

Original Article

Pattern of Plasma Lipid Profile among HIV Positive Patients on Anti-Retroviral Therapy

Atiba AS,¹ Odimayo MS,² Akande JO,^{3*} Niran-Atiba TA,⁴ Daramola AO,⁵ Oparinde DP.⁶

¹Department of Chemical Pathology, Ekiti State University, Ado-Ekiti, Nigeria

²Department of Microbial Pathology, University of Medical Sciences, Ondo City

³Department of Chemical Pathology, Bowen University, Iwo, Nigeria

⁴Department of Biomedical Sciences, Ladok University of Technology, Ogbomoso, Nigeria

⁵Department of Haematology and Blood Transfusion, Ekiti State University

⁶Department of Chemical Pathology, Ladok Akintola University of Technology, Ogbomoso, Nigeria

*Correspondence: Akande JO

Email: atiadesam08@gmail.com; prophyjoe30@gmail.com

Tel: +2347030454127; +2347066377491

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ABSTRACT

There are improvements all over the world in the management of HIV/AIDS. However, adverse reactions of drugs used in the treatment are still being observed. Patients on treatment with anti-retroviral drugs are to take these medications for life. Prolonged intake of these drugs needs to be investigated. This study was therefore set up to investigate some associated body derangements involving prolonged anti-retroviral medications such as dyslipidemias. This research was conducted on 260 patients who were HIV positive. Patients who were obese, those on lipid modifying drugs and those who are diabetic or hypertensive were excluded from the study. Parameters of lipid profile except low density lipoprotein – cholesterol were analyzed by the use of commercial kits manufactured by Randox Laboratory, Alden, USA, low density lipoprotein – cholesterol was calculated by the use of Friedewald equation. The plasma HDL-c is significantly higher in female (2.77 ± 1.22) subjects than male (2.36 ± 0.92) subjects ($p=0.015$). There were no statistically significant differences among the groups considering duration of therapy. Greater percentage of our study population had taken ART for a period less than 5 years. And there was no significant trend observed in the parameters of lipid profile. The study found no significant association between the parameters of lipid profile and duration of therapy. The greater percentage of our studied population had only taken therapy for less than five years. A regular check on lipid profile may throw more light on this subject.

Keywords: HIV/AIDS, Antiretroviral drugs, Adverse drug reaction, Lipid profile

INTRODUCTION

Over the years, treatment of HIV infection is improving.¹ Improvement in the treatment may however, comes with its own challenges. Despite this improvement, drug adverse reactions as well as drug to

drug interactions are still a thing of worry. Furthermore, there are complications of HIV infection on its own that can be worsened by these anti-retroviral drugs when administered.² Metabolic complications of lipid metabolism, characterized by signs of lipodystrophy, insulin resistance, central adiposity, dyslipidemia, increased risk of cardiovascular disease and even an increased risk of atherosclerosis have been observed among patients with HIV infection³. Studies have shown that anti-retroviral therapy (ART) compounded the effects of HIV infection by increasing lipid oxidation.^{4,5} It has been demonstrated that patients on first line ART had high levels of total cholesterol (TC), low density lipoprotein - cholesterol (LDL-c) and high TC/HDL-c ratio compared with ART-naive patients.⁶ Protease inhibitors, Indinavir and lopinavir, were found to be commonly associated with hypercholesterolemia, high LDL-c, low HDL-c, and hypertriglyceridemia while Atazanavir was apparently associated with a more advantageous lipid profile⁷ However, these studies did not consider the duration of therapy as at the time these patients were being captured into the study. This would have shown the pattern of these parameters of lipid profile over a period of anti-retroviral drugs (ARD) administration. Drug accumulation causes adverse drug reaction⁸. There are reports to support the effects of drug accumulation on some biochemical parameters.^{9,10}

Considering the above findings, and coupled with the known effects of socio-cultural habits on some parameters of lipid profile, this study was designed to look at the pattern of fasting plasma lipid profile in patients who had taken ART for a period of time.

