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Dysglycaemia and Dyslipidaemia Among Subjects Living with Human Immunodeficiency Virus Infection

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Abstract

Another dimension to the global challenge of Human Immunodeficiency Virus (HIV) is the increasing prevalence of metabolic abnormalities such as diabetes mellitus and dyslipidaemia. The current challenge in managing people living with human immunodeficiency virus (PLWH) includes the identification and monitoring of comorbid health risks associated with HIV and its treatment. This cross-sectional study was conducted among 200 HIV positive subjects (100 newly diagnosed patients and 100 on Highly Active Anti-Retroviral Therapy (HAART) attending the outpatient clinic dedicated to People Living with HIV (PLWH) at the Osun State University Teaching Hospital, Osogbo, Nigeria and 100 HIV negative individuals were monitored as controls. A structured questionnaire was administered to collect relevant medical and socio-demographic information. A multistage random technique was employed in recruiting subjects for the study. Serum glucose, total cholesterol and triglyceride were determined using spectrophotometry techniques. High Density Lipoprotein cholesterol was assayed by precipitation method while Low Density Lipoprotein cholesterol was calculated using Friedewald equation. Data were analyzed using Student t-test, Chi square test, analysis of variance and Pearson correlation coefficient. Serum glucose *(*5.39 ± 2.42 vs 4.52 ± 0.96 vs 3.65 ± 0.67, , total cholesterol *(*4.11 ± 0.84 vs 3.65 ± 1.07 vs 3.42 ± 0.61*)* and LDL (2.88 ± 0.84 vs 2.51 ± 1.05 vs 1.944 ± 0.68) were significantly higher among HIV positive subjects on HAART than HIV positive HAART naive and HIV negative controls (p<0.001*)*. Conversely, HDL (0.85 ± 0.20 vs 0.89 ± 0.19 vs 1.22 ± 0.25) were significantly lower among HIV positive subjects on HAART than HIV positive HAART naive and HIV negative controls. The management of metabolic disorders related to HIV infection is complex. Nevertheless, results from this study suggest that metabolic clinics will be beneficial to PLWH and should be an important part of HIV services especially now that all identified PLWH are linked to treatment as early as possible.

Keywords: metabolic abnormalities, dysglycemia, dyslipidaemia, HIV, HAART.

Introduction

The number of people living with HIV/Acquired Immunodeficiency Syndrome (AIDS) has increased due to the utilization and effectiveness of highly active antiretroviral treatment (HAART) (Hadigan and Kattakuzhy, 2014). Nevertheless, opportunistic infections in people living with HIV (PLWH) may lead to serious illness and be one of the causes of morbidity and mortality. Despite the fact that HAART has significantly prolonged the life span of people living with HIV (PLWH), it is associated with an increase in metabolic abnormalities. Metabolic abnormalities coexisting with HIV are quite challenging and can lead to grave consequences in the absence of medical intervention.

The increasing prevalence of metabolic abnormalities in PLWH has been majorly attributed to the inflammatory process of viral replication and the use of HAART. Though, earlier antiretroviral drugs that caused severe

toxicity (e.g pentamidine) have been removed, some of those still available have potential to precipitate toxicity. Lack of medical intervention can lead to low quality of life, poor adherence to treatment, resulting in increased morbidity and mortality. Given this, prompt diagnosis and early management intervention are very important to avoid preventable complications and possible untimely loss of life.

