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Research Paper

Apolipoprotein C3T-455C polymorphism is not associated with dyslipidemia in HIV patients on HAART in Southwest Nigeria

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ABSTRACT: *The use of Highly Active Antiretroviral Therapy (HAART) in Human Immunodeficiency virus (HIV) infection is associated with dyslipidaemia in HIV positive individuals. Studies from some climes have reported that Apolipoprotein (Apo) C3 polymorphism is a candidate gene for dyslipidaemia including hypertriglyceridaemia and decreased high density lipoprotein in HIV infection . Therefore, this study ivestigated the association of ApoC3 T-455C genetic polymorphism and altered lipid profile in HIV positive subjects on HAART and HAART Naive in a population of southwest Nigeria. One hundred individuals comprising of forty HIV positive individuals on HAART , twenty HIV HAART naïve and forty HIV negative controls were recruited. Venous blood was collected, plasma total cholesterol (TC) and triglyceride (TG) were quantified enzymatically while high density lipoprotein (HDL) was analyzed using precipitation method. Low density lipoprotein-C (LDL) was calculated using Friedewald equation, and Total cholesterol/High density lipoprotein (TC/HDL-C) using standard formular. Frequencies of ApoC3T-455C polymorphism was determined by Amplification Refractory Mutation System (ARMS) Polymerase Chain Reaction. Results were expressed as Mean ± Standard Error of Mean (SEM). One way Analysis of variance, odds ratio and confidence interval were used in analyzing the data at $p < 0.05$ level of significance. Total cholesterol and HDL-C levels for HIV positive on HAART (4.03 ± 0.15 mmol/L, 1.13 ± 0.05 mmol/L) and HAART naïve (3.36 ± 0.20 mmol/L, 0.81 ± 0.07 mmol/L) were significantly lower compared to the controls (4.30 ± 0.16 mmol/L, 1.21 ± 0.04 mmol/L) ($p=0.003$) respectively . TC/HDL-C of HAART naïve (3.81 ± 0.20 mmol/L) and HIV positive individual on treatment (4.63 ± 0.45 mmol/L) were higher than in controls (3.67 ± 0.17 mmol/L) ($p=0.04$). Non-significant changes in plasma TG, LDL, VLDL and Non -HDL concentrations of HIV positive individuals were recorded compared to controls. The frequencies of homozygous ApoC3 455C/C (40.63 %) and 455T/T(9.38 %) genotypes were higher in all HIV positive subjects than controls (21.43% and 7.14 %) whilefrequency of heterozygous 455C/T genotype was lower in HIV positive (50%) than controls (71.43%). Significant associations between ApoC3 455 gene polymorphism and HIV risk for CC genotype (OR = 0.187, CI=0.059-0.587, p =0.004); and for TT (OR = 0.008, CI = 0.001-0.051, p = 0.0001) were observed with an insignificant association for TC (OR= 2.500, CI=0.854-7.316, p = 0.120). wild type T allelic frequencies of HIV positive and control subjects were 34.38 % and 42.86 % ($P > 0.05$), while for variant C allele were 65.63% and 57.14% ($P > 0.05$) respectively. Measure of association between Apoc3 T-455C with lipid profile showed no significant difference ($p > 0.05$). Lipid abnormalities were observed in HAART naive and those on HAART even in the absence of host related risk factors for dyslipidaemia. ApoC3 T-455C gene polymorphism showed a non-significant relationship with altered lipid profile among the studied subjects. Homozygous ApoC3 T-455C genotypes was strongly associated with HIV infection. A larger sample size is required for confirmation in a further study.*

KEYWORDS: *Apo C3 polymorphism ,dyslipidemia, highly activeantiretroviral therapy, Nigerian*

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I. INTRODUCTION

The treatment of HIV infection with antiretroviral therapy has reduced susceptibility to diverse range of metabolic derangements consequently increasing the survival and life expectancy of people living with the immunodeficiency virus (1). HIV/AIDS infected individuals develop diverse metabolic abnormalities such as hyperinsulinaemia, adipose tissue redistribution, cardiovascular disease and dyslipidaemia. The pathogenesis of dyslipidemia in HIV involves the impact of the drug, chronic inflammatory status, hormonal influence, genetic predisposition or the infection itself (2). The dyslipidemia linked with HAART has been reportedly marked by reduced high density lipoprotein (HDL-C), elevated levels of total cholesterol (TC), triglyceride (TG), low density Lipoprotein (LDL-C), very low density lipoprotein (VLDL), apolipoprotein B and C3 which together constitute a highly atherogenic lipid profile (3). Hypocholesterolemia reportedly prevalent during the earliest stage of HIV infection was linked to alteration in some specific immune functions (3). Research have shown that genetic factors may be implicated in dyslipidaemia because not all HIV positive individual that are exposed to same drug regimen, with comparable demographic, virological, and immunological characteristics develop metabolic disorders associated with lipid profile variations (4).

