

Original Article

Differences in Lipid Profile Findings in HAART Naive vs. HAART Treated HIV Positive Patients

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ABSTRACT

This study was to assess the lipid profile changes present in HIV positive HAART treated vs. HAART Naive patients. Data was obtained from seventy six patients each in three groups (HAART treated, HAART Naive and Controls) who met the inclusion criteria after a written informed consent was obtained. Ethical approval was obtained from the Research and Ethics Committee of the University of Benin teaching Hospital, Benin City, Nigeria. The mean age for the treatment naïve patients was 41.39 ± 7.23 years while HAART treated and normal controls had mean age of 44.01 ± 7.13 years and 42.95 ± 9.55 years respectively. There were statistically significant differences in most anthropometric measurements of patients in all three groups. Also, Obesity was present in 7.9% of HAART treated and 6.6% of HAART naive patients. Abnormal waist circumference was also noted in 65.8% of patients in both HIV positive patient groups while an abnormal waist hip ratio was present in 43.4% and 48.7% of HAART treated and HAART naive patients respectively. Elevated total cholesterol and abnormalities in the HDL levels were most prevalent abnormal lipid profile parameters. This study showed derangements in anthropometric and lipid profile parameters in HIV positive patients compared to controls with alterations in total cholesterol levels in HAART treated patients. These effects are possibly indicative of HAART's impact on lipid metabolism through multi-factorial mechanisms which would need to be elucidated by further studies.

Keywords: HAART Naive, HAART treated, HIV Positive, Lipid Profile

INTRODUCTION

Human immunodeficiency virus (HIV) infection /Acquired Immunodeficiency Syndrome (AIDS) affects about 34 million people worldwide. The greatest burden of the disease occurs in Africa, accounting for about 70% of all HIV infected persons globally. Human

immunodeficiency virus (HIV) is a retrovirus that mostly infects components of the human immune system such as CD4 T cells, macrophages and dendritic cells. Infection with HIV causes a multisystem disease, and constitutes a global health challenge with devastating effect on the

social, economical and political aspects of any nation.²

The corner stone of management of patients with HIV infection is the use of combination antiretroviral therapy (cART), also referred to as highly active antiretroviral therapy (HAART). It consists of the use of at least three antiretroviral drugs (ARVs) that work at two different sites to help combat the effects of the virus.³

However, the introduction of HAART although beneficial is not without side effects. The use of HAART has been noted to result in an increased risk of metabolic syndrome, hyperlipidaemia and insulin resistance in HIV patients.⁴ Dyslipidaemia resulting from antiretroviral therapy has lately emerged as a matter of concern because of the likelihood of premature atherosclerosis and cardiovascular disease.⁵ Drug related cardiotoxicity has also been reported in the post - HAART era.^{6,7}

The use of HAART regimen especially Protease Inhibitors are associated with increased metabolic effects such as hyperlipidaemia, insulin resistance and somatic changes like lipodystrophic and lipoatrophic changes that are usually associated with higher risk for morbidity.⁸

These metabolic changes with the abnormal body fat distribution all increase cardiovascular risk.⁸ and may portend worsening overall treatment outcomes with possible related deaths from metabolic induced cardiovascular diseases whose aetiology may be occurring from the effects of treatment regimens targeting the HIV virus but with untoward debilitating side effects.

In developing countries like Nigeria where access to HAART is now routine, there are reports of cardiovascular diseases resulting from accelerated atherosclerosis in patients on HAART. Thus, this study aims to assess the lipid profile changes in patients who have the HIV virus but are HAART naive and those who are on treatment with HAART whilst comparing these findings with normal subjects.

MATERIALS AND METHODS

This was a descriptive comparative cross sectional study in which one hundred and fifty two (152) HIV positive

patients (consisting of seventy six (76) HIV positive HAART Naive patients and seventy six (76) HIV Positive HAART Treated Patients) and seventy six (76) HIV negative subjects (controls) were recruited from the HIV clinic (PEPFAR clinic) and general outpatient clinics of the University of Benin Teaching Hospital (UBTH), Benin City, Edo state, Nigeria.

All patients' recruited had their data obtained with anthropometric and lipid profile assessments entered into a structured questionnaire. Dyslipidaemia and metabolic syndrome was defined using the National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP) III guidelines.⁹ Increased waist circumference (WC) was defined according to the NCEP ATP III guidelines: 102 cm for males and 88 cm for females, and waist hip ratio (WHR) was said to be abnormal if >0.9 for men and >0.85 for females.