Metabolic abnormalities independently give rise to serious complications and their coexistence with HIV infection worsens the prognosis. An increased risk of metabolic abnormalities has been observed in elderly patients, males, as well as patients with high viral loads and long duration of HIV infection. Untreated metabolic abnormalities worsen immunosuppression. The prevalence of metabolic abnormalities varies across populations all over the world. Several studies have shown abnormal blood glucose levels in PLWH (Levitt *et al,* 2016; Pillay *et al,* 2016). The prevalence of disorders of the glucose metabolic process in HIV patients was estimated to range from 2.1% to 26.5% in a study conducted by Abraham *et al. (*2015). Similarly, Magodoro *et al. (*2016) stated that the prevalence of type 2 DM was found to be 2.1 % (95 % CI 1.3%–3.2 %) amongst PLWH in a public sector facility in Zimbabwe. The estimated prevalence of diabetes was higher in data from people aged 50 years and above living with and without HIV in Uganda (Mugisha *et al.*, 2015). In another study conducted by Steiniche *et al. (*2016), the prevalence was 5.8% for DM and 5.6% for impaired fasting glucose (IFG) among PLWH in Guinea-Bissau.

Dyslipidemia is very common in PLWH and manifests as low HDL (high density lipoprotein), high triglyceride, total cholesterol and LDL (low density lipoprotein). It is well established that cardiovascular risk assessment of PLWH is a critical element of care in developed countries, but not the case in developing countries. Therefore, healthcare systems in developing countries could also benefit from specialists in this area to reduce CVD in PLWH. According to a study conducted among PLWH in South Africa by Dave *et al. (*2016), hypercholesterolemia was found in 32.2%, low HDL was found in 45.7% and elevated LDL in 9.5% (95% CI 6.2–12.8). This is likely due to the effect of medications, as HAART administration is associated with higher TG (triglyceride), TC (total cholesterol), LDL and HDL than those who were treatment-naïve (Julius *et al*, 2011). In a similar study in Kenya, the prevalence of dyslipidemia was found to be 63.1% and dysglycemia was 20.7%. HAART was associated with increased total cholesterol, triglyceride and LDL levels. However, HAART is not associated with low HDL and does not affect dysglycemia. This study therefore seeks to determine dysglycemia and dyslipidaemia among HIV infected subjects.

Materials and Methods

Study Area

This study was conducted at Osun State University Teaching Hospital, Osogbo, Osun State, Nigeria.

Study Design/Population

This is a cross-sectional study with a total of 200 HIV Positive subjects (100 newly diagnosed patients and 100 on HAART) attending the outpatient clinic dedicated to People Living with HIV (PLWH) at Osun State University Teaching Hospital, Osogbo, Osun state, Nigeria and 100 HIV Negative individuals were monitored as controls. A structured questionnaire was administered to collect relevant information. A Multistage random technique was employed in recruiting subjects for the research. All participants were informed about the investigation and their consent was obtained.

Inclusion and Exclusion criteria

HIV positive male and female subjects on highly active antiretroviral treatment (HAART), those who are not yet on HAART (naïve) and HIV negative subjects as controls were included in the study. While subjects with history of dyslipidemia, diabetics, hypertension and drug addiction were excluded from the study.

Ethical approval

Ethical approval was obtained from Ethical Review Committee of UNIOSUN Teaching Hospital, Osogbo (LTH/EC/2020/01/444). All participants gave informed consent to participate in the study.

Clinical and anthropometric measurement
Clinical and anthropometric measurements regarding each participant's gender, age, weight, height and parameters of special interest such as medical records of the patient, known systemic complications, as well as treatment regimen status were collected using a standard questionnaire.

Sample Size
Using the prevalence of 1.4% as reported by the Federal Ministry of Health; Nigeria HIV/AIDs Indicator and Impact Survey (NAIIS), (2019), the minimum sample size was determined using the formula described by Araoye (2004). The minimum sample size is 21, but 200 HIV infected subjects were eventually recruited for the study.

Blood Collection/Laboratory Analysis
Venous blood sample was collected from the cubital fossa using 21 G needle and syringe, out of which 4mL was dispensed into a plain bottle (non-anticoagulant bottle). The blood was allowed to clot and centrifuged at 1200 rpm for 5 minutes to separate the serum from the cells. The serum sample was stored at -20 ^{0}C for a maximum of three weeks before analysis.