Candidate gene studies have pinpointed that single nucleotide polymorphism (SNPs) could account for alterations in blood lipid level (5). Polymorphic variants of over 400 genes that control lipid metabolism are found in humans with carriers of aberrant alleles displaying higher risk of obesity and its associated complications (5, 6) Genetic variation of enzymes, receptors and apolipoproteins, which are important for LDL-C metabolism, are partially involved in the regulation of LDL-C and total cholesterol (7).

Apolipoprotein C3, a glycoprotein produced in the liver and small intestine is a major component of chylomicron, very low and high density lipoproteins. It regulates intravascular triglyceride metabolism through inhibition of lipoprotein lipase and interference with apoE mediated triglyceride–rich lipoprotein uptake by hepatic receptors (8). ApoC3 455T-C polymorphism is linked with HAART related dyslipidemia in HIV individuals (9) while a change of thymine to cysteine at position -455 is linked with elevated triglyceride and decreased high density lipoprotein constituting a risk factor for cardiovascular disease(10).

HAART impairs hydrolysis of triglyceride-rich lipoprotein by plasma and tissue lipases (Sekhar *et al.*, 2005 (10) and alters normal post prandial catabolism of free fatty acids and lipoprotein (Van wijk *et al.*, 2005 (11). Previous studies (12,13) showed disparity in the pattern and severity of dyslipidaemia among racial groups. Foulkes et al (12) reported an association of apoC3 polymorphism with lower triglyceride and higher high density lipoprotein cholesterol levels in a black, non- Hispanic group this was in contrast with other observations of an increase in blood triglyceride in white /non -Hispanic subjects (13) and in European Carriers of APOC3 variant alleles due to HAART treatment (14).

The HIV epidemic in Nigeria is complicated as it varies widely from one state to another based on high risk sexual behavioural habits. The prevalence of HIV infection in Osun State South-western Nigeria increased from 2.0 to 2.7 percent in 2014 (1) Therefore the present research studied for the first time the prevalence of apoC3 455T/C polymorphism and its association with altered lipid metabolism in HIV positive naive patients and those on HAART regimen among a population of Osun State, Southwestern Nigeria.

II. SELECTION OF SUBJECTS

This was a consecutive case - control study carried out on 100 individuals. Of this number, 40 were HIV positive patients on first line HAART regimen (Zidovudine + Lamivudine + Nevirapine). Twenty were HIV positive naïve patients (those yet to commence HAART) attending the HIV clinic of State Specialist Hospital Osun state, Nigeria. 40 apparently healthy individuals served as controls. All participants were briefed about the objectives of the study and completed a questionnaire which captured their demographic characteristics, health status, family history. Informed consent was sought and obtained. Control subjects were screened using Determine Rapid test kit. Anthropometric measurements of all subjects were taken. Ethical approval was obtained from the Ethics and research committee of the State Hospital Asubiaro Osun State, Nigeria(REC/27/04/2015/SSHQ/016).

Subjects diagnosed of HIV from 3months, whose $CD4^+$ count were < 200 cells/μL were recruited for this study. viral load copies of ≥ 20 cp/ml was utilized in selecting subjects based on Diagnostic criteria for AIDS established by the Centers for disease control and prevention. Dyslipidemia in HIV was defined according to the NCEP/ATP III criteria for metabolic syndrome (15). These include: elevated triglyceride (≥1.69mmol/L), low HDL cholesterol (≤1.03mmol/L in men, ≤1.29mmol/L in women), hypertension (≥130/≥85mHg).

HIV positive HAART naïve individuals, HIV positive on HAART regimen and apparently healthy controls that were willing to participate in the study were included. Individuals on lipid lowering regimen, menopausal women and those on contraceptives were excluded.

III. BLOOD COLLECTION

5 ml of blood was collected through venepuncture from each of the subjects after 12 hours overnight fast. 3ml was carefully dispensed into EDTA bottle for determination of lipid profile parameters while 2ml was dispensed into tri potassium EDTA bottle for Genetic ApoC3 analysis. Plasma sample was spun at 1500 revolution per minute at 4 ˚C for 30 min, separated and stored frozen.

