International Journal of Biomedical and Health Sciences
Vol. 6, No. 4 December 31, 2010
Printed in Nigeria

0794-4748/2010 $12.00 + 0.00

http://www.asopah.org

IJBHS 2010116/6407

An assessment of renal functions in HIV-seropositive patients at Ebonyi State University Teaching Hospital, Abakaliki, South Eastern Nigeria

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(Received July 29, 2010; Accepted August 24, 2010)

ABSTRACT: In order to assess the renal functions of HIV infected subjects receiving cares at Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki, 60 consenting HIV seropositive individuals; grouped into HIV^+ not on HAART (n = 30) and HIV^+ on HAART (n = 30) with 29 apparently healthy HIV seronegative volunteers matched for age recruited between April and September 2009 were investigated. Plasma total protein, albumin, urea and creatinine and urine protein were analysed using standard laboratory techniques. Approximately sixty eight (67.5%) of the participants were female with mean age of 31.67 ± 11.10 years. While total protein was significantly ($p < 0.05$) lower in the HIV patients than the control, HIV^+ on HAART had higher ($p > 0.05$) level than HIV^+ not on HAART (7.02 ± 0.90 g/dl vs. 6.92 ± 1.31 g/dl). However, HIV^+ on HAART had significantly higher albumin level than either HIV^+ not on HAART or controls. Significantly higher proportions of HIV infected subjects had proteinuria with subjects on HAART having lower proportion than their counterparts not on HAART. Also significantly higher levels of plasma urea and creatinine were found in HIV^+ not on HAART when compared with HAART naïve patients or control but higher in patients on HAART than in controls. These findings revealed that renal dysfunction exists in HIV infected patients, irrespective of HAART, but more pronounced in patients not receiving HAART.

Key Words: Renal functions; HIV, Blood serology, Abakaliki, Nigeria.

Introduction

Since the first case was reported in the early 80s, the prevalence of HIV infection has been on the increase until recently when reductions in the prevalence were reported in some countries (1). The attenuation of HIV scourge has been partly ascribed to treatment with HAART and better cares for people living with the pandemic. However, with increased life expectancy of the affected individuals due to drug therapy, kidney disease has emerged as the possible causes of morbidity and mortality (2).

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Infection with Human Immunodeficiency virus (HIV) has been associated with many types of renal disease including acute renal failure, acute tubular necrosis, and HIV-associated nephropathy (HIVAN) which ultimately may progress to end stage renal disease (3, 4) within few months if left untreated. Studies have shown that the prevalence of HIV- associated renal disease varies according to geographical locations (5, 6) and race with estimated 14% of black patients and 6% of white patients who died from HIV infection is the United States in 1999 having renal disease (7). For instance, while Afhami *et al.* (8) in Iran found no electrolyte imbalance, proteinuria, or renal failure in HIV infected patients, azotaemia, a good marker of HIV nephropathy had been reported in Nigerians with HIV infection (9). Also, a high prevalence (38%) of renal disease measured by proteinuria and/or elevated serum creatinine had been reported in Nigerians with HIV infection (10).

In addition to HIV infections, black race (11), older age (12), HAART use (13), hypertension (14), diabetes (15), low CD4+ cell count, and high viral load (16) remained important risk factors for kidney disease. Chronic kidney disease that may progress to end-stage renal disease requiring dialysis and renal transplant can be diagnosed in its earlier stage through routine screening and careful attention to changes in renal functions (2). In economically disadvantaged settings of developing countries, where renal transplant and dialysis may not be accessible, early detection of renal disease may have some clinical and financial implications for people living with HIV/AIDS. Because of the increasing prevalence of HIV and the growing demands for HAART, the two important risk factors for renal dysfunction, this study was conducted to asses the impact of HIV infection with or without HAART on renal functions of HIV infected individuals receiving care at Ebonyi State University Teaching Hospital, Abakaliki, Nigeria.

