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Dyslipidemia in HIV Infected Children and Adolescents on Highly Active Antiretroviral Therapy in Abuja, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author AAO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors JOL and MD managed the analyses of the study. Author AAO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Compelling evidence exists on the usefulness of highly active antiretroviral therapy in the improvement of life of people living with HIV. There is however growing concern from its prolong exposure in children because of possible undesirable effects on the body lipid profile with its potential cardiovascular risks. We therefore conducted this study to evaluate the lipid profile of children and adolescents on highly active antiretroviral therapy overtime in our health institution for possible intervention.
Methods: A cross sectional hospital based study was conducted among 161 HIV-infected children and adolescents on highly active antiretroviral therapy in our health institution from February to May 2016 for the above objectives. Data collection was through questionnaire interview, and

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results of laboratory assay, while analysis was with SPSS version 21 software. P > 0.05 was set as statistically significant and confidence interval calculated at 95%.

Results: The mean age of the study participants was 10.13 ±4.5 years, with 10-14 years 72(44.7%) forming the majority of the study population. One hundred and three (64.0%) were males, their mean body mass index, systolic/ diastolic blood pressures, total cholesterol, total triglyceride, low density lipoprotein cholesterol, and high density lipoprotein cholesterol were 16.01±3.0 mg/m^2, 93.50±9.9 mmHg/ 56.43±10.3 mmHg, 149.61±39.5 mg/dl, 119.95±12.1 mg/dl, 74.93±35.3 mg/dl, 55.04±19.7 mg/dl respectively. They were on highly active antiretroviral therapy for a mean duration of 7.91±3.2 years, with 139(86.3%) being on 1st line antiretroviral medications. Total cholesterol >170 mg/dl occurred in 45(27.9%) of the subjects, 30(18.6%) had high level of total triglyceride of >150 mg/dl, 20(12.4%) had low density lipoprotein cholesterol of >130 mg/dl, while high density lipoprotein cholesterol of <35 mg/dl occurred in 28(17.4%) of the subjects. Majorities of the study subjects with dyslipidemia were of grade1 and 2 elevations for total cholesterol, total triglyceride, and low density lipoprotein cholesterol. Risk factor for dyslipidemia include BMI [OR 2.158 (95% CI 1.014-4.59) p=0.044] using total cholesterol, and types of 1st line [OR 0.107 (95% CI 0.008-1.029) p-0.033], 2nd line HAART [OR 0.042 (95% CI 0.0007-1.38) p=0.006], and BMI [OR 0.316 (95% CI 0.112-0.88) p-0.023] using high density lipoprotein cholesterol.

Conclusion: Use of first and second line highly active antiretroviral therapy regimen, and high BMI were associated with raised lipid profile. These parameters are to be monitored periodically while on these medications for any rising trends.

Keywords: Dyslipidemia; HIV infection; children; adolescents; antiretroviral therapy.

1. INTRODUCTION

The global burden of HIV is worst hit in sub-Sahara Africa which alone accounts for 71% of the infections [1,2]. Nigeria is second to South Africa in this world burden with over 3.3 million of her population living with the virus out of which 360,000 were children below 15 years [3]. Antiretroviral therapy (ART) has remarkably improved the survival of perinatal infected children into adulthood. Such children are exposed to higher risk of ongoing HIV infection, and prolong use of ART on the metabolic functions of the body.

