48±8.89	28.53±10.59	33.81±12.54	30.90±8.04

Statistical significance at *P<0.05; **P<0.01; ***P<0.001

Table 3: Distribution of subject according to BMI of HIV positive and negative participants

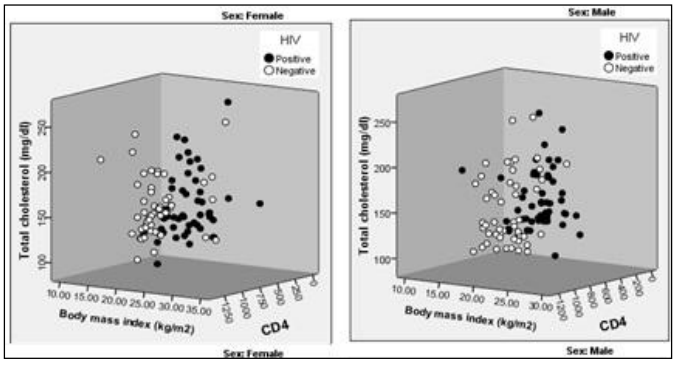
BMI	Female		Male	
	HIV Negative	HIV Positive	HIV Negative	HIV Positive
Underweight	6 (12.00)	21 (42.00)	10 (20.00)	27 (54.00)
Normal	44 (88.00)	29 (58.00)	37 (74.00)	23 (46.00)
Overweight	0 (0.00)	0 (0.00)	3 (6.00)	0 (0.00)
χ^2test	χ^2=11.416; P<0.001		χ^2=14.078; P<0.001	

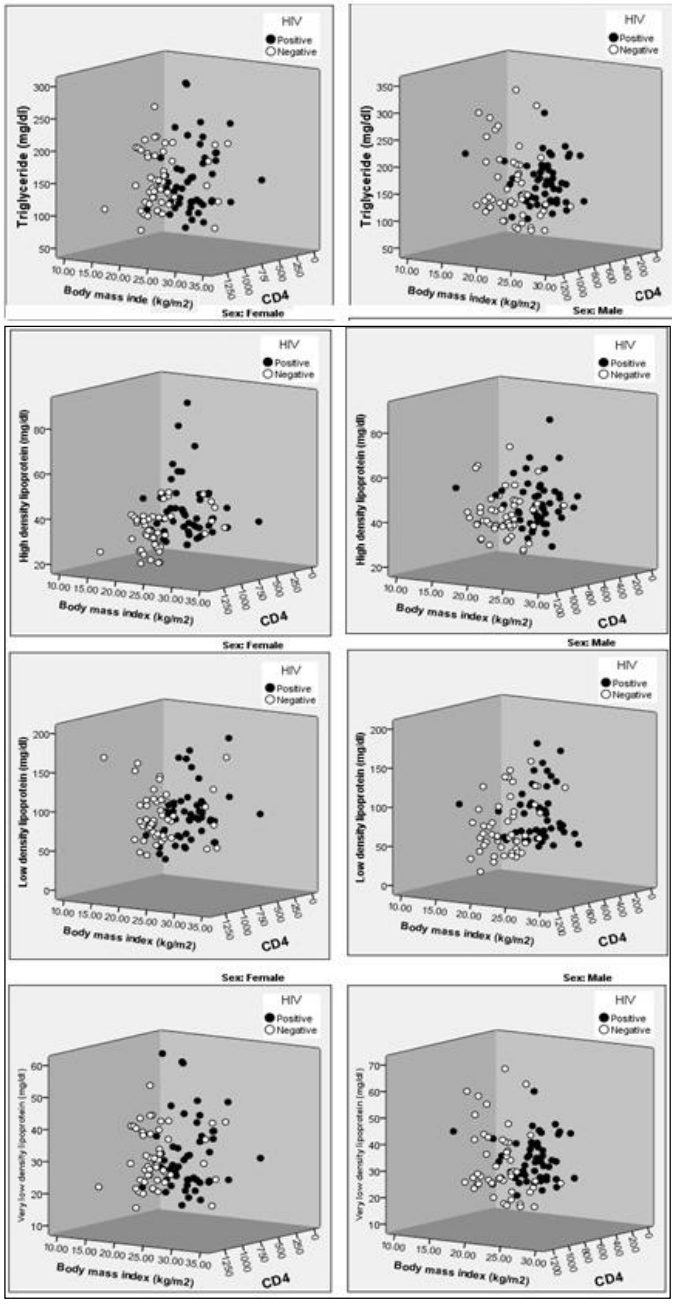
It was noted that overall 27% of female and 37% of male were under the category of the underweight group (Table 3). The 54% of HIV positive male and 42% of HIV positive female were from the underweight class. Nutritional status is one of the major factors for the mortality among the HIV positive patients. In this study, while comparing the body weight and BMI, it was being noticed that the body weight and BMI were significantly lower in case of HIV positive participants than that of the HIV negative participants of both sexes (Table 2). It was also observed that the prevalence of undernutrition was higher among the HIV positive participants than the HIV negative one (Table 3). The Odd ratio showed that HIV infected female and male were 5.31 and 4.34 times more prone to underweight respectively. While studying the Pearson product moment correlation between BMI and the lipids viz. TC, HDL, LDL, VLDL and TG among the HIV positive male and female, it was being observed that only TC and LDL among the female participants showed a significant positive association with the BMI (Table 4). Nutritional status (BMI) and CD_4^+ wise distributions of male and female total cholesterol data are shown in a typical scattered plot (Figure 1). This figure clearly showed that all the lipid parameters of the HIV positive female were too much scattered than the HIV negative individuals.

