

“Prevalence of dyslipidemia in retroviral patients on ART (TLE) –“At a tertiary care center”western UP

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Abstract:

Since the discovery of antiretroviral therapy (ART), it has significantly modified the prognosis of individuals infected by the Human Immunodeficiency Virus-1 (HIV), with marked improvement in morbidity and mortality rates worldwide¹. Although the clinical benefits are considerable, the protease inhibitors contained in these antiretroviral regimens produce a lipodystrophy syndrome characterized by changes in body fat distribution, dyslipidaemia, and insulin resistance.² The hyperlipidemia is attributable to increases in very low density lipoproteins (VLDL) and Low density lipoproteins (LDL) Total cholesterol, and decrease in HDL, it can produce serious cardiovascular complications including endothelial dysfunction and atherosclerosis.^{3,4}

Aims and objective:-

To see the prevalence of dyslipidemia in retroviral patient, who are on ART and its association with newly diagnosed HIV patient.

Methodology:-

The study was conducted at medicine department L.L.R.M Medical College Meerut. Patients were taken from ART PLUS centre L.L.R.M Medical College Meerut. We classified HIV patients who were on first line ART (TLE) for more than 1 year study duration as case and newly registered patient, on their first visit before starting any treatment, during the same period, as control. These patients were interviewed regarding their symptoms. Thorough general examination, anthropometric measurement, CD-4 count and systemic examination, and

all the relevant investigations were done. Information thus collected was tabulated.

Result:-

Out of 142 cases, 90 (63.3%) were male and 52 (36.6%) were female. In control group 48 (52.7%) were male 43 (47.2%). Maximum no. of patient both in cases and control group fall in between the range of 18-40 years of age group. On comparing anthropometric parameter (weight, waist hip ratio, and BMI) between cases and control group there were no significant difference found ($p > .05$). On comparing biochemical parameter (total cholesterol, triglyceride, HDL, VLDL) between cases and control group no significant difference were found except in LDL level. Difference in CD4 count in cases and control (cases CD4 538.13 ± 308 , control CD4 856 ± 312.69 , $p < 0.0001$) were found significant.

Conclusion:-

We concluded from our study that patients on ART had high level lipid profile derangement than control group, and difference was statistically significant ($p < 0.014$). We advocate effective life style modification and pharmacological treatment for dyslipidemia in patient on ART.

Key words:- HIV, AIDS, ART, dyslipidemia, LDL, HDL, Total cholesterol.

I. Introduction:-

Since the identification of first cases of HIV/AIDS in June 1981 in Los Angeles, USA, there have been tremendous advances in the field of HIV prevention, diagnosis, care and treatment globally. This global progress is not only limited to identification of newer molecules

that are more robust and less toxic but also includes a significant reduction in the cost of therapy. Innovative approaches to service delivery that increase access to treatment, literally transforming the disease from a virtual death sentence, a few years ago, to a chronic manageable disease now⁵.

Nevertheless, several clinical aspects have been developed along with the longer longevity of HIV individuals, most of them related to other chronic conditions or to the antiretroviral treatment (ART).⁶ Metabolic abnormalities such as insulin resistance and disturbances in glucose homeostasis, modified adiposity physiology with lipid alterations might result in clinical complications including glucose intolerance, diabetes mellitus, dyslipidemia, altered body fat distribution, with lipodystrophy (loss of subcutaneous fat mostly in the face and periphery) and lipohypertrophy (localized fat gain mostly in central and visceral adiposity).²

Some of these perturbations can be associated with ART.⁷ Protease inhibitors (PI) show direct effect on human adipose tissue and specific effects on insulin resistance which may contribute to the overall adipose tissue imbalance and development of dyslipidemia, lipodystrophy, and metabolic syndrome in HIV-positive individuals.^{7,8} In addition, nucleoside reverse transcriptase inhibitors (NRTIs) may induce mitochondrial dysfunction, which could result in effects on adipose tissue, lactic acidosis, myopathy, peripheral neuropathy, hepatic steatosis and pancreatitis as well.⁸

Though many studies are present to show the effect of ART on lipid profile but there is very less Indian data. So this study was conducted to assess the effect of ART Therapy on lipid profile and other biochemical markers.

