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Lipid Profile and Cd4$^+$ - T – Lymphocytes Counts in Naïve Human Immunodeficiency Virus Infected Pre – Menopausal Females.

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ABSTRACT

This study was aimed at determining the serum lipid levels in naive HIV-infected pre – menopausal females and in the progression of HIV/AIDS. In a bid to determine lipid abnormalities or otherwise in naïve HIV – infected pre-menopausal females, 80 HIV- positive females aged between twenty to thirty five years at the PEPFAR, HIV clinic, University of Nigeria Teaching Hospital(UNTH), Enugu and 80 apparently healthy non-HIV positive age-matched female volunteers that served as the control group were studied. The medical Ethical Committee of the UNTH, Ituku-Ozalla, Enugu, approved the study protocol and the patients' informed consents were obtained prior to sample collection. The blood samples were collected using standard methods. HIV re-screening and confirmation were carried out using WHO HIV test algorithm. Automated method using Flow cytometry was used for the enumeration of CD4$^+$ T Lymphocytes while lipid profile of the test subjects and the control group were carried out using standard methods. The results were expressed as mean ± standard deviation. The data were analyzed using graph pad Instat version 3.01, Graph pad software, San Diego, California, USA. The test of significance was based on probability (p) values of < 0.05. Comparisons between groups were performed using One-way-ANOVA, Bonferroni's multiple comparison test and student t-tests depending on the number of variables. Serum total cholesterol, HDL and LDL levels of the patients were significantly lower ($P < 0.05$) than the control groups and all decreased progressively with the progression of HIV/AIDS. However, triacylglylerols and VLDL levels were significantly higher ($P < 0.05$) than the controls and all increased with the progression of HIV/AIDS.

Introduction

Lipids are class of compounds that are soluble in organic solvents and nearly insoluble in water (Finley and deMan, 2018). They are distinct biomolecules that often occur combined either covalently or through weak bonds with members of other classes of biomolecules to yield hybrid molecule. In such biomolecules, the distinctive chemical and physical properties of their components are blended to fill specialized biological function (Rifai and Warnick, 2006 and Murzina *et al*,2020). Chemically, lipids include compounds that yield fatty acid on hydrolysis and complex alcohol that can combine with fatty acids to form ester. Generally, they are hydrophobic and are soluble in such organic solvents as petroleum, ether and benzene (hydrocarbons) and halogenated hydrocarbons (chloroform, carbon tetrachloride, and dihydroethane) (Stein, 1987 and Blanco *and Blanco*,2017).Lipids play vital roles in many cellular processes such as storage of energy, structural supports, protection and communication including their roles in the pathogenesis of different diseases, inflammation, autoimmune disease, cancer and neurodegeneration (Santos and Preta, 2018). Human immunodeficiency virus (HIV) is one of the greatest public health challenges worldwide and Africa in particular. In 2020, it was reported that 75.7 million (55.9 million – 100 million) people have become infected with HIV globally since the start of the epidemic while about 32.7 million people have died from AIDS – related illnesses during the same period. The same report also had it that about 38.0 million people were living with HIV in 2019 (UNAIDS, 2020).

Materials And Methods.

A formal approval for this work was obtained from the Medical Ethical Committee of the University of Nigeria Teaching Hospital, ItukuOzalla, Enugu. Informed consent

was obtained from the patients prior to their inclusion in this study. Two categories of subjects were used. The first category was 80 HIV positive females aged between twenty to thirty Five years at the President's Emergency Action Plan for AIDS (PEPFAR), HIV clinic, University of Nigeria Teaching Hospital, Enugu. These HIV infected females were rescreened and confirmed positive. They were counselled one on one as Data on their demographic characteristic and behavioural factors were being obtained. Pregnant women and breast feeding mothers were excluded from the study. Similarly, patients who were on antiretroviral therapy prior to this study were not selected. The HIV/AIDS patients were divided into three groups according to Centre for Disease Control and Prevention Criteria (CDC) system (CDC, 1992). This system is based on three ranges of CD4 counts *viz*: (1) ≥ 500 mm^{-3}, (2) 200 – 499 mm^{-3} and (3) < 200 mm^{-3}. The second category of subjects was the control group of 80 apparently healthy and HIV negative age-matched female volunteers. All the venous blood samples (8.0 ml) were collected from the medial cubital vein with minimal venous stasis. The collected blood samples were dispensed into plain tubes, allowed to clot and the sera separated by centrifugation at 3,000 g for 10 minutes. The sera were used for HIV serology and for lipid analyses. Where the analyses were not possible the same day, they were stored at 4^0 C till the next day for analyses. The results were expressed as Mean ± Standard deviation (M ± S.D). The data were analyzed using graph pad Instat version 3.01, Graph pad software, San Diego, California, USA, while the test of significance was based on probability $p < 0.05$. Comparisons between groups were performed using One-way-ANOVA, Bonferroni's multiple comparison test and student t-tests depending on the number of variables.