Materials and Methods

This study was conducted at Ebonyi State University Teaching Hospital Abakaliki between April and September 2009. The Ethics and Research Committee of the Institution approved the protocol for the study. The subjects were 60 consenting HIV patients (with duration of infection > 3 year) receiving cares at Out Patient Counselling and Care Centre of the Hospital. They were divided into HIV seropositive not on HAART (n = 30) and HIV seropositive on HAART (n = 30). Patients newly diagnosed or having any other clinical disorders that may affect renal functions were not allowed to participate in the study. Twenty nine (29) apparently healthy HIV seronegative individuals comprising staff and Medical students matched for age acted as controls. Age of the patients and volunteers were obtained by oral interview. Non fasting venous blood (5.0ml) and urine (5.0 ml) were collected from each participant. The blood sample was dispensed into lithium heparin bottle and centrifuged at 2000g for 5 minutes for the separation of the plasma. Plasma was frozen when analyses was not carried out immediately.

Plasma total protein was determined by Biuret method (17) as previously described while plasma albumin was determined by bromocresol green method (18). Plasma urea was determined by the method described by Jung *et al*. (19) and creatinine estimation was done by method originally described by Benedict and Behie (20) and re-evaluated by Stevens *et al.* (21). Urinalysis for the detection of proteinuria was done using reagent test strips (Makromed, Johannesburg, South Africa). Proteinuria was defined as any shade of colour change on the reagent test strip.

Statistical Analysis

Data analyses was done using SPSS version 10. Comparison of parameters was done using one way analysis of variance (ANOVA) and correlations between parameters were analysed using Pearson correlation analysis. Values are expressed as mean ± S.D. / or proportion (percentage) with statistical significant set at ≤ 0.05.

Results

The distributions of subjects are shown in Table 1. Of the 89 participants, 67.4% were female with female to male ratio of approximately 3:1 in the subjects and 1:1 in the controls.

Table 1: Sex distribution of HIV-seropositive subjects and controls (percentage in parenthesis).

Sex	Control	HIV^+ not on HAART	HIV^+ on HAART	Total
Male	14 (48.3)	8 (27.6)	7 (24.1)	29
	(48.3)	**(26.7)**	**(23.3)**	**(32.6)**
Female	15 (25)	22 (36.7)	23 (38.3)	60
	(51.7)	**(73.3)**	**(76.7)**	**(67.4)**
Total	29	30	30	89

Table 2: Age and plasma parameters of HIV seropositive subjects and controls.

Parameters	Control (n = 29)	HIV^+ not HAART (n = 30)	HIV^+ on HAART (n = 30)	p-values
Age	31.62 ± 11.1	31.43 ± 11.0	31.97 ± 11.2	0.982
Total protein (g/dl)	9.63 ± 1.95	6.92 ± 1.31	7.02 ± 0.53	0.000
Albumin (g/dl)	2.75 ± 0.77	2.63 ± 0.53	3.42 ± 0.73	0.000
Urea (mg/dl)	19.75 ± 8.39	47.72 ± 26.51	31.91 ± 11.82	0.000
Creatinine (mg/dl)	0.62 ± 0.34	1.14 ± 1.06	0.99 ± 0.70	0.027
Proteinuria (n/%)	2 (6.9)	10 (33.3)	6 (20.0)	0.041

Values are expressed as mean ± S.D.
$P < 0.05$ is considered significant

From Table 2, there was no significant age difference in the subject and control groups. Although plasma total protein was comparable between the HIV patients, there was significantly ($p < 0.05$) lower plasma total protein in the subjects compared with the controls. However, though within the reference range, plasma albumin was significantly lower in HIV^+ not on HAART and controls compared with the HIV^+ on HAART (2.63 ± 0.53 & 2.75 ± 0.77 respectively vs. 3.42 ± 0.73, $p < 0.05$).

