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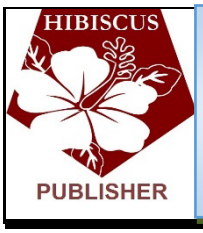

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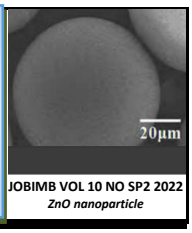

Estimation of Serum Levels of AST, LDH, CKMB AND TCK Among HIV Patients on HAART, HAART Naïve and Controls

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ABSTRACT

Human Immunodeficiency virus (HIV) infection is associated with increased of developing heart disease. Information on the cardiac status of HIV-infected Nigerians is lacking. HIV/AIDS infection is a global pandemic and poses a serious health challenge in sub-Saharan Africa, Nigeria inclusive. The 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 include arrhythmias, heart failure myocardial infarction and coronary heart disease. This study aimed to estimate serum levels of AST, LDH, CKMB and TCK among HIV patients on HAART, HAART naïve and controls subjects attending Bauchi State Tertiary hospital, Nigeria. The results showed that the mean serum total Creatine kinase, CK-MB, LDH and AST were significantly higher in HIV participants not on HAART compared with HIV participants on HAART at $P<0.05$ respectively. Similarly, the mean serum total Creatine kinase, CK-MB, LDH and AST were significantly higher in symptomatic HIV participants not on HAART compared with HIV seronegative control subjects at $P<0.05$ in each case. Once again, the mean serum total Creatine kinase, CK-MB, LDH and AST were significantly higher in asymptomatic HIV participants compared with HIV seronegative control subjects at $P<0.05$ respectively. Increased levels of some cardiac markers were seen in HIV-infected participants. The study reveals that there is a need to monitor these parameters to prevent sudden cardiovascular complications in HIV seropositive patients. Hence, it is recommended that more investigations need to be carried out to further evaluate the levels of CK-MB (cardiac-specific) isoenzyme of CK and other cardiac biomarkers such as troponins I and T, and myoglobin, among others.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is a global pandemic which is becoming a serious health problem in Sub-Saharan Africa, Nigeria inclusive [1] HIV is a lentivirus that breaks down the body's immune system, infects CD_4 lymphocytes, depletes them and gradually leads to acquired immunodeficiency syndrome (AIDS) which is a fatal illness [2]. Infection with HIV leads to a progressive impairment of cellular functions, which is characterized by a gradual decline in blood

$CD4^+$ T cell counts thereby predisposing the individual to a wide variety of opportunistic bacterial, fungal, viral, protozoa infections and cancerous growth [3]. HIV was first recognized in the summer of 1981 but has now assumed a pandemic proportion [4]. In 1998, HIV was reported as the fourth leading cause of death worldwide with estimated 2.5 million deaths annually [5].

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 [6,5]. This has significantly reduced to 34 million people living with HIV/AIDS with about 1.8 million deaths in 2010 [7]. In 2011, 1.7 million people died from AIDS-related causes worldwide [8]. 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 [6,5].

A report on the global HIV/AIDS pandemic (2006) showed that approximately 64% of the world population living with HIV is in sub-Saharan Africa. In Nigeria, a total of 3.1 million people are living with HIV as of the end of 2011 and about 300, 000 new infections are occurring annually [6]. HIV/AIDS prevalence rate in Nigeria dropped from 5.1% to 3.4% [9]. Bauchi State, with a total population of 4,653,006 with a 2016 forecast of 6,537,314 has an HIV prevalence rate of 6.0% in 2018 [10], which dropped to 3.3% in 2020, below the National prevalence rate of 4.6% [11] and raise again to 5.6% according to the HIV/AIDS prevalence ranking by states published by NACA 2022. A total of 15,095 and 18,504 people were tested for HIV in 2019 and 2020 respectively, out of which 1,238 and 1,204 individuals were positive [12]. On the total of new patients enrolled on ART, the figure showed that 714 and 525 patients are newly enrolled in 2019 and 2020 respectively [12].