Results
A total of 300 participants were recruited for the study including 123 males and 177 females with a mean age of 41.24 ± 7.73 years.

Table 1 shows the demographic and clinical characteristics of study participants. No significant differences in age, diastolic and systolic blood pressures were observed. The most frequently prescribed HAART was lamivudine-zidovudine, used by 53.1% of the subjects. Tenofovir-lamivudine, abacavir-lamivudine and didanosine-lamivudine were used by the remaining subjects. The study participants were divided into three groups: treatment naïve (HIV-positive HAART naive), those on HAART and HIV negative controls. There was no significant difference among all groups in terms of distribution of age, height, BMI and blood pressure.

Table 2 shows the Serum glucose *(*5.39 ± 2.42 vs 4.52 ± 0.96 vs 3.65 ± 0.67, p<0.001*),* total cholesterol *(*4.11 ± 0.84 vs 3.65 ± 1.07 vs 3.42 ± 0.61*)* and LDL (2.88 ± 0.84 vs 2.51 ± 1.05 vs 1.944 ± 0.68) were significantly higher among HIV positive subjects on HAART than HIV positive HAART naive and HIV negative control subjects. Conversely, HDL (0.85 ± 0.20 vs 0.89 ± 0.19 vs 1.22 ± 0.25) were significantly lower among HIV positive subjects on HAART than HIV positive HAART naive and HIV negative control subjects.

Table 3 indicates the correlation between measured metabolic parameters and viral load among PLWH. Blood glucose and lipid profile parameters did not show a significant correlation with viral load.

Table 1: Socio-demographic characteristics of the study participants

Parameters	HAART N=100	Naive N=100	Control N=100	p-value
Systolic (mmHg)	113.70±21.07	113.10±17.51	111.80±13.13	0.736
Diastolic (mmHg)	74.40±13.73	73.10±12.12	73.60±9.48	0.739
Height (m)	1.61± 0.07	1.62±0.09	1.62±0.07	0.130
Weight (Kg)	63.65±11.31	59.84±10.25	61.40±11.41	0.050
BMI (kg/m^2)	23.79±3.86	23.1±4.23	23.64±4.6	0.483

HAART= HIV positive subjects on A nti-retroviral drugs; NAIIVE=HIV positive subjects not on anti -retroviral drugs; Data presented as Mean ± Standard Deviation (SD)

Table 2: Comparison of measured variables among HIV Positive subjects

Parameters	HAART(n=100)	NAÏVE(n=100)	CONTROL (n=100)	F	*p*-value
Glucose (mmol/L)	5.39±2.42	4.53±0.96	3.65±0.67	14.317	<0.001
CHOL (mmol/L)	4.11±0.84	3.65±1.07	3.42±0.61	7.868	0.001
T.G (mmol/L)	0.64±0.21	0.54±0.21	0.55±0.22	2.926	0.057
LDL (mmol/L)	2.88±0.84	2.51±1.05	1.94±0.68	13.506	0.001
HDL (mmol/L)	0.85±0.20	0.89±0.19	1.22±0.25	32.759	0.001

Key: CHOL=Cholesterol, TG=Triglyceride, LDL -c=Low Density Lipoprotein, HDL -c= High Density Lipoprotein

Table 3: Correlation between blood glucose, lipid profile parameters and Viral load among people living with HIV

	V.LOAD	GLUC	CHOL	T.G	LDL	HDL
V.LOAD	1	.195	.118	-.070	.146	-.053
GLUCOSE	.195	1	.273**	-.017	.275**	-.061
CHOL	.118	.273**	1	.152	.958**	.005
T.G	-.070	-.017	.152	1	.062	-.075
LDL	.146	.275**	.958**	.062	1	-.236*
HDL	-.053	-.061	.005	-.075	-.236*	1

Key: CHOL=Cholesterol, TG=Triglyceride, LDL-c=Low Density Lipoprotein, HDL-c= High Density Lipoprotein