RESULTS.

1.0: Demographic parameters of the test subjects.

Table 1.0 shows the mean age (years) 29.1 ± 3.52., 29.25 ± 2.79, 29.51 ± 3.61 and 28.35 ± 3.5 for the overall test subjects, test subjects with $CD4^+$ (cells/µl) ≥500, 499-200 and <200 respectively. On comparison of the control value (29.78 ± 3.18) with the patients and their subgroups based on $CD4^+$ classification showed no significant difference ($p > 0.05$). The table also showed the breakdown of the 80 HIV patients based on the type of HIV they have as follows; HIV- 1 – 53, HIV-2 – 7 and HIV- 1 and HIV-2 – 20 patients. Different HIV types were further sub-divided using the CDC HIV staging depending on the levels of $CD4^+$. The result of the patients also showed massive proteinuria with the declining $CD4^+$ count. However, the 6.4 % proteinuria found in the control group may be as a result of latent sicknesses not captured in the course of this study since the controls were only apparently healthy.

Table 1.0: Demographic characteristics of the patients and the control group

	Control	Test subjects	$CD4^+ \geq 500$ (cells/µl)	$CD4^+$499-200(cells/µl)	$CD4^+ < 200$ (Cells/µl)
Mean Age (yrs.)	29.78 ± 3.18	29.1 ± 3.52[aa]	29.25 ± 2.79[aa]	29.51 ± 3.61[aa]	28.35 ± 3.5[aa]
HIV - 1 (n)	-	53	10	26	17
HIV -2 (n)	-	7	2	3	2
HIV 1 and 2 (n)	-	20	8	8	4
Proteinuria (%)	6.4	47	35	45	69

[aa] represents $P > 0.05$.

2.0: Lipid Profile

Table 2.0 shows the mean serum lipid profiles of various groups of the patients. Total cholesterol 3.88 ± 0.26, 4.17 ± 0.02, 3.94 ± 0.17 and 3.49 ± 0.01 mmol/L for overall patients, patients with $CD4^+$ count $\geq$ 500, 499-200 and <200 cells/µl respectively. The values in various groups of the test subjects were significantly lower ($p<0.05$) than that of the control group, 5.15 ± 0.31 mmol/L. Mean serum triacylglycerol of the patients were 2.35 ± 0.19, 2.08 ± 0.03, 2.39 ± 0.16, and 2.58 ± 0.05 mmol/L for overall patients, patients with $CD4^+ \geq$ 500, 499-200 and <200 cells/µl respectively. Values from the various groups of the test subjects were significantly higher ($p < 0.05$) than the that of the control group, 1.47 ± 0.20 mmol/L. Mean serum HDL (mmol/L) for the test subjects were 1.11 ± 0.18, 1.36 ± 0.02, 1.14 ± 0.04, and 0.87 ± 0.05 for overall patients, patients with $CD4^+$count (cells/µl) ≥ 500, 499-200 and < 200 respectively. The various groups of the test subject showed significantly lower values ($p < 0.05$) than the control group 1.59 ± 0.14. Mean serum levels of LDL (mmol/L) of the patients were 1.70 ± 0.17, 1.87± 0.03, 1.76 ± 0.07, and 1.44 ± 0.07 for the overall patients, patients with $CD4^+$ T-lymphocyte count (cells/µl) $\geq$ 500, 499-200, and < 200 respectively. Comparison of various groups of the patients showed a progressive decrease ($p < 0.05$) with the progression of HIV/AIDS compared with the control value of 2.87 ± 0.41. Mean serum VLDL levels of the patients 1.07 ± 0.08 mmol/L was significantly higher ($p < 0.05$) than that of the control group 0.67 ± 0.07 mmol/L. On comparison, the values for various $CD4^+$ group of the patients 0.95 ± 0.01, 1.07 ± 0.01, and 1.17 ± 0.03 mmol/L for patients of CD4 $\geq$ 500, 499-200 and < 200 cells/µl respectively were significantly higher ($p <0.05$) than that of the control mentioned above.

