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Effects of Anti-Retroviral Therapy on Some Liver Parameters of Hiv Sero-Positive Individuals in Rivers State, Nigeria

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Abstract

This study was carried out to determine the effect of antiretroviral therapy on some liver parameters of HIV sero-positive individuals in Rivers State, Nigeria. A total of 300 HIV patients, undergoing treatment were recruited in this study, aged 20-70 years. They were classified into three groups; Group 1 was made up of HIV sero-Positive infected individuals on highly antiretroviral therapy as the test subjects. Group 2 was HIV sero-Positive infected individual but not on highly active antiretroviral therapy as control 1, while Group 3 was HIV sero-negative individual as control 2. Ethical approval for the study and informed consent from the participants were obtained. The results revealed a statistically significant increase (P<0.005) in AST F=8.781, P=0.000, ALT F=29.052, P=0.000, ALP F=6.078, P=0.000, TP F=62.830, P=0.000, ALB F=899.014, P=0.000 of test subject and control I compared to control II, also statistically significant increase (P<0.005) in AST F=3.756, P=0.000, ALP F=361.489, P=0.000 in relation to sex (male and female) test subject and control I compared to control II. Also statistically significant increase (P<0.005) in AST F= 2.481, P=0.000, ALT F=5.534, P=0.000, ALP F=1.260, P=0.0233, TP F=10.560, P=0.000, ALB F=141.120, P=0.000 of the test subject and control I compared to control II, in relation to age groups. Based on duration of therapy, 0-2years, the results revealed no significant increase (P>0.05) in AST and ALB levels, however, a statistically significant increase (P<0.05) was observed in ALT, ALP and TP; for 2-5 years, no significant increase (P>0.005) in AST, ALT, ALP, TP, ALT, ALB, TP, ALB. For 5-10years, there was no significant increase (P>0.05) in AST, ALT, ALP, TP, ALT, ALP of the test subjects compared to the control I and control II respectively. This study demonstrated that long term administration of HAART to HIV infected positive subjects could lead to metabolic disorder such as dyslipidaemia which could predispose the patient to high risk of conorary heart disease.

Keyword: Anti-retroviral drugs, Highly Active Antiretroviral Therapy, HIV sero-negative individual, HIV seropositive individuals, Liver parameters

Introduction

Human Immunodeficiency Virus (HIV) is a lentivirus (a member of the retrovirus family) that causes Acquired Immunodeficiency Syndrome (AIDS), (Weiss, 1993), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells.

According to current estimates, HIV is set to infect 90 million people in Africa, resulting in a minimum estimate of 18 million orphans. In the last years, the retroviral disease, caused by the human immunodeficiency virus (HIV), turned from an incurable to a chronic disease. This fundamental thing happened due to a huge progress in the understanding of the pathogens and treatment of this infection. However, one question still remains open: what is the best time to introduce therapy? The CD4 count is the point of reference to start off the treatment in H10 infected patients. Tendency to introduce highly active antiretroviral therapy (HAART) as early as possible has been observed recently. HAART should be started when CD4 count reaches 2500 cells/µl. However, the question of when to begin an antiretroviral therapy remains still open. The pivotal result of the antiretroviral treatment is reduction of HIV viral load, and protection or eventually reconstruction of the immune system. This leads to a reduction of HIV transmission and decrease of HIV related mortality.

Drug-induced liver injury can be considered predictable (high incidence) or unpredictable (low incidence) (Kaplowitz, 2001). Liver injury may result from direct toxicity of the drug or its metabolites or may be an idiosyncratic response in persons with a characteristic genetic predisposition. The latency period between the initiation of therapy and the onset of liver disease provides clues to its etiology. Predictable hepatotoxic reactions are close dependent and host independent, with the classic example being paracetamol (acetaminophen) toxicity (Kaplowitz, 2001). Early-onset toxicity (within a few days) is strong evidence for direct drug toxicity, particularly if there has been no previous exposure. Unpredictable hepatotoxic reactions are host dependent and not dose related (Zimmerman, 1999). Unfortunately, the vast majority of drug reactions are unpredictable. They occur when the drug is transformed into an intermediate metabolite that is either toxic (host-mediated metabolism) or provokes an immunological response (hypersensitivity reaction), there are four known mechanisms involved in the development of hepatotoxicity associated with the use of antiretroviral medications. Multiple aberrant pathways may coexist within the same individual.

