Journal of Natural Sciences Research
ISSN 2224-3186 (Paper) ISSN 2225-0921 (Online)
Vol.2, No.7, 2012

Assessment of the Effects of Highly Active Antiretroviral Therapy on the Renal Function of Patients with HIV-1 in a Rural Setting of South Eastern Nigeria

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ABSTRACT
A study to assess the effects of Highly Active Antiretroviral Therapy on the renal function of patients with HIV-1 in a rural setting of South Eastern Nigeria was conducted. One hundred and forty seven adult patients with mean age of 31 years comprising of 65 females and 82 males were enlisted for this study. This investigation was carried in the Federal Teaching Hospital Abakaliki where the subjects were registered and placed on antiretroviral therapy and evaluated for eighteen months with respect to renal function parameters such as creatinine and urea in correlation with CD4 T-cell count. Personnel factors such as age, sex and social status were also considered. The result revealed that 42 (28%) patients showed elevated serum urea and creatinine values above normal range as indicated by mean values of 71.6mg/dl and 3.92mg/dl from initial values of 50.71mg/dl and 1.24mg/dl at baseline respectively in the 18th month respectively the value are significant as $p<0.05$ and had a correlations coefficient of .975 .829 at 0.01 level with CD_4^+ T-cell. Also the CD_4^+ T-cell count increased from mean value of 81±16 cell/µl to 521±27 cell/µl at 18th months. The result shows that while the antiretroviral therapy may show good prognosis when considered on the basis of CD_4^+ T-cell turn over the impact on renal function is significantly deleterious. While the treatment of HIV infected person with anti retroviral is receiving wider attention, the side effects of these drugs are continually manifesting among some recipients especially in rural poor setting. This may not be unconnected with concomitant administration of other drugs such as antimalarial. There is therefore the need for proper monitoring of patients on antiretroviral therapy for adverse effect on renal function.
Keywords: Assessment, antiretroviral, HIV-1, creatinine, urea, CD_4^+ T-cell.

INTRODUCTION

The impact of HIV infection has become a global phenomenon. This is more felt in rural areas with poor economic and social background (Abruzzo *et al*., 2002).

The development of anti-retroviral therapy has however brought some relief to the menace of HIV infection. These drugs are able to arrest some of the replication processes leading to reduction in viral load and a concomitant reconstitution of the immune system. The cardinal target of the most antiretroviral therapy is the disruption of the viral genome which leads to termination of the viral replication process. Once the viral replication cycle is disrupted the host cell mechanism can be restored with the boost in the lymphoproliferative system (Alioum *et al*., 2001).

Despite the remarkable improvement with the antiretroviral therapy, the side effects and toxicities have continued to present a major challenge to the users. This is more felt among the rural dwellers who are confronted with other challenges such as poverty, poor nutrition and infection with other diseases that require treatment (Baderi *et al.,* 2003).

Most of the side effects or toxicity has been aggravated by concomitant administration of antimalarial drugs. It is to be noted that some antiretroviral therapy are potent inhibitors of cytochrome P450 enzyme system which is also a major pathway for antimalaria metabolism and therefore have the potential effect of interacting with such antimalaria. In some cases the remission of HIV viral load leads to accumulation of immune complexes which can be deposited in some vital organs of the body including the glomeruli leading to interference in the renal function of the individual (Hoffman-Terry *et al*., 2000).

Renal function can be adversely impaired due to interaction of the antiretroviral with some immune complex and also due to direct toxicity on the renal organs (Bondi and Rosender, 2004). This study was aimed to assess the effects of Highly Active Antiretroviral Therapy on the renal function of patients with HIV-1 attending Federal Teaching Hospital, Abakaliki, Nigeria.

MATERIALS AND METHODS

Subject: One hundred and forty seven adult patients comprising of 65 females and 82 males were enlisted for this study. They were placed on antiretroviral therapy of highly active antiretroviral therapy (HAART) and monitored for eighteen months.

Location of Study: This study was carried out at the Federal Teaching Hospital, Abakaliki, the state capital of Ebonyi State, Nigeria. The hospital is one among those designated for administration of antiretroviral therapy.

Ethical Approval: Ethical approval was sought for and obtained from the hospital ethic committee. Also personal consent was obtained from each of the patients after explanation.

Sampling Technique: Each patient was sampled 5 times corresponding to baseline i.e. before commencement of the antiretroviral therapy, and then three months on HAART, six months, twelve months and eighteen months respectively.

Laboratory Methods

i. **CD_4^+ T Cell Count:** This was done using the cyflow cytometer (Patec Germany). Whole blood was collected in a citrated tube and aspirated through the probe of the cytoflow. Results are displayed automatically.

ii. **Measuring Serum Urea:** The method used was Diacetyl monoxime method as modified by Cheesbrough (2006). In this method 20µl of serum was added to 4ml of freshly constituted urea reagent, incubated at 100°C for 15 minutes and absorbance was read at 530nm.

iii. **Measuring Serum Creatinine:** This was measured using the Jaffe and Slot method as modified by Cheesbrough (2006). In this technique 0,2ml of serum was added to 2.0ml of creatinine standard, allowed to stand at room temperature for 20 minutes and absorbance was read at 500nm using spectrophotometer.