Table 4: Correlation between BMI (kg/m^2) and different lipid parameters among HIV Positive group

Variables	Female	Male
TC (mg/dl)	0.305*	0.053
TGL (mg/dl)	0.037	0.03
HDL (mg/dl)	-0.03	0.126
LDL (mg/dl)	0.333*	0.005
VLDL (mg/dl)	0.038	0.051

Statistical significance at *P<0.05





LDL level was negatively associated with CD_4^+ in the female

Fig 1: Nutritional status (BMI) and CD4 state wise dispersion pattern in female and male data from different groups of cholesterol level.

Discussion

The study group consisted of 100 HIV positive and 100 HIV negative participants explored no significant changes in lipid profile between the HIV positive and negative participants. group. Previous study established that patients with AIDS show an intense abnormality in their total lipid concentrations in plasma [14].

A few authors suggested that lipid related disorders are commonly progressed with an increase of immunological

deficiency and development of HIV infection [15-16]. Previous study observed [17] significant reduction of CD_4^+ cells in HIV/AIDS compared to controls and highlighted significantly decreased levels of TC, HDL-C and LDL-C in AIDS cases compared to controls which did not confirm by the findings of the current study where we observed that at the preliminary stage of infection there was no changes in TC, HDL-C but significantly lower levels of LDL-C in female compared to controls. A study reported that HIV sero-conversion is associated with the decreased TC, HDL-C and LDL-C concentrations [18]. Another study suggested that the alterations in cholesterol metabolism in HIV-infected patients could be explained by lipid peroxidation [19]. The cytokine tumor necrosis factor (TNF)-α plays a role in plasma lipoprotein peroxidation in HIV-infected patients by stimulating the production of reactive oxygen species [20]. These modifications might have major effects on the immune system.

Further study conducted by Khiangte *et al*., on the correlation between the changes in lipid profile and the progression of HIV infection also observed significantly decrease in TC, HDL-C, LDL-C with associated increase in VLDL-C along with significant reductions in CD_4^+ cell count as the disease progressed gradually [21]. The observations made in this study showed no changes in TC and HDL-C levels among positive cases when compared to HIV negative individuals. The changes were proportional to the lowering of CD_4^+-lymphocyte counts, which reflect the severity of the infections. A study conducted by Khiangte *et al*. showed that HDL-C level decreased as the disease progressed parallel with the deterioration of CD_4^+ count [20].

The HIV infection can lead to malnutrition and the patient suffers from protein loss and weight loss that may have an important role in the changing of the plasma lipid profile levels [22]. Various infections, which occur as a result of a weakened immune system in HIV-infected people; and can affect appetite and the ability to eat. Diarrhea could lead to malabsorption of fat from food. HDL cholesterol, which is mainly supplied by fat from food will therefore be reduced as the disease progresses. Crook and Mir reported that LDL cholesterol significantly changed in HIV-positive group compared to seronegative controls. The present study also indicates the similar findings in case of female but not for the male [12].

HIV infection affects several key processes in regulating the levels of lipids and in conjunction with tumor necrosis factor (TNF) and other cytokines and this influences lypolysis and insulin resistance during infection [9]. As insulin sensitivity decreases in HIV-infected subjects along with reduction in CD_4^+ counts, uptake of glucose into skeletal muscle. This finally resulted in an increased circulatory level of free fatty acid and reduced storage of triglycerides in adipose tissues. Thus, higher triglyceride levels are observed amongst sero-postives compared to the seronegative controls [23]. This finding is consistent with this report where HIV/AIDS is characterized by high prevalence of hypertriglyceridaemia and hypercholesterolemia [3]. This indicates decreased cholesterol and cholesterol containing lipoprotein in both AIDS and HIV infection precede the appearance of hypertriglyceridaemia.

The development of AIDS, the subsequent increase in interferon (IFN) may have contributed to increase in plasma TG levels by decreasing the clearance of plasma TG [3]. Findings showed that INF and interleukin increased plasma TG levels by stimulating hepatic lipogenesis and that IFN and interleukin-6 also increase hepatic lipogenesis [24]. VLDLs are composed predominantly of triglycerides. Most LDL particles are derived from VLDL [25]. This is seen in the concomitant increase in LDL-C in HIV-positive subjects as the levels of CD_4^+ reduce. The presence of opportunistic infections lipid parameters were influenced and concluded HIV infection is associated with dyslipidaemia, and becomes increasingly unbearable as immunodeficiency progresses.

In the early stages of HIV infection HDL-C was found to be lower than in controls, while TG and the atherogenicity index increased and TC and LDL-C decreased in the advanced stages of immunodeficiency. The decrease CD_4^+ count among the patient the severity of the HIV infection increases in the body. The negative oxidative stress, ketogenesis and fat emulsification are common phenomenon in this stage.

Conclusion

This study found that the serum LDL was increased with the increasing body weight and BMI among the female HIV+ patients, but no such association was observed in case of TC, TG, HDL and VLDL. The fat homeostasis is severely affected among the HIV infected persons. The atherogenic lipids; LDL, VLDL and TG have been found to increase as the CD_4^+ T-lymphocyte count of HIV positive participants decreases. Levels of good cholesterols (HDL) reduce as the disease progresses. Subjects with CD_4^+ T- lymphocyte count of < 200 cells/µl were at the highest risk of coronary heart disease since this group showed the highest level of dyslipidaemia. Lipid profile can be a good index of disease progression in HIV/AIDS patients. There is a need for proper check on lipid levels as the CD_4^+ count reduces with infection states. This will help the doctors to choose the type of antiretroviral therapy to administer to the patients as certain combinations of these drugs increase the levels of these atherogenic lipid.

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