WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

SJIF Impact Factor 2.786

Volume 4, Issue 03, 153-160. Research Article ISSN 2278 – 4357

BIOCHEMICAL ALTERATIONS IN ADULT HIV PATIENTS ON ANTIRETRQVIRAL THERAPY

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Article Received on
26 Dec 2014,

Revised on 21 Jan 2015,
Accepted on 14Feb 2015

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ABSTRACT

Some biochemical alterations in adult Human Immunodeficiency Virus (HIV) patients on Antiretroviral Therapy were investigated at the Federal Medical Centre Owerri, Imo Stale, Ngeria. Subjects were made up of twenty (20) adult HIV patients on antiretroviral therapy (9 males and 11 females) and twenty (20) adult HIV patients not on any antiretroviral therapy (11 males and 9 females) (control) with mean age of 34 years. The period of exposure to therapy was between 1-10 months. The results showed that the mean values of Alanine amino transferase (ALT), Aspartate aminotransferase (AST) as well as alkaline phosphatase (ALP) were significantly ($P<0.01$) reduced in adult HIV patients on antiretroviral therapy when compared with the controls. On the other hand, there was no significant ($P>0.05$) increase in the concentration of total and conjugated bilirubin (TB and CB) in the adult HIV patients on antiretroviral therapy when compared with the controls. The findings of the study show that antiretroviral Therapy especially within the duration investigated in the study does not have any adverse effect on the

liver that may cause hepatotoxicity.

KEYWORDS: Biochemical Alteration, Adult HIV Patients, Antiretroviral therapy, Hepatotoxicity.

INTRODUCTION

Human Immunodeficiency Virus (HIV) is the etiologic agent of AIDS. It is a retrovirus derived from Primate lentiviruses (Jawetz *et a.*,, 2004). HIV is a global pandemic with the first cases reported since 1981. Infection with human immunodeficiency virus (HIV) has been estimated to have occurred in 150 million people with a record of 50 million deaths (Rodriguez - Rosado *et al.*, 2004).

The first case of HIV in Nigeria was reported in 1986. Since then, the number of people living with HIV or AIDS (PLWAS) steadily increased and the epidemic moved into *a* "generalized" state with an increase of seroprevalence from 1.8% in 1991, 4.5% in 1996, to 5.8% in 2001 and 5.0% in 2003. This meant that Nigeria had over 3.5 million infected persons, the third highest in the world (WHO, 2006).

The high burden of the disease, associated mortality, and morbidity despite the concerted efforts of the Federal Government of Nigeria, International and local partners to combat the disease continue to be a major public health concern for the country. The epidemic has impacted on many segments of the society. It has markedly reduced gains in life expectancy which Nigeria had achieved over the past four decades since her independence and further weakened and threatens to overwhelm the already weak Nigeria health care system.

Antiretrovirals have been developed to manage infected individuals. However, issues on compliance and adverse effects have now become evident as a limiting cause of benefit in a substantial proportion of individuals. Amongst others, Liver toxicity is now one of the leading reasons for withdrawn treatment (Sulkowski *et al.*,2005).The effects of prolonged exposure to this therapy on the liver have attracted the attention and interest of many researchers worldwide (Wit *et al.*,2002).

The Liver is the central Organ that coordinates and modulates most biochemical activities in the body. The presence of Liver enzymes - Alanine amino transferase (ALT) and aspartate amino transferase (AST) at levels above normal values suggest an increased rate of tissue destruction. Measurement of these plasma enzyme levels can provide a valuable evidence for the toxicity of the tissue. This study therefore will determine whether prolonged exposure to these antiretrovirals have any effects on some biochemical indices of Liver Function in Adult HIV Patients.

MATERIALS AND METHODS

The study was conducted at the Federal Medical centre Owerri, the Imo State Capital. Owerri is strategically located in the Eastern states of Nigeria; sharing boundaries with and being a gateway to Umuahia and Aba in Abia State, Rivers State, the Eastern Nigeria part city Anambra State. It lies on Latitude 5027^{1} - $5°31^{1}$N, and Longitude 6°55 - $7°03^{1}$ E. It has a population of 127, 213 (National Population Commission, 2005) and is cosmopolitan, being home to many non indigenes apart from the ethnic Igbo.

Federal Medical Centre where the study was conducted, is a Federal Government Owned tertiary health care institution and serves as the Government approved centre for HIV/AIDS treatment, under the Federal Government's NACA (National Action Committee on AIDS) programme. The subjects therefore represent a subgroup of Adult HIV patients on antiretroviral therapy in Nigeria.

And the subject from when in further with respect to age, sex and duration of therapy were also obtained.The study group comprised of 40(20 apparently healthy HIV individual and 20 HIV seropositive patients) both screened and confirmed with western blot.