Host differences in drug metabolism may lead to an excess of potentially harmful reactive drug metabolites when genetic polymorphisms affect critical metabolizing enzymes (Bissell *et al*., 2001). The latency of onset is long (from 2 to 12 months), which poses problems for patient monitoring (Nathwani and Kaplowitz, 2006). Prototypical examples include isoniazid and troglitazone; these aberrant metabolic pathways may also underlie one 1’orm of drug injury seen in association with the non-nucleosidc reverse transcriptase inhibitors (NNRTI) and the protease inhibitors (PI) (Haas *et al*., 2006 and Ritchie *et al*., 2006). Some drugs may potentiate the activation of T cell death receptor s and/or intracellular stress pathways, leading to increased oxidative stress (Leist *et al*., 1998). In response, hepatocytes promote mechanisms of cytoprotection, such as the formation of heat shock proteins, which protect the liver against toxic metaholites (Bissell *et al*., 2001). This cytoprotective response may explain the spontaneous normalization of liver enzymes that may occur despite maintenance of HAART (or other medications, such as isoniazid). Alternatively, the rise and fall of serum

aminotransferase concentrations after initiation of medications may be related to a phenomenon of 'adaptation, whereby liver Function tests noma1izc despite ongoing drug exposure (Kaplowitz, 2004).

Biochemical markers play an important role in accurate diagnosis and also for assessing risk and adopting therapy that improves clinical outcome. Over decades, research and utilization of biomarkers has evolved substantially. A biomarker as the characteristic that is objectively measured and evaluated as an indicator of normal biological, pathologic processes, or pharmacologic responses to a therapeutic intervention (Ramachandran, 2006).

Aspartate aminotransferase (AST) or serum glutamic oxaloacetate transaminase (SGOT), is a pyridoxal phosphate (PLP)-dependent transaminase enzyme (EC 2.6.1.1). AST catalyzes the reversible transfer of an amino group between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism. AST is found in the liver, heart, skeletal muscle, kidneys, brain, and red blood cells, and h is commonly measured clinically as a marker for liver health. Aspartate transaminase catalyzes the interconversion of oxaloacetate and glutamate to aspartate and α α -ketogIutarate.

Alanine transaminase or ALT is a transaminase enzyme (EC 2.6. 1.2). It is also called serum glutamic pyruvic transaminase (SGPT) or alanine aminotransferase (ALT). ALT is found in serum and in various bodily tissues, but is most commonly associated with the liver. It catalyzes the two parts of the alanine cycle. It catalyzes the transfer of an amino group from alanine to α α -ketoglutaratc, the products of this reversible transamination reaction being pyruvate and glutamate.

glutamate + pyruvate = α α -ketoglutarate + alanine.

It is commonly measured clinically as a part of a diagnostic evaluation of hepatocellular injury, to determine liver health. When used in diagnostics, it is almost always measured in international units/liter (U/L). While sources vary on specific normal range values, most show between 5-60 U/L as being normal. Alanine transaminase shows a marked diurnal variation.

Alkaline phosphatase (ALP, ALKP) (EC3.1.3.1) is a hydrolase enzyme responsible for removing phosphate groups from many types of molecule including nucleotides, proteins, and alkaloids. The process of removing the phosphate group is called dephosphorylation. As the name suggests, alkaline phosphatases are most effective in an alkaline environment. It is sometimes used synonymously as basic phosphatase (Tamaset *et al*., 2002). In humans, alkaline phosphatase is present in all tissues throughout the entire body, but is particularly concentrated in liver, bile duct, kidney, hone, and the placenta. Humans and most other mammals contain the following alkaline phosphatase isozymes:

Liver disease is classified broadly into two categories of injury: cell necrosis and cholestasis. A classification of liver disease that best facilitates effective laboratory test strategy and interpretation of results is as follows:

Antiretroviral therapy (ART) has been reported to improve the health and prolong the lives of most sero-positive patients, as compared to other therapies. HAART is observed to alter the course of HIV disease dramatically with decreased mortality and morbidity since its introduction in the 1990s.

There are few research reports about effects of ART among patients on HAART in Nigeria. Also, the roles of socio-demographic characteristic, psychosocial factors as predicators of effects have produced largely inconsistent results. This work is therefore carried out to evaluate the effect of anti-retroviral therapy on the biochemical indices of HIV sero-positive individuals in Rivers State, Nigeria.