Ethical Approval was obtained from the Research and Ethics Committee of the University of Benin Teaching Hospital (UBTH), Benin City, Edo state, Nigeria. A written informed consent was obtained from all participants in the study. In addition, all HIV positive HAART naïve patients were counselled and commenced on HAART immediately on completion of data collection.

Data obtained was analyzed using the International Business Machines Statistical Product and Service Solutions (IBM-SPSS) version 22.0. A p-value 0.05 was considered significant for all statistical comparisons.

RESULTS

The mean age for the treatment naïve patients was 41.39 ± 7.23 years while HAART treated and normal controls had mean ages of 44.01 ± 7.13 years and 42.95 ± 9.55 years respectively. The female to male ratio in the study was 1.9:1, 1.8:1 and 1.4:1 in the HAART naïve, HAART treated and control groups respectively with 65.8% and 64.5% HIV infected population in the treatment Naive and HAART treated groups being women.

The most common highly active antiretroviral medication used by patients in the treatment experience group was

lamivudine (98.7%). Zidovudine (46.1%), Nevirapine (46.1%), Tenofovir (40.8%), and Efavirenz (38.2%) in descending order were also commonly used with Abacavir, Lopinavir/Rotinavir and Dolutegravir seldomly prescribed. [Figure I]

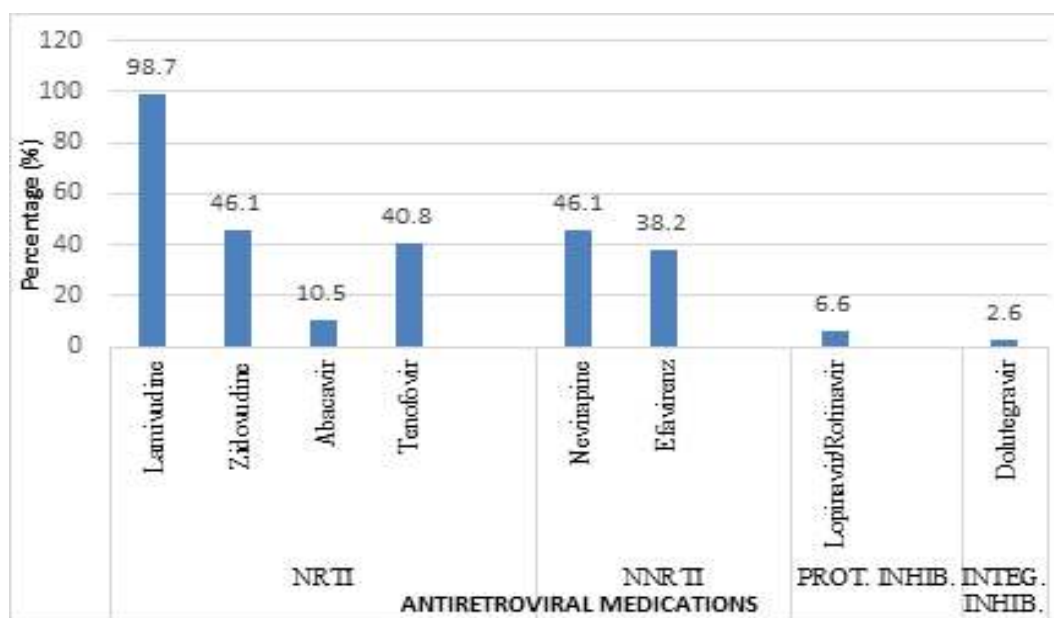
HIV positive HAART treated patients weighed more than treatment-naïve patients with controls weighing the most. The mean height and body surface area of patients were almost same with little differences in the standard deviations. Also, controls were noted to be slightly overweight with a body mass index of both HIV groups within normal ranges. In addition, there were statistically significant differences in the weight ($p < 0.001$), height ($p < 0.001$), body surface area ($p < 0.001$), body mass index ($p = 0.012$), waist circumference ($p < 0.001$) and hip circumference ($p < 0.001$) of patients in all three groups. [Table I]

Tukey's Post Hoc comparisons showed significant post hoc comparisons of weight ($p < 0.001$), height ($p < 0.001$), waist circumference ($p < 0.001$), hip circumference ($p < 0.001$) and body surface area ($p = 0.01$), for HAART

naive vs. Control patients; height ($p < 0.001$), waist circumference ($p < 0.001$), hip circumference ($p < 0.001$) and body surface area ($p = 0.01$) for HAART naive vs. HAART treated patients; and significant post hoc comparison of weight ($p < 0.001$), body surface area ($p = 0.004$) and body mass index ($p = 0.012$) for HAART treated vs. Control patients.