*** Correlation is significant at the 0.01 level (2-tailed)*
**Correlation is significant at the 0.05 level (2tailed)*

Discussion

Human immunodeficiency virus (HIV) remains a persistent public health concern in sub-Saharan Africa. With the prolonged survival of PLWH, metabolic abnormalities are fast becoming an issue of concern in PLWH and also for health systems in developing countries (Mendenhall and Norris, 2015). Diabetes mellitus and dyslipidemia are increasingly seen in PLWH. Progressively diabetes and dyslipidaemia are developing among low-wage populations that additionally are most burdened by social anxiety and disease (Mendenhall *et al.*, 2015) and PLWH are at particular risk (Kagaruki, 2014). Furthermore, metabolic abnormalities commonly cause organ specific damage with exacerbation of socioeconomic burden (Hadigan and Kattakuzhy, 2014).

The increased glucose level in PLWH which is further exacerbated in those on HAART as shown in this study can be a result of pancreatic beta-cell lipotoxicity, which may be due to drug-induced effects, or to the consequences of lipodystrophy or both (Gan *et al,* 2001). In the homeostasis of blood glucose level, insulin supports glucose uptake by activating insulin receptors on cell surfaces. This sets up a course of phosphorylation of key cell substrates that results in translocation of glucose transporter 4 (GLUT4) from the cell cytosol to the surface of the cell, where it encourages glucose entry into the cell. Within this pathway, the action of insulin may be interrupted at numerous points, resulting in insulin resistance (Samaras, 2009). In addition, the increase may also be due to disrupted glycemic control which is often attributed to PIs (Protease Inhibitors) but

Efavirenz, Zidovudine and Stavudine have also been implicated with an increased risk of developing diabetes (Erlandson *et al*, 2014; Karamchand *et al*, 2016). Several studies have demonstrated that use of the early PIs (such as indinavir) increases insulin resistance. In spite of its role in reduction of the burden on PLWH, HAART is observed to be connected with type 2 DM (Dimala *et al*, 2016). PLWH on HAART has greater risks for developing DM compared to those who are not on HAART (Maganga *et al*, 2015).

Dyslipidaemia as revealed in this study may largely be related to PI, fatty liver and use of HAART. Ngala *et al*, 2013 reported that HAART was associated with lipodystrophy, and the risk of developing type II diabetes among the HAART-experienced group was 5 times higher than the treatment-naïve group. In Nigeria, high cholesterol, LDL-c and triglyceride were seen in 28%, 24% and 35%, respectively. A study conducted by Salami *et al. (*2009) reported that PI worsens dyslipidemia. In Tanzania, low HDL was found in 67% and increased triglyceride was recorded 28%. High triglyceride and low HDL levels were associated with lipodystrophy in the same study. PLWH now live longer and are increasingly encountering a series of challenging metabolic disorders like diabetes, obesity, dyslipidemia and subsequent increase in the risk of CVD. Furthermore, in developing countries, CVD has become one of the major causes of death in HIV patients due to the high prevalence of metabolic disorders like diabetes mellitus and dyslipidemia.

Conclusion

Findings from this study revealed that PLWH are at greater risk of having metabolic abnormalities like diabetes mellitus and dyslipidemia which could be further pronounced in those who are on HAART. Thus, cardiovascular risk reduction and lifestyle modifications should be essential components of the control program. Also, careful selection of the HAART according to underlying metabolic abnormalities and risk factors is of great importance. Therefore, since PLWH are increasing and have an ageing population to address, a metabolic clinic may be a good choice not only to meet the clinical demand for clinical services but also to provide a useful opportunity to collect data for further clinical research.

Ethical approval

Ethical approval was obtained from the Ethical Review Committee of LAUTECH Teaching Hospital, Osogbo (**LTH/EC/2020/01/444**). All participants gave informed consent to participate in the study. The study was part of a larger study.

Conflict of Interest

The authors declare no conflict of interest.

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