Based on the WHO-recommended guidelines for the treatment of HIV-positive patients, a total of 1.5 million (30%) people infected with HIV infection in Nigeria are on therapy [13]. Highly active antiretroviral therapy (HAART) has dramatically decreased the morbidity and mortality associated with HIV infection and rebuilt the immune system [14]. A number of side effects such as dyslipidaemia and lipodystrophy have been reported to be induced by HAART [15]. Cardiovascular disease accounts for more than 20% of death [16].
The cardiac disease may occur at any stage of HIV infection [1] but important manifestations are more frequent with advanced immunodeficiency.

Moreover, it has been reported that complications from HIV infection include arrhythmias, heart failure myocardial infarction and coronary heart disease [17]**.** Heart 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 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) [18].

The heart is enclosed in a double-layered fibrous membrane (sac) called the pericardium. The myocardium contains striated muscle fibres that alternate between contraction and relaxation, which allows the heart to do its work. These fibres are composed of cardiac-specific contractile proteins called actin and myosin and regulatory proteins called troponins. In addition, these fibres also contain a - number of enzymes such as creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) that have been used as markers of cardiac injury. CK: this is also known as creatine phosphokinase. An enzyme expresses by various tissue and cell types that are generally associated with ATP regeneration in contractile or transport systems.

Its predominant physiological function occurs in muscle cells where it is involved in the storage of high-energy creatine phosphate. CK is widely distributed in tissues with the highest activity found in skeletal muscles, heart muscles, and brain tissues and present in small amounts in tissues like the bladder, placenta, GIT, thyroid, uterus, kidney, lungs, spleen, liver, and pancreas.CK levels are frequently elevated in disorders of cardiac and skeletal muscles. The CK level is considered a sensitive indicator of acute myocardial infarction (MI) but they are not entirely specific.CK enzymes has 3 isoform- CK-BB (Brain type), CK-MB (Hybrid), and CK-MM (Muscle type) with CK-MB coming from the myocardium of the heart.

Lactate dehydrogenase is present in the cytoplasm of all tissue cells in the body. There are five main isoenzymes, the sixth being present only in the testicular tissue. The LDH convert lactic acid to pyruvic acid at 8.8 to 9.8 pH. The action is reversible at 7.4 to 7.8 PH. It markedly increases a few hours after myocardial infarction and remains high for about 1 to 2 weeks. There is also moderately increase activity in disorders such as megaloblastic anaemia, hepatitis, renal infarction, pulmonary infarction, leukaemia, haemolytic anaemia, most liver disease and hypothyroidism. It follows therefore that an increase does not generally indicate any specific disorder [19].

Highly active antiretroviral therapy (HAART) is the name given to aggressive treatment regimens used to suppress HIV viral replication and the progression of HIV disease [9] The usual HAART regimen combines three or more different drugs such as two nucleosides reverse transcriptase inhibitors (NRTIs) and a protease inhibitor (PI), two NRTIs and a non-nucleoside reverse transcriptase inhibitor (NNRTI) or other such combinations. These HAART regimens have proven to reduce the amount of active virus and in some cases can lower the number of the active virus until it is undetectable by current blood testing techniques [9].

HAART provides effective treatment options for treatment-naive and treatment-experienced patients. Six classes of antiretroviral agents that currently exist are as follows: Nucleoside reverses transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), Protease inhibitors (PIs), Integrase inhibitors (IIs), Fusion inhibitors (FIs), Chemokine receptor antagonists [11].

Each class of HAART targets a different step in the viral life cycle as the virus infects a CD_4^+ T lymphocyte or other target cells.

The use of these agents in clinical practice is largely dictated by their ease or complexity of use, side-effect profile and efficacy based on clinical evidence, practice guidelines and clinician preference [2]. Resistance, adverse effects, pregnancy and co-infection with hepatitis B virus or hepatitis C virus present important challenges to clinicians when selecting and maintaining therapy [11]

MATERIALS AND METHODS

Study Population
One hundred and eighty subjects were randomly recruited for this study. Using the World Health Organization (6), staging for HIV as a guide, the participants were grouped, comprising of 60 symptomatic HIV subjects on HAART, 60 symptomatic HIV subjects not on HAART and 60 (male = 49; female = 11) HIV seronegative control subjects. These participants have no history of any disease which was obtained using a questionnaire and they were randomly recruited from the voluntary and counselling unit (VCT) of Tertiary Hospital.

