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## STUDY OF LIPID PROFILE IN NEWLY DIAGNOSED HIV POSITIVE PATIENTS IN CORRELATION WITH CD4+COUNT

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**ABSTRACT:** Human Immunodeficiency Virus (HIV) is the causative agent for Acquired Immuno Deficiency Syndrome (AIDS). AIDS is a fatal illness which burns down the body's immune system making the victim vulnerable to multiple life threatening opportunistic infections, neurological disorders or unusual malignancies. A variety of endocrinologic, metabolic and nutritional disturbances are common during the course of HIV infection. Most HIV infected patients develop multiple metabolic abnormalities including insulin resistance, lipodystrophy and dyslipidaemia. An observation on the nature of dyslipidaemia in HIV positive patients with reference to correlation if any that exists between CD4+ levels and lipid profile in these patients was performed. Results revealed that the total cholesterol, HDL and LDL decreased while triglycerides and VLDL were found to increase as CD4+ levels depleted. It can be concluded that changes in lipid profile can be a good index of disease progression in HIV infection.

**KEYWORDS:** Lipid profile, HIV, CD4+.

**INTRODUCTION:** AIDS is a fatal illness caused by a retrovirus known as the Human Immunodeficiency Virus (HIV) which breaks down the body's immune system, leaving the victim vulnerable to a host of life threatening opportunistic infections, neurological disorders, or unusual malignancies.<sup>1</sup> India is estimated to have around 1.6 lakh annual new HIV infections among adults and around 14,500 new HIV infections among children in 2011. OF the 1.16 lakh estimated new infections in 2011 among adults, the previously high HIV prevalence States of Andhra Pradesh, Karnataka, Maharashtra ,Tamil Nadu, Manipur and Nagaland account for 31% of new infections, where some low prevalence states (Odisha, Jharkhand, Bihar, Uttar Pradesh, West Bengal, Gujarat, Chhattisgarh, Rajasthan, Punjab and Uttarakhand) together account for around 57% of new infections.<sup>2</sup> AIDS is affecting mainly the young people in sexually active age group. The majority are infected through unprotected sex.

Impoverished, unemployment under employed, mobile, and migrant youth, and street children are also particularly vulnerable to HIV or access to preventive measures, and they may face repeated risks of HIV infection. The immune system disorders associated with HIV infection/AIDS are considered to occur primarily from the gradual depletion in a specialized group of white blood cells (lymphocytes) called T-Helper or T-4 cells. The full name of T-Helper cells is CD4+ T lymphocyte and is commonly known as CD4+ cell. These cells play a key role in regulating the immune response. HIV selectively infects T-Helper cells apart from several other cells. When the virus reproduces, the infected T-Helper cells are destroyed. Consequently people with AIDS tend to have low overall white blood cell count.<sup>3</sup> A variety of endocrinologic, metabolic and nutritional disturbances are common during the course of HIV infection. Most HIV-infected

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patients develop multiple metabolic abnormalities including insulin resistance, lipodystrophy and dyslipidemia.<sup>4</sup> Metabolic disturbances in the HIV infected patients are incriminated to be risk factors of accelerated atherosclerosis and cardiovascular diseases<sup>5</sup> and altered lipid metabolism is known to affect immune processes.<sup>6</sup>

Racial variations in serum lipid levels of HIV-infected patients have been observed by Gadd.<sup>7</sup> In view of the increasing incidence of new HIV infection in previously low prevalence state like Bihar and especially North Bihar (Kosi region) where a large population are migrant workers and exposed to unprotected sex due to ill literacy, unemployment and poverty, the present study was undertaken to find out any correlation between the changes in lipid profile and CD4+ levels in these patients.

**MATERIALS AND METHODS:** The study was carried out on HIV positive patients attending the outpatient department of Katihar Medical College and Hospital, Katihar for a period of 8 months i.e. from January 2014 to August 2014 which was preapproved by the Ethical Committee of this institution review board. 88 participants (58 males, 30 females) were enrolled for the present study. 56 patients were HIV positive patients (36 males, 30 female) and 32 healthy controls(20 males,12 female) were recruited for the study. For diagnosis and confirmation of HIV infection we followed the National Aids Control Organization (NACO) recommendations for HIV testing. All the patients were subjected to detail history taking and clinical examination.

