Lipid profile in HIV/AIDS patients in Nigeria

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Abstract

Introduction: Alterations of serum lipid profiles have been reported widely among Human Immuno deficiency Virus (HIV) positive patients on Highly Active Anti Retroviral Therapy (HAART). However, there are few data on serum lipid profile among treatment naïve HIV positive patients in our environment.

Objectives: To describe the pattern of lipid profile among treatment naïve HIV positive patients and changes following HAART initiation.

Methods: One hundred and thirty HIV positive patients seen in HIV center in an urban area in Nigeria and 44 matched individuals were recruited. Data were collected on socio demographic characters, baseline lipid profiles and CD4 count. Values of lipid parameters were retrieved after 12 months on HAART.

Results: The mean Low density lipoprotein(LDL) was 2.26+ 0.9 mmol/l among the test group compared with 0.96+0.39mmol/L among the control ,p value =0.000 .The mean High density lipoprotein (HDL) was also significantly lower,0.8+ 0.6mmol/L reaching a dyslipidemic level, in the HIV positive group than the control, p value = 0.00. Tuberculosis /HIV co infected patients had a significantly elevated mean LDL, p=0.002.

Conclusion: Abnormality of serum lipid is common among treatment naïve HIV patients seen in Nigeria. The NNRTI regimen is associated with elevation of HDL and some stabilization of TC and TG.

Key words: lipid profile HIV

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Introduction

The global HIV/AIDS pandemic, in most developing sub Saharan countries, is reaching proportions that is potentially threatening any previous gains in health, causing further reduction in life expectancy and overstressing already weak health system .In Nigeria, 3.9% of adults between ages 15-49 are living with HIV/AIDS. Although the sero-prevalence rate of HIV is lower in Nigeria than in other African countries like South Africa or Zambia, the size of Nigeria's population meant that by the end of 2006, there were estimated 2. 9Million infections with HIV with approximately 220,000 deaths from HIV alone in 2006. [1, 2]

Untreated HIV infection usually progresses to AIDS. With the introduction of HAART in mid to late 1990s, HIV associated morbidity and mortality in treated patients have significantly reduced so that they no longer succumb to opportunistic infections.[3] This is especially true, especially in developed countries. The efforts of international donors and organizations have assisted in providing easy access to HAART in most developing countries like Nigeria. However, patients with HIV are subject to dyslipideamia and other complications secondary to HAART that are often referred to as HIV metabolic syndrome [4]. Even before the availability of HAART, studies in HIV infected individuals have shown a variety of lipid abnormalities. [5,6] Low levels of total cholesterol (TC), High density Lipoprotein (HDL) and Low density Lipoprotein (LDL) have been reported in HIV infection [5]. Mondy K et al observed low HDL and elevated TG in their study population in the US [7]. In Uganda, recent reports showed that HIV infected patients have infrequent elevations in serum TC, LDL and TG.[8]

The association between HAART especially Protease Inhibitor (PI) based regimen and the occurrence of abnormal lipid changes in lipid and lipoprotein profiles is well known. [9] In another study, HIV-infected HAART-naïve subjects had lower concentrations of LDL and HDL and a higher concentration of TG than healthy controls. After

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receiving PI-based HAART, LDL-C and TG concentrations increased, while HDL-C concentrations remained unchanged [10]. However, Nevirapine based regimen has been shown to have increase TC, HDL and this changes persist even at 24 weeks of treatment. [11]

In Nigeria, Akpa MR et al, have looked at the serum lipid levels in healthy Nigerians [12] .They found elevated mean TC and LDL but reduced Triglyceride(TG) and HDL. In a similar work among patients with type 2 diabetes, several combinations of abnormal lipid parameters including reduced HDL and raised TG were noted. [13]

However, data about patterns of lipid profile in treatment naïve HIV positive patients is scarce and near non existence in Nigeria. The aim of this study was to determine the pattern of lipid profile in treatment naive HIV patients, to determine associated factors and pattern of change after 12 months of HAART initiation. We hypothesized that HIV infected treatment naïve patients in our environment, have multiple abnormal lipid profiles which is quite different from HIV negative persons. Secondly, that short term treatment with HAART has impact on lipid level.