Ethical Clearance
Ethical approval was obtained from the ethical committee of Abubakar Tafawa Balewa University Teaching Hospital. Informed consent was also obtained from all the participants. Abubakar Tafawa Balewa University Teaching Hospital.

Sample Collection and Processing
About four millilitres (4 mL) of blood sample was taken into a plain container by venepuncture. This was performed using a vacutainer needle into the plain container after sterilizing the site with methylated spirit. The antecubital fossa was cleaned with methylated spirit and allowed to dry. A tourniquet was applied a few centimetres above the antecubital fossa to distend the veins. The blood sample (4 mL) was drawn using a 23G needle. The blood was transferred into a plain bottle, allowed to clot for 30 minutes and centrifuged at 3000 rpm for 5 minutes. The serum was harvested and put into sample bottles and analysed for serum TCK, CK-MB, LDH and AST levels. However, it is not possible to carry out the analysis immediately due to a logistic problem, the sera were stored frozen at – 20 ^{o}C until the following day.

Equipment
Benchtop centrifuge ALC 4235 Anno Di fabric Milano (Italy) will be used to spin the blood specimens'.UV-Vis spectrophotometer Beckman Coulter DU- 720 (Germany) will be used for the measurements of serum LDH, AST and CK.

Reagents
All reagent kits used in the study were obtained from Agappe Diagnostics, Switzerland. All the reagents were of analytical grade.

Analytical Methods

Quantitative determination of Aspartate aminotransferase (AST).
Serum AST activities were estimated using the method of Reitman and Frankel [20].

Principle
Aspartate aminotransaminase transfer amino group from aspartate to α – ketoglutarate to produce glutamate and oxaloacetate. The oxaloacetate is reduced by malate dehydrogenase to malate and there is concomitant oxidation of NADH to NAD. The decrease in NADH is proportional to enzyme activities.

Procedure
The procedure was as described by the manufacturer (Agappe Diagnostics, Switzerland). 100 µl of standards, specimens and controls were dispensed into appropriate test-tubes. 1000 µl of working reagent (Tris buffer, 88 mmol/L, L-aspartate, 260 mmol/L, MDH, > 600 U/L, LDH > 900 U/L, NADH, 0.20 mmol/l, α- ketoglutarate 12 mmol/L)) were dispensed into each test tube respectively, gently mixed and incubated at 37 ^{o}C for 100 seconds. The change in absorbance per minute was measured within 3 minutes at 340 nm.

Calculation
AST Activity (U/L) = (▲OD/ 3 minutes) x 1768

Quantitative determination of serum lactate dehydrogenase
LDH activities were estimated using a modified method base on recommendations of the Scandinavian Committee on Enzymes (SCE).

Principle

LDH catalyses the following reaction

$$\text{Pyruvate} + \text{NADH} + H^{+} \rightarrow NAD^{+} + \text{L-Lactate (catalysed by LDH)}$$

At 340 nm wavelength (ultraviolet spectrophotometer), NAD has no absorbance where as $NADH_2$ absorbs strongly in an ultraviolent spectrophotometer.

Procedure
The procedure was as described by the manufacturer (Agappe Diagnostics, Switzerland). 10 µl of standards, specimens and controls were dispensed into appropriates test tubes. 1000 µl of working reagent (Tris buffer, 80 mmol/L, pyruvate 1.6 mmol/L, sodium chloride, 200 mmol/L NADH, 240 mmol/L) were dispensed into each test-tube respectively, gently mixed and incubated at 37 ^{o}C for 1 minute. The change in absorbance per minute was measured within 3 minutes at 340 nm.

Calculations
LDH Activity (U/L) = (▲OD/ 3 minutes) x 16030.