IV. BIOCHEMICAL MEASUREMENTS

Total cholesterol and Triglyceride concentrations were determined by enzymatic and hydrolysis methods as previously described (16,17) using Biosystems kit (S.A. Barcelona) while,high density lipoprotein cholesterol was determined using precipitation method.

Low density Lipoproteins was calculated using Friedewald formula (18):

LDL-Cholesterol = total cholesterol (mmol/L) – triglyceride /2.2 (mmol/L) – HDL

while very low density lipoprotein and Non –HDL were calculated using these formulae:

VLDL = Triglyceride/2.2

Non –HDL = TC – HDL-C

V. DNA EXTRACTION AND GENOTYPING

DNA was extracted from the sample using Bioline DNA extraction kit (Bioline USA) according to manufacturer's instruction.

The ApoC3T-455C polymorphism was detected using Amplification Mutation refractory system (ARMS) based on PCR reaction, out of 100 samples, only 60 were successfully genotyped. All PCR product reactions were ran in a final volume of 20µl comprising of 8.9µl of distilled H_2O, 2.5µl of 10X PCR buffer, 0.8 µl of dNTPs, 1.0 µl of $Mgcl_2$, 0.8µl of forward C and T primers, 0.8µl of reverse primer, 0.2 µl of Taq polymerase and 5µl of DNA. The polymerase chain reaction was performed under the following conditions; Initial denaturation at 95˚C for 5min, followed by 30 cycles of 94˚C for 45 seconds, Annealing temperature 58˚C for 30 seconds, 72˚C for 1min while the final extension step was done at 72˚C for I0 min. The DNA fragments were separated on a 2% Agarose gel and the bands visualized under 300nm ultraviolet transillumination. The primers of T-455C were Forward C 5'-GGGAAATGGCTTGGACATAG-3' Forward T 5' TCTGTGCCTTACTCCAAACAT-3' Reverse CT 5'GGGAAATGGCTTGGACATAG3' while the Amplicon base pair was 200kbp

The statistical analysis was done using SPSS version 20.0 software packages. Results were expressed in mean ± standard error of mean, one–way analysis of variance (ANOVA) was employed to compare the differences between the subjects. Chi-square test was used to examine the significance of the association in frequency distribution of variables. Pearson correlation was used to determine the association between variables; Odds ratio (OR) and 95 % confidence interval were computed. Also tests were considered significant at $p < 0.05$.

VI. RESULTS

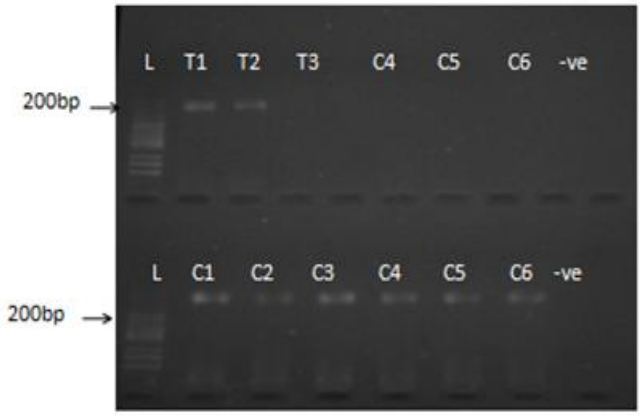

Figure 1: 2 % Agarose gel electrophoresis picture showing the DNA fragment using Amplification Restriction Mutation System for ApoC3 T-455C genotyping. Lane 1-3 TC heterozygous, lane C4-C6 homozygous (CC) L- ladda, -ve Negative

6.1Lipid profile levels in the study group

Results obtained from the comparison of biophysical parameters of HIV positive subjects on HAART, HAART Naïve and controls are shown in Table 1 . There were significant differences in the mean ages of HIV subjects on HAART and HIV naïve subjects compared to controls ($p < 0.05$). However, no significant differences were observed in the mean values for height, systolic blood pressure, diastolic blood pressure and body mass index.

From table 2, the mean plasma valuesof total cholesterol and high density lipoprotein was significantly lower in HAART users and treatment naïve groups compared to controls ($p<0.05$). Higher values of TC/HDL ratio was recorded in HAART naïve and HIV subjects on HAART than controls ($P < 0.05$).

