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Full Length Research Paper

Effect of highly active anti-retroviral therapy (HAART) on lipid profile in a human immunodeficiency virus (HIV) infected Nigerian population

Francis M. Awah[1,2]* and Onyinye Agughasi[2]

[1]Department of Biochemistry, University of Nigeria, Nsukka, Nigeria.
[2]Department of Biochemistry, Madonna University, Elele Campus, Rivers State, Nigeria.

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Nigeria remains the country with the third highest number of human immunodeficiency virus (HIV) infected individuals with over 600,000 HIV-infected subjects requiring antiretroviral therapy (ART). Since there is little or no data on the effect of highly active antiretroviral therapy (HAART) on the lipid profile of HIV-infected subjects in Nigeria, this study was aimed at evaluating the dyslipidaemia associated with HAART in HIV/AIDS (acquired immune deficiency syndrome) subjects. The lipid profile of the HIV-infected subjects taking HAART (n=25) was compared to that of the HIV-infected without ART (n=25) and the seronegative control (n=25). Total cholesterol, triglyceride, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol was determined using standard enzymatic methods. The results showed that HAART caused dyslipidaemia in HIV-infected subjects. Total cholesterol, triglycerides and LDL-cholesterol levels significantly increased in those receiving HAART (*p<0.05*) compared to those without treatment and the seronegative subjects. HDL-cholesterol levels were however, not significantly different (*p>0.05*) in the subjects. Triglyceride, LDL and HDL cholesterol levels were not significantly different between the sexes. It could therefore be concluded that HIV-infected subjects on HAART are predisposed to develop hypercholesterolaemia and conditions associated with it like coronary heart diseases. The lipid profile of HIV-infected subjects about to commence ART and those on HAART should be determined prior to and during treatment.

Key words: HIV/AIDS, HAART, lipid profile, dyslipidemia, Nigerian population.

INTRODUCTION

The human immunodeficiency virus (HIV) has thus far infected over 22.4 million people in sub-Saharan Africa and Nigeria remains the country with the third highest number of HIV-infected subjects in the world (WHO/UNAIDS, 2009). Since HAART was introduced in the mid 1990s, as a treatment for HIV/AIDS, the morbidity and mortality associated with HIV/AIDS has reduced considerably. According to the 2005 HIV Sentinel Survey and National HIV Prevalence AIDS Estimates Reports, an estimated 645,810 HIV-infected Nigerians would have been requiring ART by 2010 (FMOH, 2006). HAART regimens typically include a combination of at least three drugs, such as different association of protease inhibitors (PI), non-nucleoside reverse transcriptase inhibitors (NNRTI) and nucleoside reverse transcriptase inhibitors (NRTI). HAART however, has been reported to be associated with a number of side effects in HIV/AIDS subjects among which dyslipidaemia and lipodystrophy are common metabolic disorders with increased risk of cardiovascular diseases and diabetes in the HIV-infected subjects (Carr et al., 1999; Roula et al., 2000; Mulligan et al., 2000; Currier, 2002). Studies have also shown that

*Corresponding author. E-mail address: awambuh@yahoo.com. Tel: (+234)-805-743-1113.

Abbreviations: HIV, Human immunodeficiency virus; **ART,** antiretroviral therapy; **HAART,** highly active antiretroviral therapy; **AIDS,** acquired immune deficiency syndrome; **HDL,** high-density lipoprotein; **LDL,** low-density lipoprotein; **PI,** protease inhibitors; **NNRTI,** non-nucleoside reverse transcriptase inhibitors; **NRTI,** nucleoside reverse transcriptase inhibitors; **TG,** triglycerides; **SPSS,** statistical package for social sciences; **SEM,** standard error of the mean; **ANOVA,** analysis of variance; **VLDL**, very-low-density lipoprotein.