Ongoing chronic inflammation from HIV infection even in face of good viral suppression, and use of highly active antiretroviral therapy (HAART) are all associated with metabolic derangements such as dyslipidaemia, and changes in fat distribution [4,5]. Abnormal lipid profile has been reported in patients infected with HIV before the implementation of ART [6,7]. Serum triglyceride (TG) was found to be higher, while total cholesterol (TC), low density lipoprotein cholesterol (LDL-c) and high density lipoprotein cholesterol (HDL-c) were all lower in HIV positive patients without treatment when compared to uninfected controls [6,8,9]. Possible mechanism for the deranged lipid metabolism in HIV infected include alteration in the cytokine profile, decreased lipid clearance, and increased hepatic synthesis of VLDL [10]. Cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) appear to promote lipid peroxidation, and the production of reactive oxygen species [11]. Use of ART with the six classes' currently available is also associated with alteration of lipid profile. In a cross-sectional surveys of HIV-infected children and adolescents receiving ART by some researchers showed a high frequency of dyslipidemia, lipodystrophy, and high risk for cardiovascular diseases [12-15]. Triant et al. [14] in their study found a significantly higher prevalence of hypertension (21.2% vs 15.9%), diabetes (11.5% vs 6.6%) and dyslipidaemia (23.3% vs 17.6%) in HIV-infected patients than in the non-HIV cohort (p<0.0001 for each comparison. The TC, HDL-c, LDL-c, and apolipoprotein B which were all low with HIV infection are all markedly elevated following HAART administration [12-15]. The lipoatrophic and lipohypertrophic changes common in infected patients typically start to manifest after 6–12 months of ARV therapy [16]. Lipoatrophy which denotes a decrease in adipose tissue volume, and lipohypertrophy meaning the opposite occur commonly in visceral adipose tissue and in the upper trunk. These have clear clinical implications such as modifications of body image with its adherence challenges, ectopic fat distribution into the heart and liver tissues that will eventually lead to increased cardiovascular risk [16,17]. As reported recently, more than 800 HIV/AIDS patients on nucleoside reverse transcriptase inhibitors (NRTI) based

medication, and protease inhibitors (PI) based regimens were associated with a high risk for developing lipohypertrophy (OR=2.1, 95% CI 1.7 to 3.3, p<0.01; OR=6.1, 95% CI 4.1 to 9.7, p<0.01, respectively) [18]. Patients who use PI for a long period of time frequently present with hypertriglyceridemia, elevated levels of LDL-c, reduced HDL-c levels, and accumulation of apolipoprotein E and apolipoprotein CIII (apoCIII) [19-22]. PIs have been involved in this process through several pathways that include inhibition of apolipoprotein B degradation, and conversely, thymidine analogue regimens [stavudine, zidovudine] were associated with a high risk of lipoatrophy [19,20]. Studies evaluating fat redistribution and abnormalities in lipid metabolism are rare in children and adolescents with HIV/AIDS in most developing countries of the world with Nigeria inclusive. Going by this, the aim of the present study is to provide information on lipid values of HIV infected children and adolescent on HAART in our hospital because of cardiovascular risks associated with its use. This will not only provide baseline information, but also guide for possible intervention.

2. METHODS

We conducted a cross sectional survey of HIV infected children and adolescents on HAART in our paediatric out-patient special treatment clinic (POSTC) of the university of Abuja teaching hospital (UATH) from February to May 2016. POSTC provides out-patient clinic service for HIV infected children and exposed babies for treatment and monitoring. Doctors, nurses, adherence counselors, record clerks, pharmacists, nutritionists and home base-care provide daily health services for their clients from Monday-Friday, and from 7.30 am to 4 pm.

