Novelty Journals

ISSN 2394-7330

International Journal of Novel Research in Healthcare and Nursing
Vol. 8, Issue 2, pp: (192-198), Month: May - August 2021, Available at: www.noveltyjournals.com

LIPID PROFILE OF HIV-SEROPOSITIVE PERSON'S ON ANTI- RETOVIRAL THERAPY IN RIVERS STATE

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***Abstract*: Assessment of lipid profile may be a good index of disease progression in HIV- infected patients following the association between CD4 count and total cholesterol, triglyceride and LDL-cholesterol. The lipid profile and atherogenic profiles of a cohort of HIV-seropositive subjects on anti-retroviral therapy (ART) and those that were ART-naïve were compared to healthy HIV-seronegative subjects. Results showed that there was a statistically significant difference in the mean age of the study subjects (p = 0.004). Systolic blood pressure in the healthy subjects was 124.4 ± 4.0mmHg, followed by 122.9 ± 7.5mmHg in the experimental subjects and 118.8 ± 8.7mmHg in the ART-naïve subjects. The difference in the systolic blood pressure of the study subjects was significantly significant (p = 0.001). The mean total cholesterol was 3.9 ± 1.1 in the healthy subjects, 3.8 ± 0.6 in the ART-naïve seropositive subjects and 3.6 ± 0.8 in the seropositive subjects on ART, while the difference in the average total cholesterol was statistically significant (p = 0.10). Among the female subjects, the AIP in healthy subjects was 0.28±0.12, -0.22±0.02 in ART-naïve seropositive subjects and 0.22±0.12 in seropositive subjects on ART. The study shows that HIV infected patients on ART were more at risk for CVD especially among seropositive male subjects.**

***Keywords*: LDL, HDL, HIV, ART.**

1. INTRODUCTION

A variety of endocrinologic and metabolic abnormalities like hypertriglyceridemia, low total cholesterol (TC), low high-density lipoprotein (HDL-c), reduced low density lipoprotein (LDL-

c) levels as well as, insulin resistance and endothelial dysfunction are often common among HIV patients.[1] Human immunodeficiency Virus (HIV) infection is a leading cause of death in Africa and a worldwide health problem that affects about 34 million men and women.[2] Nigeria, records the second highest number of people (about 3 million) with HIV infection, after South Africa with about 5.6 million.[3] Approximately 24% of infected adult population are on highly active antiretroviral therapy (HAART).[4] This has resulted in improved survival of HIV patients. However, morbidity and mortality in these patients are still linked to organic diseases which include dysfunctional lipid profile and peripheral vascular disease implicated in cardiovascular system.[5] To this end, lipid abnormalities have been recorded in both highly active antiretroviral therapy (HAART)-naïve HIV patients and those on HAART, and the presence of this dyslipidemia may lead to increased risk of cardiovascular disease (CVD).[6] It is reported that lipid profile may be a good index of disease progression in HIV-infected patients as a result of presence of association between CD4 count and total cholesterol, triglyceride and LDL-cholesterol. Hypertriglyceridemia, low total cholesterol (TCH) and reduced low density lipoprotein

(LDL) levels have been observed in HAART-naïve patients.[7] Also, Low levels of high-density lipoprotein (HDL) were also found to be common especially in those with reduced CD4 count.[8] To this end, lipid abnormalities have been recorded in both highly active antiretroviral therapy (HAART) naïve HIV patients and those on HAART, and the presence of this dyslipidemia may lead to increased risk of cardiovascular disease (CVD).[6] This study was carried out to assess the lipid profile of HIV-infected persons in a bid to identify risks for cardiovascular diseases among people receiving treatment.

2. METHODS

Study Design

The cross-sectional study design was adopted for the study, where haematological and lipid profile of a cohort of HIV-seropositive subjects on anti-retroviral therapy (ART) and those that were ART-naïve were compared to healthy HIV-seronegative subjects.

Study population

Four hundred individuals were recruited for the study. They were grouped as follows; 300 HIV- seropositive subjects on ARV therapy, 150 patients who were ARV naïve confirmed with Western blot attending ARV clinic in UPTH, Port Harcourt.