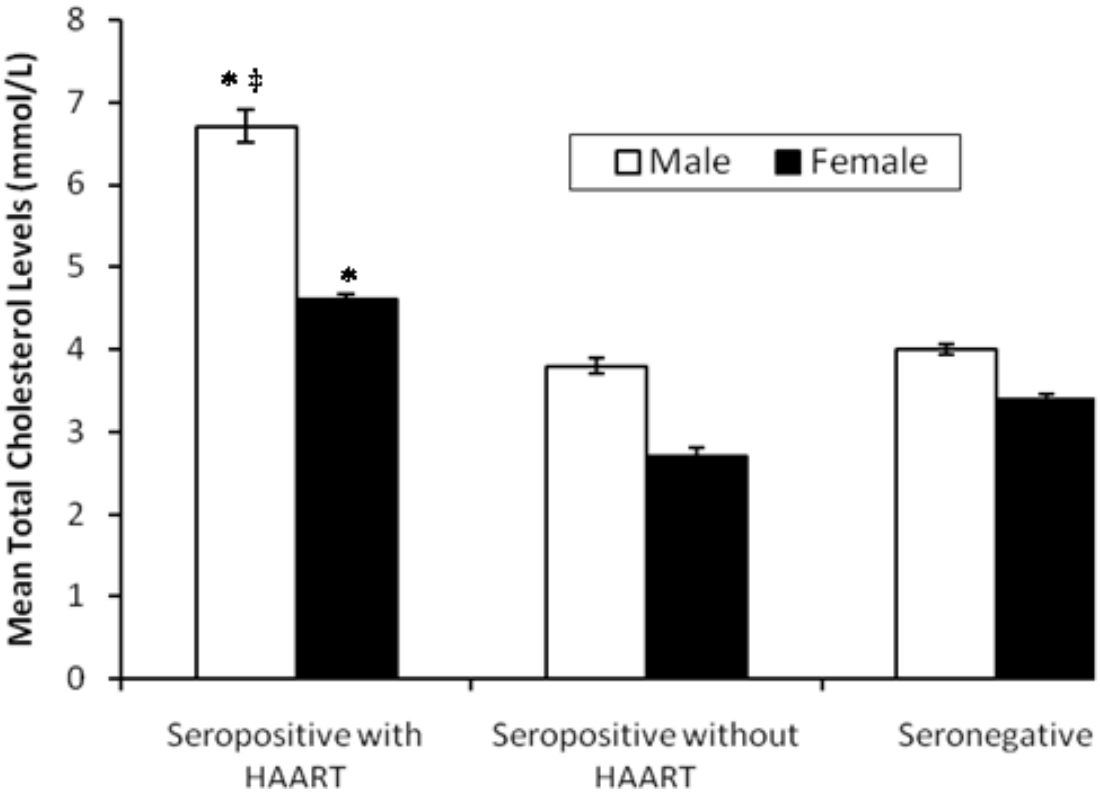

Figure 1. Serum cholesterol level of HIV-infected subjects on HAART compared to those without HAART and the seronegative. *$p < 0.05$, statistical significance of difference from seropositive without HAART and seronegative control. ‡$p < 0.05$, statistical significance of difference from females.

HAART treatment, especially those including protease inhibitors, is associated with hypertriglyceridaemia, hypercholesterolaemia, hypo HDL-cholesterolaemia and hyperinsulinaemia (Miserez et al., 2002; Vigano et al., 2003; Clotet et al., 2003; Palacios et al., 2006; Khiangte et al., 2007). Considering the number of HIV subjects in Nigeria taking HAART, the aim of this study was to evaluate the lipid profile of HIV-infected subject with or without HAART treatment in a bid to assess the potential risks of dyslipidaemia, if any, in male and female subjects who are about to or are enroll on HAART in a Nigerian population.

MATERIALS AND METHODS

Study area and subjects

A total of fifty (50) HIV-infected volunteers aged between 25 to 57 years, attending the General Hospital, Asaba, Delta State, Nigeria between July to October 2008 were surveyed for biochemical investigations and thereafter included in this study. Twenty five (25) of the subjects were on the first line HAART regiment while 25 were not yet on antiretroviral treatment. For both groups there were 13 females and 12 males. Age and sex matched HIV seronegative Madonna University students and staff were used as control (n=25). Selection was based on the subject's availability within the period of study.