Materials and Methods

Study Area

This study took place in the University of Port Harcourt Teaching Hospital, Choba, Port Harcourt, Rivers State, Nigeria. This is the largest hospital in the Southern region of Nigeria. University of Port Harcourt Teaching Hospital serves as both a primary contact hospital and a regional referral hospital. Currently, the ART clinic provides HIV related services for both adults and children.

Port Harcourt, the capital of the oil rich Rivers State, is located in Southeastern Nigeria (07^{o} 3' E, 04^{o} 51'N, and 10m altitude above sea level) in the humid forest zone of the Niger Delta region, Nigeria. It is densely populated and home to multinational oil and gas companies and as such witnesses the influx of people in search of better living.

Port Harcourt features a tropical wet climate with lengthy and heavy rainy seasons and very short dry seasons. Temperatures throughout the year in the city are relatively constant, showing little variation throughout the course of the year. Average temperatures are typically between 25^{o}C -28^{o}C in the city.

Study Population

300 subjects within the age range of 20-70 years, who are undergoing treatment for HIV infection, were recruited for this study. They were classified into three groups: (1) HIV sero-positive infected individuals on ART (2) Control 1 – HIV sero-positive infected individual but not on ART. (3) Control 2 – HIV negative individual. The first batch was 100 in number, that is, HIV sero-positive on ART for the minimum of seven months, and the second batch was 100 in number for HIV sero-positive infected without ART.

The third batch was 100 that is HIV negative. 300 sample size was determined using the formula below:

N = Z2 P (I-P)/ D2
Where
N = Sample size
Z = Statistic for a level of confidence
P = Expected prevalence or proportional
D = Precision
n= z2pq

$$\frac{}{d2}$$

n= sample size minimum
z= 95% confidence interval = 1.96
p= proportion of the target population (15.5%) (prevalence rate)
q= 1.0 – p

d= degree of accuracy (0.05)

$$n = \frac{3.8146 \times 0.15 \times 15}{2.5 \times 10\text{-}5} = \frac{8.6436}{0.0025} = 3.457 \text{ Sample size}$$

Selection Criteria

A Inclusion

1. HIV sero-positive individuals with ART for 7 months and above
2. HIV sero-positive individuals with ART within the age bracket of 20-70 years
3. HIV sero-positive individuals with ART on a given consent
4. HIV sero-positive individuals without ART on a given consent
5. HIV sero-negative individuals

B Exclusion Criteria

1. Subjects with chronic disease aside HIV, e.g. liver disease, renal disease
2. HIV sero-positive individuals outside the age bracket
3. Those who refuse to give their consent

Parameters for Study

The parameters evaluated in this study are as follows: ALT, AST, ALP, TP, ALB

Study Design

For the HIV sero-positive on anti-retroviral drugs (ART), those that are sero-positive without antiretroviral drugs, and those that are HIV negative. Blood samples were collected within 9am-12pm to reduce variability. Samples were centrifuged and stored at -20^{o}C. This study was divided into 3 stages:

A Stage I: Confirmation of sero-positive subjects using the national algorithm.
B Stage II: Evaluation of biochemical parameters using appropriate techniques.

Laboratory Procedure

All reagents and kits for the work were commercially purchased and the manufacturer's SOPs were strictly adhered to.

A HIV confirmation using the national algorithm.
(i) Determine commercial kit (Alere medical Co, Japan, 2013; Catlog No.: 7D2344; Lot No.: 66329k100R)

Principle
The Alere determine HIV ½ is an immunochromatographic test for the qualitative detection of antibodies to HIV-1/2 in human serum, plasma or whole individuals. Sample was added to the sample pad. As the sample migrates through the conjugate pad, it reconstitutes and mixes with the selerium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized recombinant antigen and synthetic peptides at the patient's window site. If antibodies to HIV-1 and/or HIV-2 are present in the sample, the antibodies bind to the antigen-selenium colloid and to the antigen at the patient's window site. If

antibodies to HIV-1 and /or HIV-2 are absent, the antigen-selenium colloid flow past the patient's window and no red line is formed at the patient's window site. Molecular masses of 8-10kDg and show approximately 20-50% sequence homology among each other at the protein level.