Biochemical analysis

The qualitative test for HIV antibodies in blood was carried out with rapid H1V-1 and HlV-2 spot test by Biosystems Diagnostic Inc. U.S.A. The confirmatory test for HIV antigens in blood was carried out with Immunocomb I1 HIV I and 2 Combfirrn Kit by Ogenics Ltd, Yavne, Israel. A serum sample yielding a minimum of two circular, coloured antigen spots, including are representing gp41 or gp 36 is defined as HIV positive Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) level were estimated by the method reported by Ritman and Frankel (1957).Alkaline phosphates activity was estimated by the modified King Amstrong method (1954) while total and conjugated bilirubin were assayed by standard techniques reported by Malley and Eveyn 1932.

STATISTICAL ANALYSIS

The computational analysis was done using population of mean and standard deviation. Test of significance was by student t-test, and ($P<0.01$) was considered as statistically significant.

RESULTS

The results of serum alanine aminotransferase (ALT), aspartate aminotransferase (ALT), and alkaline phosphatase (ALP) of Adult HIV patients on antiretroviral therapy and control groups sare presented

in table 1 below, The mean values of ALT, (5.8 ± 3.4 IU/L), AST (7.8 ± 4.4 1U/L), ALP (64.6 ± 14.3 IU/L) of Adult HIV patients on antiretroviral therapy were significantly (P<0.01) reduced when compared to the mean values of ALT (19.3 ± 7.7 IU/L), AST (20.9 ±11.5 IU/L) and ALP (63.9 ± 23.0 IU/L) in control subjects.

Table 1: Activities of serum ALT, AST and ALP of Adult HIV Patients on Antiretroviral Therapy and Control

Parameter	Control	Adult HIV Patients on ARV Therapy	T - Test
ALT (IU/L)	19.3 ±7.7	5.8 ±3.3	P<0.01
AST (IU/L)	20.9 ±11. 5	7.8 ±4.4	P<0.01
ALP (IU/L)	63.9 ± 23.0	64.6 ±14.3	P<0.01

Table 2: Mean values of serum Bilirubin (mg/d!)

Parameter	Control	Adult HIV Patients on ARV Therapy	T-Test
TB (mg/dl)	0.89+0.15	0.86+0.13	P>0.05
CB (mg/dl)	0.59±0.13	0.59±0.13	P>0.05

Table 2 shows the results of total bilirubin (TB) and conjugated bilirubin (CB) of patients and controls. The slight difference observed in the means values of TB (0.89 ±0.15 mg/dl) and CB (0.59 ±0.13 mg/dl) in the control was statistically insignificant (P>0.05) when compared to TB (0.86 ±0.13 mg/dl) and CB (0.59 ±0.13 mg/dl) in subjects.

Table 3: Activities of serum ALT, AST and ALP for Adult HIV Patients on antiretroviral therapy with respect to duration of therapy.

PARAMETER	PARAMETER	DURATION OF THERAPY		t - TEST
		1-5 months	6-10months	
ALT (IU/L)	19.3 ±7.7	4.9 + 3.4	6.6 ± 3.4	P<0.01
AST (IU/L)	20.9+11.5	7.6 ±4.5	8.0 + 4.8	PO.01
ALP (IU/L)	63.9 + 23.0	65.0 ±15.1	64.1 + 15.1	PO.01

Table 3 shows the activities of ALT, AST and ALP of Adult HIV patients on antiretroviral therapy with respect to their duration of therapy. The mean values of ALT (4.9 ± 3.4 IU/L) and (6.6 ± 3.4 IU/L) of subjects from 1 - 5 months and 6 - 1 0 months respectively were reduced significantly (P<.0.01) when compared with the mean value of ALT (19.3 ± 7.7 IU/L) in controls. AST (7.9 ± 4.5 IU/L) and (8.0 + 4.8 IU/L) in subjects from 1 - 5 months and 6 - 1 0 months respectively were reduced significantly (P<0.01) when compared to the mean values of AST (20.9 ±11.5 IU/L) in controls. ALP (65.0 ± 15.1 IU/L) and (64.1 ± 15.0 IU/L) in subjects from 1 - 5 months and 6 - 1 0

months respectively decreased significantly (P^O.01) when compared to the mean values of ALP (63.9 ± 23.0 IU/L) in the controls.