Blood collection

Fasting blood samples (5 ml) were collected from all the study subjects by venipuncture into plain sample tubes. The blood samples were allowed to coagulate and spun at 5,000 rpm for 10 min. The serum was collected and stored at 4°C until assayed for biochemical indices within 4 days after collection. Subject's files were checked for their sex, age, stage of infection and antiretroviral therapy usage.

Lipid profile analyses

The serum total cholesterol, triglycerides (TG) and HDLcholesterol were determined in sera using commercial kits supplied by Randox (UK). These analyses were carried out according to the manufacturer's protocol. LDL cholesterol was calculated using the Friedewald's equation.

Statistical analysis

The results were analysed using the Statistical Package for Social Sciences (SPSS) version 10.0 for Windows. All the data are expressed as mean ± standard error of the mean (SEM). Two-way analysis of variance (ANOVA) was used to compare means, and values were considered significant at $p<0.05$.

RESULTS AND DISCUSSION

Metabolic disorders and other adverse drug side effects

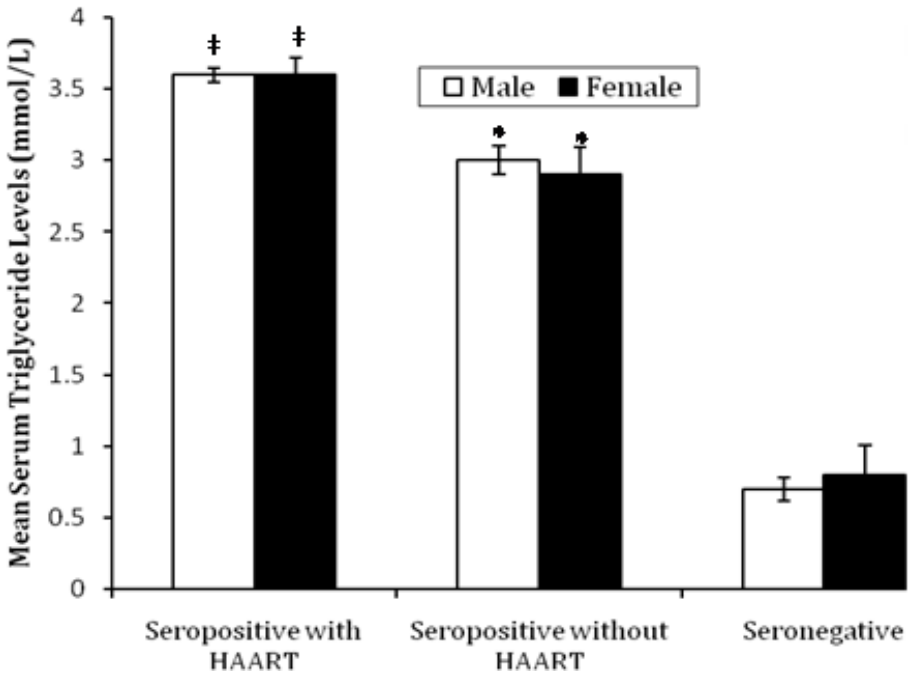

Figure 2. Serum triglyceride level of HIV-infected subjects on HAART compared to those without HAART and the seronegative. *$p < 0.05$, statistical significance of difference from seronegative control. ‡$p < 0.05$, statistical significance of difference from seropositive without HAART and seronegative control.

