Correlates of Impaired Renal Function in Highly Active Antiretroviral Therapy (HAART) Naive HIV Infected Patients in Maiduguri, Nigeria

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Abstract

Background : Although renal function may be abnormal in as many as 30

Index terms— Highly active antiretroviral therapy, human immunodeficiency virus, correlates, serum creatinine.

1 Introduction

espite the widespread use of highly active antiretroviral therapy (HAART), HIV disease remains associated with increased kidney an often unrecognised problem as kidney function may be abnormal in up to 30% in HIV population (Gupta et al.,2005; **??**zczechet al.,2002). HIV-infected patients may HIV-associated nephropathy (HIVAN) is traditionally the most common renal lesion affecting HIVinfected patients; it is the commonest cause of end stage renal disease (ESRD), often requiring renal replacement therapy. Although HIVAN has been documented in indigenous African patients, little is known about the prevalence or risk factors for renal disease in this population (Winston et al., 1999; **??**osgrove et al., 2002; **??**zczechet al.,2004).

The aim of this study was to determine the factors associated with impaired renal function among the patients initiating highly active antiretroviral therapy.

2 II.

Patients and Method disease risk **??**Phair and Palella,2011) Kidney function can be measured by determining the glomerular filtration rate (GFR), the decrease in GFR has been shown to correlates with the severity of kidney disease. The Cockcroft-Gault equation, which estimates GFR using serum creatinine and anthropometric variables has been shown to predict renal function **??**Cockcroft and Gault,1976). The use of this equation in assessing GFR has been validated among black HIV positive patients **??**Chukwuonye,2007). such as Cameroon, Niger and Chad Republics. Maiduguri the capital of Borno State is situated in the north eastern Nigeria and the largest settlement near the Lake Chad.

Study procedure : Cross-sectional data of 415 HIV positive patients were abstracted for the purpose of this study.

Variable abstracted included age, gender, weight and WHO clinical stage of HIV disease. Blood samples were collected for CD4 count using standardized flow cytometricCyflow machine (manufactured by Cytec, Partec, Germany 2005). While plasma HIV RNA levels was measured using freshly frozen specimen separated within 6 hours of phlebotomy utilizing the Amplicor HIV-1 Monitor Test, version 1.5 Manufactured by Roche® Germany, with a minimum cut off value of 200 copies per ml. Enzyme linked immunosorbentassay kits was used to detect the presence of HBsAg and HCV antibodies (DIA, PRO, DiagosticBioprobes Sri, via columella no 20128 milano-Italy).

The estimated Glomerular Filtration Rates (eGFRs) were calculated from serum creatinine measurements using the Cockcroft Gault equation Statistical analysis : Data were analyzed using SPSS ® , version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using Chi-square test, group means were compared the students t-test. Mann Whitney test was used to compare variables that did not follow normal distribution.

Factors associated with reduced eGFR (defined as <60mL/min) were tested for inclusion in a multivariate logistic regression model. A P-value of < 0.05 was considered statistically significant.

3 III. Results

4 a) Stratification of participants based on gender

A total of 415 HIV positive, highly active antiretroviral therapy (HAART) naive patients with mean age of 43.65±9.70 (95% CI; 42.77 -44.52), were considered for this study. Out of this 182 (43.6%) participants were males, with a mean age of 47.43±9.00, they were older than their female counterpart that had a mean age of 40.54±9.08 ($p<0.05$). Female gender was associated with significantly low haemoglobin, viral load, and proportion significantly high proportion of participants infected with hepatitis B virus, while the body mass index and AIDS status between the males and females were not comparable as shown in Table On multivariate analysis, with younger age(<50 years), Hb?10g/dl,WBC?3X10 9 /l, platelets?150x10 9 /l, HIV-1RNA?100000copies/ml, no AIDS status, Normal BMI(18.5-25.0kg/m2) as a referent, it shows that older age (?50 years), anaemia (Hb<10g/dl), abnormal BMI (<18.5kg/m 2 or >25.0 kg/m 2) had significant associations with reducedeGFR (eGFR<60ml/min) as shown in Table **??**.

5 IV. Discussion

Our study examined the pattern of renal impairment and its associated factors among highly active anti retroviral naive HIV infected individuals. The prevalence of renal impairment as defined by an eGFR<60 ml/min/1.73m2 among HIV patients in our cohort was 14.7% similar to previous studies that reported a prevalence rate of 10 to 30% (Weiner et al., 2002; **??**zczechet al., 2004; **??**inston et al., 1979) characteristicsincluding demographic characteristics, stage of HIV infection, and access to health care services. Of note, our population was relatively young (mean age 44 years), presented at late stage of the disease.Although somehow expected, this finding of prevalence of 14.7% in our cohort was worrisome for us. We used Cockcroft-Gaultequations to estimate glomerular filtration rate (eGFR), and since these equations can underestimate the actual GFR or creatinine clearance in patients with malnourishment or reduced muscle mass related to advance HIV, it is possible that the true prevalence of CKD in our cohorts is underestimated.