Quantitative determination of total Creatine kinase (CK) in Human sera
Serum TCK activities were estimated according to the International Federation of Clinical Chemistry (IFCC) and offered the advantage of the sensitive and specific test system.

Principle
Creatine kinase catalyses the formation of ATP from creatine phosphate and ADP. Glucose was converted to glucose-6-phosphate by hexokinase using ATP as a source of PO4 moiety. G-6-P was oxidized by G-6-PDH to 6-phosphogluconate reducing NADP to NADPH. The reaction after the lag phase was monitored by the increase in absorbance at 340nm and directly proportional to the creatine kinase activities. (i.e. the formation of NADPH is in equimolar amount as that of the formation of creatine)

The kinetic determination of CK is based on the following reactions;

Creatine phosphate + ADP→Creatine + ATP (Catalysed by CK)
ATP + Glucose →ADP + Glucose-6-phosphate G6P+$NADP^{+}$ (Catalysed by HK)
6-phosphogluconate + NADPH + H^{+} (Catalysed by G6P-DH)

Procedure
The procedure was as described by the manufacturer (Agappe Diagnostics, Switzerland). 100 µl of standards, specimens and controls were dispensed into appropriate test tubes. 1000 µl of working reagent (D-glucose 125 mmol/L, N-Acetyl-L-cysteine 25 mmol/L, magnesium acetate, 12.5 mmol/L, NADP 2.4 mmol/L, EDTA 2 mmol/L, Hexokinase > 6800 U/L, creatine phosphate 250 mmol/L, ADP 15.2 mmol/L, AMP, 25 mmol/L, Di-adenosinepentaphosphate 103 mmol/L, G-6-PDH > 8800 U/L) were dispensed into each test-tube respectively, gently mixed and incubated at 37 ºC for 1 minute. The change in absorbance per minute was measured within 3 minutes at 340 nm.

Calculation

Creatine kinase Activity (U/L) = (▲ OD/ 3 minutes) x 4127

Quantitative determination of Creatine kinase (CK)- MB in Human sera
Serum CK MB activities will be estimated using CKMB (NAC act.) KIT
(Immuno-inhibition / modified IFCC method)

Principle
CK-M fractions of the CK-MM and the CK-MB in the sample are completely inhibited by an anti-CK-M antibody present in the reagent. Then the activity of the CK-B fraction is measured by the CK (NAC act.) method. The activity of the non-inhibited CK-B subunit is then assayed by the following series of reactions;

Phosphocreatine + ADP→Creatine + ATP (catalysed by CK)
ATP + Glucose→ADP + Glucose-6-phosphate (catalysed by HK)
G6P + $NADP^+$ → 6-phosphogluconate + NADPH + H^+ (catalysed by G6P-DH)

The rate of NADPH formation, measured photometrically, in proportion to the catalytic concentration of CK-B present in the sample.

Procedure
The procedure was as described by the manufacturer (Agappe Diagnostics, Switzerland). 40 µl of standards, specimens and controls were dispensed into appropriate test tubes. 1000 µl of working reagent (imidazole (pH 6.7), 125 mmol/L, D-glucose 25 mmol/L, N-Acetyl-L-cysteine 25 mmol/L, magnesium acetate, 12.5 mmol/L, NADP 2.52 mmol/L, EDTA 2.02 mmol/L, Hexokinase > 6800 U/L, creatine phosphate 250 mmol/L, ADP 15.2 mmol/L, AMP, 25 mmol/L, Diadenosinepentaphosphate 103 mmol/L, G-6-PDH > 8800 U/L) were dispensed into each test-tube respectively, gently mixed and incubated at 37 C for 100 seconds. The change in absorbance per minute was measured within 3 minutes at 340 nm.

Calculation

Creatine kinase –MB Activity (U/L) = (▲ OD/ 3 minute) x 8254.

Quality Control
Quality control sera were run along tests in each batch of analysis these were compared with the reference values of the control sera. Standard deviation and coefficient of variation were calculated on them. Five per cent (5%) hypochlorite solution was used to deprotonate while deionised water to flush before and after every use of the semi-auto analyser.