such as dyslipidaemia are important factors associated with reduced quality of life among HIV infected patients taking HAART (Pujari et al., 2005). The results of this study showed a significant increase in the serum total cholesterol levels ($p<0.05$) of the males and females HIV subjects on HAART compared to the HIV subject without HAART and the seronegative control (Figure 1). Total cholesterol levels were significantly higher in the males HIV-infected subjects compared to the females. These disturbances of cholesterol metabolism upon HAART treatment have been reported by other researchers (Falkenbach et al., 1990). The high levels of oxidative stress and lipid peroxidation associated with HIV/AIDS may, in part, explain the alterations of cholesterol metabolism in HIV-positive patients. Significant higher cholesterol in male subjects on HAART compared to females suggests that males could be more predisposed to hypercholesterolaemia due to HAART treatment compared to females probably due to hormonal differences. Serum triglyceride levels were also significantly higher ($p<0.05$) in the both the male and female seropositive subjects on HAART compared to the seropositive without HAART and the seronegative control. There was no significant difference ($p>0.05$) in the mean triglyceride levels between the male and female HIV-infected subjects. Furthermore, TG levels were significantly higher ($p<0.05$) in the HIV seropositive subject not on HAART compared to the control seronegative subjects (Figure 2). This indicates that HIV-infection may be associated with a disturbance in TG metabolism and HAART treatment further aggravates the metabolic disturbance. Hypercholesterolemia and hypertriglyceridemia has therefore been seen in HAART users compared to the normal control. Both decreased TG clearance and increased Very-low-density lipoprotein (VLDL) overproduction have been found in HIV-positive patients (Grunfeld et al., 1992) and could be the reason the increase serum TG observed.

There was no significant difference ($p<0.05$) in the means serum HDL-cholesterol ($p>0.05$) levels of the HIV-infected subjects on HAART compared to those without HAART and the seronegative (Figure 3). Compared to the normal HIV seronegative female subjects and HIV-infected female subject not on HAART, HIV-infected female subjects on HAART had significantly higher ($p<0.05$) LDL-cholesterol levels (Figure 4). The HIV-infected male subject on HAART and those not on HAART had no significant difference in their LDL-cholesterol levels, however both groups had significantly higher ($p<0.05$) mean LDL-cholesterol compared to the seronegative control (Figure 4). The mechanisms responsible for metabolic disorders associated with antiretroviral drugs are not fully understood. Lipid disturbances in HIV patients receiving PI treatment are more evident (Leitner et al., 2006). The protease inhibitors could inhibit lipogenesis and impair the activity of adipocyte regulatory proteins (Carr et al., 1998) while NRTI may induce mitochondrial toxicity in subcutaneous fat tissues (Carr

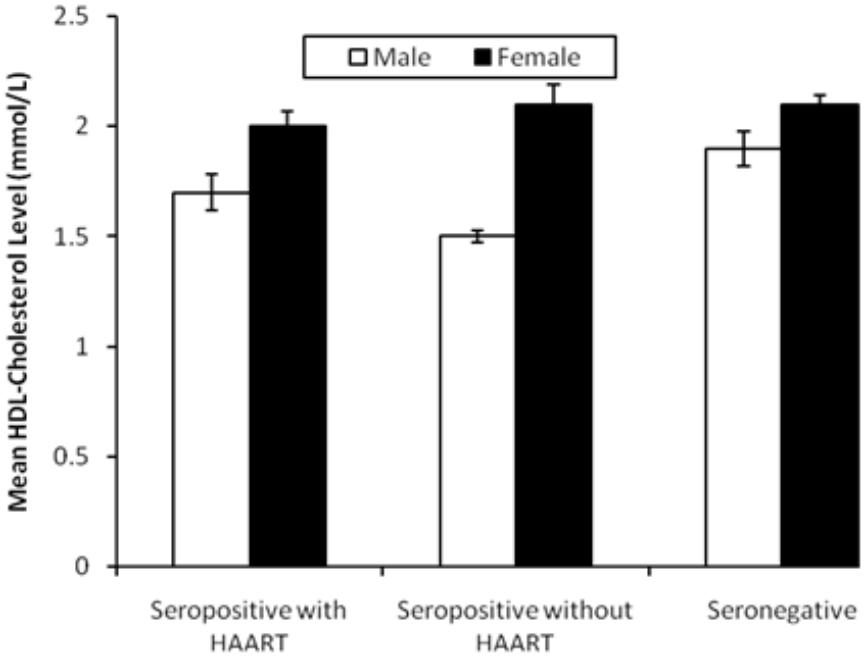

Figure 3. Serum HDL-cholesterol level of HIV-infected subjects on HAART compared to those without HAART and the seronegative.

