

Pattern of Blood Pressure, Body Mass Index and Some Cardiac Enzymes in HIV Seropositive Patients in Sokoto, Nigeria

Bello, A.
Mainasara, A. S.
Liman, H. M.
Umar, H.
Abubakar, A. F.
Saidu, K.
Abdullahi, A. U.

ABSTRACT

HIV/AIDS infection is a global pandemic, and poses a serious health challenge in sub-saharan Africa, Nigeria inclusive. Cardiac disease may occur at any stage of HIV infection, but important manifestations are more frequent with advanced immunodeficiency. Moreover, it has been reported that complications from HIV infection includes arrhythmias, heart failure myocardial infarction and coronary heart disease. The present study is designed to investigate the pattern of blood pressure and some cardiac enzymes in HIV seropositive subject in Sokoto metropolis Nigeria. A total of one hundred and forty seropositive patients on HAART and HAART naïve patients were investigated and compared with seventy seronegative controls. HIV infection result into a lot of clinical manifestation cardiovascular disorder inclusive. The result shows that CKMB and LDH were significantly increase in patients on HAART as compared to those not on HAART, however, there was also significant increased in systolic BP, Diastolic BP and body mass index but not in total CK. When compared with control there is significant increase in all the parameters in the study groups than in controls. The study observes that there is need to monitor these parameters to prevent sudden cardiovascular complications in HIV seropositive patients.

Keywords: HIV Seropositive, HAART, Cardiac enzymes, Blood Pressure

INTRODUCTION

Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) infection is a global pandemic which is becoming a serious health problem

**Bello A, Mainasara A.S, Abubakar A F and Saidu K. are Lecturers in the Department of Chemical Pathology and Immunology, Faculty of Basic Medical Sciences, College of Health. Liman, H. M and Umar H. are Lecturers in the Department of Internal Medicine, Faculty of Clinical Sciences, College of Health Sciences. Abdullahi A.U. is a Lecturer in the Department of Morbid Anatomy and Forensic Medicine, Faculty of Basic Medical Sciences, College of Health Sciences. All in Usmanu Danfodiyo University, Sokoto.*

**E-mail: aminubellodange@gmail.com*

in Sub-Saharan Africa, Nigeria inclusive (Oluboyo A., Okogun, Duru, Oluboyo B., *et al.*, 2006). Human Immunodeficiency Virus (HIV) is a lent virus, a member of retrovirus family that causes Acquired Immunodeficiency Syndrome (AIDS). Human immunodeficiency virus was first recognized in the summer of 1981 but has now assumed a pandemic proportion (Fauci, 1999). In 1998, HIV was reported as the fourth leading cause of death worldwide with estimated 2.5 million deaths annually (WHO, 1999). In Nigeria HIV was first recognized in 1985 and reported in 1986 (Abdulsalami and Tekena, 2006). By the end of 2005, the estimated number of people living with HIV and AIDS has risen to 38.6 million with about 2.8 million deaths (UNAIDS/WHO, 2006). This has significantly reduced to 34million people living with HIV/AIDS with about 1.8 million deaths in 2010 (UNAIDS, 2011). In 2011, 1.7 million people died from AIDS-related causes worldwide (UNAIDS, 2012). This represents a 24% decline in AIDS-related mortality compared with 2005 when 2.3 million deaths occurred.

However, more than 25 million people are living with HIV/AIDS since 1981 (UNAIDS/WHO, 2006). A report by the global HIV/AIDS pandemic (2006) showed that approximately 64% of world populations living with HIV are in the sub-Saharan Africa. In Nigeria, the prevalence of HIV is about 5% in the entire population as at the end of 2003 (FMOH Report, 2004). National AIDS/STDS control program (NASCP, 2005) reported the prevalence of 3.5% for the north western zone of the country, Sokoto inclusive. The prevalence of 2.1% was reported in north western zone in 2010 (NACA, 2012). The HIV/AIDS prevalence rate in adult population in Nigeria is reported to be 3.6 % (CIA report, 2009). The national HIV Seroprevalence level, obtained from sentinel surveys of antenatal care attendees, increased from 1.8 per cent in 1991 to 5.8 per cent in 2001 and then declined to 5.0 per cent in 2003 and further to 4.4 per cent in 2005. This was followed by a rise to 4.6 per cent in 2008 and then a recent decline to 4.1 per cent in 2010 (NACA, 2012). Cardiac disease may occur at any stage of HIV infection (Oluboyo *et al.*, 2006) but important manifestations are more frequent with advanced immunodeficiency.