(ii) UNIGOLD commercial kit (Trinity Biotech Plc, Ireland, 2013; Catlog No: 1206502; Lot No.: HIV 4090014).

Principle

Recombinant proteins representing the immuno-dominant region of the envelope proteins of HIV 1 and HIV 2, glycoprotein gp41, gp120 (H10) and glycoprotein gp (HIV2) respectively are immobilized at rest region of the nitrocellulose strip. These proteins are also linked to colloidal gold and impregnated below the test region of the device. A narrow band of the nitrocellulose membrane is also sensitized as a control region. During testing, two drops of serum, plasma and whole blood is applied to the sample paste, followed by two drops of buffer and allowed to react. Antibodies of an immunoglobulin class, with linked antigen antibody protein colloidal gold complex moves chromatographically along the membrane to the test and control region of the test device. A positive reaction is visualized by a pink/red band in the test region of the device. A negative reaction occurs in absence of human immunoglobulin antibodies to HIV in the analyzed specimen. Consequently, no visually detectable band develops in the test region of the device.

(iii) STAT PAK Commercial kit (Chembio Diagnostic System, 2013).

The chembio HIV 1/ 2 STAT PAK assay employs a unique combination of a specific antibody binding proteins, which is conjugated to colloidal gold dye particles and HIV 1/ 2 antigen which are bound to the membrane solid phase, the sample is applied to the sample well followed by addition of running buffer in reactive sample, dye conjugative immune complex migrate on the nitrocellulose membrane and is captured by the antigen immobilized in the test area producing a pink/purple line the test area.

B. ASPARTATE AMINOTRANSFERASE (AST) kit by Randox

Principle

Aspartated Aminotransferase (AST) belongs to the group for transaminase which catalyses the conversion of amino acids to the corresponding ∞-keto acids and vice versa. It is widely distributed in tissue, principally hepatic, cardiac, muscle and kidney. Elevated serum levels are found in diseases involving these tissues. Hepatobiliary diseases such as carhosis, metastatic caracinomaamd viral hepatitis also increase serum AST levels as well as myocardial infarction. Patients undergoing renal dialyses are those with vitamin B6 deficiency may have decreased serum AST. AST present in samples catalyses the transfer of an amino group, between the L- aspartate and 2-oxoglutarate to form oxaloacetate and L-glutamate. The oxaloacetate then reacts with NADH, in the presence of malate dehydrogenase (MDH) to form NAD+ pyridoxal phosphate serves as a coenzyme in the amino transfer reaction. It ensures full enzymes activation. The rate of NADH oxidation is directly proportional to the catalytic AST activity. It is determined by measuring the decrease in absorbance.

L – Aspartate + ∞-ketoglutarate AST oxaloacetate + L – glulamate
MDH

Procedure
Label 5 tubes B(blank) and 1-4, Add reagents accurately into each. Add 0.1ml of distilled water to each tube and mix well. Add 0.5ml of DNPH reagent to each tube. Mix well. Leave at room temperature for 20 minutes for colour development. Add 5ml of 0.4 N sodium hydroxide solution to each tube. Mix well. Leave at room temperature for 5 minutes. Read the absorbance of the pyruvatt standard solutions at 505nm (blue-green filter). Zero the instrument with the blank solution B. On a sheet of graph paper, plot the absorbance of each standard solution. Express in µ/l. Determine the enzyme activity from the calibration curve.
Normal values = 7-21µ/l

C. Alanine Aminotransferase (ALT) Kit By Randox

Principle
Glutamate pyruvate transaminase (alanine aminotransferase) belongs to the group of transaminase which catalyses the conversion of amino acids to the corresponding ∞-keto acids and vice versa by transfer of amino group. Elevated transaminase levels can indicate myocardial infarction, hepatic disease, muscular dystrophy and organ damage. Although the highest concentrations of alanine aminotransferase occur in the liver, smaller activities are found in the kidneys, heart, skeletal muscle, pancreas, spleen and lungs tissue. However, increased serum activities of GPT (ALT) are largely specific for liver parenchymal disease whereas GOT (AST) is not a liver-specific enzyme, ALT, also known as glutamate pyruvate transaminase (GPT) is a transaminase. ALT catalysis the transfer of the amino acid group of the L-alanine to ∞-ketoglutamate to give L-glutamate.
∞-ketoglutamate + alanine ALT glutamate + pyruvate
Pyruvate + NADH + H+ LDH L- lactate + NAD+
LDH = Lactatedehydrogenase