One hundred and sixty one (161) consecutive eligible children attending the POSTC were recruited and enrolled into the study after caregivers has provided written informed consent and children 7 years and above provided verbal assent. Inclusion criteria include: HIV positive children aged 6months to 18 years on HAART, those willing to participate in the study, and those not living very far away from the study area for easy collection of fasting blood sample for lipid profile. Exclusion criteria: Caregiver and older children unwilling to participate in the study, recent hospitalization, children with other chronic illnesses like diabetics, hypertension. Questionnaire was administered to eligible children and their parents/caregivers. Information obtained among others were: the age of the child, the sex, date of commencement of ART, type of HAART, their religion, place of abode, etc. Weight, length/height of all the enrolled children were measured using electronic Seca beam weighing scale accurate to the nearest 0.01 kg, and Roche standiometer /infantometer accurate to 0.1 cm, and body mass index calculated. Blood pressure (B/P) was measured with (*Accosson Sphygomanometer*, *Accoson Works, Parkway, CM19 5QP England)* with appropriate cuff for age, together with CD4 cell count, using automated Partec Cyflow easy count kit (*Partec code no. 05-8401 Western Germany*), and viral load (VL) measurement with (*Roche Smp /prep /cobs Taqman 96, USA)* for those who have not done their VL measurement in the last 6 months. The plasma total TC, TG, and HDL-c were estimated using Fully Automated Chemwell Awareness Machine, and LDL-c calculated using Friedwald equation. Desirable, borderline and undesirable levels of TC, LDL-c, HDL-C, and TGs were as follows: Desirable level (mg/dL) for TC is < 170, for LDL-c is < 110, HDL-c is >45, and TGs is < 150 [23,24]. Borderline level (mg/dL) of TC is between 170-199, LDL-c is between 110-129, HDL-c between 35-45, and no borderline values for TGs [23,24]. Undesirable level of these lipid profiles (mg/dL) include: TC of ≥200, LDL-c of ≥130, HDL-c of < 35, and TGs o f ≥125 [23,24].

Ethics clearance was obtained from the ethics committee of the health institution before the commencement of the study. Data analysis was computed using SPSS version 21.0 computer software packages. Tests of significance was with Chi-square or Fisher exact test (whenever the expected frequency in one of the cells was less than 5) and logistic regression was used for categorical variables, and analysis of variance or Student's *t*-test for continuous variables. Differences between groups were considered significant at p<0.05.

3. RESULTS

Table 1 is the characteristics of the 161 patients studied according to sex. There were 103 (64.0%) males and 110(68.3%) Christians. Majority of the study population 72(44.7%) were between the ages of 10 - 14 years, the least group 12(7.5%) being 15-18 years. Their mean age, weight, length/height, BMI, systolic/ diastolic blood pressure, CD4 cell count, and viral load (VL) were 10.13 ±4.5 years, 30.63±12.3 kg, 134.54±17.8 cm, 16.01±3.0 kg/m^2, 958.57±480.2

cells/µl, and 14,076.3±741.9 copies/ml respectively. They also had a mean TC, TG, LDL-c, and HDL-c of 149.61±39.5 mg/dl, 119.95±12.1 mg/dl, 74.93±35.3 mg/dl, 55.04±19.7 mg/dl respectively. Their average duration on HAART was 7.9±3.2 years, with 137(85.1%) being on 1st line ART. No statistically significant was observed in all the parameters studied for male and female subjects (Table 1).

Table 2 depicts lipid profile and duration on HAART. Using TC, 116 (72.0%) of the study population had normal TC, while 45(27.9%) had various degrees of dyslipidemias. Thirty (18.6%) had abnormal high level of TG using <150 mg/dl as the upper limit of normal, 20 (12.4%) had abnormal LDL-c, while 28(17.4%) had undesirable HDL-c level of < 35mg/dl. The majorities of the study subjects with abnormal lipid profile were of grades 1 and 2 elevation for TC, TG and LDL-c, however 28 (17.4%) had an undesirably high level of HDL-c. While no significant difference was seen in the lipid profile for ≤10 years and ≥10 years, there was however statistically significant difference in the VL of the two groups (≤10 years and ≥10 years), [5,192.07±3,587.75 Vs 10,581.78±8,085.76, (p=0.003)], (Table 2).