Aim and Objectives:-

To see the prevalence of dyslipidemia in retroviral patient, who are on ART and its association with newly diagnosed HIV patient.

II. Methodology:-

This study was conducted in the department of Medicine and ART Plus centre L.L.R.M Medical College, Meerut. We have taken all the patients enrolled in ART PLUS center from October 2018 to September 2019, who fulfilled the inclusion and exclusion criteria. The Ethical clearance was taken

from Institutional ethics committee LLRM Medical college (no/S-I/2019/9157 dated 11-12-2019). After taking informed consent we classified HIV patients who are on first line ART (TDF, 3TC and EFV), for more than one year as case and newly registered patients during their first visit of ART center, during same period, who have not on treatment yet as control. These patients were interviewed regarding their symptoms. Thorough general examination, anthropometric measurement, and systemic examination were done. All the relevant investigations like CBC with ESR, LFT, KFT, HbA1C, fasting lipid profile, blood sugar fasting and PP, were carried out. Information thus collected was tabulated in MS-Excel and analysed by applying appropriate statistical test by using IBM-SPSS version 21. For parametric quantitative data the results are depicted as mean and standard deviation, comparison were made by chi square test and unpaired t-test for quantitative variables between two groups.

We measured fasting lipid profile and study variables were defined. We defined dyslipidemia when total cholesterol levels were more than 200 mg/dl, triglyceride levels more than 150 mg/dl, HDL level less than 40 mg/dl for male less than 50 mg/dl female, LDL level more than 130 mg/dl, VLDL more than 30 mg/dl.

Anthropometric measurements like weight was taken in kg, WHR in meter, and BMI in kg/cm²

INCLUSION CRITERIA:

Selection of cases:-

1. All retroviral patients on ART (first line regimen TDF-Tenofovir, 3TC-Lamivudine and EFV-efavirenz) for more than 1 year
2. Age > 18 years.
3. Willing to give consent.

Selection of controls:

1. Newly diagnosed retroviral patients not on treatment at their first visit before starting any treatment, sample for lab investigations were collected.
2. Age > 18 years.
3. Willing to give consent.

EXCLUSION CRITERIA:

1. Age < 18 years.
2. Not willing to give consent.
3. Pregnant women.

Patients with hypothyroidism, DMT2,

CKD,CLD,CHF,CADpancreatitis:

1. Patient on drugs causing dyslipidemia- Betablocker, Glucocorticoids, Amiodorone, Immunosuppression drug (cyclosporine), Thiazide diuretics.
2. Obese patient (BMI > 30).

III. Observations and Results:-

. Among 142 cases, 90 (63.3%) patients were male and 52 (36.6%) were female. In control group out of total 91 patients 48 (52.7%) were male and 43 (47.2%) were female. It was seen that in both cases and controls groups male were more than female in our study.

We divided patients in two groups, age between 18-40 years and age between 41-60 years. Among cases 95 (66.9%) patients were between the age of 18-40 years and 47 (33.09%) patients were between 41-60 years of age group. In control group 67 (73.6%) patients were in 18-40 years of age group whereas 24 (26.3%) patients were in 41-60 years of age group. It shows that maximum no of patient were in age group between 18 to 40 years both in cases as well as in control group. So there is no variation in age and sex, in both cases and control.

Table 1:- Comparison of Anthropometric parameters between Case and Control

Anthropometric Parameters	Case	Control	p-value
Weight	62.07±12.97	60.24±6.80	0.22
WHR(m)	0.94±0.03	0.95±0.01	0.17
BMI	23.45±4.45	23.91±2.5	0.37

Table no 1 shows the comparison of anthropometric distribution between cases and control. Among cases mean weight was 62.07 with SD 12.97 and among control 60.24 with SD 6.80, with p value (0.22). The difference of weight both in cases and control was statistically not significant.