Sample size and Sampling

The minimum sample size required for this study was determined using the formula (Araoye, 2003) below

$$n = \frac{z^2 pq}{d^2}$$

Where n = minimum sample size

z = 95% confidence interval = 1.96

p = prevalence of the target population = 24% q= 1-p=1.0-0.24 =0.76

q = 1

d = degree of accuracy desired (at 0.05) n= $(1.96)^2$ (0.45) (1-0.45)/0.05^2

$$= \frac{3.8416 \times 0.45 \times 0.55}{0.0025}$$

$= 380.3 \approx 400$

The calculation was based on a prevalence rate of 45% (Lesi *et al*., 2009) observed for hyperlipidemia in a cohort of HIV-positive Africans on highly active antiretroviral therapy done in Lagos State, Nigeria. The confidence level was set at 95% giving a calculated minimum sample size of 380 subjects, which was rounded up to reach 400 subjects and grouped as follows;

200 were HIV seropositive on ART,

100 were HIV seropositive ART naïve and

100 were HIV seronegative apparently healthy control.

A systematic sampling technique was used to select the subjects, at an interval of every 5th individual that meets the following criteria;

Inclusion criteria

1). HIV positive patients attending anti-retroviral clinic in UPTH who give informed consent.

International Journal of Novel Research in Healthcare and Nursing
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Exclusion criteria

1). Patients who are on lipid lowering drugs, known hypertensive and diabetic patients 2). Patients with evidence of kidney disease was excluded.

3). Patients Significant history of alcohol use, renal disease and those with family history of dyslipidemia and cigarette smoking will also be excluded from the study.

Sample collection and Analysis

Blood samples was taken from all participants after 8-12 hours fasting to determine the lipid profile and FBS. The blood for serum lipid profile was collected in plain bottles. Serum total cholesterol (TC) and triglyceride (TG) was determined by enzymatic estimation while high density lipoprotein cholesterol (HDL-c) was determined by enzymatic estimation after precipitation. Low density lipoprotein cholesterol (LDL-c) was determined from the values of the aforementioned using the Friedewald's formula.

LDL= TC – HDLc - (TG/2.2) mMol / L

TG was measured using the colorimetric enzymatic method.

Formulas for Mean Arterial Pressure (MAP) = (Diastolic × 2) + systolic / 3). Pulse Pressure = systolic pressure – Diastolic pressure

Body Mass Index (BMI) = weight / (height) ^{2}

A clinical chemistry analyser (vitro Scient-vs 10) which is a semi auto analyser was used (montiselio(RN)- Italia).

Data Analysis

Data was entered and analysed using Statistical Package for Social Sciences SPSS Version 20.0. Continuous variables were presented using means and standard deviation for data, whereas the difference between continuous variables was analysed using the one-way ANOVA. Multiple comparisons of the different groups were also assessed using the LSD tests. A p value < 0.05 was considered to be significant

3. RESULTS

Table 1 shows that the anthropometric measurements of the female subjects. The healthy patients (control subject) were between 19 – 52 years old, with a mean age of 31.5 ± 8.3 years. The ART- Naïve HIV seropositive patients were between 19 – 60 years and had a mean age of 34.3 ± 10.8 years).

Table 1: Sociodemographic Data of Study Subjects

		Frequency	Percent
Age (Mean/SD)		**36.7±9.6**	
Age groups (years)	18 – 35	230	57.50%
	36 – 55	159	39.75%
	>56	11	2.75%
	Total	400	100.00%
Sex			
	Female	257	64.25%
	Male	143	35.75%
	Total	400	100.00%