Statistical Analysis
The data obtained were expressed as Mean ± Standard Error of Mean (Mean ± SEM) and presented in form of tables and figures. The analyses were performed with the use of the Statistical Package for Social Sciences (SPSS) statistical software package, version 20.0. P <0.05 is considered statistically significant. Serum cardiac enzymes (CK, CK-MB, LDH and AST) obtained from HIV patients on HAART, naive-HIV patients and controls were compared using one-way analysis of variance (ANOVA). Where there was a significant difference, a post-hoc analysis was carried out using the Student t-test statistical method. A p-value equal to or less than 0.05 ($p \leq 0.05$) was considered significant.

RESULTS

A total of one-hundred and eighty (180) subjects (60 naïve patients, 60 HIV on HAART patients and 60 controls) were enrolled on the study. Naive patients were 25 males and 35 females with a mean age of 31.47 ± 1.03 years, HIV on HAART subjects were 20 males and40 females with a mean age of 34.67±1.47 and control had a mean age of 25.22 ±0.48 years. The mean concentrations of AST, LDH, CKMB and TCK are shown. In all parameters, the values were lower in patients on treatments than in HAART naïve patients, while they were higher in patients on treatment than in controls. The p-values (0.027, <0.000, 0.000, and 0.014) are statistically significant for serum AST, LDH, CKMB and TCK respectively. The detailed results are shown in **Tables 1** to **10,** respectively.

Table 1. Socio-demographic characteristics of the study subjects.

Characteristics	Control (n=60)	On HAART (n=60)	Naïve (n=60)
SEX			
Male	49	20	25
Female	11	40	35
RELIGION			
Islam	54	53	53
Christianity	6	7	7
MARITAL STATUS			
Single	58	10	8
Married	2	35	31
Divorced	0	2	3
Widowed	0	13	18
TRIBE			
Hausa	35	45	49
Yoruba	12	4	0
Igbo	4	0	5
Others	7	11	4

Table 2. The Comparison of Mean serum levels of AST, LDH, CKMB, and TCK (mean± SEM) between the three Groups of Study.

Subjects	n	AST(U/L)	LDH(U/L)	CKMB(U/L)	TCK(U/L)
Naïve(A)	60	43.43±4.91	310.25±13.79	183.97±12.33	118.75±915.51
HAART(B)	60	37.02±2.71	255.15±18.30	168.92±8.86	103.98±6.93
Control(C)	60	30.73±1.15	222.72±8.59	120.10±13.48	75.47±6.66
P-value		0.027	<0.001	<0.001	0.014

Where n = Number of subjects, AST= Aspartate transaminase, LDH = Lactate dehydrogenase, CKMB= creatine kinase MB, CKT= creatine kinase total, and HAART =highly active antiretroviral therapy. There are significant statistical differences ($p<0.05$) in the mean concentration of AST, LDH, CKMB and TCK levels between HAART naïve, HAART group and controls, using one-way ANOVA.

Table 3. Age, BMI, and duration of disease of the study subjects.

Subjects	Naïve	HAART	Control	P-value
Age(years)	31.47±1.03	34.67±1.47	25.22±0.48	<0.0001
BMI(kg/m^2)	21.17±0.52	22.09±0.51	20.93±0.35	0.183
DOD(years)	3.45±0.11	2.87±0.08	-	<0.0001

Table 4. Correlation of age and biochemical parameters in HIV patients on HAART.

Markers	N	R	p-value
AST(U/L)	60	-0.075	0.568
LDH(U/L)	60	-0.154	0.240
CKMB(U/L)	60	-0.223	0.086
TCK(U/L)	60	-0.138	0.292

Table 5. Relationship between BMI and serum biochemical parameters in HIV Patients on HAART using Pearson correlation.