MATERIALS AND METHODS

This study was conducted in the Department of Chemical Pathology of the Ekiti State University Teaching Hospital, Ado-Ekiti. Research assistants who were NYSC members in the Department were trained to take records from HIV clinic into the research

protocol designed. This protocol was designed to accommodate variables like patients' ages, duration of treatment as at the time patients were being recruited. After patients were carefully recruited based on the set inclusion and exclusion criteria, they were scheduled for routine plasma lipid profile. This included Total cholesterol (TC), Low density lipoprotein -cholesterol (LDL-c), High density lipoprotein – cholesterol (HDL-c) and Triglyceride (Tg).

This research finally recruited 260 patients who were HIV positive into the study. Patients who were also HBsAg⁺ positive were not included in the study. Patients who were obese as evident by increased body mass index (BMI), those on lipid modifying drugs, those who were diabetic or hypertensive were excluded from the analysis. Patients with obvious dyslipidemia as reported in their case notes during physical examination were also excluded from the analysis.

In the laboratory, patients were asked to fast for a minimum period of ten hours overnight before three to four milliliters of whole blood sample was collected inside lithium heparin specimen bottle. This blood sample was centrifuged on its arrival in the laboratory at about 3000Xg for five minutes to harvest supernatant plasma. The plasma was kept frozen for the maximum period of five days before the analysis of parameters of lipid profile. The parameters of lipid profile were analyzed using ready to use commercial kits manufactured by Randox Laboratory, Alden, USA. These kits employed enzymatic method except for the LDL-c that was calculated by the use of Friedewald equation.¹¹

Variables were later entered and analyzed using SPSS 25.00. Data were presented in form of tables. ANOVA was used to compare association within different groups of patients and p- value <0.05 was considered significant

We sought and got ethical approval (EKSUTH/A67/2020/018) to conduct this study from the Ethics and Research Committee of the Ekiti State University Teaching Hospital, Ado-Ekiti.

RESULTS

The study, as shown in table1, 95 (37.3%) of the study population were between the ages of 20 and 34, 95 (36.5%) were between the ages of 35 and 44, 62 (23.9%) were between the ages of 45 and 64 and only 6 (2.3 %) were above 65 years of age. Sixty-six (25.4%) of the patients recruited were males while 194 (74.6%) of them were females. Thirteen (6.7%), out of female population recruited had body mass index (BMI) kg/m² less than 18.5 while 181 (93.7%) had BMI between 18.5 and 29.9 kg/m². Among male population recruited, 11 (16.7%) had BMI less than 18.5 kg/m² while 55 (83.3%) had BMI between 18.5-29.9 kg/m². Seven (3.6%) of female and one (1.5%) of male populations had CD4 count less than 200 cell/μl. Ninety (46.4%) of female, 20 (30.3%) of male had CD4 count between 200-500 cell/μl while 97 (50%) of female and 45 (68.2%) of male had CD4 count of greater than 500 cell/μl.

Table 1: Socio-demographic Data and CD4 (cell/μl) count of the Subjects

Variables	Group	n (%)
Age (year)	20-34	97 (37.3%)
	35-44	95 (36.5%)
	45-64	62 (23.9%)
	>65	06 (2.3%)
Sex	F	194 (74.6%)
	M	66 (25.4%)
BMI (kgm ⁻²)	F	
	<18.5	13 (6.7%)
	18.5 – 29.9	181 (93.3%)
	M	
<18.5	11 (16.7%)	
18.5 – 29.9	55 (83.3%)	
CD4 count (cell/μl)		
	F	
	<200	07 (3.6%)
	200 – 500	90 (46.4%)
	>500	97 (50%)
	M	
<200	01 (1.5%)	
200 – 500	20 (30.3%)	
>500	45 (68.2%)	

Table 2 shows mean distribution of the parameters of lipid profile between males and females subjects. There were no statistically significant differences in the parameters except for HDL-c when compared. The plasma HDL-c is significantly higher in female (2.77±1.22) subjects than male (2.36±0.92) subjects (p=0.015)

Table 3 shows comparison of parameters of lipid profile among different age groups. There were no statistically significant differences in any of the biochemical parameters among different classes of age.