Moreover, it has been reported that complication from HIV infection includes arrhythmias, heart failure myocardial infarction and coronary heart disease (Mahmoud *et al.*, 2005, Mahmoud, 2008). Lactate dehydrogenase catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and Nicotinamide adenine dinucleotide (NAD⁺). It converts pyruvate, the final product of Glycolysis, to lactate when oxygen is absent or in short supply and it performs the reverse reaction during the Cori cycle in the liver. At high concentrations of lactate, the enzyme exhibits feedback inhibition, and the rate of conversion of pyruvate to lactate is decreased. It also catalyzes the dehydrogenation of 2-Hydroxybutyrate, but it is a much poorer substrate than lactate. There is little to no activity with beta-hydroxybutyrate. Functional lactate dehydrogenase isoenzymes are homo- or hetero- tetramers composed of M and H protein subunits

encoded by the *LDHA* and *LDHB* genes respectively: LDH-1 (4H) - in the heart, LDH-2 (3H1M) - in the reticuloendothelial system, LDH-3 (2H2M) - in the lungs, LDH-4 (1H3M) - in the kidneys, placenta and pancreas, LDH-5 (4M) - in the liver and striated muscle. The five isoenzymes that are usually described in the literature each contain four subunits. The major isoenzymes of skeletal muscle and liver, M_4 , has four muscle (M) subunits, while H_4 is the main isoenzyme for heart muscle in most species, containing four heart (H) subunits. The other variants contain both types of subunits. Creatine kinase (CK), also known as creatine phosphokinase (CPK) or phospho-creatinekinase, is an enzyme expressed by various tissues and cell types. CK catalyses the conversion of creatine and consumes adenosine triphosphate (ATP) to create phosphocreatine (PCr) and adenosine diphosphate (ADP). This CK enzyme reaction is reversible, such that also ATP can be generated from PCr and ADP.

In tissues and cells that consume ATP rapidly, especially skeletal muscle, but also brain, photoreceptor cells of the retina, hair cells of the inner ear, spermatozoa and smooth muscle. PCr serves as an energy reservoir for the rapid buffering and regeneration of ATP in situ, as well as for intracellular energy transport by the PCr shuttle or circuit. Thus creatine kinase is an important enzyme in such tissues. In the cells, the “cytosolic” CK enzymes consist of two subunits, which can be either B (brain type) or M (muscle type). There are, therefore, three different isoenzymes CK-MM- in the skeletal muscles, CK-BB- in the brain tissues, CK-MB- in the cardiac muscles. Highly active antiretroviral therapy (HAART) has prolonged many patients’ lives, but the cardiac sequelae may progress despite HAART. Heart muscle disease is the most important cardiovascular manifestation of HIV infection and is likely to become even more prevalent as HIV infected patients live longer. This may present as myocarditis, dilated cardiomyopathy or isolated left or right ventricular dysfunction.

Heart muscle disease results in symptomatic heart failure in up to 5% of HIV patients. Both adults and children are affected with severity ranging from incidental microscopic inflammatory findings at autopsy to clinically significant cardiac disease with chronic cardiac dysfunction. HIV has gone from a fatal syndrome to a chronic disease in persons receiving highly active antiretroviral therapy (HAART) (Cheryl and Jonathan, 2009).

METHOD

This study was conducted at three major hospitals in Sokoto metropolis. These are Usmanu Danfodiyo University Teaching Hospital (UDUTH), Specialist Hospital Sokoto (SHS) and Maryam Abacha Women and Children Hospital (MAWCH) Sokoto, Nigeria. Blood samples were collected from confirmed HIV seropositive subjects attending IHVN center of UDUTH and SHS and ARV clinic of MAWCH. The permission to performed the research was obtained from ethical

committee of UDUTH and that of Sokoto State Ministry of Health and informed consent was signed by each subjects recruited into the study. All subjects were 15 years and above (age range 15-80 years). Interim African Region version for persons aged 15 years or more with positive HIV antibody test or other laboratory evidence of HIV infection (WHO, 2005). The number of subjects for inclusion in the study was determined using the sample size formula for estimating sample size for descriptive studies (Araoye, 2003).

$$\text{That is } n = Z^2 \frac{pq}{d^2} \dots\dots\dots 1$$

The subjects were divided into three groups comprising Seventy HIV positive HAART naïve patients, Seventy HIV positive patients on HAART and Seventy age and sex matched HIV negative individuals as controls. Therefore, a total of two hundred and ten subjects were recruited for the study.

