GLYCAEMIC AND LIPID PROFILES IN HIV POSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY IN SOKOTO STATE, NIGERIA

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ABSTRACT

Background: This study assessed the effects of Human Immunodeficiency Virus (HIV) and Antiretroviral Drugs (ARVs) on glycaemic and lipid profiles, and to determine the pattern of glucose and lipid abnormalities at different periods of the treatment. Method: Two hundred (200) participants were enrolled in the study, which comprised fifty (50) HIV negative, fifty (50) HIV positive not on therapy (HAART naïve), fifty (50) on therapy for 1-6 months and fifty (50) on HAART for 7-12 months. Glycaemic and lipid profiles were analyzed using enzyme based methods while CD4 cell counts were enumerated using flow cytometry. Results: Total Cholesterol, TAG, VLDL-C and FBS of control group did not differ significantly (P>0.05) in the entire three groups. The mean HDL-C was significantly lower (p<0.05) in the HAART naïve group, and those on treatment for 1-6 months compared to control subjects. HDL-C increased with the increase in the level of CD4 cell counts. The LDL-C in the control was observed to be significantly lower (p<0.05) than those on treatment for 1-6 months. A significant increase (P<0.05) in LDL-C/HDL-C ratio was observed in the entire groups, except those on therapy for 7-12 months compared to control group. Conclusions: From our study we suggest that glycaemic and lipid profile should be part of routine test for all HIV patients as part of monitoring their management.

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[1] BACKGROUND

Human immunodeficiency virus (HIV) belongs to the genus lentivirus, a family of lentivirus [1]. Acquired immunodeficiency syndrome (AIDS), is incurable illness caused by human immunodeficiency virus (HIV), which are known by long period of replication before manifestation of the disease [2]. Losses of cellular immunity due to metabolic syndrome are one of the effects of AIDS [3].

The acquired immunodeficiency syndrome (AIDS) was initially identified in 1981 [4]. In Nigeria, the first two cases of AIDS were identified in 1985 and reported in 1986 during an International AIDS conference [5].

The HIV has thus far infected between 21.6 and 24.1 million people in Sub-Saharan Africa with South Africa having the highest figure followed by Nigeria [6]. Another report released by WHO [7] showed that 9.1 million of HIV infected people in Sub Saharan Africa are receiving antiretroviral therapy in 2013, which make the region to has the highest HIV positive patient on HAART worldwide.

In Nigeria, a total of 3.1 million people are living with HIV as at the end of 2011 and about 300, 000 new infections are occurring annually [6]. The national prevalence rate is 3.6% and 3.1% in 2011 and 2012 respectively [8]. Furthermore, about 1.5 million of people living with HIV in Nigeria have access to antiretroviral therapy [6].

Sokoto State, with a total population of 3,702,676 (2006 National Census Figures) has a HIV prevalence rate of 6.0% in 2008 [9], which dropped to 3.3% in 2010, below the National prevalence rate of 4.6% [10]. A total of 15,095 and 18,504 people were tested for HIV in 2013 and 2014 respectively, out of which 1,238 and 1,204 individuals were positive [11]. On the total of newly patient enrolled on ART, the figure showed that 714 and 525 patients are newly enrolled in 2013 and 2014 respectively [11].

Based on the WHO recommended guidelines for the treatment of HIV positive patients, a total of 1.5 million (30%) people infected with HIV infection in Nigerian are on therapy [6]. HAART has dramatically decreased the morbidity and mortality...
associated with HIV infection and rebuilds the immune system [12].

A number of side effects such as dyslipidaemia and lipodystrophy have been reported to be induced by HAART [13, 14]. Cardiovascular disease account for more than 20% of death [15] and diabetes [16,17]. Previous studies has associated ARVs particularly protease inhibitors with lipid and glucose abnormalities such as hyperglyceridaemia, hypercholesterolaemia, hypo HDL- Cholesterolemia, hyperinsulinaemia [18, 19], high levels of LDL-C [18], insulin resistance, impaired glucose tolerance and diabetes mellitus, which leads to ischaemic heart disease [20, 21].

In Sokoto State antiretroviral drugs have been used for the management of HIV infection since 1998. Although, glycaemic and lipid profiles in HIV patients on ART has been widely studied in many places across the globe, none has been documented from Sokoto State. Thus, this study is set out to examine if some factors like viral virulence, genetic, race and environmental difference can modify the outcome of management of AIDS patients and whether some measures need to be taken to ensure that better therapies are received by the people living with HIV in the state.