Among cases mean BMI (basic metabolic rate) was 23.45 with SD of 4.45 and among control mean BMI was 23.91 with SD of 2.5 with p value 0.37. We observed that relationship of BMI between two groups is statistically not significant ($p \geq 0.05$).

Among cases mean WHR (waist hip ratio) was 0.94 with SD of 0.03 and among control group

mean WHR (waist hip ratio) was 0.95 with SD of 0.01 and p value of 0.17. The difference of waist hip ratio both in cases and control is statistically not significant.

The Mean value of CD4 count among cases were 538.13 with SD (± 308.26) and among control were 856.47 with SD (± 44.80). CD4 count were found to be in lower range than newly diagnosed HIV Patients. We observed that relationship of CD4 count between case and control was statistically significant. There was significant difference in cd4 count both in cases and control group.

Table 2: Prevalence of dyslipidemia in study groups (cases and control)

GROUP	Case (n=142)	Control (n=91)	Statistics
Dyslipidemia	115 (81.60%)	60 (67%)	chi square 5.94 P value 0.014
Non-Dyslipidemic	27 (18.4%)	31 (33%)	

Table no 2 shows the distribution of dyslipidemia in both cases and controls. Dyslipidemia (any type of lipid abnormality) among cases were 81.6% and among control group, it was 67%. Chi square value between case and control was 5.84 and the relation between case and control was found to be statistically significant ($p < 0.05$).

Table-3: levels of lipid profile in cases and controls.

GROUP	Case(n=142)	Control (n=91)	Chi Squarevalue	Pvalue
HIGHTG* \geq 150 mg/dl	88(61.9%)	51(56%)	0.58	0.44
HIGHTC* \geq 200 mg/dl	44(30.9%)	28(30.7%)	0.001	0.97
LOWHDL* \leq 40mg/dl	30(21.1%)	12(13.1%)	1.86	0.17
HIGHLDL* \geq 130 mg dl	23(16.19%)	6(6.59%)	3.85	0.04*
HIGHVLDL* \geq 30mg/dl	86(60.5%)	53(58.2%)	0.046	0.83

*(TG-triglyceride,TC-total cholesterol,HDL-high density lipoprotein,LDL-low density lipoprotein,VLDL-very low density lipoprotein)

When various values of lipid profile were assessed, it was observed that 61.9% cases had hypertriglyceridemia (triglyceride level > 150) whereas in control group hypertriglyceridemia were present in 56% patients. Chi square value between case and control was 0.58 and we observed the relation between two were statistically nonsignificant ($p=0.44$) hypercholesterolemia were found in 30.9% cases and in control group hypercholesterolemia were present in 30.7%. Chi square value between case and control was 0.001 and p value was 0.97 and we observed the relation between two was statistically nonsignificant ($p>0.05$)

Prevalence of low HDL in cases group were 21.1% and in control group were 13.1%. Chi square value between case and control was 1.86 and we observed the relation between case and control was statistically non-significant ($p=0.17$).

Prevalence of high LDL in cases were 16.19% and in control group were 6.59%. Chi square value between case and control was 3.85 and we observed the relation between two were **statistically significant ($p = 0.04$)**

Prevalence of high VLDL in case was 60.5% and in control group was 58.2% Chi square value between case and control was 0.046 and we observed the relation between these two was statistically non significant ($p=0.83$).

IV. DISCUSSION

Patients receiving ART specially protease inhibitors develop hyperlipidemia and insulin resistance. Protease inhibitor have high affinity for the catalytic site of HIV protease and may bind and alter the function of an homologous human proteins

involved in lipid metabolism.²In addition, nucleoside reverse transcriptase inhibitor (NRTIs) may induce mitochondrial dysfunction, which could result in effect on adipose tissue.