Table 3 is showing the lipid profile and types of 1st and 2nd line HAART. One hundred and fourteen (83.2%) of subjects on 1st line HAART had normal TC, while 16.8% had elevated level. For those on 2nd line 13(54.5%) had normal TC, while 45.8% had elevated TC. For TG, 110/137 (80.3%) had normal values for those on 1st line while 11/24 (52.4%) had high values for the 2nd line group. Normal value for LDL-c for those on 1st line drugs was 125/137 (91.2%), elevated level was seen in 12/137 (8.8%). For those on 2nd line, normal LDL-C was 14/24 (58.3%) while high values were recorded in 10/24 (41.7%). Normal HDL-c was recorded in 117/137 (85.4%) of subjects on 1st line ART, while 20/137 (14.6%) had abnormal high HDL-c. For those on 2nd line medications 20/24 (83.3%) had normal values, while 4/24 (16.7%) had abnormal values. No significant difference was seen in lipid profiles of subjects on 1st and 2nd line HAART, however the VL for those on 1st line HAART showed significant difference in their lipid profile, [6,699.4±34.2 Vs 281.67±22.8 Vs 59.0 ±2.1 (p = 0.008)].

Table 1. Characteristics of the study population according to sex

Parameters	Male (%)	Female (%)	Total (%)	P values
Number	103 (64.0)	58 (36.0)	161 (100.0)	0.744
Age (years)	*9.62±3.77	*11.29±5.21	*10.13 ±4.5	0.347
6mths-4yrs	16 (66.7)	8 (33.3)	24 (14.9)	0.927
5-9yrs	47 (65.3)	25 (34.7)	72(44.7)	0.822
10-14yrs	32 (60.4)	21 (39.6)	53 (32.9)	0.567
15-18yrs	8 (66.6)	4 (33.3)	12(7.5)	0.722
Type of HAART				
1st line HAART	90(64.7)	49(35.3)	139 ()	0.733
2nd line HAART	13(59.1)	9(40.9)	22(13.7)	0.608
ARV duration (years)	*8.46±3.26	*7.35±3.21	*7.9±3.2	0.734
Religion				
Christianity	74 (67.3)	36 (32.7)	110 (68.3)	0.201
Islam	29 (56.9)	22 (43.1)	51(31.7)	0.821
Anthropometry				
Weight (kg)	*29.99±7.4	*30.09±3.0	*30.63±12.3	0.962
Length/Height (cm)	*134.68±1.66	*134.31±3.7	*134.54±17.8	0.910
BMI (kg/m^2)	*16.60±0.69	*15.83± 0.61	*16.01±3.0	0.534
Blood pressure (mmHg)				
Systolic BP	*93.20±1.82	*93.47±2.2	93.50±9.9	0.870
Diabolic BP	*56.09±0.78	*58.12±2.3	56.43±10.3	0.187
Lipid Profile				
TC (mg/dL)	*151.18±36.3	*141.63±56.6	*149.61±39.5	0.311
TG(mg/dL)	*120.86±13.8	*123.66±15.5	*119.95±12.1	0.818
LDL-c (mg/dL)	*75.69±34.0	*71.9±39.5	*74.93±35.3	0.669
HDL-c (mg/dL)	*54.34±14.7	*57.27±14.8	* 55.04±19.7	0.557
CD4 and Viral Load				
CD4 cell count (cells/µl)	*904.78±439.35	*1,054.12±536.1	*958.57±480.2	0.058
Viral load (copies/ml)	*18,507.8±908.1	*6,206.6± 237.6	*14,076.3±741.9	0.314

*TC: Total cholesterol, TT: Total triglyceride, LDL-c: Low density lipoprotein cholesterol, HDL-c: High density lipoprotein cholesterol, BMI: Body mass index, ARV: Antiretroviral therapy, BP: Blood pressure, *values are mean ±SD*