Markers	N	R	p-value
AST(U/L)	60	-0.067	0.613
LDH(U/L)	60	-0.203	0.121
CKMB(U/L)	60	0.154	0.240
TCK(U/L)	60	0.288	0.026

Table 6. Relationship between Duration of Disease and serum biochemical parameters In HIV treated patients using Pearson correlation.

Markers	N	R	p value
AST(U/L)	60	-0.008	0.954
LDH(U/L)	60	0.075	0.571
CKMB(U/L)	60	0.264	0.042
TCK(U/L)	60	0.212	0.104

Table 7. Relationships between BMI and serum levels of biochemical parameters in Controls subjects.

Markers	N	R	p value
AST(U/L)	60	0.305	0.018
LDH(U/L)	60	0.190	0.146
CKMB(U/L)	60	-0.153	0.243
TCK(U/L)	60	0.283	0.028

Table 8. Relationship between age and biochemical parameters in control.

Markers	N	R	p-value
AST(U/L)	60	0.289	0.025
LDH(U/L)	60	0.327	0.011
CKMB(U/L)	60	0.181	0.166
TCK(U/L)	60	0.137	0.296

Table 9. Comparison of mean between HAART and HAART naïve Patients using t-test

Subjects	N	AST	LDH	CKMB	TCK
HAART	60	37.02±2.71	255.15±18.30	168.92±8.86	103.98±6.91
NAÏVE	60	43.43±4.91	310.25±13.79	183.97±12.31	118.75±15.51
P-value	-	0.256	0.018	0.324	0.386

Table 10. Relationship between age and serum biochemical parameters in HIV naïve Patients.

Markers	N	R	p value
AST(U/L)	60	0.097	0.460
LDH(U/L)	60	0.049	0.713
CKMB(U/L)	60	0.053	0.685
TCK(U/L)	60	0.027	0.839

DISCUSSION

In this study, serum levels of TCK, CK-MB, LDH and AST were significantly higher in HIV-positive individuals not on treatment compared with seronegative control subjects. Generally, the increases in the levels of cardiac enzymes were more marked in symptomatic HIV individuals not on HAART than those on treatment. This finding is the same as [21] reported that the mean serum total Creatine kinase, CK-MB, LDH and AST were significantly higher in symptomatic HIV participants not on HAART compared with HIV seronegative control subjects at $P<0.05$ in each case. Once again, the mean serum total Creatine kinase, CK-MB and AST were significantly higher in asymptomatic HIV participants compared with HIV seronegative control subjects at $P<0.05$ respectively. Another research which is in support of this result was carried out by [1] and reported statistically significant differences in TCK, CKMB and AST between HIV positive patients on HAART and those not on HAART, but not in LDH.

In the present study, there was a statistically significant difference in TCK, LDH, AST and CKMB. These Increased levels of some cardiac enzymes which were seen in HIV-infected participants may be due to the direct effects of the human virus on the heart [23], the chronic inflammatory effect of the virus itself on the myocardium [22] and the presence of [23]. Also, individuals infected with HIV have been linked with heart problems such as pericarditis [25] and endocarditis [24] However, another study carried out by Bello et al [28] shows no statistically significant difference in TCK and CKMB but there is a significant difference in LDH. In addition, the present study has found a significant statistical difference in age and DOD among patients on HAART and those not yet on HAART. It also recorded a significant correlation between the serum levels of TCK, CKMB, AST and LDH and BMI in patients and controls respectively.

In the present study, there is a significant difference in BMI among HIV seropositive patients on HAART and biochemical parameters. Furthermore, the present study has shown no significant correlations between the serum levels of AST, LDH, CKMB and TCK and age in HIV treated. And also, between serum levels of AST, LDH, CK MB and TCK and naïve HIV patients. It was also recorded by Bello *et al.* [28] no significant correlation between the serum levels of TCK, CKMB and LDH and BMI in patients and controls respectively.