Table 2: Mean Distribution of Lipid Profile between Genders

Variables	Male (66)	Female (194)	t-test	p-value
T-Chol (mmol/L)	4.00±1.01	4.27±1.29	-1.542	0.124
HDL-Chol (mmol/L)	2.36±0.92	2.77±1.22	-2.438	*0.015
LDL-Chol (mmol/L)	1.11±0.3	1.04±0.31	0.410	0.151
TG (mmol/L)	1.11±0.63	1.07±0.71	0.682	0.682

Table 3: Mean Distribution of Lipid Profile among Age (year) Categories

Variables (mmol/l)	N	Mean	X ²	Df	p-value	
TC	20-34	96	4.16±1.27	0.108	3	0.976
	35-44	92	4.21±1.68			
	45-64	65	4.24±1.21			
	=65	7	4.30±1.80			
HDL-C	20-34	96	2.61±1.16	0.228	3	0.919
	35-44	92	2.70±1.10			
	45-64	65	2.72±1.19			
	=65	7	2.56±1.89			
LDL-C	20-34	96	1.06±0.31	0.064	3	0.721
	35-44	92	1.07±0.31			
	45-64	65	1.05±0.35			
	=65	7	0.93±0.42			
Tg	20-34	96	1.07±0.66	0.359	3	0.520
	35-44	92	1.14±0.79			
	45-64	65	1.00±0.58			
	=65	7	1.30±0.73			

Table 4 shows biochemical parameters considering different durations of therapy. There were no statistically significant differences among the groups. Greater percentage of our study population had taken ARD for a period less than 5 years. And there was no significant trend observed.

In table 5, parameters of lipid profile were compared among patients placed on different anti-retroviral drug regimen. The study observed no statistically significant differences among the studied groups.

Table 4: Mean Distribution of Lipid Profile Considering Duration (Year) of Anti-retroviral Treatment

Variables (mmol/l)	N	Mean	X ²	Df	p-value
TC			1.950	3	0.277
<1	12	3.61±1.90			
1-3	154	4.17±1.18			
>3-5	91	4.31±1.21			
>5	3	4.60±1.21			
HDL-C			1.339	3	0.398
<1	12	2.14±1.72			
1-3	154	2.65±1.13			
>3-5	91	2.74±1.14			
>5	3	2.90±0.98			
LDL-C			0.087	3	0.473
<1	12	0.92±0.35			
>3-5	154	1.07±0.32			
1-3	91	1.06±0.33			
>5	3	1.10±0.00			
Tg			0.194	3	0.749
<1	12	0.91±0.55			
1-3	154	1.11±0.76			
>3-5	91	1.05±0.59			
>5	3	1.10±0.10			

Key (Table 5)

AZT= Zidovudine, 3TC= Lamivudine, EFV= Efavirenz, NVP= Nevirapine, ALLUVIA= Alluvia-ritonavir boosted lopinavir, FTC= Emtricitabine

Table 5: Mean Distribution of Parameters of Lipid Profile among Patients on different Anti-Retroviral Regimen

Variables	N	Mean	X ²	Df	p-value
TC			1.597	6	0.389
AZT,3TC,EFV	18	4.03±1.08			
AZT,3TC,NVP	24	4.28±1.23			
TDF,FTC,NVP	6	3.47±1.05			
TDF,3TC,ALLUVIA	5	3.70±1.97			
TDF,3TC,NVP	12	4.28±0.83			
TDF,3TC,EFV	8	4.03±0.46			
Others	7	3.54±1.97			
HDL-c			1.249	6	0.479
AZT,3TC,EFV	18	2.57±0.98			
AZT,3TC,NVP	24	2.73±1.17			
TDF,FTC,NVP	6	2.23±0.75			
TDF,3TC,ALLUVIA	5	2.24±2.07			
TDF,3TC,NVP	12	2.65±0.97			
TDF,3TC,EFV	8	2.40±0.47			
Others	7	1.93±1.74			
LDL-c			0.21	6	0.977
AZT,3TC,EFV	18	1.05±0.21			
AZT,3TC,NVP	24	1.06±0.33			
TDF,FTC,NVP	6	1.03±0.33			
TDF,3TC,ALLUVIA	5	0.96±0.38			
TDF,3TC,NVP	12	1.10±0.20			
TDF,3TC,EFV	8	1.14±0.33			
Others	7	1.06±0.47			
Tg			0.562	6	0.312
AZT,3TC,EFV	18	1.22±0.70			
AZT,3TC,NVP	24	1.10±0.71			
TDF,FTC,NVP	6	1.25±0.8			
TDF,3TC,ALLUVIA	5	0.70±0.48			
TDF,3TC,NVP	12	0.78±0.37			
TDF,3TC,EFV	8	1.08±0.61			
Others	7	0.71±0.69			

DISCUSSION

Greater percentage of our studied population falling below 44 years of age as shown in table 1 is in agreement with reported age group commonly affected by HIV/AIDS. World Health Organization and UNAIDS reported similar prevalence in this same age group.^{12,13} The prevalence of HIV has been reported to be higher in females than males.¹⁴ Our observation was in agreement with this.