Methods

Study population

This is a cross sectional case controlled study among HIV positive individuals seen at the adult HIV clinic of the National Hospital, Abuja, Nigeria. The HIV clinic is supported by PEPFAR initiative.

Case records of 130 patients whose names were randomly selected from the clinic register were retrieved and reviewed for analysis. Information obtained from the case notes includes socio-demographic characters, baseline anthropometric parameters like weight, height and Body mass index (BMI), baseline value of lipid profiles i.e. serum LDL, HDL, TG and TC, results of serological markers for HIV, for HBV i.e. Hepatitis B surface antigen (HBsAg) and for HCV i.e. anti HCV .Forty four consented individuals, non hypertensive or diabetic who were matched with the patients were recruited as controls from the outpatient department. Data were also collected on the HAART regimen the patients were on.

Lipid profile

Fasting venous blood sample drawn from consented subjects after adequate disinfection of the area was separated to obtain plasma which was then frozen stored till analyzed. TC was determined using ferric perchlorate method while HDL was determined after precipitation of LDL with phosphotungstate and magnesium was calculated from Friedwald's formula:

LDL= TCx HDL (TG/5)[14].

TG was measured using the colorimetric enzymatic method.

Information on lipid profiles, anthropometric parameters and other parameters

obtained above were also retrieved after 12 months on HAART.

Statistical analysis

For data collection and analysis, SPSS version 11 (Chicago IL, USA) were used. Descriptive statistics were computed with standard methods and are presented as mean and standard deviations (SD) .Chi square test was used to compare association between categorical variables and independent t- test was used to compare the mean value of some laboratory parameters and socio demographic and between control and patients while paired sample t test was used to analyze for difference in the mean values of lipid parameters at baseline and at 12 months on HAART. Independent t test was also used to analyze for association between some HIV associated variables and mean value of lipid profile.

A p value of <0.05 was considered to be statistically significant.

Results

Table I shows the socio demographic characteristics of the patients and control. As shown majority of the patients were in the 30 -39 age group, representing 58% and 54.5% of patients and control respectively. There was no statistical significant association between patients (HIV positive) and the control in age (p value =0.2) and sex distributions (p value =0.2) , marital status and alcohol use (p value=0.05 each) .However they differ significantly in their smoking status and mean BMI. As shown, 23% of the HIV positive patients are smokers compared with 16% of the control, p value =0.02. Also, the mean BMI was significantly higher among the control group compared with the test group; 28.5 + 2.3kg/m^2/ 23.4 + 2.3kg/m^2 .

Table 1: Socio- demographic characteristics of study subjects

Characters	HIV Pos. n=130 (%)	Control n=50 (%)	Total	P-value
Age group				
20-29	30(23)	12(27)	12 0	0.7
30-39	76(58)	23(55)	99	0.5
40-49	17(13)	6(14)	23	0.6
50-59	7(5)	3(6.8)	10	0.7
Sex				
M	40(31)	14(32)	103	0.6
F	90(69)	30(68)	77	0.8
Marital status				
Married	75(58)	25(57)	100	0.06
Single	55(42)	19(43)	74	0.7
Smoking, Yes	30(23)	8(16)	38	0.02#
Alcohol, Yes	40(31)	16(28)	56	0.6
Mean,BMI kg/m^2	23.4+ 2.3	28.5 +2.1		0.04*

Chi square was used to test for association, with significance level at 0.05

*Independent t test was used # significant association.

Table 2 shows the pattern of lipid profile among the HIV positive patients and HIV negative control. Mean LDL was higher among the HIV positive subjects compared with control (2.26 + 0.9mmol/l v 0.96 + 0.39mmol/l respectively),p value 0.000.Significant difference were also obtained in the mean HDL and TC. HDL and TC were significantly higher among the control (2.48 +0.7mmol/l v 0.8 +0.6mmol/l) and (4.17+0.8mmol/l v 3.6+0.92mmol/l), p value 0.00 and 0.03 respectively. There was no statistically significant difference in the mean TG for both the patients and the control, though it was in the dyslipidemic range for the two.