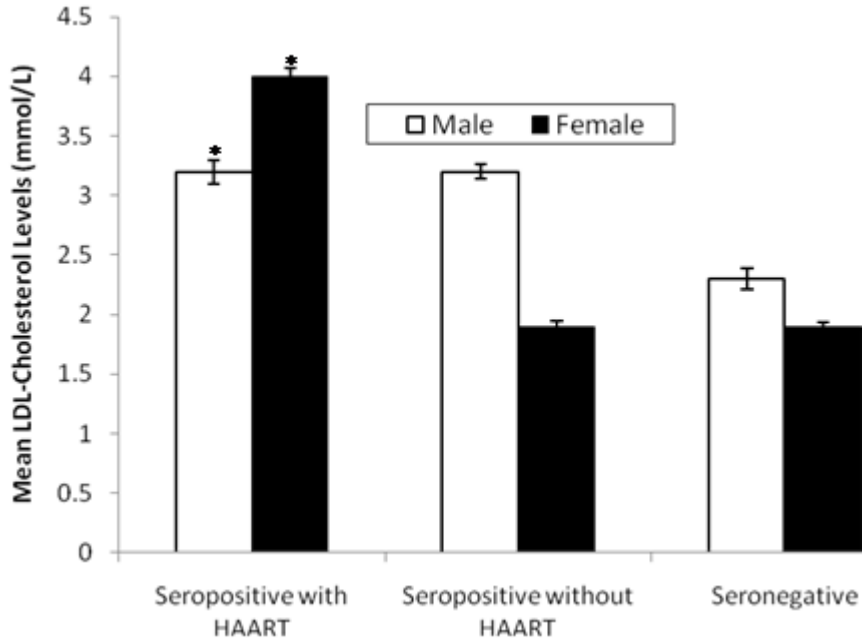

Figure 4. Serum LDL-cholesterol level of HIV-infected subjects on HAART compared to those without HAART and the seronegative. *$p < 0.05$, statistical significance of difference from seronegative control.

and Cooper, 2000). Increase serum concentrations of TG and LDL-cholesterol have been considered independent risk factors for coronary artery diseases and myocardial infarction (Stampfer et al., 1996; Assmann et al., 1998). Abnormalities in lipid metabolism make HIV-positive subjects to be at high risk for the development of coronary heart disease (Asztalos et al., 2006). The observations of this study are in conformity with studies in other countries, which have shown that HIV/AIDS subjects exhibit dyslipidaemia characterized by increase

in total cholesterol, triglyceride, and LDL cholesterol (Grover et al., 2005; Asztalos et al., 2006; Obirikorang et al., 2010). This suggests that the dyslipidaemia observed may not be not related to HIV infection itself, given that the total cholesterol and LDL-cholesterol levels of the HIV-infected subjected without HAART treatment was significantly lower than that of HIV-infected subjecting taking HAART.

Conclusion

It is evident from the above findings that long term administration of HAART to HIV-infected subjects could lead to metabolic disorders such as dyslipidaemia which could predispose the patients to high risk of coronary heart diseases. HIV-infected subjects in Nigeria should therefore be assessed for their lipid profile before enrolment for HAART and the lipid profile should also be assessed periodically in the course of the treatment. Elucidating the mechanism via which antiretroviral therapy is associated with metabolic disturbances which could contribute to premature cardiovascular disease is of major importance. It is recommended that further research be carried out with larger sample sizes and additional information regarding other risk factors for dyslipidaemia in Nigerian populations be assessed to better understand the effects of HAART on lipid profile and other metabolic disturbances.

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