There was a significant higher plasma level of HDL-c

in females than males among our study population. This is not an unfamiliar finding as there are reports in the literature to support this observation.^{15,16} The study by HyeJin *et al.*, carried out in a Korean population reported as observed in our study.¹⁷ This has therefore been postulated to be due to the fact that there is a close association between plasma HDL-c and smoking as well as alcohol consumption of which men are more likely to indulge in such acts.¹⁸ Obesity and increasing age are also known to have close association with plasma HDL-c. However, these may not be factors to consider in our subjects as we observed no significant differences in the age and BMI (kg/m²) between male and female population of our subjects. Furthermore, the general belief that estrogen has a positive correlation with plasma HDL-c could be a factor to explain this result. It is said that postmenopausal women do have a decreased plasma level of HDL-c. The higher level of HDL-c in females than males as observed in our study can be also due to the fact that the majority of our studied population are below menopausal age. Women in their menopause ages do have lower estrogen plasma level as this is one of the biochemical parameters being used in the confirmation of menopausal state.

The observed pattern of total cholesterol in different age groups are not different from what has been observed in previous studies as found in the literature. The highest plasma level of total cholesterol was seen in subjects above 65 years of age. The study by Tarig *et al.* observed significantly raised value of total cholesterol in populations above 55 years of age.¹⁹ The findings on other parameters of lipid in different age groups are not significant. This may be due to the fact that the studied groups are apparently healthy patients. This is evidenced by the levels of CD4 count which majority has within normal range and one does not expect any form of dyslipidemia at such levels.

Drugs are often given to get the desired therapeutic effects. However, these are not always without adverse reactions. Adverse drug reaction may come in form of type A or type B. Type A follows the usual

pharmacological effects which may be associated with drug accumulation over a period of time. This is the reason we recruited patients who had taken medications over a period of time. Adverse drug reactions may be detected based on some observed unexpected clinical signs and symptoms while some are linked to biochemical derangements. Our study observed parameters of lipid profile in patients who were on ART. In our study, the observed no statistically significant differences in patterns of lipid profile and duration of anti-retroviral medications is not that different from the study of Doddigarla *at al.*²⁰ In our study which was comparative as against theirs which was longitudinal, there were statistically significant differences between patients with HIV infection on treatment and newly diagnosed HIV infection in all the parameters of lipid (TC, Tg, HDL-c, LDL-c). Despite the significant differences observed in their study all the mean values of all the parameters of lipid were within the acceptable normal limits. Findings of our study in this regard were not different. However, the consideration of five years and below duration of medication may be a limitation. Different antiretroviral drug regimens are known to be associated with different forms of dyslipidemias and majority of these are reported in isolation or as a case report.³

A comparison of parameters of lipid profile in patients on different antiretroviral regimen showed no significant differences. The is in contrary to the reports from other earlier studies.^{7,15,21} It has been reported that administration of protease inhibitor such as indinavir has association with hypercholesterolemia, raised LDL-c, reduced HDL-c and hypertriglyceridemia. In the same vein, patients on neucloside reverse transcriptase inhibitors such as zidovudine have been linked to having hypertriglyceridemia.⁷ The background lipid metabolism, genetics as well as diet and environmental factors before the commencement of ARD could play a significant role in the overall lipid profile status after the commencement of the therapy. This may be a factor among our people in our

environment. A look into individual drug may give a more elaborate information about the ARD effects on plasma lipids in the community but this may prove difficult as patients are placed on combination therapy.

CONCLUSION

The present study has shown that there were no significant associations between the parameters of lipid profile and duration of therapy as a greater percentage of our studied population had only taken therapy for a period less than five years. This duration on the average may be too short to draw definite conclusions. A regular check on lipid profile over a considerably longer period may throw more light on the topic. Also, the effect of individual drugs on parameters of lipid profile may further throw more light on the subject.

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