Table 2 showed that experimental subjects (HIV infected patients on ART) were between 21 – 65 years old and had a mean age of 36.5± 8.2 years old. The difference in the mean age of the various groups was found to be statistically significant (p = 0.001). The mean systolic blood pressure of healthy subjects was 122.5±4.4mmHg, systolic blood pressure in ART-naïve seropositive subjects was 120.2±13.8mmHg and 120.8± 8.1mmHg in HIV infected subjects on ART (Experimental group). There was no statistical difference in the systolic blood pressure between the three groups (p = 0.341). The diastolic blood pressure in the Control subjects was 81.5 ± 2.7mmHg, 79.5 ± 7.5mmHg in ART-naïve HIV-seropositive subjects and 79.1 ± 6.6 in the experimental subjects. No significant difference was observed in the diastolic

blood pressure of the subjects (p = 0.048). The mean arterial pressure was 95.2±3.2mmHg in control subjects, 93.1± 9.2mmHg in ART-naïve HIV infected subjects and 93.0 ± 6.0mmHg in Experimental subjects. No difference was observed in the mean arterial pressure of the subjects (p = 0.083). The pulse pressure of the control subjects was 41.0 ± 2.5mmHg, and 40.7 ± 8.6 in the ART-naïve HIV infected patients, while it was 41.6 ± 8.2mmHg in the Experimental subjects and there was no difference in the mean arterial pressure (p = 0.666). The average weight of the control subjects was 64.3 ± 12.6kg, and 66.8± 8.4kg in ART-naïve HIV infected subjects, while it was 70.6 ± 8.4kg in experimental subjects (p < 0.0001). The average height was 1.6 ± 0.1m in all groups of subjects respectively. The average Body Mass Index (BMI) of the control subjects was 23.9 ± 3.6 m/kg^2, 25.7 ± 2.9 m/kg^2 in the ART-naïve infected subjects and 26.8 ± 3.2 m/kg^2 in the experimental subjects. The difference in the BMI of the subjects was significantly different (p < 0.0001

Table 2: Age/Blood Pressure/Anthropomeric Measures of Female Subjects

Parameters	Healthy seronegative n = 58	Seropositive ART naïve n = 58	Experimental = 141	nTotal n = 257	ANOVA
Age (years)	31.5 ± 8.3	34.3 ± 10.8	36.5 ± 8.2[a]	34.9 ± 9.1	0.001*
Systolic Blood Pressure(mmHg)	122.5 ± 4.4	120.2 ±13.8	120.8 ± 8.1	121.0 ± 9.1	0.341
Diastolic Blood Pressure(mmHg)	81.5± 2.7[b]	79.5 ± 7.5	79.1 ± 6.6	79.8 ± 6.3	0.048
MAP (mmHg)	95.2 ± 3.2[b]	93.1 ± 9.2	93.0 ± 6.0	93.5 ± 6.4	0.083
Pulse Pressure (mmHg)	41.0 ± 2.5	40.7 ± 8.6	41.6 ± 8.2	41.3 ± 7.4	0.666
Weight (Kg)	64.3 ± 12.6	66.8 ± 8.4	70.6 ± 8.4[a]	68.3 ± 9.8	<0.0001*
Height (M)	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	0.161
BMI (m/kg^2)	23.9 ± 3.6	25.7 ± 2.9[a]	26.8 ± 3.2[a,c]	25.9 ± 3.4	<0.0001*

All values are given as Mean ± Standard Deviation MAP: Mean Arterial Pressure, BMI: Body Mass Index.

a significantly different compared to the Healthy Seronegative (p<0.05)

b significantly different compared to the HIV On ART (p<0.05)

c significantly different compared to Seropositive ART Naïve (p<0.05)

The mean CD4 count of female subjects showed that the healthy subjects (control) had a mean CD4 count of 905.7± 302.3, the CD4 count of the HIV infected subjects on ART was 512.8±294.3 and the mean CD4 count of the ART-naïve subjects was 271.6±119.9. The difference in the average CD4 of the different groups was statistically significant (p < 0.001). Among the male subjects, the mean CD4 count was 933.5 ± 181.1 in healthy subjects, 244.7 ± 64.9 in ART-naïve seropositive patients and 283.1 ± 176.0 in seropositive patients on ART, while the difference in the CD4 count was statistically significant (p<0.0001) as presented in Table 3.