[II] EXPERIMENTAL DESIGN

2.1. Research location

The research was carried out in Sokoto State, Nigeria. The sample was collected from HIV Clinics of Usman Danfodiyo University Teaching Hospital and Specialist Hospital, Sokoto. An estimated 70 to 80% of the HIV positive patients in the state receive treatment from the two HIV clinics, hence the two centres are the major ART centres and enrolled about three fourth of the patients in the state. Ethics and Research Committee’s approval of the two hospitals were obtained. Patients enrolled were informed using a standard informed consent form and written interview to subjects that gave their consent to participate in the study.

2.2. Sample Size

A total of two hundred (200) samples comprising fifty (50) apparently healthy HIV negative volunteers, fifty (50) sample from HIV positive pre-HAART (HAART naïve), fifty (50) HIV positive patients on treatment for 1 to 6 months, and fifty (50) HIV positive patients on HAART for 7 to 12 months.

2.3. Sample Collection and Sample treatments

On enrollment, 5mls of blood samples were collected using multiple sample needles with sterile vacutainers blood specimen bottle and centrifuged for five minutes at 3000g. The serum was removed and transferred into serum container by means of disposal transfer pipette for the assay of biochemical parameters.

[III] MATERIALS AND METHODS

3.1. Reagents

All reagents used were of analytical grade. For quantitative determination of total cholesterol, HDL-Cholesterol, triglyceride and fasting blood glucose in serum, enzymatic calorimetric kits were procured from Randox Laboratories Limited, United Kingdom. Kit for CD4 count was procured from Partee Munster, Germany.

3.2. Statistical Analysis

Statistical analysis was performed using Graph pad Instat version 3.02 (Graph pad Corp., San Diego, USA). The data was described using descriptive statistics and analysis of variance (Benferroni compare all columns) to test for the level of significance between the mean. A P value < 0.05 was taken as statistically significant.

[IV] RESULTS

The fasting total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), Atherogenic index (AI), Triglyceride (TAG), fasting blood glucose, and CD4 count were evaluated.

The fasting total cholesterol and TAG of the three groups (HIV positive HAART naïve, those on HAART for 1-6 months and 7-12 months on HAART) did not differ significantly (P>0.05) in comparison to control [Supplementary Figures-1 and -2].

The serum HDL-C levels of the three HIV positive groups were significantly lower (P<0.05) than the control group [Supplementary Figure- 3]. The level of HDL-Cholesterol increases with the increase in CD4 cell count, though no positive or negative significant correlation exists between the two parameters in the entire groups as shown in Supplementary Figure- 4. LDL-C level of the three HIV positive groups are higher compared to control, though not statistically significant (P>0.05) except those on treatment for 1 to 6 months [Supplementary Figure- 5].

The VLDL-C levels of all the three HIV positive groups were not statistically significant (P<0.05) when compared with control subjects [Supplementary Figure-6]. A significant increase (P<0.05) in LDL-C/HDL-C ratio was observed in the two HIV positive groups (treatment naïve and those on treatment for 1-6 months) when compared with control [Supplementary Figure- 7].

Moreover, HIV positive subjects have higher level of fasting blood sugar when compared with the control, though the increase in not statistically significant (P>0.05) as shown in Supplementary Figure-8 below. The glucose level of HIV positive subjects have been shown to increase with the increase in the level of CD4 T-cell count, even though the two indices are not significantly correlated throughout the groups [Supplementary Figure- 9].
[III] DISCUSSION

No significant difference (P>0.05) in total cholesterol, triglycerides and very low density lipoprotein cholesterol of the HAART naïve groups, those on treatment for 1 to 6 months and 7 to 12 months on treatment compared to control, though there is a slight increment in the level of the three parameters, but is statistically insignificant.

Our findings on the lipid and glycaemic profiles are consistent with a report by Iffen et al. [22], in which no significant difference in the levels of fasting total cholesterol of control group when compared with HIV positive subjects was reported. Likewise, Kumar and Sathian [23] reported no significant change in TAG level of HIV positive patient when compared with the control. A study by Kumar et al. [24] revealed that very low density lipoprotein cholesterol were markedly elevated in HIV/AIDS patients compared to normal subject, which are in conformity with our finding, though the elevation is not significant.

Francis and Onyinye [25] reported significant increase in the serum total cholesterol, triglycerides and very low density lipoprotein cholesterol of HIV positive patients when compared with the control group. This study contrasts the finding of the present study.

The VLDL-C consists mainly of triglycerides, which may substitute the reason for no significant change in the VLDL-C level was observed when no significant change in TAG was also noticed among the three HIV positive groups.