Table **??** : Multivariate analysis of correlates of reduced eGFR (< 60ml/min) among HIV-infected patients.

6 2004), 3% reported in California (Crum-Cianfloneet

This study demonstrates older age, abnormal weight (under weight or over weight/obesity) and anaemia at presentation to be independent predictors of renal impairment in our cohort. Renal function is known to decline with age. Older age is an established risk factor for a decline in creatinine clearance in the general population (Davies and Shock, 1950). Similarly, older agehas been independently associated with renal function decline among HIV-infected subjects.

(Mocroftet al.,2007; Cheung et al., 2007).The preponderance of renal impairment in our male cohort may be related to significantly older male than female population.

The mean CD4 count of 222 cells/ul in patients with normal renal function was significantly higher than 182 cells/ul in our cohort with renal impairment. This is consistent with earlier studies that reported an association between impaired renal function in HIV infected patients with significantimmuno suppression, having CD4 cell count less than 200ul/L. Immunological AIDS (CD4 count <200ul/L) is known to be associated with development of opportunistic infections, malignancies and other organ diseases that affects kidney functions. (Winston et al.,1999; Szczech et al., 2004; Winston et al.,2001; Krawczyket al.,2004). CD4 cell had a protective role in the development of renal Reports from sub-Saharan Africa, indicated that the prevalence of decreased eGFR is high and varied substantially depending on the estimating method used **??**Chukwuonye,2007;Van Deventer et al.,2008;Eastwood et al.,2010). However the use of Cockcroft-Gault equations have been validated for use as it has been shown to predicts renal function in black HIV population (Chukwuonye, 2007)

7 V. Limitations

This study is limited in its retrospective design, with the greater proportion of HIV-infected with AIDS with advanced clinical disease, it implies that prevalence estimates derived from this study may not be generalizable to patients with early stage of HIV infection. In addition, we were limited by the use of a single serum creatinine, hence spurious results were not excluded. Finally, there was no assessment for protenuria; however, this was the standard of care in the centre at the time of this study.

Figure 1: (

undergo renal damage related to the HIV infection itself, to the presence of co-infection, arterial hypertension, diabetes or to the exposure to nephrotoxic drugs. Consequences of kidney disease in HIV-infected persons include increased risk of atherosclerosis and mortality, in addition immunosuppression that is known to be associated with development of opportunistic infections, malignancies and other organ diseases that affects kidney functions. (Choi A et al.,2010; Choi AI et al.,2010).
highly
active antiretroviral therapy for effective and proper management.

[Note: Results : A total of 415 participants with mean age of 43.65±9.70 (95% CI; 42.77 -44.52), were considered for this study. Out of this 182 (43.6%) were males, with a mean age of 47.43±9.00, they were older than females with mean age of 40.54±9.08 (p<0.05). A total of 61(14.7%) had an eGFR<60mL/min, with disproportionately more males (17.0%vs 12.5%) having eGFR<60mL/min than females (p<0.05). On multivariate analysis, older age (?50 years), anaemia (Hb<10g/dl), abnormal BMI (<18.5 kg/m 2 or >25.0 kg/m 2) had significant associations with reduced GFR. Conclusion : Older age, anaemia and abnormal weight are independently associated with risk of having impaired renal function in our cohort. We therefore recommend renal function tests to HIV infected patients at commencement of]

Figure 2:

1

Males(n=182)	Females (n=233)	P-value

Figure 3: Table 1 :

2

	(eGFR?60mL/min) N=356	(eGFR<60ml/min) N=61	P-value
Age (years)	42.46±8.90	49.87±11.07	0.000*
Gender			
Male, no (%)	161(83.0%)	31(17.0%)	0.000*
Female, no (%)	104(87.5%)	29(12.5%)	0.000*
Mean Hb (g/dl)	11.60±2.05	10.19±2.31	0.000*
Mean WBC	5.05±1.93	5.68±2.90	0.115
Mean platelets	262.12±103.00	251.32±113.34	0.471
Mean CD4 count(cells/µl)	222.04±152.03	182.21±105.46	0.013*
Mean viral load (copies/ml)	4.96±5.44	4.97±5.27	0.958
Hepatitis C	3	0	
Hepatitic B	48(13.5%)	10(16.4%)	0.000*
BMI	22.77±4.48	20.70±3.90	0.013*
AIDS status, no=231			
yes	193(83.5%)	38(16.5%)	0.000*
no	162(88.0%)	22(12.0%)	0.000*

BMI (body mass index).
*Statistically significant.

Figure 4: Table 2 :

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Figure 5:

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