Table 2: Pattern of lipid profile according to HIV status

Characters	HIV negative n=44	HIV positive n=130	P value
Mean LDL	0.96+0.39	2.26+0.9	0.000*
Mean HDL	2.48+0.7	0.8+0.6	0.00*
Mean TC	4.17+0.8	3.6+0.92	0.031*
Mean TG	3.0 + 0.8	3.29 + 2.4	0.4*

Independent T test was used to test for association with significant level p<0.05

*Mean concentration is in mmol/l.** = Significant association

Table 3 shows the association between lipid profiles and some HIV associated conditions.

Female sex was associated with a significance elevation in the mean TC compared with male, p value =.003. Presence of TB was associated with a significance elevation of the mean LDL concentration (2.55+ 0.5mmol/l v 1.49+0.9mmol/l). There were no association between hepatitis serology status (i.e. HepBsAg, Anti-HCV or both), hypertension and any of the lipid parameters. No association was also observed between CD4 count level and any of the lipid parameters.

Table 4 shows the changes in lipid profiles over a 12 month period of initiating HAART. As shown, there were significant increase in the mean BMI (22.4±2.6kg/m2 to 27.2+ 3.6kg/m2) and mean HDL (0.8+0.6mmol/l to 1.43+0.7mmol/l) from baseline and at 12 months. Though there were reductions in the mean LDL, TC and TG, these did not reach statistical significance.

Table 3: Association between lipid profiles and HIV associated variables

Characters	LDL Mmol/l	HDL Mmol/l	TG Mmol/l	TC Mmol/l
Sex				
F	1.73+ 0.97	1.59 + 0.84	2.60 + 1.78	4.15 +0.83**
M	1.38 + 0.91	1.78 + 1.19	4.26 + 0.87	3.7 + 0.9
P value	0.1	0.4	0.5	0.03
Hypertension				
Yes	2.40+ 0.64	1.39 + 1.36	3.24 + 1.85	3.84 + 1.22
No	1.54 + 0.95	1.69 + 1.02	3.30 + 2.47	3.95 + 0.92
P value	0.2	0.6	0.7	0.08
CD4 Count				
0-99	1.63 + 0.76	2.40 + 0.92	3.57 + 2.70	3.09 + 1.30
100 and above	0.70 + 0.36	0.81 + 0.6	3.24 + 2.39	3.83 + 0.84
P value	0.06	0.7	0.7	0.08
Tuberculosis				
Yes	2.55+ 0.5*	1 15+ 0.64	2.52 + 1.3	4.19 +0.7
No	1.49+0.9	1.74+1.0	3.48+2.6	3.9+0.9
P value	0.01	0.2	0.3	0.4
Hepatitis				
Positive	1.36+1.26	0.1+0.02	5.1+ 3.4	3.23 + 0.07
Negative	2.33+0.96	0.8+0.60	3.1+2.22	3.72+ 1.03
P value	0.1	0.6	0.5	0.5

Table 4: Changes in lipid profile over a 12 month period on HAART

Parameters	Mean ±SD at 0 month mmol/l	Mean ±SD at 12 month mmol/l	P value
LDL	2.3+0.9	1.9+0.7	0.2
HDL	0.8+0.6	1.43+0.7	0.02
TC	3.6+ 0.9	3.4+1.5	0.9
TG	3.29+2.4	3.3+1.5	0.9
BMI kg/m2	22.4±2.6	27.2+ 3.6	0.000

Discussion

This study included data on 130 HIV positive patients and 50 HIV negative controls that were matched in all parameters except in their smoking status and BMI. HIV positive patients ,has shown in this study has a variety of lipid abnormalities including significant elevation of LDL and reduced level of HDL and TC compared with HIV negative controls. Higher level of serum TG was recorded among HIV positive patients, though this is not significant. The level of HDL and TG meet the criteria for dyslipidemia as defined by the National Cholesterol Education Program (NCEP-ATP III), with mean serum level of less than 1.03mmol/l and greater than 2.3mmol/l respectively[15]. Even though the mean LDL was significantly higher than control, it did not reach dyslipidemic level. The finding of low HDL in treatment naïve patients was similar to the Nutrition for Healthy Living (NFHL) cohort in the United States [16]. In that study, HIV patients who are not yet on HAART have an adjusted OR of 2.7 for low HDL compared with general population. This is equally supported by recent study in Spain [17]. This finding of low HDL is also similar to results obtained among diabetics, diabetics and hypertensive in Nigeria[12].