The present study corroborates the finding by Khiangte et al. [26] who reported the mean HDL-C to be significantly higher in HAART group compared with HAART naïve group. The finding of this study is also consistent with the a study by Ducobu and Payen [27], where he reported that HIV infection induces early decrease of HDL-C, which is proportional to the lowering of CD4 count, which revealed the severity of infections. Chandrasekaran et al. [28] suggested that use of non-nucleoside reverse transcriptase inhibitors based therapy (which was mostly used by the patients of this study) result in an elevation in HDL- levels and therefore may be less atherogenic than protease inhibitors.

Khiangte et al. [26] reported a decrease in the level of HDL-C as progression of HIV disease continues by concomitant decline in the levels of CD4 cells. Progression of HIV infection was fully known with depletion of CD4 cells count which is also accompanied by decrease in HDL-Cholesterol as reported by Obirikorang et al. [29]. As the virus (HIV) weaken the immune system various co-infections may likely to occur, which may lead to fever, malnutrition, diarrhea, loss of appetite etc. Fat from the food is the major source of HDL-C, which will reduce as a result of malabsorption of fat from the food caused by diarrhea [26].

The study by Francis and Onyinye [25] on the effects of HAART on lipid profile in HIV infected people contradict the finding of the present study, where they observed no significant difference (P>0.005) in the mean serum HDL-C levels of the HIV infected subjects on HAART compared to those without HAART and HIV seronegative individuals.

Additionally the study revealed that level of LDL-C in the treatment naïve subject, those on HAART for 1-6 months and patient on HAART for 7 – 12 months are lower (thought not significantly) compared to control subject.

Ducobu and Payen [27] also reported that patient with AIDS had higher levels of LDL-C when compared with seronegative group, which conform to the finding of this current study. Other studies [24, 22] reported higher LDL-C levels in HIV positive patients when compared with control group.

Miserez et al. [30] reported that HIV positive patients taking ARVs commonly have high levels of LDL-Cholesterol, which conform to the present finding in this study as it was observed in 1-6 month of treatment group. The mechanisms by which ARVs result in metabolic disorders are not fully understood, but lipid abnormalities in HIV patients receiving protease inhibitors (Pis) treatment are more evident [31].

The LDL/HDL-C ratio (Atherogenic Index) of HAART naïve and those on HAART for 1-6 months was significantly higher (P<0.05) compared to control, but at subjects on HAART for 7-12 month the difference was insignificant.

Furthermore, the result of the study revealed that, the fasting blood glucose in HIV positive subject is higher, though not statistically significant compared to control subjects. Muthumani et al. [32] showed no significant change in the level of fasting blood sugar of HIV positive subjects compared to the control group, which corroborate to the finding of this study. Hadigan et al. [33] reported that fasting blood sugar levels remain in normal range in most of the patients receiving potent antiretroviral therapy. Gadd [34] reported that low CD4 count in HIV positive subjects is associated with high glucose level, which may be serve as the reason for the higher (not statistically significant) glucose level in all the three groups when compared with control (with highest CD4 cell count).

[IV] CONCLUSION

In conclusion, from the finding of our study the total cholesterol, Triglyceride, very low density lipoprotein and fasting blood sugar remain significantly unaltered in all the three HIV positive groups in comparison with the control. HDL-C was found to be significantly altered in the three HIV positive groups compared with HIV negative group, which was also observed to increase as the CD4 T-cell count increase. A slight higher (not statistically significant) level of LDL-C was found in all the three HIV positive groups except those on HAART for
1-6 months, where LDL-C level was significantly increased in comparison with control. Our study was limited to one year (12 month) duration of treatment which may not have been enough to assess long term changes in lipids and glucose profiles. Data on individual dietary history are unavailable; therefore role of dietary intake cannot be commented on. The study did not include hypertensive and diabetic individuals throughout the study.

CONFLICT OF INTEREST
The authors have declared no conflict of interest. The authors further declared that no other relationships or activities that could appear to have influenced this study.

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Supplementary Information (As provided by author)

**Supplementary Figure 1**: Total-Cholesterol level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)

**Supplementary Figure 2**: Triglyceride level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)

**Supplementary Figure 3**: HDL-Cholesterol level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)
**Supplementary Figure 4**: HDL-Cholesterol and CD4 T-cell Count of HIV negative subject, HIV positive, HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)

**Supplementary Figure 5**: LDL-Cholesterol level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)

**Supplementary Figure 6**: VLDL-Cholesterol level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)
Supplementary Figure 7: Atherogenic Index of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)
Supplementary Figure 8: Fasting Blood Glucose level of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 month and 7-12 months on HAART (n=50)
Supplementary Figure 9: Fasting Blood Glucose and CD4 T-cell Count of HIV negative subject, HIV positive HAART naïve, Positive on HAART for 1-6 months and 7-12 months on HAART (n=50)