The informed consent was obtained from the patients before enrolling them for the study. The inclusion criteria was those patients with confirmed cases of HIV infection without anti-retroviral therapy were included and the exclusion criteria was that subjects who were smokers, obese and on anti-hypertensive drugs for more than three months and patients on lipid lowering drugs and antioxidants, vitamin supplements were excluded. To assess the effect of immunological changes due to the HIV infection and its impact on lipid profiles, the HIV-positive subjects were grouped into three based on different CD4+ counts/ranges.

- Group 1 – CD4+ count < 200 cells/mm<sup>3</sup>
- Group 2 – CD4+count 200-499 cells/mm<sup>3</sup>
- Group 3 – CD4+ count ≥500 cells/mm<sup>3</sup>

Lipid profile of all the patients and control was estimated by enzymatic methods.<sup>8,9</sup> The CD4+ lymphocyte count was estimated by fluorescence activated cell sorter (FACS) count system (Becton Dickinson). Other routine investigations were also done One-way Analysis of Variance(ANOVA) was used to compare the mean valued of lipid profiles of the three HIV positive groups and control HIV negative subjects. Tukey's Test was used for post hoc analysis on mean lipid levels that differed significantly among the groups.

**OBSERVATIONS:** Observations are represented below in tables and figures.

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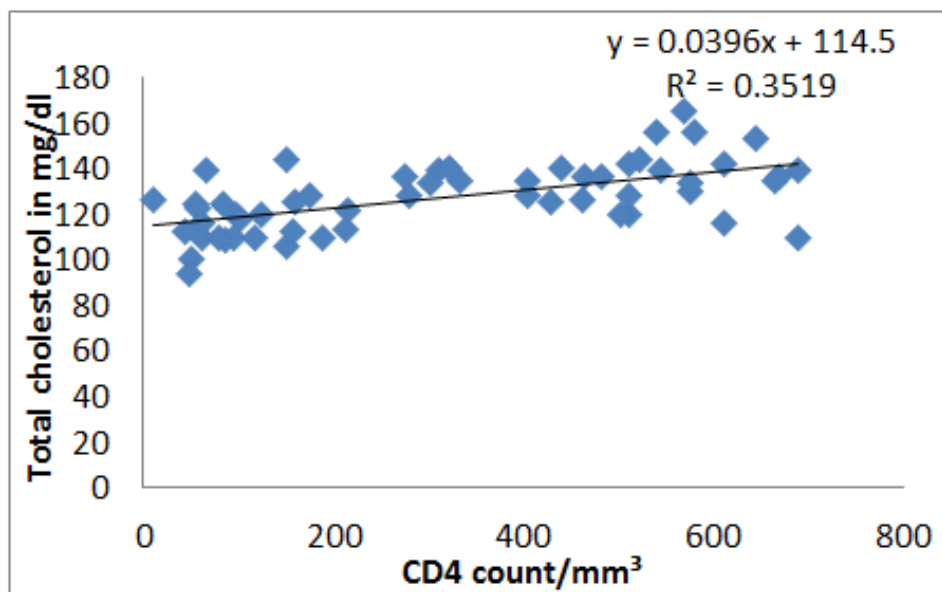


Fig. 1: Correlation plot between Total Cholesterol and CD4 levels of HIV-positive subject enrolled in the study (n=56,  $p < 0.0001$ ).