Table 1: Biophysical parameters of the study population **(**Mean ± S.E.M)

Parameters	HIV positive HAART (n=40)	HAART Naïve (n=20)	Control (n= 40)	p-value
Age (yrs)	41.90 ± 1.37	38.50 ± 2.42	34.78 ± 1.90	0.01**
Height (M^2)	1.66 ± 0.02	1.66 ± 0.03	1.65 ± 0.01	0.65
Weight (Kg)	61.65 ± 2.13	61.35 ± 4.44	58.63 ± 1.81	0.60
SBP (mmHg)	122.78 ± 2.79	121.40 ± 4.03	121.33 ± 2.27	0.91
DBP (mmHg)	80.83 ± 1.80	79.35 ± 2.47	76.60 ± 1.56	0.21
BMI (kg/m^2)	22.28 ± 0.70	22.30 ± 1.29	21.95 ± 0.97	0.96

**significant@p = 0.01

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, BMI: Body Mass Index,

Table 2: Plasma lipid profile of the study population (N= 100) (Mean ± SEM)

Parameters	HIV positive on HAART (n= 40)	HAART Naive (n= 20)	Controls (n=40)	p-value
TC (mmol/L)	4.03± 0.15	3.36± 0.20	4.30±0.16	0.003**
TG (mmol/L)	1.51± 0.09	1.53± 0.13	1.45±0.08	0.82
HDL (mmol/L)	1.13± 0.05	0.81± 0.07	1.21±0.04	0.00**
LDL (mmol/L)	2.21± 0.15	1.83± 0.16	2.43±0.20	0.70
VLDL (mmol/L)	0.68± 0.04	0.73± 0.07	0.65±0.03	0.62
TC/HDL(mmol/L)	3.81± 0.20	4.63± 0.45	3.67±0.17	0.04*
Non –HDL	2.90± 0.15	2.55± 0.18	3.09±0.16	0.12

significant@*p<0.05, **p<0.01

TC: Total Cholesterol, TG: Triglyceride, HDL: High density Lipoprotein,
LDL: Low density Lipoprotein, VLDL: very low density lipoprotein

Of the 60 individuals from the study population that were successfully genotyped. 28 (46.7%) were apparently healthy controls, 20 (33.3%) were HIV positive subjects on HAART while 12 (20.0%) were HAART naïve. the largest percentage (60.0%) of the population have heterozygous TC genotype while 31.7 % were CC and 8.3 % were TT homozygotes

Table 3 shows that the mean Age value was significantly higher in HIV subjects compared to controls ($P < 0.05$). The mean HDL-C was significantly lower in HIV subjects compared to control subjects. The mean Height, weight, BMI, systolic blood pressure, diastolic blood pressure was not significant ($p > 0.05$).) Very low density lipoprotein, triglyceride, TC/HDL and Non-HDL expressed no significant differences.

Table 3: Biophysical and Biochemical parameters of the genotyped population (N=60) (Mean ± SEM)

Parameters	HIV positive n=32	Controls n=28	p-value
Age (years)	39.72 ± 1.74	32.39 ± 1.99	0.01**
Height (meters)	1.69 ± 0.02	1.64 ± 0.01	0.90
Weight (Kg)	65.94 ± 3.32	59.00 ± 2.23	0.98
SBP(mmHg)	123.16 ± 2.99	118.82 ± 2.42	0.27
DBP (mmHg)	80.50 ± 1.93	75.75 ± 1.86	0.84
BMI (kg/m^2)	23.28 ± 1.07	22.18 ± 1.31	0.52
TC(mmol/L)	3.90 ± 1.05	4.09 ± 0.81	0.43
TG(mmol/L)	1.54 ± 0.63	1.42 ± 0.49	0.42
HDL (mmol/L)	1.04 ± 0.44	1.23 ± 0.29	0.03*
LDL (mmol/L)	2.17 ± 0.96	2.20 ± 0.77	0.91
TC/HDL (mmol/L)	4.21 ± 1.89	3.48 ± 0.97	0.99
VLDL (mmol/L)	0.70 ± 0.29	0.65 ± 0.22	0.70
Non–HDL-C (mmol/L)	2.84 ± 0.98	2.86 ± 0.75	0.39

significant@*p = 0.05, ** 0.01

Homozygous Apo C3 455 CC and TT genotypes showed a significant association with HIV occurrence but a non significant association was observed with 455TC genotype. TC genotype has the highest distribution in HIV positive individuals compared with CC and TT respectively. A similar pattern of genotypic frequencies was observed in control subjects. The allelic distribution of 455T and 455 C was not significantly associated with HIV infection. A prevalence of 34.4 % for 455T wild type and 65.6% for 455C variant were observed at polymorphic sites in HIV positive subjects. 42.9% and 57.14% prevalence were observed at T-455C polymorphic sites respectively in controls (Table 4**)**