Table 2. Lipid profile and duration on HAART

Variables	≤10 years [n=146] (%)	≥10 years [n=15] (%)	Total (%)	P value
TC mg/dl <170 [normal value]	104(71.2)	12(80.0)	116(72.0)	0.77
TC mg/dl 170-199 [Grade 1 elevation]	29(19.9)	1(13.3)	31(19.3)	
TC mg/dl 200-299 [Grade 2 elevation]	13(8.9)	1(6.7)	14(8.7)	
TC mg/dl > 300 [Grade 3 elevation]	0(0.0)	0(0.0)	0(0.0)	
TG (mg/dl) <150 [normal value]	116(79.5)	13(86.7)	129(80.1)	0.88
TG (mg/dl) 150-300 [Grade 1 elevation]	26(17.8)	2(13.3)	28(17.4)	
TG (mg/dl) 301-500 [Grade 2 elevation]	2(1.4)	0(0.0)	2(1.2)	
TG (mg/dl) >500 [Grade 3 elevation]	2(1.4)	0(0.0)	2(1.2)	
LDL-c (mg/dl) <130 [normal value]	129(88.3)	12(80.0)	141(88.1)	0.88
LDL-c (mg/dl)130-159[Grade1 elevation]	11(7.5)	0(0.0)	11(6.8)	
LDL-c (mg/dl)160-189[Grade2 elevation]	4(2.7)	1(6.7)	5(3.1)	
LDL-c (mg/dl) >190 [Grade3 elevation]	2(1.4)	2(13.3)	4(2.5)	
HDL-c (mg/dl) >35 [normal value]	120(82.2)	13(86.7)	133(82.6)	0.07
HDL-c (mg/dl) <35 [Undesirable]	26(17.8)	2(13.3)	28(17.4)	
CD4 cell count (ul/ml)	913.32±38.2	732.22±68.21	958.57±37.8	0.73
Viral Load (copies/ml)	5,192.07±3,587.75	10,581.78±8,085.76	9,717.38±47.2	0.003

Table 3. Lipid profile and types of 1st and 2nd line HAART

Variables	1st Line HAART				2nd Line HAART				
	AZT+ 3TC+ NVP [n= 88] (%)	**ABC+ 3TC+ NVP [n= 45] (%)**	**D4T+ 3TC+ EFV [n= 4] (%)**	**P value**	**AZT+ 3TC+ LP/r [n= 11](%)**	**ABC+ 3TC+LP/r [n= 6] (%)**	**TDF+ 3TC+ LP/r [n= 4](%)**	**TDF+ FTC+ LP/r [n=3] (%)**	**P value**
TC mg/dl <170 [normal value]	**61 (69.3)**	**38 (84.4)**	**2 (50.0)**		**6 (54.6)**	**4 (66.7)**	**2 (50.0)**	**1 (33.3)**	
TC mg/dl 170-199 [Grade 1 elevation]	17(19.3)	7(15.6)	1(25.0)		2(18.2)	2(33.3)	0(0.0)	0(0.0)	
TC mg/dl 200-299 [Grade 2 elevation]	10(11.4)	0(0.0)	1(25.0)	0.15	2(18.2)	0(0.0)	1(25.0)	1(33.3)	
TC mg/dl > 300 [Grade 3 elevation]	0(0.0)	0(0.0)	0(0.0)		1(9.1)	0(0.0)	1(25.0)	1(33.3)	0.16
TG (mg/dl) <150 (normal value)	**63 (71.6)**	**45 (100.0)**	**2 (50.0)**		**5(45.5)**	**4 (66.7)**	**1 (25.0)**	**1 (33.3)**	
TG(mg/dl) 150-300 [Grade 1 elevation]	24(27.3)	0(0.0)	1(25.0)		2(18.2)	1(16.7)	0(0.0)	0(0.0)	
TG (mg/dl) 301-500 [Grade 2 elevation]	0(0.0)	0(0.0)	1(25.0)	0.22	2(18.2)	1(16.7)	2(50.0)	1(33.03	0.54
TG (mg/dl) >500 [Grade 3 elevation]	(1.1)	0(0.0)	0(0.0)		1(9.1)	0(0.0)	1(25.0)	1(33.3)	
LDL-c (mg/dl) <130 [normal value]	**81 (92.0)**	**42 (93.3)**	**2 (50.0)**		**6(54.6)**	**5(83.3)**	**2 (50.0)**	**1 (33.3)**	
LDL-c (mg/dl)130-159 [Grade1 elevation]	5(5.7)	3(6.7)	1(25.0)		2(18.2)	1(16.7)	0(0.0)	0(0.0)	
LDL-c (mg/dl)160-189 Grade2 elevation]	2(2.3)	0(0.0)	1(25.0)	0.94	2(18.2)	0(0.0)	1(25.0)	0(0.0)	0.09
LDL-c (mg/dl) >190 [Grade3 elevation]	0(0.0)	0(0.0)	0(0.0)		1(9.1)	0(0.0)	1(25.0)	2(66.7)	
HDL-c (mg/dl) >35 [normal value]	**76 (86.4)**	**39 (86.7)**	**2(50.0)**		**8 (72.7)**	**5 (83.3)**	**4 (100.0)**	**3 (100.0)**	
HDL-c (mg/dl) <35 [elevated]	12(13.6)	6 (13.4)	2(50.0)	0.98	3(27.3)	1(16.7)	0(0.0)	0(0.0)	
CD4 (µl/ml)	889.47±36.3	869.5±211.6	1,185.51±6.1	0.79	892.7±35.9	901.7±13.3	1183.7±12.8	938.5 ±14.5	0.96
VL(copies/ml)	6,699.4±34.2	281.67±22.8	59.0±2.1	0.008	2,994.0±35.6	481.1±15.8	54.7±2.8	20.0±0.0	0.26