In a study, myocardial infarction was observed in HIV subjects [26] In another study, Friis *et al* [27] shows that old age, current or former smoking, and previous cardiovascular diseases were associated with an increased risk of myocardial infarction. This may be due to the fact that HIV infects myocytes but is not abundant (1 in 2000 cells) or highly multiplicative in these cells [22]. Despite the paucity of evidence of direct myocyte involvement, HIV infection clearly causes structural and functional injury to the heart as a whole. The virus persists in reservoir cells in the cerebral cortex and in macrophages that may be present between myocardial cells, even after effective anti-retroviral therapy (ART) [29].

Much of the evidence for HIV effects on the heart was published before the era of highly active ART (HAART), and thus, the beneficial effects on the heart of more thorough suppression of HIV infection with HAART are generally less well understood. Reservoir cells and associated cytokine signalling may be important in the development and progression of cardiomyopathy and encephalopathy. Reservoir cells may hold HIV on their surfaces for extended periods. It is also possible that the reservoir is in cytoplasmic vacuoles, with the virus inducible through the Golgi apparatus, where progressive tissue damage is caused by the virus-induced chronic release of cytotoxic cytokines [29].

In this study, we conclude that the serum activities of total creatine kinase (CK), lactate dehydrogenase (LDH), creatine kinase MB and Aspartate aminotransferase (AST) were significantly increased in HIV-positive subjects. The finding may suggests possible impairment of cardiac function and this may

lead to cardiovascular disorder in HIV infected patients. It could be recommended from the findings of the present study that:

i. Cardiac markers are included as a routine test for evaluating the cardiac function of people infected with HIV. This could improve the management of this group of individuals.

ii. Further study to be carried out to evaluate the levels of CK-MB (cardiac-specific) isoenzyme of CK and other cardiac biomarkers such as troponins I and T, and myoglobin, among others.

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ANOVA	Analysis of variance
AST	Aspartate Aminotransaminase
AZT	Zidovudine
CD4	Cluster of differentiation
CDC	Center for Disease Control and Prevention
CK-MB	Creatine Kinase- M.B
DNA	Deoxyribonucleic Acid
GRID	Gay-Related Immunodeficiency
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HTLVS	Human T-lymphotrophicViruse
KS	Kaposi's Sarcoma
LDH	Lactate Dehydrogenase
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
PCP	PneumocysticCarinii Pneumonia
TCK	Total Creatine Kinase
UDUTH	UsmanuDafodiyo University Teaching Hospital
UNAIDS	Joints United Nations Program on HIV/AIDS