Obesity was present in 7.9% of HAART treated and 6.6% of HAART naive patients. Abnormal waist circumference was also noted in 65.8% of patients in both HIV positive patient groups while an abnormal waist hip ratio was present in 43.4 and 48.7 of HAART treated and HAART naive patients respectively. [Table III]

Lipid profiles parameters of patients showed statistically significant differences in total cholesterol ($p = 0.016$) between all three groups [Table II] with Tukey's post hoc comparison showing significant difference ($p = 0.018$) between HAART treated vs. Control groups. HDL levels were also lower in HAART naive patients although not statistically significant. [Table II] Elevated total cholesterol and abnormalities in the HDL levels were



NRTI: *Neucloside / Nucleotide Reverse Transcriptase Inhibitors*; NNRTI: *Non-neucloside Reverse Transcriptase Inhibitors*; PROT INHIB: *Protease Inhibitors*; INTEG INHIB: *Integrase Inhibitors*.

more prevalent compared to other lipid profile parameters as 40.8% and 42.1 % of HAART treated patients had elevated total cholesterol and abnormal HDL levels while 13.2% and 57.9% of HAART naive patients had elevated total cholesterol and abnormal HDL [Table III]

Table I: Anthropometric Characteristics of Patients

	HIV Positive (Treatment Naïve) N=76 N (%)	HIV Positive (HAART Treated) N=76 N (%)	Control N=76 N (%)	F	p-value
Weight(Kg)	61.41 (9.77)	65.39 (11.21)	72.71 (15.75)	15.97	<0.001
Height(metres)	1.60 (0.10)	1.67 (0.77)	1.68 (0.70)	20.26	<0.001
BSA	0.06 (0.005)	0.06 (0.005)	0.06 (0.007)	23.28	<0.001
BMI(kg/m2)	24.21 (4.19)	23.67 (25.86)	25.86 (5.28)	4.54	0.012
WC(cm)	74.42 (9.81)	84.88 (11.71)	84.93 (9.08)	25.52	<0.001
Hip Circum (cm)	85.53 (10.39)	97.61 (10.77)	98.50 (8.75)	4.10	<0.001
WHR	0.87 (0.49)	0.87 (0.06)	0.86 (0.64)	0.55	0.577

BSA: Body Surface Area; **BMI:** Body Mass Index; **WC:** Waist Circumference;

Hip Circum: Hip Circumference; **WHR:** Waist Hip Ratio

Table II: Lipid Profile Assessment of Patients

	HIV Positive (Treatment Naïve) N=76 N (%)	HIV Positive (HAART Treated) N=76 N (%)	Control N=76 N (%)	F	p-value
TC(mg/dl)	177.66 (17.36)	187.04 (32.78)	174.66 (29.88)	4.19	0.016
HDL – C(mg/dl)	52.47 (18.06)	54.92 (16.13)	52.39 (18.26)	0.51	0.600
LDL – C(mg/dl)	119.79 (21.94)	119.92 (27.98)	115.05 (30.77)	0.79	0.454
TG(mg/dl)	93.05 (13.75)	94.12 (26.56)	86.66 (20.61)	2.81	0.062

TC: Total Cholesterol; **HDL_C:** High Density Lipoprotein Cholesterol; **LDL_C:** Low Density Lipoprotein

Cholesterol; **TG:** Triglyceride

Table III: Relationship between Anthropometric / Lipid Profile assessments and HIV HAART naive vs. HAART treated patients' groups