Table 3: CD4 counts of Study subjects

Parameters	Healthy Seronegative n = 58	Seropositive ART naïve n = 58	HIV on ART n =Total 141	n = 257	ANOVA
Female	905.7± 302.3[c,b]	271.6±119.9[a,b]	512.8±294.3[a,c]	547.03±343.34	<0.0001*
Male	933.5 ± 181.1[c]	244.7 ± 64.9	283.1 ± 176.0[a]	462.9 ± 341.1	<0.0001*

All values are given as Mean ± Standard Deviation

a significantly different compared to the Healthy Seronegative (p<0.05)

b significantly different compared to the HIV On ART (p<0.05)

c significantly different compared to Seropositive ART Naïve (p<0.05)

The clinical chemistry of the male subjects is presented in Table 4. The mean total cholesterol was 3.4 ± 0.8 in the seropositive subjects on ART, 3.7 ± 0.9 in the healthy subjects and 3.9 ± 0.8 in the ART-naïve seropositive subjects, while the difference in the average total cholesterol was statistically significant (p = 0.10). Triglyceride levels was 1.09 ± 0.4 in

ART-naïve seropositive subjects, 1.08 ± 0.3 in healthy subjects and 0.96 ± 0.4 in seropositive subjects on ART, with no significant difference in the triglyceride levels of the different groups (p = 0.161). HDL levels were 1.4 ± 0.5 in the seropositive subjects on ART, 1.5 ± 0.6 in the healthy (control) subjects and

1.9 ±0.4 in the ART-naïve seropositive subjects and the difference in the HDL levels across the groups was statistically significant (p < 0.0001). LDL levels was 1.5 ± 0.4 in the ART-naïve seronegative subjects, 1.5 ± 0.5 in the seropositive subjects on ART and 1.7 ± 0.7 in the healthy (control) subjects, while the difference was not statistically significant (p = 0.109).

Table 4: Lipid Profile of Female Subjects

Parameters	Healthy Seronegative n = 58	Seropositive ART naïve n = 58	HIV on ART n =Total 141	n = 257	ANOVA
Total cholesterol (mmol/l)	3.9 ± 1.1[b]	3.8 ± 0.6	3.6 ± 0.8	3.7 ± 0.9	0.016
Triglyceride (mmol/l)	1.1 ± 0.3[b]	1.03 ± 0.4	0.9 ± 0.5	0.9 ± 0.4	0.078
HDL (mmol/l)	2.1 ± 1.9[b]	1.7 ± 0.5	1.5 ± 0.5	1.7 ± 1.0	0.002*
LDL (mmol/l)	1.8 ± 0.7	1.7 ± 0.4	1.6 ± 0.6	1.7 ± 0.6	0.314
FBS (mmol/l)	0.73 ± 0.27	0.7 ± 0.25	0.8 ± 0.1	0.8 ± 0.4	0.297

HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, FBS: Fasting blood sugar.

All values are given as Mean ± Standard Deviation

a significantly different compared to the Healthy Seronegative (p<0.05)

b significantly different compared to the HIV On ART (p<0.05)

c significantly different compared to Seropositive ART Naïve (p<0.05)

The clinical chemistry of the male subjects is presented in Table 5. The mean total cholesterol was 3.4 ± 0.8 in the seropositive subjects on ART, 3.7 ± 0.9 in the healthy subjects and 3.9 ± 0.8 in the ART-naïve seropositive subjects, while the difference in the average total cholesterol was statistically significant (p = 0.10). Triglyceride levels was 1.09 ± 0.4 in ART-naïve seropositive subjects, 1.08 ± 0.3 in healthy subjects and 0.96 ± 0.4 in seropositive subjects on ART, with no significant difference in the triglyceride levels of the different groups (p = 0.161). HDL levels were 1.4 ± 0.5 in the seropositive subjects on ART, 1.5 ± 0.6 in the healthy (control) subjects and

1.9 ±0.4 in the ART-naïve seropositive subjects and the difference in the HDL levels across the groups was statistically significant (p < 0.0001). LDL levels was 1.5 ± 0.4 in the ART-naïve seronegative subjects, 1.5 ± 0.5 in the seropositive subjects on ART and 1.7 ± 0.7 in the healthy (control) subjects, while the difference was not statistically significant (p = 0.109).