The aim of this study was to assess the prevalence of dyslipidemia (lipid profile derangements) among HIV-infected patients receiving first-line ART, and their comparison with newly diagnosed HIV patients not on ART.

In our study males are more than females in both cases and controls. It shows that prevalence of HIV infection is more in males than females. It is opposite to Dave et al⁹ where they had took 551 case out of which 78% were female and 22% were male and among control group 406 patients were selected out of which 76% were female and 24% were male.

Maximum no of patients in both case and control group were in the age group 18 to 40 years, this difference of distribution among various age groups were statistically not significant ($P \geq 0.05$). In a study by Dave et al⁹ the median age of participants were 34 years which is similar to our study. Another study by Dickson et al¹⁰ which show median age of participants were 43.4 ± 11.0 years which was also like our study in which maximum no of patients fall between 18 -40 years of age group.

We analyze the various parameters of obesity like **weight WHR and BMI** between two groups. It shows that there were no significant difference in weight, waist hip ratio as well as in BMI in cases as well as control groups. A Study by Dave et al⁹ showed that obesity ($BMI > 30 \text{Kg/m}^2$) was more common in ART naive patient than ART treated participant. A similar study by Lucia et al¹¹ which found significant BMI rise after one year

followup on patient on ART.

The Mean values of CD4 count among cases were 538.13(\pm 308.26) and among control were 856.47 (\pm 44.80). There were significant difference in cd4 count both in cases and control group. A study by Dave et al⁹ showed median CD4 count in ART naïve female patient was 278 (IQR 159,440) and in males 227 (IQR 134, 411), in patient ART median CD4 count in females was 371 (IQR242, 525) and in males 278 (IQR 199, 387) in their study triglyceride level correlates negatively with CD4 count.

On analyzing lipid profile we found that 81.6% among cases and 67% among control group had at least one parameter of lipid profile deranged.

There was an approximately 15% difference in the prevalence of dyslipidemia in patient on ART and in newly diagnose d patient (control group). The relationship between two groups were found statistically significant ($p < 0.05$). A similar study was done by Tadewos et al¹² which included 113 HIV infected patients treated for a minimum of one year with first-line ART regimens and others 113 who had never received ART (Pre-ART group). 82.5% of ART And 76.9% Pre ART patient had at least one laboratory abnormality¹².

There were no significant difference in the level of total cholesterol , triglyceride and HDL level between cases and controls in our study .These findings in cholesterol levels are opposite to a study by Dickson et al¹⁰, which shows the prevalence of total cholesterol (≥ 200 mg/dl) was 51.0 % in patients on ART and 9.6% Pre-ART patients ($p < 0.0001$). On comparing HDL levels with Dickson et al¹⁰, which shows prevalence of HDL below 40 mg /dl are not statistically significant between pre ART and ART group .Finding of our study are not in accordance with the findings of Pujari et al¹³, in whose study 18 months treatment with first line ART were associated with significant increase in HDL level.

In our study prevalence of high LDL in cases were 16.19% and in control group were 6.59%.we observed the relation between two was statistically significant ($p < 0.05$). A similar study by Dickson et al¹⁰ which showed LDL-cholesterol ≥ 130 mg/dl occurred in 36.9% ART patients and in 7.7% pre ART patients respectively, with ($p = 0.0001$).

V. CONCLUSION

We can conclude from our study that HIV-infected patients receiving first-line ART have a high

prevalence of lipid profile derangements when compared to those non- treated HIV-infected patients. Uses of first-line ART regimens are significantly associated with atherogenic lipid profiles. Therefore, the findings indicate the need to assess lipid profiles at baseline before initiation of ART treatment and lipid profile monitoring during therapy to monitor any rising trends. Additionally, the results also recommend implementation of well- controlled cohort studies for the evaluation of long-term effects of ART treatment on lipid profiles.

We advocate effective lifestyle and pharmacological intervention to prevent and treat dyslipidemia in patient on ART therapy.

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