Table 4 and 5 showed logistic regression and risk factor for hyperlipidemia using TC, and HDL-c. Only BMI showed risk factor for hyperlipidemia using TC, [OR 2.158(1.014-4.59), p=0.044], others showed no risk factors. Using HDL-c, multiple risk factors were identified: types of 1st and 2nd line HAART, and BMI, [OR, 0.107 (0.008-1.029), p=0.033] for 1st line HAART, [OR 0.042 (0.0007-1.38), p=0.006] for 2nd line, and [OR 0.316 (0.112-0.88), p=0.023 for BMI.

4. DISCUSSION

In this study, the prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-c, and low HDL-c were 27.9%, 18.6%, 12.4%, and 17.4% respectively. Hypercholesterolemia and hypertriglyceridemia, recorded in this study was far much lower than 62.5%, 79.2% obtained from Mexican study, [23] 68%, 28% from Houston, [24] and 60% from Brazilian study [25]. Among adult population, figures derived were also much higher: TC (43.4%), TG (55.8%), LDL-c (33.6%), and HDL-c (43.4%) than the present study. [26] The findings however appeared similar to what was obtain from European Paediatric Lipodystrophy study Group, [27] 27% (95% CI, 21.6-32.7) for hypercholesterolaemia and 21% (95% CI, 16.4-26.6) for hypertriglyceridaemia. Similar findings was also observed in Thailand by Aurpibul et al. [28] where hypercholesterolaemia of 23% was recorded and HDL-c of 26% seen after 144 weeks of initiation of HAART when lower cut-off point for normal TC of 150 mg/dl was used, and >200 mg/dl was used for TG. Other studies [29,30] also showed similar dyslipidemia findings with the present study, ranging from 13% to 22%. The similarities and differences in the various studies might not be un-connected to the differences in the study design used for the various studies, differences in the sample sizes used, and different cut off points used for types of dyslipedemias.

Abnormal lipid metabolism has been associated with HIV infection itself [6-11] and use of ART [12-15,31-33] in both adults and children. Use of ART with the six classes' of drugs have shown high frequency of dyslipidemia, lipodystrophy, and high risk for cardiovascular diseases [12-15]. Those who develop lipodystrophy have been shown to have higher serum concentrations of inflammatory cytokines (IL-6 and TNF-α). There is evidence based relationship between increase in IFN-α and increased level of TC, TG, VLDL, apoB, and apoB/apoA1 [34]. PIs bind to LDL receptor-related protein (LRP), thus reducing the

Table 4. Logistic regression and risk factor for dyslipidemia using total cholesterol