Procedure
Set up two test tubes, test and control. Stand at room temperature for 5-10 minutes. Read absorbance at 505nm (Yellow-green filter).
Normal Range = 6-21µ/l

D. Alkaline Phosphatase (ALP) Randox kit.

Principle
The enzyme alkaline phosphatase hydrolyses the substrate, disodium phenyl phosphate to release phenol. The quantity of phenol released under standardized conditions of urine, temperature and pH, is measured by the absorbance of the red colour it assumes in alkaline solution. The phenol reacts with 4- aminophenazone in the presence of alkaline potassium ferricyanide to produce the red colour.

Procedure
Aspirate fresh ddH20 and perform a new gain calibration in flow cells mode. Select ALP in the run test screen and carry out a water blank. Mix and aspirate into the Rx monza; or Pipette into cuvette, macro, semi-micro and micro and mix, read initial absorbance and start timer simultaneously. Read again after 1, 2 and 3minutes.

Calculation
µ/l = 3300 x ΔA 405nm/min macro
µ/l = 2760 x ΔA 405nm/min semi-micro

µ/l = 2760 x ΔA 405nm/min micro		
Normal Range = 250C	300C	370C
Men/women 60-170µ/l	73-207µ/l	98-279µ/l

Knowledge, Attitude and Practice

A structured questionnaire assessing their knowledge of HIV infection, prevention, treatment, laboratory testing in area of disease monitoring was administered. Considering socio-economic impact of HIV in society, there is the need to know how they would like to be treated as regards family, work place and the society at large. To develop self-esteem, increase adherence to treatment and reduce the spread of HIV infection, understanding the mechanism of antiretroviral therapy in the pathogenesis of AIDS. Also, this knowledge will help in development of improved diagnostic approaches. However, it will help the Health Service Providers on specific ways of handling or managing PLWHA.

Statistical Analysis

Results were analyzed using Statistical Package for Social Sciences (SPSS) version 15. The data were expressed using descriptive statistics and Analysis of Variance (ANOVA). Multiple comparisons for the parameter were done using Post Hoc Turkey (HSD) to test for the level of significance between means. Values were expressed as mean ± Standard Deviation (m ± SD) and values above the 95% confidence unit ($P<0.05$) were considered statistically significant.

Results

The result of the study showed that there was statistically significant difference ($P< 0.05$) in AST ($F=8.781$, $P=0.000$), ALT ($F=29.052$) $P=0.000$), ALP ($F=6.078$, $P=0.000$), TP ($F=62.830$, $P=0.000$) and Alb ($F=899.014$, $P=0.000$) of HIV positive without HAART, HIV positive with HAART compared with the control (HIV negative), as shown in Table 1 below:

Table 1. Effect of HAART on Liver Function parameters (enzymes) of HIV positive individual of the study population

Group	**AST (U/L)**	**ALT(U/L)**	**Alkaline Phosphatase (U/L)**	**Total Protein (g/l)**	**Albumin (g/l)**
Control (A)	15.4000±.78406	11.1400±..62118	138.37±3.39178	70.8900±1.02296	40.8600±.51287
HIV Positive (B)	16.5716±..67349	17.0780±..62659	103.63±8.51026	155.06±9.91359	79.9400±.92166
HIV Positive on HAART (C)	12.8300±..42783	15.8907±..49097	141.59±11.60712	81.7600±.86054	44.9150±.65447
F	8.781	29.052	6.078	62.830	899.014
P	.000	.000	.000	.000	.000

Also, the result of the study showed statistically significant difference (P< 0.05) in AST (F=3.756, P=0.003), ALT (F=12.399, P=0.000), ALP (F=2.534, P=0.0029), TP (f=25.396, P=0.000), and Alb (F=361.498, P=0.000) of male and female HIV positive without HAART, HIV positive on HAART, compared with their respective controls, as shown in Table 2 below:

Table 2. The effect of HAART on Liver function in different sex of HIV subjects

Group	**AST (U/L)**	**ALT(U/L)**	**Alkaline Phosphatase (U/L)**	**Total Protein (g/l)**	**Albumin (g/l)**
male control (A)	15.7419±.94422	11.9032±.77974	140.10±4.45969	71.9032±.97989	41.1129±.69451
Female control (B)	14.8421±1.38449	9.8947±1.00694	135.55±5.21142	69.2368±2.16017	40.4474±.73974
male Positive (C)	16.3254±1.15312	17.4714±.96320	95.9357±3.64578	143.02±16.81837	77.7857±1.57473
Female Positive (D)	16.6674±.82542	16.9250±.78865	106.62±11.74064	159.74±12.14070	80.7778±1.11492
male Positive with HAART (E)	13.6064±.73517	16.5694±.80779	136.12±1.11354	84.0500±1.39521	45.3278±.75589
Female Positive with HAART (F)	12.3933±.52164	15.5089±.61768	144.67±18.16571	80.4719±1.06620	44.6828±.93315
F	3.756	12.399	2.534	25.396	361.498
P	0.003	0.000	0.029	0.000	0.000

There was also statistically significant difference (P< 0.05) in AST (F=2.481, P=0.003), ALT (F=5.534, P=0.003), ALP (F=1.266, P=0.233), TP (F=10.560, P=0.000) and Alb (F=141.120, P=0.000) of HIV positive without HAART, HIV positive on HAART in age groups 20-30, 31-40, 41-50, 51-60, and 61-70, compared with their respective controls, as shown in Table 3 below:

Table 3. The effect of HAART on Liver function in different age groups of HIV subjects

GROUP	Age group (years)	**AST (U/L)**	**ALT(U/L)**	**Alkaline Phosphatase (U/L)**	**Total Protein (g/l)**	**Albumin (g/l)**
Control	20-30	24.0000±4.50925	15.0000±4.50925	157.67±21.26290	75.0000±2.64575	42.3333±.88192
	31-40	15.6071±1.80559	11.5000±1.58907	132.96±5.37816	70.1786±1.44021	40.4643±1.00985
	41-50	15.0000±1.07361	10.8085±.75159	136.74±4.51162	71.6170±1.28952	40.6596±.81910
	51-60	15.6875±1.54574	10.6875±1.29653	143.69±12.26299	68.1875±4.31008	42.5625±.87067
	61-70	12.5000±2.24722	11.3333±1.89150	152.50±13.54437	73.6667±3.84419	39.0000±1.96638
HIV POSITIVE	20-30	15.3109±1.06975	15.6114±1.05178	95.4714±4.52830	139.80±10.61415	81.4857±1.35682
	31-40	16.5037±1.15837	18.0571±1.10710	123.96±23.55314	153.27±17.26067	80.0857±1.67652
	41-50	17.9960±1.64070	18.7500±1.41575	88.7550±4.44985	191.20±32.45439	76.4000±1.99789
	51-60	16.5412±1.84095	14.5875±1.46061	93.9000±5.41915	149.12±26.85173	82.2500±3.94493
	61-70	25.7000±5.30000	18.8500±2.25000	78.3500±3.35000	115.50±54.50000	76.5000±6.50000
HIV POSITIVE ON HAART	20-30	13.2900±.81088	16.1600±1.03529	132.72±1.34124	80.8259±1.74645	43.0481±1.23763
	31-40	13.1626±.66123	16.6180±.70374	150.63±25.29420	82.3848±1.26866	46.6196±1.08370
	41-50	11.3616±.82664	13.2274±1.02105	134.81±1.41512	81.5842±1.92879	43.6368±.94365
	51-60	12.8525±1.68995	17.1250±1.18800	135.65±2.71003	81.7375±3.11660	44.4500±1.73771
	61-70	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
	F	2.481	5.534	1.266	10.560	141.120
	P	.003	.003	.233	.000	.000

Table 4 shows the effect of HAART on liver function parameters in HIV subjects based on duration of therapy. For HIV positive patients who have been on HAART for 0-2 years, the results revealed that there was no significant difference in AST (F=0.161, P=0.968) and Albumin levels (F=2.044, P=0.500); however, a statistically significant difference was observed in ALT (F=0.000, P=0.000), alkaline phosphatase (F=0.000, P=0.000) and total protein (F=0.000, P=0.000).