Table 4: Mean values of Serum Bllirubin mglal respect of therapy to deviation

PARAMETER	CQMTRGL.	DURATION OF THERAPY		T-TEST
		1 -5. months	8-10 months	
TB (Mg/d!)	0.89 ±0.1 5	0.84 ±0.1 6	0.88 ±0.12	P>0.05
CB (Mg/dl)	0.59 ±0.13	0.60 ±0.1 8	0.57 ±0.11	P>0.05

Table 4 shows the mean values of Total Bilirubin (TB) and Conjugated Bilirubin (CB) for adult HSV Patients on antiretrovira! therapy with respect of their duration of therapy. The mean values of TB (0.84 ±0.16 mg/dl). (0.88 ± 0.12 mg/dl) and CB (0.60 ± 0.16 mg/dl), (0.57 ± 0.11 mo/dl) of subjects from 1 - 5 months and 6-10 months respectively, statisScaly were insignificant (P>0.05) when compared with the controls.

DISCUSSION

In the study, reduction in the activities of serum alanine aminostransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP with respect to the duration of therapy were significant (P<0.01) when compared with Aduit HIV Patients not on antiretrovira] therapy. This decrease was also observed in these enzymes when their mean values in aduit HIV patients on antiretrovira! therapy were compared with those of the control patients.

This could be a proof of the useful synergistic of the combination therapy as not being hepatotoxic, hence a reduction of liver enzyme levels. This is in agreement with the study done by Ujowundu *et a!* (2007) ,who reported that there was significant (P<0.05) elevation in the activities of liver enzymes (ALT, AST and ALP) in Adult HiV Patients not on any antiretrovirals (NARV). In a similar investigation carried out by Emejulu ef *al* (2007), it was reported that the serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT)' and alkaline phosphatase were highly < in newly infected Adult HIV subjects not on drugs.

Elevation of the serum enzymes indigenous to the liver is an indication of hepatotoxicity (Nwanjo and Oze, 2006) Hence hepatotoxicity may be attributed to the destructive effects of the human immunodeficiency virus on the hepatocytes and may not be because of the antiretroviral therapy. This is in accordance with the work done by Nunez (2006) who recommended the use of certain antiretroviral drugs like Lamivudine (3TC) in combination with other antiretroviral regimens such as stavudine and protease inhibitors for clearing of HIV from the blood circulation, thereby reducing

the rate of Liver *cell destruction* which gives rise to elevated Liver enzyme levels. However, the Liver of those Adult H/V patients who are not on any antiretroviral therapy are prone to assault which can cause destruction of Liver cells resulting in the release of Liver enzymes above baseline.

The difference in the mean values of total and conjugated Bilirubin concentrations in Adult HIV patients on ant/retroviral therapy and the control subjects was not significant. This observation agrees with the report of Ujowundu *et al.* (2007) that there are no significant differences in the concentrations of total and conjugated Bilirubin in patients on antiretroviral therapy. This is an indication that suitable combinations of therapeutic dose of antiretrovirals may not be responsible for hepatotoxicity in Adult HIV patients on antiretroviral therapy. Although the findings disagrees with earlier findings of Mouton *et al.* (1997), which stated that there was an increased level of at least twofold with respect to normal value of Liver enzymes, bilirubin rising above 2.5 mg/dl in 187 Adult HIV patients who began Highly Active Antiretroviral Therapy (HAART) in a reference centre for HIV/AIDS located in Madrid, Spain and that HAART is associated with hepatotoxicity as claimed by Lapadula *et al.* (2007). The cause of the elevation of these Liver enzymes and Bilirubin as claimed may be as a result of unsuitable and imperfect combination of these drugs and the dosage taken, which results to hepatotoxicity. As revealed by Dybul et al. (2002), the combinations of antiretrovirals are subject to positive and negative synergies, which limit the number to useful combinations, including their complicated dosing schedules and often severe side effects such as Liver toxicity.

Also in this study, it was observed that the dosage of the antiretrovirals taken by these subjects with respect to the duration of therapy (i.e. between 1-10 months) has no side effect on the hepatic function, In conclusion, the use of suitable combinations of antiretroviral therapy may not cause hepatotoxicity, considering the results of the study, since measurement of these Liver enzymes are sensitive indices for hepatocellular damage. Hence, more verification should be done and results of such findings be given wide publicity in order to educate people and to encourage Adult HIV patients to freely go to treatment centres like F.M.C. Owerri. This finding contradicts the general notion that people on antiretrovirals suffer as a result of the drugs. Therefore, the use of combination therapy with less hepatotoxicity should be a research priority. Findings here from could be a useful guide to health care providers and care and support organization on HIV/AIDS management

ACKNOWLEDGEMENT

We wish to acknowledge the cooperation of the patients who gave consent to the study. We are equally grateful to the members of the Ethical Committee of the F.M.C, Owerri for permission to carry out the study, and the Medical Laboratory scientists of the Hospital for their assistance as well as the nurses for their co-operation.

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