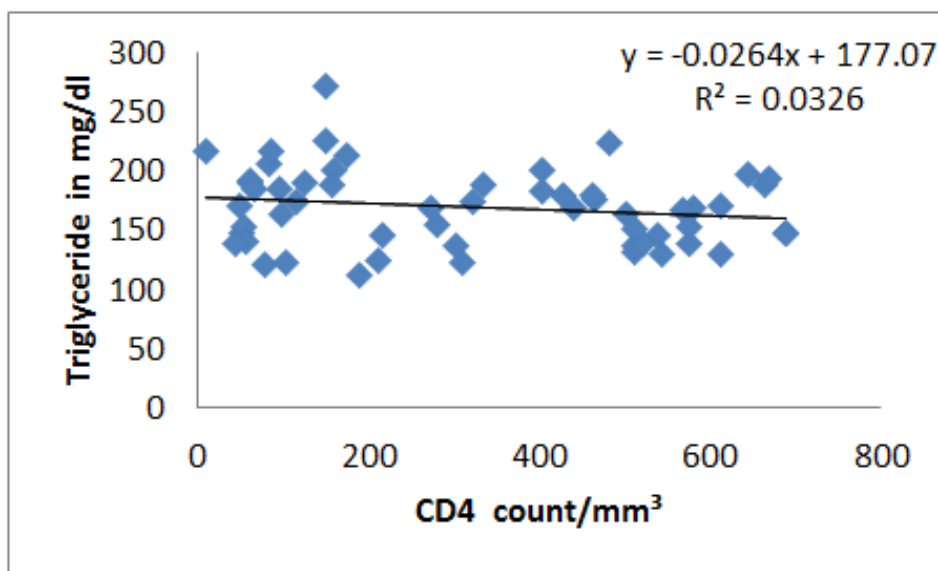


Fig. 2: Correlation plot between Triglyceride and CD4+ levels of HIV subjects enrolled in study (n=56,  $p < 0.0001$ )

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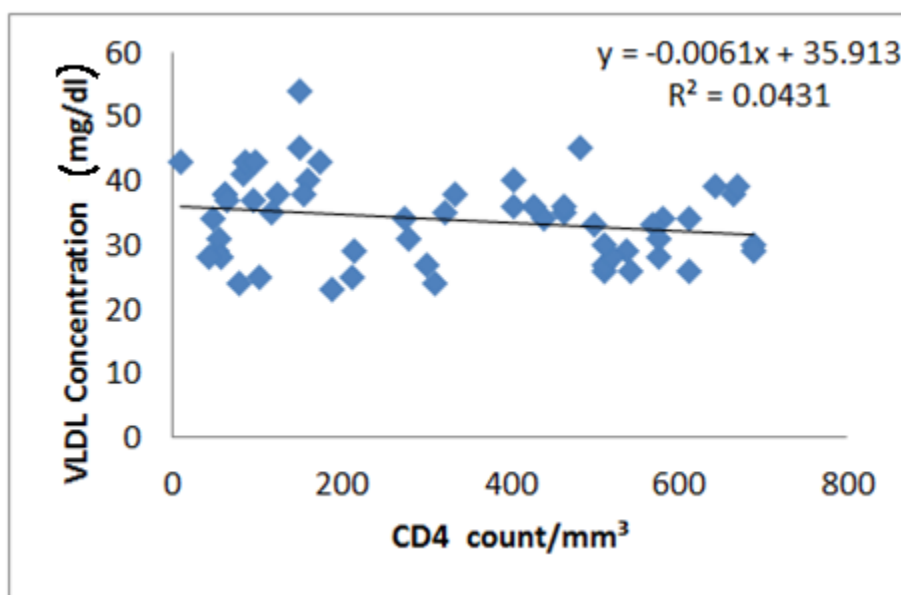


Fig. 3: Correlation plot between VLDL Cholesterol and CD4+ levels of HIV subjects enrolled in study (n=56,  $p < 0.0001$ ).