Variables (n)	TC		OR (95% CI)	P value
Duration of HAART	**<170 (%)**	**>170 (%)**		
<10 years (146)	104(71.2)	42(28.8)		0.471
>10 years (15)	12(80)	3(20)	0.619 (0.166-2.306)	
Type of 1st line HAART				
1(88)	62(70.5)	26(29.5)	1	0.888
2(45)	30(66.7)	15(33.3)	1.21 (.019-23.9)	
3 (4)	3(75.0)	1(25.0)	0.61 (0.119-6.4)	
Type of 2nd line HAART				
1(11)	4(33.3)	7(66.7)	1	0.456
2(6)	3(50.0)	3(50.0)	0.33(0.14-8.3)	
3(4)	3(75.0)	1(25.0)	0.667(0.037-10.14)	
4(3)	2 (66.7)	1(33.3)	0.125(0.002-3.07)	
Systolic blood pressure				
<120(159)	115(72.3)	44(27.7)		0.484
>120 (2)	1(50)	1(50)	2.614(.160-42.702)	
Viral load of >400 and <400 copies/ml				
<400(123)	86(69.9)	37(30.1)		0.273
>400(38)	30(78.9)	8(21.1)	0.62(.26-1.479)	
CD4 cell count of <200 and >200				
<200(3)	2(66.7)	1(33.3)		0.834
>200(158)	114(72.2)	44(27.8)	0.772(0.068-8.73)	
BMI of <15 and >15				
<15(63)	51(81)	12(19)		0.044
>15(98)	65(66.3)	33(33.7)	2.158(1.014-4.59)	
Sex				
Male (103)	76(73.8)	27(26.2)		0.513
Female (58)	40(69)	18(31)	1.267(.624-2.573)	

Table 5. Logistic regression and risk factor for dyslipidaemia using high density cholesterol

Variables (n)	HDL-c		OR (95% CI)	P value
Duration of HAART	**<35 (%)**	**>35 (%)**		0.074
<10 years (146)	26(17.8)	120(82.8)		
>10 years (15)	0(0)	15(100)		
Type of 1st line HAART				
1(88)	12(13.6)	76(86.4)	1	0.033
2(45)	0(0.0)	45(100.0)		
3 (4)	2(50.0)	2(50.0)	0.107 (0.008-1.029)	
Type of 2nd line HAART				
1(11)	0(0)	11(100.0)		0.006
2(6)	0(0)	4(100.0)		
3(4)	1(33.3)	2(66.7)	1	
4(3)	3(75.0)	1(25.0)	0.042 (0.0007-1.38)	
Systolic blood pressure				
<120(159)	26(16.4)	133(83.6)		0.532
>120 (2)	0(0)	2(100)		
Viral load of >400 and <400 copies/ml				
<400(123)	19(15.4)	104(84.6)		0.663
>400(38)	7(18.4)	31(81.6)	0.809 (0.311-2.102)	
CD4 cell count of <200 and >200				
<200(3)	0(0)	3(100)		0.443
>200(158)	26(16.5)	132(83.5)		
BMI of <15 and >15			-	
<15(63)	5(7.9)	58(92.1)		0.023
>15(98)	21(21.4)	77(78.6)	0.316(0.112-0.88)	
Sex				
1(103)	17(16.5)	86(83.5)		0.870
2(58)	9(15.5)	49(84.5)	1.076(0.446-2.597)	