Table 4: Genotypic and allelic distributions of Apoc3 T455-C of the genotyped population in the studied subjects(n=60)

Variable	HIV Positive (n=32)	Controls (n=28)	OR (95 % CI)	p-value
455 Genotype				
455CC	13(40.63)	6(21.43)	0.187(0.059-0.587)	0.004**
455TC	16 (50.0)	20(71.43)	2.500(0.854-7.316)	0.12
455TT	3(9.38)	2 (7.14)	0.008(0.001-0.051)	<0.0001***
Allelic Frequency				
455T	22(34.38)	24(42.86)	1.871(0.590-5.890	0.40
455C	42(65.63)	32(57.14)	0.67(0.259-10.82)	0.67

significant@ ** p = 0.01,*** 0.001

Table 5 showed the biochemical parameters in HIV positive subjects and controls analyzed separately based on Apoc3 T455-C genotypes and the results showed no significant differences in all analyzed parameters (p > 0.05).

Table 5: Comparison of biochemical parameters according to Apoc3 T455-C polymorphism among HIV subjects and Controls (Mean ± S.E.M)

	HIV subjects				Controls			
Lipid Parameters/ ApoC3 genoytpes	455CC (n=13)	455TC (n=16)	455TT (n=3)	p –value	455CC (n=6)	455TC (n=20)	455TT (n=2)	p -value
TC (mmol/L)	3.98±0.34	3.69± 0.18	4.67±1.02	0.33	3.60±0.23	4.30± 0.17	3.50±0.90	0.96
TG (mmol/L)	1.64 ± 0.15	1.52 ± 0.18	1.48±1.02	0.52	1.13 ±0.77	1.50 ±0.11	1.18 ±0.64	0.29
HDL-C (mmol/L)	1.08 ± 0.11	0.99 ± 0.08	1.06±0.30	0.84	1.11± 0.12	1.29 ±0.06	0.99 ±0.07	0.20
LDL-C (mmol/L)	2.18 ± 0.31	1.99 ± 0.17	3.08±0.78	0.21	1.91 ±0.19	2.32 ±0.19	1.85± 0.69	0.43
Non-HDL-C (mmol/L)	2.90 ± 0.32	2.69 ± 0.19	3.61±0.72	0.34	2.49 ±0.17	3.01± 0.17	2.51± 0.97	0.27
TC/HDL	3.98 ± 0.38	4.32 ± 0.60	4.67±0.47	0.82	3.42 ±0.38	3.48± 0.22	3.62± 1.17	0.97
VLDL (mmol/L)	0.75 ± 0.07	0.70 ± 0.08	0.54±0.12	0.53	0.51± 0.03	0.68 ±0.05	0.67± 0.29	0.29

Table 6 showed that the duration of drug used correlated significantly with age (r = 0.306, p = 0.02), while duration of infection correlated positively with age and DBP respectively (r = 0.385, p = 0.00; r = 0.289, p = 0.03).

Table 6 : Correlation of biophysical and biochemical parameters in all study group (N= 100)

Parameter (mmol/l)		Age (yrs)	Height (meter)	Weigh (kg)	SBP (mmHg)	DBP (mmHg)	BMI(kg/m^2)
TC	r	0.05	0.09	0.169	0.118	0.138	0.198*
	P	0.13	0.372	0.093	0.243	0.17	0.04
TG	r	0.046	0.088	0.128	-0.066	0.036	0.099
	P	0.651	0.382	0.205	0.512	0.725	0.326
HDL	r	-0.069	-0.019	-0.096	0.091	0.033	-0.091
	P	0.498	0.85	0.342	0.366	0.747	0.371
	r	0.088	0.091	0.199*	0.107	0.131	0.230*
LDL	P	0.383	0.367	0.047	0.291	0.194	0.021
	r	0.079	0.106	0.219*	0.097	0.14	0.249*
NonHDL	P	0.434	0.295	0.03	0.335	0.164	0.012
	r	0.119	0.05	0.153	0.017	0.139	0.177
CHOL/HDL	P	0.238	0.62	0.128	0.867	0.167	0.077
	r	0.092	0.072	0.106	-0.049	0.041	0.086
VLDL	P	0.364	0.474	0.296	0.631	0.685	0.396