For HIV patients who have been on HAART for 2-5 years, the results revealed that there was no significant difference in AST (F=1.015, P=0.534), ALT (F=0.604, P=0.892), alkaline phosphatase (F=1.311, P=0.397), total protein (F=0.751, P=0.717) and albumin (F=0.781, P=0.699). For HIV patients who have been on HAART for 5-10 years, the results revealed that there was no significant difference in AST (F=0.641, P=0.780), ALT (F=3.774, P=0.102), alkaline phosphatase (F=4.978, P=0.343), total protein (F=0.751, P=0.717) and albumin (F=0.781, P=0.699). For HIV patients who have been on HAART for 10 year and above, the results revealed that there was a statistically significant difference in AST (F=0.000, P=0.000), ALT (F=0.000, P=0.000), alkaline phosphatase (F=0.000, P=0.000), total protein (F=0.000, P=0.000) and albumin (F=0.000, P=0.000).

Table 4. Effect of HAART on Liver Function parameters in HIV Subjects based on Duration of Therapy

Group	Duration of Therapy	AST (U/L)	ALT(U/L)	Alkaline Phosphatase (U/L)	Total Protein (g/l)	Albumin (g/l)
HIV Positive on HAART	0-2 years	14.7792±5.20812	17.4508±4.20494	135.212±6.563	79.6250±11.10767	45.0455±5.87918
	F	0.161	0.000	0.000	0.000	2.044
	P	0.968	0.000	0.000	0.000	0.500
	2-5 years	12.5024±4.07567	15.7702± 4.80163	131.693± 15.00049	81.9623± 7.44610	43.5303± 5.06992
	F	1.015	0.604	1.311	0.751	0.781
	P	0.534	0.892	0.397	0.717	0.699
	5-10 years	12.3067± 4.47963	15.3312± 4.97575	133.732± 6.40399	81.3061± 7.44610	43.5303± 5.06992
	F	0.641	3.774	4.978	0.751	0.781
	P	0.780	0.102	0.343	0.717	0.699
	10 years and above	13.1067 ± 5.70142	14.3700 ± 7.63326	12.7532 ± 6.38462	88.6667± 1.52753	40.6667± 8.51254
	F	0.000	0.000	0.000	0.000	0.000
	P	0.000	0.000	0.000	0.000	0.000

Discussion

The study on effect of antiretroviral therapy on HIV positive patients focused on the liver functions.

The results of this study showed statistically significant difference (P<0.005) in AST, ALT, ALP, TP, and Alb of HIV positive individuals without HAART and HIV positive individuals with HAART. This could be as a result of the fact that the main consequences of HIV infection are to damage the liver hepatocytes; Hepatotoxicity is the most frequent (30%)

toxicity of antiretroviral drugs, which has appeared as one of the leading causes of HIV related illness, death and treatment withdrawal (Nunez, *et al*; 2006). The extensive use of antiretroviral drugs by HIV positive patients as well as the new antiretroviral medications results in negative impacts on the clinical outcome of the patients (Palella, *et al*; 2006).

Increase levels of liver enzymes are generally a result of liver disease associated with some degree of hepatic necrosis such as cirrhosis, caranoma, viral or toxic hepatitis and obstructive jaundice. Elevated levels of the parameters have also been found in extensive trauma and muscle disease, circulatory failure with shock, hypoxia, myocardial infarction and hemolytic disease (Penttila, *et al*; 1975; Auston, 1993).

Elevated activities of these enzymes indicate cell damage which has resulted from several mechanisms. These include metabolic host-mediated injury, mitochondrion toxicity, hypersensitivity reaction and immune reconstitution.

Conclusion

This study demonstrated that long-term administration of HAART to HIV infected positive subjects could lead to metabolic disorder such as dyslipidaemia which could predispose the patient to high risk of coronary heart disease. Hepatotoxicity was induced in HAART-experienced HIV patients who were treated with antiretroviral drugs not known to be associated with hepatotoxicity. The effect of HAART on hepatotoxicity was time dependent. There is strong evidence that co-infection with hepatitis B virus increases the risk of hepatotoxicity while taking antiretroviral therapy (Aranzabal et al., 2005; Kontorinis and Dieterich, 2003). Regular monitoring of transaminases is therefore recommended when HIV patients are being treated with antiretroviral drugs even if they do not include PIS. This will help to decide on discontinuation of treatment if toxicity levels become too high. Further research should be carried out with larger sample sizes and additional information regarding other risk factors for dyslipidaemia in Nigerian populations should be assessed to better understand the effects of HAART on lipid profile and other metabolic disturbances.

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