		HIV Positive (Treatment Naïve) N=76 N (%)	HIV Positive (HAART Treated) N=76 N (%)	²	p-value
Body Mass Index	Normal	32 (42.1)	45 (59.2)	5.80	0.122
	Obese	5 (6.6)	6 (7.9)		
	Overweight	31 (40.8)	18 (23.7)		
	Underweight	8 (10.5)	7 (9.2)		
Waist Hip Ratio	Abnormal	37 (48.7)	33 (43.4)	0.42	0.515
	Increased	50 (65.8)	50 (65.8)	0.00	1.000
Waist Circumference	TC	10 (13.2)	31 (40.8)	14.73	0.001
	HDL – C	Abnormal	44 (57.9)	32 (42.1)	3.79
LDL – C	Elevated	3 (3.9)	3 (3.9)	0.00	1.000
	TG	Elevated	0 (0.0)	2 (2.6)	2.03

TC: Total Cholesterol; **HDL_C:** High Density Lipoprotein Cholesterol; **LDL_C:** Low Density Lipoprotein Cholesterol; **TG:** Triglyceride

DISCUSSION

This study showed a higher female prevalence of HIV. Women account for about 60% of all infected adults in regions around West Africa (including Nigeria) a trend which is the reverse in the developed world.¹⁰ Also, the practices in most African cultures increase female vulnerability as there is a great number of un-empowered women.¹⁰ Thus, the findings of higher HIV prevalence in a vulnerable population in these society is consistent with over 60% of women diagnosed HIV positive in the treatment naïve and HAART treated groups respectively in this study. In addition, UNICEF has reported that young girls are twice more likely to contract HIV/AIDS in sub-Saharan Africa compared to males of the same age group¹¹ a finding similar to the female to male ratio observed in this study.

This study shows a significantly higher difference in body mass index (BMI) in treatment naïve patients compared to controls with a higher hip circumference also noted in HAART treated compared to treatment naïve patients. The use of HAART has been known to result in complications such as increase in BMI plus alterations in other parameters that constitute the term metabolic syndrome.¹² However, the Fat Redistribution and Metabolic Changes in HIV Infection Study has shown that there is no association between peripheral and central lipoatrophy in a greater percentage of HIV infected individuals.¹³

Furthermore, this study showed a higher mean (SD) waist circumference in patients on HAART [84.88 (11.71)cm in HAART treated versus 74.42(9.81)cm in treatment naïve patients], a similar finding by Muhammad et al., in their study of Nigerian HIV patients on HAART.¹⁴ In addition, the HAART naïve group had fewer patients with normal body mass index compared to HAART treated patients, a finding consistent with pre-existing data.¹⁵

The total cholesterol recorded in HAART treated patients was significantly higher than values observed in treatment naïve patients; a finding which was statistically significant. Dyslipidaemia increases the chances of

developing metabolic syndrome in HAART treated patients. These effects are indicative of HAART's impact on lipid metabolism through multifactorial mechanisms including alterations in adipose tissue function, genetics and lifestyle.¹⁶

Earlier research has shown that Nucleoside / Nucleotide Reverse Transcriptase Inhibitors (save Rilpivirine), Non-nucleoside Reverse Transcriptase Inhibitors (save Nevirapine), and Protease Inhibitors contribute to dyslipidaemia.¹ Furthermore, existing literature has also shown that Integrase Inhibitors and Entry Inhibitors have a neutral effect on lipid metabolism¹ while Nevirapine based regimes may offer additional benefits of stabilizing lipid profiles via its positive effects in relieving oxidative stress and increasing HDL levels.^{1,17,18}

Prior to the onset of HAART, the usual lipid profile findings in HIV positive treatment naïve patients were hypocholesterolaemia, reduced HDL and LDL values as seen in HIV positive treatment naïve patients in this study with findings of lower mean total cholesterol, TC and reduced HDL and TG in control healthy Nigerian subjects in this study as similarly documented by Akpa et al., in Portharcourt, Nigeria.¹⁹ The presence of reduced HDL-C levels in treatment naïve patients may be due to the result altered lipid metabolism which is known to occur in association with HIV infection.¹⁴

CONCLUSION

There was significantly higher cholesterol values recorded in HAART treated patients. The use of HAART has been known to result in complications such as increased in BMI and dyslipidaemia multiplying the chances of developing metabolic syndrome in HAART treated patients. These effects are indicative of HAART's impact on lipid metabolism through multifactorial mechanisms which would need to be elucidated by further studies. It is thus noteworthy that consistent assessment of HIV positive patients' lipid profile and management to prevent the complications that may arise from metabolic

syndrome be a priority for clinicians.

Conflict of Interest

The Authors also wish to emphatically declare that there are no Conflict of Interests. This study was self sponsored by the authors

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