* Correlation is significant at the 0.05 level (2-tailed)
DI- duration of infection, DDU – duration of drug use

VII. DISCUSSION

The menace of HIV/AIDS has reduced the survival rate of infected individuals thereby threatening social, developmental achievement and economic advancement of a nation. Nigeria has a growing population of individuals infected with HIV/AIDS (1). The use of HAART has significantly reduced the mortality rate and increased longevity of infected individuals, however, HIV infection with or without drug regimen is reported to cause lipid profile abnormalities (1,3), with genetic variations accounting for disparities in humans (5). Our literature search does not reveal any available data on association of ApoC3 455T/C genotypes with altered lipid profile during HAART use in HIV positive individuals of Southwestern Nigeria descent. These relationships were investigated in this study.

Decreased high density and low density lipoproteins have been reported in earlier stage of HIV and as the disease progresses there is an increase in triglyceride-rich lipoproteins (19, 20). In the present study, a reduction in the mean plasma total cholesterol and high density lipoprotein levels, which are features of altered lipid profile, was recorded among HIV positive naïve subjects and HAART users. This is in accordance with previous investigations (3,21). The nutritional status of HIV 1 infected individual with protein and weight loss, might contribute to reduced total plasma cholesterol, HDL-C and LDL-C levels (22). In addition, HIV infection weakens reverse cholesterol transport in monocyte and macrophages in vitro and this could result in decreased high density lipoprotein production leading to an atherogenic condition (20).

A moderate, though statistically non-significant increase in TG and VLDL-C levels among HIV naive in comparison with HIV positive individuals on HAART and controls was observed in present study. This could be due to inflammation as HIV infection characterized by increased triglyceride and cholesterol levels is associated with elevated levels of cytokines. IFN- α was shown to bring about increased TG levels through a decrease in TG clearance as well as an increase in de novohepatic lipogenesis and VLDL synthesis (22). However we did not analyze for cytokines in blood of participants in this study.

Mean plasma TC/HDL-C value was significantly different among our study groups. The lower mean TC/HDL-C ratio observed in controls in comparison with HIV positive individual on HAART and HIV naïve individuals suggested that control subjects have a lower risk of developing coronary artery disease. These findings were at variance with the results obtained by Yusuf et al (23) that showed a significantly lower TC/HDL-C ratio among HIV positive individual on HAART compared with HIV naïve individuals and controls but is in agreement with another study (22) who observed a significantly increased TC/HDL-C in HIV HAART users compared to both treatment naïve and controls.

The gene area of Apolipoprotein C-III (ApoC3) contains three polymorphisms linked with HAART related dyslipidaemia (14).

A low prevalence of ApoC3 T-455 wild type allele and higher frequency of ApoC3 -455C variant was discovered among HIV positive individuals in this study. Similarly, an earlier study(24) on genetic variants of ApoC3 promoter gene reported a low prevalence of ApoC3 T-455 and a higher variant frequency of ApoC3−455C

allelesamong HIV positive cohorts in their Northern South African population, they thereafter proposed that this pattern predisposes individuals to lipid disorder including elevated triglyceride thus posing a higher risk of metabolic disorders.

From this study, the frequency of ApoC3 - 455 T /C genotype was highest in HIV subjects compared to CC and TT homozygous, a similar pattern was seen among control subjects. A contradictory observation of higher frequency of CC genotype among South Africans compared to European and Indian population was earlier reported (24).

Our results showed non- significant increases in total cholesterol and low density lipoprotein in the CC and TT homozygous groups than the TC heterozygous. These results are in agreement with an earlier report (25) but at variance with another (20) that established wild type ApoC3 455-TT polymorphic site has been linked with lower risk of metabolic complications in Africans thereby conferring a better lipid profile than with Caucasians. The impact of polymorphism is dependent on environmental interactions, being overweight, physical inactivity or smoking that predispose individuals to dyslipidaemia (27).

The significant positive correlation of total cholesterol and BMI in all study participants implies that as total cholesterol increases there is a significant increase in BMI levels. This result conforms with observations of Yusuf *et al.* (23). A significant positive correlation was also observed between the duration on HAART and low density lipoprotein (LDL) which suggested a predisposition of HIV subjects to hypercholesterolemia-linked metabolic disorders. These findings are in line with others (28) who reported additional incidences of cardiovascular disease with nearly 75 % of the plasma cholesterol incorporated into the LDL particles hence increasing risk of myocardial infarction.