Low HDL is a well recognized independent risk factor for adverse cardiovascular outcomes and this has even been shown to be true in HIV infected individuals, irrespective of other risk factors[18].

In this study, we found no significant association between mean values of lipid parameters and serological status for hepatitis B, C or both, hypertension and CD4 count.

Hypocholesterolemia has been reported in HIV infection [6] and as shown in this study it is significantly lower in HIV positive patients than control. However, female patients with HIV had a significantly elevated level of TC compared with males. This finding is corroborated by the findings of Shor-Posner et al, where hypocholesterolemia with or without hypertriglyceridemia was found in male

patients with early infection with HIV -1 [19]. Reduced level of cholesterol has been demonstrated in AIDS, early HIV infection and some other infections[20,21] . This has been found to be negatively related to Tumor Necrosis Factor-alpha[18], but the mechanisms are not yet clear [19].

The lack of association between any of the lipid parameters and hypertension may be related to the duration of the hypertension, the degree of blood pressure control or the degree of immune suppression. Even in previously diagnosed hypertensives, who have been on medication or those with a positive family history of cardiovascular events in a first degree relative, there were no significant correlation between hypertension and abnormal lipid profile, especially low HDL [18]. This may suggest that HIV infection may constitute an additional and independent cardiovascular risk in hypertensive patients.

The reason for lack of association between lipid parameters in this cohort of HIV positive patients and the immune status may be related to the close similarity in the CD4 count as most patients are in the CD4 count range 50 -220 cell/mm3. Despite this, it has been demonstrated that the reduction in HDL in HIV infection persist all along all CD4 levels from the beginning of infection [19].Elevated TG was shown to positively correlate with interferon alpha ,advanced /opportunistic infection when immunity is markedly reduced and delayed clearance due to reduced lipoprotein lipase activity.[22, 23]

We found no significant association between hepatitis serological status and abnormalities of the lipid profiles. Other studies have reported low LDL, low TC and low HDL in HIV positive patients especially low TC in those co- infected and with advanced stage of liver disease [16, 24, 25].Though the findings were not significant, absolute values of these parameters are lower in those with hepatitis infection.

Tuberculosis is a common infection in HIV/AIDS patients with a prevalence of 12.7% in Ile Ife [26], and 28.1% in Ibadan [27]. With co infection, there is a synergism between the two infections leading to progression of the two diseases and ultimately death, if not treated. As revealed in this study, HIV patients co infected with TB had a significantly higher mean LDL compared with HIV positive patients who were not co- infected. This may indicate an exaggerated state caused by HIV/ TB co infection.

At the end of 12 month therapy with a NNRTI based regimen, there were significant changes in the mean BMI and HDL from the pre treatment value. Though there were reductions in the mean LDL, TC and TG concentrations, these were not statistically significant. HAART can cause severe dyslipidemia especially regimen including protease inhibitors [8] .NNRTI regimen have been noted to have additional protective factors against low HDL [28]. This is especially strong with nevirapine[27]. This anti - atherogenic effect of Nevirapine based regimen may be related to its protection against oxidative stress[29]. In resource limited setting, where access to PI may be limited due to cost, this study has shown that nevirapine based regimen may offer additional benefit of stabilizing lipid profiles particularly enhancing HDL.

Some limitations were noted and must be acknowledged in this study. The number of study subjects was not high, thereby limiting power and accuracy of the analysis. Secondly, associations could not be said to be causal because of the transversal nature of the study.

Despite these limitations, our findings indicate that HIV infected individuals have a host of variations in their lipid profiles compared with HIV negative control in our environment. Low HDL, reaching the dyslipidemic range, high LDL and TG were found compared with controls. TB is associated with a high LDL. NNRTI based regimen could have additional advantage of enhancing HDL and may be associated with reduced risk of cardiovascular events.

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