RESULTS

One hundred and forty seven adult patients were sampled for 18 months, 42 (28%) showed evidence of renal infection as indicated by a rise in the serum creatinine and urea above normal ranges from initial baseline mean value of 1.24±0.8 to 3.92 and 50.7±19 at baseline to 72.0±50 respectively at 18 months. The CD_4^+ T cell count also showed significant improvement from mean values of 81±16 cells/µl to 5.10±27 at 18 months as indicated in Table 1.

Table 1: Mean values of CD_4^+ T cell count

	1	**2**	**3**	**4**
CD_4^+ T cell range	**0-100**	**101-200**	**201-350**	**351-500**
Mean T cell at baseline	81±16	162±26.7	279±41	406±43.7
Mean T cell at 3 months	141±32.5	165±27.4	305±48	458±51.9
Mean T cell at 6 months	154±36	178±29	340±68.3	460±85
Mean T cell at 12 months	188±41.9	210±45	360±82	499±18
Mean T cell at 18 months	196±48	251±32	385±61	510±27
Control	850±51	850±51	850±51	850±51

Table 2: Mean value of creatinine

GP	Baseline	3 Months	6 Months	12 Months	18 Months
1	1.24±0.8	2.6±11.5	2.68±2.18	2.47±2.0	3.12±2
2	1.18±0.95	3.09±1.6	3.42±1.8	3.92±0.69	3.96±1.8
3	1.17±0.9	2.16±1.8	2.68±1.5	2.82±2.93	2.82±1.6
4	1.17±1.8	1.42±0.7	1.44±0.5	1.51±0.91	2.04±0.9

Table 3: Mean value of urea

GP	Baseline	3 Months	6 Months	12 Months	18 Months
1	50.7±4.19	70.7±44.8	73.5±45.7	69.3±41.3	71±31
2	50.7±4.19	67.7±44.8	71.4±45.7	71.6±41.3	72±50
3	56.93±24.2	56.0±36.4	56.9±45.2	57.9±45.2	57.9±35
4	45±18	54.23±25.2	56.4±21.5	60.5±18.6	62±41

The subject population was divided into four groups based on the initial CD_4^+ T cell count at baseline. The Table 1 shows the value of the CD_4^+ T cell in all the groups. As shown, the lowest value was recorded in group 1 with mean value of 81±16 at baseline, while the highest baseline value was recorded in group 4 with 196±48. There was remarkable rise in the CD_4^+ T cell count of the groups to maximum of 510±27 as shown in the table within the 18 months of the study.

Table 2 shows the mean value of creatinine in the groups. The highest rise in mean creatinine value was recorded in group 2 with mean value of 3.96±18 in the 18th month. The mean creatinine value remained fairly high among the four groups studied but there were more rise in the values among group 1. All the groups showed high elevation of mean creatinine value above the normal range of 0.6-1.5.

Table 3 shows the values of urea in the group studied. There was a rise in the mean value of urea in all the groups studied, most especially in group with the highest value of 72±50 mg/dl. All the value are statistically significant ($P<0.05$) and correlate significantly with the CD_4^+ T-cell count.

DISCUSSION

The result shows a major evidence of renal function abnormality which is associated with the use of antiretroviral therapy. The renal parameters shows evidence of cellular damage as indicated by rise in the urea and creatinine values. This may not be unconnected with immunological damages or direct cellular toxicity of the antiretroviral drugs.

Although these parameters cannot be taken completely as a conclusive evidence of renal infarction, it has been described as one of the greater indicators of renal impairment (Bondi and Rosender, 2004).

In this study it was observed that about 28% of the population showed elevation in both serum urea and creatinine. This observation is in conformity with the earlier work done by Harris et al. (2005). Most renal dysfunction is due to damage in glomeruli, the tubula and interstitial tissue. Pathogenesis of such damage has been attributed mostly to immunological mechanism. Bondi and Rosender (2004) has described immune complex deposition as a single independent factor responsible for glomeruli damage and probably some other form of damage to renal tubules (Law *et al*., 2003). Immune complex formation has been shown to be more important than direct toxic effect in the damage and pathology of glomerulonephritis. Two distinct mechanisms are responsible for induction of glomerulonephritis and nephrotic syndrome: These are deposition of antibody complexes in the glomeruli and fixation of circulating antibody to antigen located in the glomeruli basement. There are evidences to indicate that both these mechanisms may be applicable in this study (Floege and Feehally, 2009). This is because most of the patients studied already had evidence of presence of high level of circulating immune complex in serum.

Also observed was the evidence of proteinuira in about 52% of the subjects studied. This observation was also in conformity with earlier works done by Harris et al. (2005). Most renal classes arise due to damage to glomeruli, tubules and interstitial tubules. Pathogenicity of such damage may also be attributed to immune complex deposition.

In conclusion, since there is overwhelming evidence among the HAART users of renal function in the rural areas, we recommend that adequate and regular monitoring of such patients be incorporated in routine health checkup of patients on HAART.

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