In conclusion, the abnormal lipid profile found in this work showed that HIV infection irrespective of HAART use is associated with dyslipidemia. Patients on HAART regimen should be monitored for cardiovascular disease and other related abnormalities. Although some studies reported that Apo C3T-455C polymorphism is strongly associated with dyslipidemia, this study did not establish such a relationship. However, results from our study revealed for the first time a baseline knowledge that heterozygous genotype of ApoC3 T-455C polymorphism has the highest prevalence among HIV positive subjects in our southwestern Nigerian population. We believe this information will be useful in decision making on management of HAART-related dyslipidemia in people living with HIV in this locality. It is recommended that genetic testing prior to HAART drug initiation in HIV positive subjects should be undertaken for possible risk of lipid disorders.

A limitation of this study is the small sample size that may be responsible for lack of statistical significance of some analyzed parameters among study subjects. A further study involving alarger population size would be undertaken for confirmation of the role of Apo C3 C−482T and 3238C-G polymorphisms on the promoter region in the expression of ApoC3 protein and HAART-related dyslipidemia in Southwest Nigeria.

REFERENCES

[1]. Federal Ministry of Health. Annual report on HIV/ AIDS Health Sector Response in Nigeria by The National AIDS and STIs Control Programme. Pp 11-13, 30-39, *2014*

[2]. Fisher SD, Miller TL, Lipshultz SE. (2006). Impact of HIV and Highly Active Antiretroviral therapy on leukocyte adhesion molecules arterial inflammation. *dyslipidaemia and atherosclerosis*185(1): 1-11.

[3]. Riddler, S. A., Smit, E., Cole, S. R., *Ellen, S., Li, R.*(2003). Impact of HIV Infection and HAART on Serum Lipids in Men. *JAMA* 289(22): 2978–2982.

[4]. Egana-Gorrono L, Martinez E, Cormand B, Escriba T.(2013). Impact of genetic factors on dyslipidemia in HIV patients on ART. *AIDS* 27(4), 529-38

[5]. Kathiresan S, Willer CJ, Peloso GM.(2009). Common variants aa 30 loci contribute to polygenic dyslipidemia. *Nat Genet.* 41(1):56-65

[6]. Masebe T, Bessong PON, Dip RN, Meyer D. (*2014*). Genetic Variants of AApoc3 promoter and HLA –B gene in HIV infected Cohort in Northern South Africa" pilots study. *International Journal of Molecular Science* 15: 11403-11415.

[7]. Salazar, L. A., Hirata, M. H., and Forti, N. (2000). Pvu II intron 15 polymorphism at the LDL receptor gene is associated with differences in serum lipid concentrations in subjects with low and high risk for coronary artery disease from Brazil. *Clinical Chimica Acta*. **293(**1-2):75–88.

[8]. Jong MC, Hofker MH, Havekes LM (1999). Role of ApoCs in lipoprotein metabolism: functional differences between ApoC1, ApoC2, and AApoC3. *Arteriosclerosis, thrombosis, and vascular biology* 19(3):472–484. pmid:10073946

[9]. de Almeida ER, Reiche EM, Kallaur AP, Flauzino T, WatanabMA. (*2013*). The roles of genetic polymorphisms and Human Immunodeficiency Virus infection in lipid metabolism. *Biomedical Research International*836790.

[10]. Sekhar, R. V., Jahoor, F., Pownall, H. J., Rehman, K., Gaubatz, J.Lyer, D. and Balasubramanyam, A. (2005). Severely dysregulated disposal of postprandial triacylglycerols exacerbates hypertriacylglycerolemia in HIV lipodystrophy syndrome. *American Journal of Clinical Nutrition.* 81**:**1405–10.

[11]. Van Wijk, J. P., Cabezas, M. C., de Koning, E. J., Rabelink, T. J., van der Geest, R., and Hoepelman, I. M. (2005). In vivo evidence of impaired peripheral fatty acid trapping in patients with Human immunodeficiency virus-associated lipodystrophy. *Journal of Clinical Endocrinology Metabolism*. 90:3575–3582.

[12]. Allain CC, Poon LS, Chan CS., Richmond W, Fu PC. (*1974*).*Clinical Chemistry* 20 (4); 470-475.

[13]. Foulkes AS, Whol DA, Frank J, Pulev E., Restine S, Wolfe ML et al.(2006). Associations among race/ethnicity, apoC-III genotypes, and lipids in HIV-1-infected individuals on antiretroviral therapy. *PLoS Medicine*3(3):337–347.