Table 5: Lipid profile of Male Subjects

Parameters	Healthy Seronegative n = 42	Seropositive =ART naïve n = 42	HIV on ART n = 59	Total n = 143	ANOVA
Total Cholesterol (mmol/l)	3.7 ± 0.9	3.9 ± 0.8[b]	3.4 ± 0.8	3.6 ± 0.9	0.010*
Triglyceride (mmol/l)	1.08 ± 0.3	1.09 ± 0.4	0.96 ± 0.4	1.03 ± 0.4	0.161
HDL (mmol/l)	1.5 ± 0.6	1.9 ±0.4[a,b]	1.4 ± 0.5[c]	1.6 ± 0.5	<0.0001*
LDL (mmol/l)	1.7 ± 0.7	1.5 ± 0.4	1.5 ± 0.5	1.5 ± 0.5	0.109
FBS (mmol/l)	2.9 ± 0.9[c]	0.6 ± 0.2	0.8 ± 0.4[a]	1.3 ± 0.9	0.057

HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, FBS: Fasting blood sugar.

All values are given as Mean ± Standard Deviation

a significantly different compared to the Healthy Seronegative (p<0.05)

b significantly different compared to the HIV On ART (p<0.05)

c significantly different compared to Seropositive ART Naïve (p<0.05)

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4. DISCUSSION

Lipid profile refers to some routinely done biochemical tests to assess the atherogenic status of individuals at risk of cardiovascular disease (CVD). The Framingham heart study over years has established the role of deranged lipid profile in the progression of CAD and deranged LDLc levels are the primary target for treatment. Assessment of certain ratios using these parameters especially in situations where LDLc levels are below target range may increase the identification of at-risk individuals. In addition to the usual risk factors for CVD seen in the general population, People living with HIV (PLWH) may have additional risks. Endothelial dysfunction and metabolic disorders associated with chronic inflammation in HIV infection itself and the use of the very life-saving Anti-retroviral therapy (ART) may be responsible for the observed excess risk for CVD.[9,10]

In this study the mean age of female HIV infected patients was 36.5 ± 8.2 years which is consistent with the findings of previous studies indicating that HIV is mostly prevalent among young people.[11,12] The average blood pressure of the female subjects was within normal limits, as there was no significant elevation in blood pressure observed. The weight and BMI of the seropositive subjects on ART was found to be higher than that of the ART-naïve seropositive patients and the control subjects.[13,14] There has been a variation in the average weight and BMI reported among

HIV infected patients on ART. Elevated BMI and weights have been a consistent outcome of HIV infected patients on ART compared to the initial weight and BMI values recorded prior to the commencement of treatment.[15,16] The average age of the male seropositive subjects was 39. 3 ± 10.1 years, which was slightly higher in comparison to the female subjects. This may be attributed to health seeking habits of male subjects which is quite low compared to females especially in sub-Saharan Africa.[9,10] The higher mean age of the male subjects may also be attributed to other unique socio-cultural factors in the population of interest.[1,17] Similarly, male seropositive patients on ART were seen to weigh more and have a higher average BMI, similar to the observations in the female subjects. The higher values of weight and BMI have also been reported in similar studies.[1,18]

The results of the study are in agreement with the findings of Kumar et al.,[19] which reported a significantly higher level in serum triglyceride LDL-cholesterol and HDL-cholesterol in ARV- naïve patients compared to controls and seropositive patients on ART. Further study by Adewole et al.,[11] on the effect of antiretroviral therapy on lipid profile in HIV patients in Abuja, Nigeria, observed significantly higher levels of LDL-cholesterol and lower HDL-cholesterol in patients compared to controls which is in contrast with the findings of this study as higher HDL- cholesterol was observed in seropositive ART-naïve subjects. The higher serum triglyceride observed among controls compared to patients in this study may be due to better nutritional status in controls or absence of other underlying disease conditions.

5. CONCLUSION

The present study indicates that CVD risk seemed to be more likely in HIV patients on ART when considering HDL-cholesterol (HDLc) and triglyceride (TG) levels in the company of atherogenic index of plasma (AIP), there seemed to be high risk of CVD in antiretroviral therapy (ART) treatment-naïve group of the patients.

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