cleavage of fatty acids from circulating triglycerides by the LRP-lipoprotein lipase complex on vascular endothelium, and thus impairing the uptake of remnant hepatic chylomicrons and VLDL [11,35]. In addition to the above mechanism of action, PIs may also directly stimulate hepatic triglyceride synthesis through up-regulation of mRNA production in hepatic cells for key enzymes involved in the triglyceride biosynthetic pathway, leading to the hepatic accumulation of triglyceride-rich lipo-particles [20]. They are also known for their inhibitory actions on lipogenesis, adipocyte differentiation, and stimulation of lipolysis in the subcutaneous fat. NRTIs also exhibit similar inhibitory actions on lipognesis, adipocyte differentiation, lipolysis of the subcutaneous fats, as well as toxic effect in the mitochondria that will inhibit mitochondrial DNA polymerase γ, leading to the depletion of mitochondrial DNA. ART in general have also shown additional increase in central visceral fat and the levels of fatty acids in blood, with a further increase of fatty acids oxidation [10,34]. In a multicenter study by Verkauskiene et al. [32] HIV-infected children with symptoms of fat redistribution showed decrease in adiponectin, insulin resistance, increase of TG and reduction of HDL-C. Though adiponectin and insulin resistance were not part of the study protocol in the present study, elevated levels of TC, TG, LDL-C and decrease levels of HDL-C were all recorded in this study as well as in other several studies, [28-33] and points to dyslipidemis activities of ART in lipid metabolism together with, chronic HIV infections on the subjects. While duration on HAART does not appear have any statistical implication on dyslipidemia in this study, other studies have shown elevation of lipid profiles after initiation of HAART which plateaus off with time as demonstrated by Carter et al. [20] when they were evaluating the cumulative risk of exposure to HAART therapy and dyslipidemia. They found an increased linear relationship between median cholesterol and duration of first PI-inclusive regimen which did not persist after 24 months and remained fairly constant thereafter.

Derangement in the lipid profile was more marked with 2nd line than 1st line HAART. This is not surprising considering the fact that all 2nd line had PIs and NRTIs in their composition. PIs especially ritonavir containing regimen when in high dosage, and thymidine analogue regimens [stavudine, zidovudine] were associated with a high risk of lipoatrophy, [19,20] with its

associated dyslipidemias. This was more pronounced with TDF+FTC+ LP/r combination in 2nd line medications, and D4T+3TC+ EFV in 1st line ARVs.

The present study also observed relationship between BMI and TC [OR 2.158 (95% CI 1.014-4.59) p=0.044], and between BMI and HDL-c [OR 0.316 (95% CI 0.112-0.88) p-0.023]. Other studies [36,37] have also reported similar relations between obesity (high BMI) with high blood pressure, high TC, and low levels of HDL-c in both men and women of diverse racial and ethnic groups, and among children [38]. Association between BMI and dyslipidemia was also documented among HIV infected children on HAART, and those not on HAART [12-15]. In Triant et al. [14] study, a significantly higher prevalence of dyslipidaemia (23.3% vs 17.6%) was seen in HIV-infected patients than in the non-HIV cohort (p<0.0001). Also, TC, HDL-c, LDL-c, and apolipoprotein B which were all low in HIV infection were noticed to be markedly elevated following HAART administration [12,13,15]. As earlier explained, this elevation could be as a result of alteration in the cytokine profile, decreased lipid clearance, and increased hepatic synthesis of VLDL from effect of chronic HIV infection and use of HAART [10,11]. Elevation with resultant misdistribution in fats will directly affect BMI and body image through the process of lipoatrophy and lipohypertrophy.

Though not part of objectives of the present study, there is clear evidence of virological failure from the mean VL of the study participants after long period on HAART (≤ or ≥ 10 years). This could be as a result of non-regular VL monitoring in our center because the HIV program in our facility does not support such regular monitoring until recently. VL assay is requested by the attending physician only when there is clear evidence of immunological or clinical failure. It is a well-documented fact that virological failure occurs as first event, followed by immunological and clinical failure usually months or years afterwards [39]. For this reason peculiar to us, and I believe to most HIV centers in resource limited settings where VL is not routinely done, patients with virological failure are not detected earlier enough for possible switch to 2nd line medication. However, most recently, there is a change in policy which supports twice yearly monitoring of VL for all patients on both 1st and 2nd line HAART, hence patients with virological failure will be detected early enough for switch to 2nd line medication.

5. CONCLUSION

Use of 1st and 2nd HAART, and patients with high BMI were associated with raised TC, and HDL-c. This was more evidence with 2nd line HAART. Lipid profiles to be monitored periodically while on treatment with these medications for any rising trends to be controlled.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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