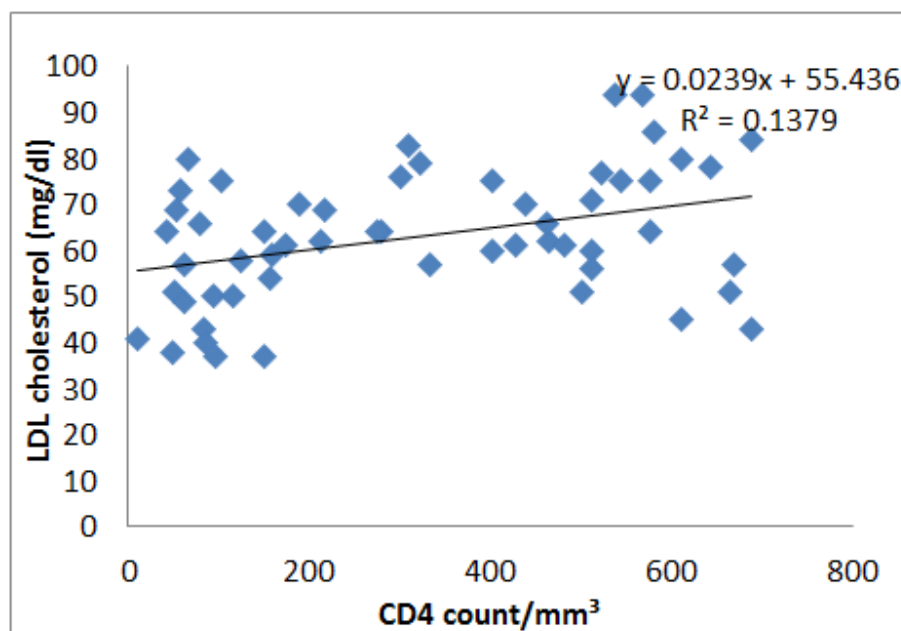


Fig. 4: Correlation plot between LDL Cholesterol and CD4+ levels of HIV subjects enrolled in study (n=56,  $p = 0.000434$ )

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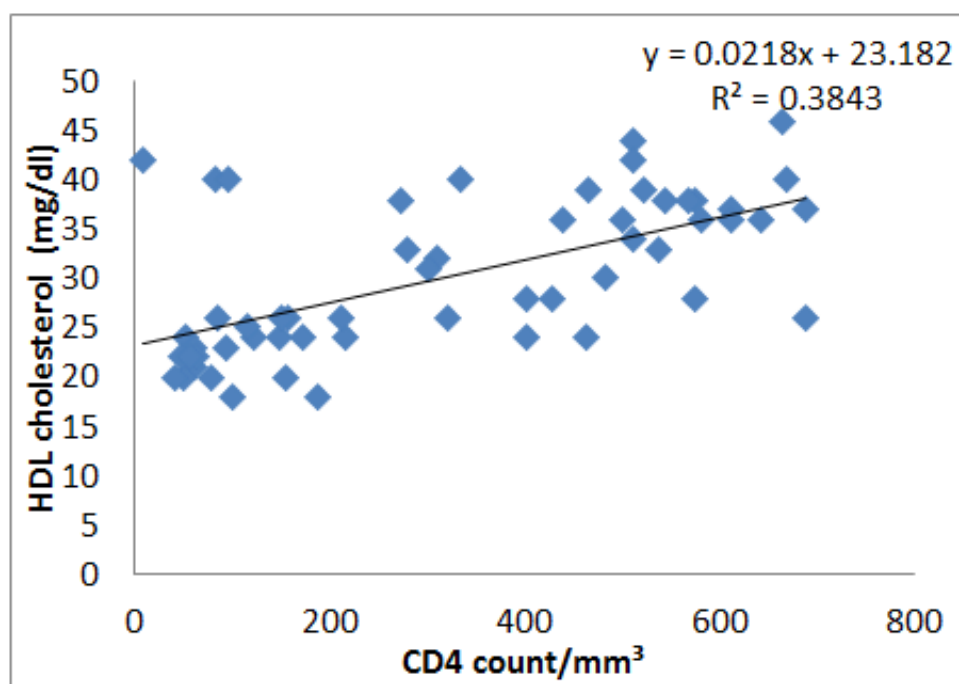


Fig. 5: Correlation plot between HDL Cholesterol and CD4 levels of HIV subjects enrolled in study (n=56, p <0. 0001).

Lipid types (Mean mg/dl)	Controls n=32	CD4≥500 n=18	CD4=499-200 n=15	CD4 ≤ 200 n=23	P Value
Total Cholesterol ± SD	142.3438 ±18.91	136.9444 ±14.87	131.5333 ±7.6613	116.9565 ±11.5423	<0.0001
Total Triglyceride± SD	131.7188 ±18.0684	155.3333 ±21.5461	168.4 ±27.7869	178.9565 ±38.6458	<0.0001
Total VLDL± SD	26.3438 ±3.6598	31.1111 ±4.3506	33.6667 ±5.6653	36.2609 ±7.7648	<0.0001
Total LDL ± SD	75.1563 ±19.7241	68.9444 ±16.1335	67.2667 ±7.7779	55.913 ±12.9752	0.000434
Total HDL ± SD	40.8438 ±6.2533	36.8889 ±4.8615	30.6 ±5.5908	24.7826 ±6.7214	<0.0001