The procedure for blood collection was explained to the participants in the language they understood. This was performed using vacutainer needle into plain container after sterilizing the site with methylated spirit. The antecubital fossa was cleaned with disinfectant and allowed to dry; a tourniquet was applied a few centimeters above the cubital fossa to distend the veins. Blood was drawn using 23G needle. A wide bore needle was then used to collect five milliliters of blood using standard technique of venipuncture and transfer into a plain bottle which was then transported to the laboratory. The serum was harvested within sixty minutes of collection, the enzymes assay were done immediately while the remaining sample were frozen at -20°C for analysis of troponin I later. Total creatine kinase (ck) and one of its isoenzymes CKMB were estimated using acetylcystein NAC activated method (Szasz, Gruber and Bernt, 1976). Lactate dehydrogenase catalyzes the oxidation of lactate to pyruvate with simultaneous reduction of NAD to NADH. The rate of NAD reduction can be measured as an increase in absorbance at 340nm with AGAPE Germany (Gay, Robbert and George Jr, 1968)

Blood Pressure Measurement: The blood pressure was taken at rest by the researcher with the client at sitting position and sphygmomanometer placed at same level with heart. The cuffs of the sphygmomanometer were placed on upper arm to occlude the brachial artery. The systolic pressure was recorded at first audible sound, while diastolic blood pressure at last audible sound.

Anthropometric Measurements: The procedure of Abdoul (2010) was employed in the anthropometric measurement. Body Weight (Wt) of the patients were weighed using regularly calibrated weighing health scale (Stadiometer model ZT120) to the nearest 0.1kg with minimum clothing. The height (Ht) of each subject was measured using a calibrated stadiometer model 220. The subjects stood erect and barefooted on the stadiometer to the nearest 0.1cm using vertex

as land mark. Body Mass Index (BMI) was determined using the weight in kg divided by square of the height in meter, weight (kg)/height (m²) (kg/m²). The data obtained from the study is presented in form of tables and figures. The results were analyzed using Microsoft excel spreadsheet and statistical software analyze for Microsoft excel version 2.25 excel12⁺. Each parametric value was analyzed using descriptive statistics, t-test and Analysis of variance (ANOVA). For nonparametric value/score and ranks the result was analyzed using median, ranges and Spearman correlation. Comparison of mean values was done using Student's t-test (Harry and Steven, 1995). Proportion was compared using chi-square (with Yates correction), where figures are small, Fishers exact probability test was used (Swinscow, 1985).

RESULTS AND DISCUSSION

One hundred and forty (140) seropositive subjects were used in the study of which 89 (63.6%) were females, while 51 (36.4%) were males. Forty seven 47 (33.6%) of the females (n = 89) were HIV positive on anti-retroviral drugs (HAART) and forty two 42 (30%) were HIV positive not on drugs. Twenty three 23 (16.4%) of males (n = 51) were HIV positive on anti-retroviral drugs (HAART) while twenty eight 28 (20%) were HIV positive not on drugs. Out of the 140 patients, only 9 (6%) are smokers, 2 (1%) are females and remaining 8 (5%) are males. Among controls 6 (9%) are smokers and were males.

Oluboyo *et al.* (2006) report statistically significant difference in TCK and CKMB between HIV positive patient on HAART and those not on HAART, but not in LDH. In the present study there were no statistically significant difference in TCK and CKMB (p value 0.347 and <0.069) respectively, but there significant difference in LDH with (p value <0.0036). There is significant statistical difference in SBP and DBP among patients on HAART and those not yet on HAART. This is contrary to findings of Oluboyo *et al.*, (2006) who found no significant difference among the two groups. Though none of the study subjects had clinical evidence of myocardial injury, yet the relatively low blood pressure recorded among some of the subjects may play a role in the cardiac event (90/60mmHg) or high blood pressure in some cases (180/100mmhg). Some studies reported high prevalence of cigarette smoking among HIV positive patients up to 22% (Virginia, Triant-Hang, Colleen and Steven, 2007) while its only 4.3% in the present study, this may not be unrelated to the culture and type of patients in the study (females). The study shows that there is no significant difference in BMI among HIV seropositive patients on HAART and that of control but it's statistically significant among HIV seropositive HAART naïve patients on HAART and controls. Furthermore, the present study has shown no significant correlation between the serum levels of CKT, CKMB and LDH and body mass index (BMI) in patients and controls respectively.