[14]. Cheng S, Pang BO, Gu C, Sun SP, An C, Zhan ZP et al. Association between apolipoprotein C3 gene promoter polymorphisms and fasting triglyceride levels. A meta-analysis. *frontiers in laboratory medicine 2017*. 1:151-157 http;//doi.org./10.1016/j.flm

[15]. Eric B, Jacques B, Josette F, Patrice M, Jean-Bernard R. (2007),*AIDS Research and Human Retroviruses*24 (2). https://doi.org/10.1089/aid.2007.0076).

[16]. Artiss JD, Zak B.(1997), Measurement of cholesterol concentration. In N. Rifai, G.R. Warnick, M.H. Dominiczak. (eds). *Handbook of Lipoprotein Testing*.AACC Press, Washington. 99-114.

[17]. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2001),*JAMA* 285:248-2497.

[18]. Artiss, J. D., and Zak, B. (1997): Measurement of cholesterol concentration. In N. Rifai, G.R. Warnick, M.H. Dominiczak. (eds). *Handbook of Lipoprotein Testing*. AACC Press, Washington. 99-114.

[19]. Friedwald WT, Levy RI, Frederickson DS (1972) Estimation of the Concentration of Low Density Lipoprotein cholesterol in Plasma without use of preparative ultracentrifugation. *Clinical Chemistry*18:499-502.

[20]. Bernal, E., Masiá, M., Padilla, S., and Gutiérrez, F. (2008). High-density lipoprotein cholesterol in HIV-1 Infected patients: evidence for an association with HIV-1 viral load, antiretroviral therapy status, and regimen composition. *AIDS Patient Care STDs*. 22:569–575.

[21]. Mujawar Z., Rose H., Morrow M. P., Pushkarsky T.,Dubrovsky L.,Mukhamedova N.(2006) Human immunodeficiency virus impairs reverse cholesterol transport from macrophages. *PLoS Biol.* 4:e365.

[22]. Adedokun K A., Olisekodiaka J M., Adeyeye AD, Adepeju AA, Muhibi MA. (2017) CD4+ Cell Count, Lipid and Lipoprotein Levels In HIV Patients on Drug Treatment. *International Journal of AIDS Res*. 4(**1**): 145-151.

[23]. Grunfield SC, Kotler DP, Hamadeh R, Tierney A, Wang J, Person RN (1989). Hypertriglyceridemia in acquired ImmunodeficiencySyndrome. *American Journal of Medicine*86**:** 27-31.

[24]. Yusuf, R., Sambo, A. I., Mohammed, M. H., and Abdulazeez, H. (2014). Lipid profile of HIV patients attending Antiretroviral clinic in Zaria North Western Nigeria. *Sub-Saharan African Journal.* 14**:** 31-33.

[25]. Naran, N. H, Raal, F. J., and Crowther, N. J. (2009). Frequencies of the T-455C and C-482T apoCIII gene polymorphisms in different South African population groups and their relationship to fasting triglyceride levels.

[26]. Padmapriyadarsini, C., Ramesh, 1. K., Sekar, L., Ramachandran, 1. G., Reddy, D., Narendran, G., Sekar, S., Chandrasekar, C., Anbarasu, D., Wanke, C., and Swaminathan, S. (2015). Factors affecting high-density lipoprotein cholesterol in HIV-infected patients on nevirapine-based antiretroviral therapy. *Indian Journal of Medical Research.* 145: 641-650.

[27]. Clarke, H., and Mousa, S. A. (2009). The implications of pharmacogenomics in the treatment of HIV-1 infected patients of African descents. *Pharmacogenomics Personalized medicine.* 2: 93–99.

[28]. Freeman, D. J., Griffin, B. A., Holmes, A. P., Lindsay, C.M.,Gaffney,D., Packad,C.J., Shepherd,J.,(1994). Regulation of Plasma HDL cholesterol and sub fractiondistribution by genetic variation and environmental factors ; Association between the Taq B RFLP in the CETP gene and smoking and obesity. *Arteriosclerosis and Thrombosis.* 14(3):336-344.

[29]. Kumar, D., Bohra, S. K., Agarwal, M., Khicha, S., Choudary, S., and Midha, N. (2018). Prediction of CVS risk using Framingham and data on adverse effect of Antiretroviral drug risk in relation to lipodystrophy in HIV patient on HAART. *Journal of global infection Disease*. 10:182 -187.