Table 2.0: Effects of HIV/AIDS on lipid profile parameters

			CD4 counts (cells/µl)		
Parametors	Controls	Test subjects	≥500	499 - 200	<200
Total cholesterol (mmol/L)	5.15 ± 0.31	3.88 ± 0.26**	4.17 ± 0.02**	3.94 ± 0.17**	3.49 ± 0.01**
Triacylglycerols (mmol/L)	1.47 ± 0.20	2.35 ± 0.19**	2.08 ± 0.3**	2.39 ± 0.16**	2.58 ± 0.05**
HDL (mmol/L)	1.59 ± 0.14	1.11 ± 0.18**	1.36 ± 0.02**	1.14 ± 0.04**	0.87 ± 0.05**
LDL (mmol/L)	2.87 ± 0.41	1.70 ± .17**	1.87 ± 0.03**	1.76 ± 0.07**	1.44 ± 0.07**
VLDL (mmol/L)	0.67 ± 0.07	1.07 ± 0.08**	0.95 ± 0.01**	1.07 ± 0.01**	1.17 ± 0.03**
	N = 80	N = 80	n = 20	n = 37	n = 23

Mean ± SD

**Indicates significant difference P < 0.05 using one-way ANOVA/Bonferroni's multiple comparison test. HDL : High density lipoprotein, LDL : Low density lipoprotein and VLDL : Very low density lipoprotein.

Discussion.

The results on lipid profile in this study revealed gross dyslipidaemia with significant decrease of serum total cholesterol, HDL and LDL levels with increased serum levels of triacylglycerols and VLDL. This dyslipidaemia, a cardiovascular risk factor, was observed to occur with the progression of HIV infection measured with the progressive declining levels of $CD4^{+}$T-lymphocyte counts in the subjects. This corroborates the work of Anyabolu, 2017, who reported dyslipidaemia in people living with HIV/AIDS. In his work, he reported a hypercholesterolemia as against hypocholesterolaemia in this study. This may be the effects of drugs as his subjects were already on antiretroviral therapy while mine were not. There is evidence that antiretroviral therapy is associated with lipodystrophy syndrome, a lipid metabolism characterized by dyslipidaemia, insulin resistance and fat maldistribution, and metabolic bone disease; osteopenia and/or osteoporosis (Souzal, *et al, 2013*). Increased immune activation in HIV infection had been implicated in contributing to increased venous and arterial thromboses which is attributed to be one of the causes of the altered lipid profile in HIV infection (Funderburg and Mehta, 2016). Lipid profile abnormality may also be as a result of abnormal lipid metabolism reported in HIV-patients such as underpinning mechanism whereby increased hepatic *de novo synthesis of fatty acids leads to increased release of VLDL-cholesterol with decreased clearance of triacylglycerol-rich lipid fraction and increased release of fatty acids for hepatic re-esterification* (Ngu, *et al*, 2010*), e*xcessive hepatic synthesis of triacylglycerols as a result of carbohydrate intolerance and or insulin resistance, stimulation of hepatic synthesis by free fatty acids released from tissue triacylglycerols store by lipolytic hormones and diminished triacylglycerols clearance from the plasma compartment (Kokot*et al*, 1971 and van Welzen, *et al, 2019*). Re-esterificaiton of fatty acids, a reaction in which molecules of fatty acids and glycerol react reversibly to yield triacyglycerol was proposed as yet another mechanism for the altered lipid metabolism. In this process, fatty acids are mobilized from the periphery where they are repackaged into triacylglycerols. Such process in addition to de-novo lipogenesis in the liver is believed to result in an increased very low density lipoprotein, the major carrier for triacylglycerols thus contributing to hypertriacylglycerolaemia (Feingold *et al*, 1990 and Calza, *et al*, 2016). The results, therefore, are also in concurrence with the works of these scholars who reported dyslipidaemia long before the introduction of Protease Inhibitors – based antiretroviral therapy during the course of HIV/AIDS (Penzak and Chuck, 2000 and Oh and Hegele, 2007).

Conclusion.

There were gross dyslipidaemia amongst the subjects which progressed with the progression of HIV/AIDS in this study. The proteinuria found in the control groups may be as a result of undisclosed or hidden sickness(s) not captured prior to their inclusion in the study as the controls were only apparently healthy.

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