Table 1: Age, BMI, BP, and Duration of disease (Mean ± SEM) in patients and controls.

Parameters	Naïve	HAART	Controls	p value
Age (years)	34.2±1.29	37.5±1.28	29.2±1.12	<0.0001
BMI (kg/m ²)	21.01±0.586	22.69±0.708	22.58±0.540	<0.0001
SBP (mmHg)	113.±2.3	123±3.01	118±1.60	0.0042
DBP (mmHg)	74.1±1.24	77.6±1.80	74.1±1.14	0.0104
DOD (years)	1.23±0.26	2.8±0.29	-	<0.0001

0.0001 is statistically significant among same variables

n = number of subjects, BMI = Body mass Index, SBP = systolic blood pressure, DBP = Diastolic blood pressure, HAART = Highly active antiretroviral therapy DOD = duration of HIV disease. There are statistical significant difference ($p < 0.05$) in the mean age, BMI, SBP, DBP and duration of HIV disease between HAART naïve patients, HAART group and controls using one way ANOVA.

Table 2: Comparison of mean Serum level of CKT, CK-MB and LDH levels (Mean ± SEM) in patients and Controls

Subjects	Naïve	HAART	Controls	p value
CKT(IU/L)	83.52±9.69	72.53±6.47	54.86±5.82	0.0265
CKMB(IU/L)	30.79±2.02	51.02±10.86	15.60±1.63	0.0007
LDH(IU/L)	439.8±17.72	517.4±19.32	353.3±23.40	<0.0001

n = number of subjects, CKT = creatine kinase, CKMB = creatine kinase MB subunit, LDH = lactate dehydrogenase HAART = highly active antiretroviral therapy. There are significant statistical difference ($p < 0.05$) in the mean concentration of cTnI, CKT, CKMB and LDH levels between HAART naïve, HAART group and controls, using one way ANOVA

Table 3: Mean blood pressure level (Mean ± SEM) in patients on treatments (HAART), HAART naïve patients and controls.

Subjects	Code	SBP (mmHg)	DBP (mmHg)
		Mean± SEM	Mean± SEM
HAART	HAART	123.9±3.01	77.5±1.80
	HAART Naïve	112.6±2.30	74.1±1.24
Controls	controls	118.1±1.64	74.1±1.14
P value	-	0.0042	0.0104

SBP = Systolic blood pressure, DBP = Diastolic blood pressure, SEM = standard error of mean. There are significant statistical difference ($p < 0.05$) in both systolic blood pressure and diastolic blood pressure among HAART naïve, HAART group and controls. Using one way ANOVA.

Table 4: Serum CKT, CKMB and LDH levels (Mean ± SEM) in hypertensive and Non hypertensive patients and Controls

Subjects	n	CKT(IU/L)	CKMB(IU/L)	LDH(IU/L)
HAART				
HPT	20	63.28±6.466	31.01±3.193	548.9±44.93
NHPT	50	91.62±13.183	30.70±2.540	504.8±20.28
p-value	-	0.188	0.946	0.306
HAART Naïve				
HPT	6	54.17±6.794	29.67±4.224	442.2±60.95
NHPT	64	74.26±7.023	53.02±11.848	439.5±18.67
p-value	-	0.389	0.551	0.966

Controls				
HPT	6	44.00±17307	7.13±2.848	333.5±68.79
NHPT	64	55.88±6.180	16.40±1.737	355.2±24.90
p-value	-	0.572	0.113	0.798

where n = number of subjects, $cTnI$ = cardiac troponin I, CKT = creatine kinase total, $CKMB$ = creatine kinase MB, LDH = lactate dehydrogenase, $HAART$ = highly active antiretroviral therapy, HPT = hypertensive and $NHPT$ = Non hypertensive. All parameters there are statistically significant elevation ($p < 0.05$) in patients than in controls using one way ANOVA.

CONCLUSION

HIV/AIDS result into many serious clinical manifestation such as cardiovascular disease with increase evidence in heart disease in patients treated with HAART. This study found elevated level of total CK, CKMB, LDH and blood pressure more in HAART treated group than in HAART naïve patients and controls. These finding suggest that there is need to monitor these parameter closely more especially in patient receiving HAART medication in order to prevent cardiovascular complications in HIV patients.

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