Table 1: Lipid Profile of the three groups of HIV positive subjects and HIV negative controls

Results are presented as Mean ± SD. SD= Standard Deviation

A positive correlation was found between total cholesterol levels and the CD4+ T lymphocyte levels of HIV positive subjects (Figure. 1,  $y=0.039x + 114.5$ ), i.e. as the CD4+count levels continue to drop there will be a corresponding decrease in total cholesterol levels. However there is negative association was found between Triglyceride and VLDL with CD4+ T lymphocyte

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levels of HIV positive subjects as is evident from the negative correlation coefficients ( Fig.2 & Fig.3,  $y = -0.026x + 177.0$  &  $y = 0.006x + 35.91$  respectively). The graph in Fig.4 shows a falling trend with steadily reducing value of LDL levels with reference to the decrease of CD4+ levels ( $y = 0.023x + 55.43$ ). A similar correlation was found between HDL levels and the CD4+ T- lymphocyte levels of HIV positive subjects (Fig.5  $y = 0.021x + 177.0$ ).

Proper assessment of Table-1 revealed that there is very significant increase of mean triglyceride and VLDL as CD4+ levels decreases ( $p < 0.0001$ ). However there is significant overall fall of mean value of Total cholesterol, LDL and HDL is seen ( $p < 0.0001$ ,  $p = 0.000434$  &  $p < 0.0001$  respectively). The 'p' values shows low to very high significance in the different CD4+ ranges; the unequal significance may be due to small sample size.

**DISCUSSION:** This study included data on 56 HIV positive subjects and 32 HIV negative controls. The study observed alteration in lipid profile of HIV positive subjects compared to the control. There is increase of triglyceride and VLDL as the disease progresses but LDL, HDL and total cholesterol decreases as CD4 decline. Previous studies have demonstrated that patients with AIDS exhibit highly abnormal total lipid concentration in plasma<sup>10</sup> study conducted by Pashupatiet al<sup>11</sup> observed significant deduction of CD4 cells in HIV/AIDS compared to controls. Their study observed significantly decreased levels of TC, HDL-C and LDL-C in AIDS cases compared to controls which conform to the finding of the current study.

Further study conducted by Khaingle et al<sup>12</sup> on correlation between the changes in lipid profile and the progression of HIV infection also observed significant decrease in TC, HDL-C with concomitant .increase in VLDL-C along with significant reduction in CD4 cell count as the disease progressed gradually. The observations made in this study again support our study. Shor Posner et al<sup>13</sup> reported similar finding in which they showed significant low levels of total cholesterol, HDL, LDL cholesterol in HIV infected patients when compared to seronegative controls ( $P < 0.05$ ) However Crook and Mir<sup>14</sup> reported significantly higher levels of LDL-Cholesterol in HIV positive subjects compared to seronegative controls, which did not conform to the finding of the current study. HIV infection has been shown to affect several key processes regulating the levels of lipids.

Increased tumour necrosis factor (TNF) and other cytokines which occur during infection increases lipolysis and insulin resistance.<sup>4</sup> HIV/AIDS is characterized by high prevalence of hypertriglyceridaemia and hypercholesterolaemia is usually associated with elevated level of cytokines.<sup>15</sup> Also, Grunfeld et al<sup>15</sup> reported decreased cholesterol and cholesterol containing lipoprotein in both AIDS and HIV infection precede the appearance of hypertriglyceridaemia. Matsuyama T et al<sup>16</sup> highlighted the influence of cytokines produced by the host immune system during HIV infection and concluded that cytokines-especially TNF $\alpha$  and are amplifiers of HIV infection. Among the cytokines, the most consistent and potent inducers of HIV expressions are the pro-inflammatory cytokines TNF $\alpha$ , IL-1 $\beta$ , IL-6.<sup>17</sup> Hence, we can establish the association of lipid profile with HIV infection; therefore lipid profile can be a good index of disease progression in HIV/AIDS patients.

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**CONCLUSION:** We have observed that a relation can be established between lipid profile and disease progression in HIV / AIDS patients. Thus lipid profile will prove to be a good index of disease progression in such cases.

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