While plasma urea was significantly higher in HIV subjects, either on HAART or not on HAART than the control, the level was higher in HIV patients not on HAART compared with patients on HAART. Also, Plasma creatinine was significantly higher in HIV patients not on HAART compared with those on HAART and controls but higher in patients on HAART than in controls (0.99 ± 0.70 vs. 0.62 ± 0.34). Proteinuria was found in significantly ($p < 0.05$) higher proportion of HIV infected patients either on HAART or not than in the controls but more in HIV^+ not on HAART than their counterparts on HAART.

Discussion

This study has shown that HIV infection affects renal functions which are ameliorated by treatment with HAART. In the present study renal dysfunction characterized by elevated urea, creatinine and proteinuria was observed in HIV infected subjects compared with the controls with dysfunction more in patients not receiving HAART than in patient receiving HAART. These findings suggest that HAART-use may have positive impact on renal dysfunction associated with HIV infection. This suggestion is consistent with the findings of Steel-Duncan *et al.* (22) where renal syndrome was resolved after eight months of HAART initiation. Several studies have shown beneficial effects of HAART and aldosterone converting enzyme (ACE) inhibitors on reducing proteinuria and slowing the progression of renal disease in HIV-infected cohorts (23-27). Evidence suggests a direct role of HIV infection in the pathogenesis of HIVAN (28, 29), hence effective control of viral replication should result in slow

progression of renal disease. It has been found that risk of death from any cause or opportunistic infections, risk of major cardiovascular, renal, or hepatic disease, and risks of cardiovascular and renal disease separately were statistically significantly lower in the viral-suppression group than in the drug-conservation group (30). Also, the substantial improvement in the survival of HIV-infected patients on dialysis noted after 1995 has been attributed to HAART (31). Recent evidence suggests that the addition of cyclosporine to HAART may offer other long-term beneficial effects (32) as cyclosporine and mycophenolate may have anti-retroviral effects. However, some studies have implicated drug toxicity in the aetiology of HIV-associated renal disease (9, 33, 34).

Significantly lower plasma total protein in HIV seropositive subjects in the present study corroborates earlier studies (9, 35) but however contrasts the higher levels reported by Audu *et al*. (36). Although the reason for the discrepancy in the findings is unknown, it may be connected with disease severity. Although serum total protein estimation has limited diagnostic importance when compared to albumin because of the compensatory increases in other serum proteins (the globulins) during infections, its relevance in the evaluation of patients with some clinical conditions such as malnutrition, malignancy, renal and liver diseases and immune disorders cannot be ignored (37).

Decrease in plasma/serum total protein in HIV infection has been associated with either increased losses and/or catabolism or as a result of reduction in intake and/or absorption due to sores in the mouth, pharynx and/or oesophagus, fatigue, depression and side effects of medications (38). However, HAART users were found to have significantly higher serum total protein than non-users (7.02 ± 53 mg/dl vs. 6.92 ± 1.31 mg/dl). This is also in corroboration of the earlier findings (9, 39). The significantly higher plasma total protein in HAART users in the present study therefore suggests that HAART-use improves protein metabolism by improving the CD4 count (40), although it could not be established if the lower serum protein levels in HIV/AIDS patients in the present study were related to CD4 count.

Reduction in protein loss through diarrhoea and catabolism in HAART users may also be a factor. However, with HIV progression protein loss may be more pronounced as it has been shown that about 0.6-1.2g of protein per kilogram body weight per day are lost in adults due to infection as a result of mobilisation of amino acids from skeletal muscles in response to the release of cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α) (40). These losses have been found to be highest in diarrhoea and dysentery, which are common in HIV infection. This is evidenced by the significantly lower plasma albumin in HIV^+ not on HAART when compared with that of patients on HAART. Serum albumin is a useful marker of body protein stores and decreased level has been found in protein wasting and diarrhoea disease as in HIV infection (36). Form this study, it is concluded that renal disorders exist among HIV infected subjects in Abakaliki, which appeared to be ameliorated by HAART therapy. We therefore recommend routine renal function tests for HIV-infected individuals, and institution of HAART therapy for the at risk groups despite the potential toxicity of HAART, as renal dysfunction may be even greater when HIV is left untreated for too long.

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