REFERENCES

1. Oluboyo AO, Okogun GR, Duru LA, Oluboyo BO, Emenike F, Obasikene CN. Pattern Of Blood Pressure, Cd4+ T Cells Count And Some Cardiac Enzymes In Hiv Seropositive Subjects. J Biomed Invest. 2006;4(2):37-41
2. Rasool, ST, Tang, H, Wu J., and Li, W. Increased level of IL- 32 during human immunodeficiency virus infection suppresses HIV replication. Immun Lett. 2018;117: 161-167.
3. Kumar, Vinay. Robbins Basic Pathology (9th ed.). 2012;147.
4. Fauci, AS. The Epidemic. New England J Med. 1999;341:1046-1050.
5. World Health Organization. Interim WHO clinical staging of HIV/AIDS and HIV/ AIDS case definitions for surveillance (African Region) Access July 26th, 2016.World Health Organization (1999) World Health Report; making a difference. 2005;Geneva.
6. UNAIDS Report on the Global AIDS Epidemic. UNAIDS 10th Anniversary Special Edition, Geneva, (2006).
7. UNAIDS (2011).World AIDS report. Joint United Nations program on HIV/AIDS UNAIDS/ JC2216E.
8. UNAIDS. The Global report, UNAIDS Report on global AIDS epidemic Joints united nation program on HIV/AIDS UNAIDS/JC2417E. 2012
9. NACA,HIV/AIDS prevalence ranking by states, published by National Agency for the Control of Aids(NACA). 2015
10. FMOH. Technical Report of National HIV/Syphilis Sero-prevalence Sentinel Survey among Pregnant Women attending Ante-natal clinics in Nigeria' Abuja, Nigeria. 2018
11. FMOH. Technical Report of National HIV/Syphilis Sero-prevalence Sentinel Survey among Pregnant Women attending Ante-natal clinics in Nigeria' Abuja, Nigeria. 2020
12. SOSACA. 2013 and 2014 Health Sector HIV/IDS Data presented during state M&E meeting by Director, M&E. 1–7. 2015
13. CIA. Adult prevalence rate, 2012 CIA World Factbook, Adapted from www.cia.gov.retrieved on February, 2010.
14. Bonnet, F, Moriat, P, Chene, G. Causes of death among HIV-infected patients in the era of highly active antiretroviral therapy, Bordeaux, France, 1998–1999, HIV 2002;Med 3:195–199.
15. Currie, PF and Boon, NA. Immunopathogenesis of HIVrelated heart muscle disease: current perspectives. AIDS, 2003;17(1):21–28.
16. Crum, NF, Riffenburgh, RH, Wegner S. Comparison of causes of death and mortality rates among HIV-infected persons: analysis of the pre-, early and late HAART eras. J Acquir Immune Defic Syndr. 2006; 41:194–200.
17. Sani MU, Okeahialam BN, Aliyu SH, Enoch DA. Human immunodeficiency virus (HIV) related heart disease: a review. Wien Klin Wochenschr. 2005 Feb;117(3):73-81.
18. McDonald CL, Kaltman JR. Cardiovascular disease in adult and pediatric HIV/AIDS. J Am Coll Cardiol. 2009 Sep 22;54(13):1185-8.
19. Ochei, J and Kolhatkar A. Medical Laboratory Science theory and practice. Tata McGraw Hill. Sixth edition, 2000;p168.
20. Reitman, S, Frankel, S. Am J Clin Pathol.1957;28:56.
21. Ezeugwunne IP, Onyenekwe CC, Ahaneku JE, Ahaneku G, Ifeanyichukwu M, Meludu SC, Chukwuanukwu RC, Serah W, Nnaemeka OJ, Nnadozie O, Onah CE. Assessment of Some Cardiac Biomarkers in Adult HIV Seropositives in Nnewi, Nigeria. Assessment. 2014;6(7).
22. Lewis, W. Cardiomyopathy in AIDS: a pathophysiological perspective. Prog Cardiovasc Dis. 2000;43(2):151–170.
23. Malnick, S. & Goland, S. Dilated cardiomyopathy in HIV-infected patients. New Engl J Med. 1998;339 (16):1093–1099.
24. Miro, JM, Del Rio, A, & Mestres, CA. Infective endocarditis and cardiac surgery in intravenous drug abusers and HIV-1 infected patients. Clin Cardiol. 2003;21:167–84.
25. Sudano I, Spieker LE, Noll G, Corti R, Weber R, Lüscher TF. Cardiovascular disease in HIV infection. Am Heart J. 2006;151(6):1147-55.
26. Carr A, Miller J, Law M, Cooper DA. A syndrome of lipoatrophy, lactic acidaemia and liver dysfunction associated with HIV nucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. Aids. 2000;14(3):F25-32.
27. Friis-Møller N, Weber R, Reiss P, Thiébaut R, Kirk O, Monforte AD, Pradier C, Morfeldt L, Mateu S, Law M, El-Sadr W. Cardiovascular disease risk factors in HIV patients–association with antiretroviral therapy. Results from the DAD study. Aids. 2003;17(8):1179-93.
28. Bello A, Mainasara AS, Liman HM, Umar H, Abubakar AF, Saidu K, Abdullahi AU. Pattern of Blood Pressure, Body Mass Index and Some Cardiac Enzymes in HIV Seropositive Patients in Sokoto, Nigeria. https://www.researchgate.net/publication/285236757_Pattern_of_Blood_Pressure_Body_Mass_Index_and_Some_Cardiac_Enzymes_in_HIV_Seropositive_Patients_in_Sokoto_Nigeria. Accessed 25th Dec 2022.
29. Orenstein, JM. Replication of HIV-1 in vivo and in vitro. Ultras Pathol. 2007;31:151–167.