ORIGINAL ARTICLE

Predictors of impaired renal function among HIV infected patients commencing highly active antiretroviral therapy in Jos, Nigeria

Oche O. Agbaji, Adamu Onu, Patricia E. Agaba, Muhammad A. Muazu, Kakjing D. Falang, John A. Idoko

Department of Medicine, HIV Clinic, Jos University Teaching Hospital, Jos, Nigeria

ABSTRACT

Background: Kidney disease is a common complication of human immunodeficiency virus (HIV) infection even in the era of antiretroviral therapy, with kidney function being abnormal in up to 30% of HIV-infected patients. We determined the predictors of impaired renal function in HIV-infected adults initiating highly active antiretroviral therapy (HAART) in Nigeria. **Materials and Methods:** This was a retrospective study among HIV-1 infected patients attending the antiretroviral clinic at the Jos University Teaching Hospital (JUTH), between November 2005 and November 2007. Data were analysed for age, gender, weight, WHO clinical stage, CD4 count, HIV-1 RNA viral load, HBsAg and anti-HCV antibody status. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault equation. Statistical analysis was done using Epi Info 3.5.1. **Results:** Data for 491 (294 females and 197 males) eligible patients were abstracted. The mean age of this population was 38.8±8.87 years. One hundred and seventeen patients (23.8%; 95% CI, 20.2-27.9%) had a reduced eGFR (defined as <60 mL/min), with more females than males (28.6% vs. 16.8%; *P*=0.02) having reduced eGFR. Age and female sex were found to have significant associations with reduced eGFR. Adjusted odds ratios were 1.07 (95% CI, 1.04, 1.10) and 1.96 (95% CI, 1.23, 3.12) for age and female sex, respectively. **Conclusions:** Older age and female sex are independently associated with a higher likelihood of having lower eGFRs at initiation of HAART among our study population. We recommend assessment of renal function of HIV-infected patients prior to initiation of HAART to guide the choice and dosing of antiretroviral drugs.

Key words: Highly active antiretroviral therapy, human immunodeficiency virus, predictors, renal function, serum creatinine

Address for correspondence:
Dr. Oche O. Agbaji,
Department of Medicine,
Jos University Teaching Hospital,
Jos, Nigeria.
E-mail: oagbaji@yahoo.com

INTRODUCTION

Kidney disease is a common complication of human immunodeficiency virus (HIV) infection even in the era of Antiretroviral Therapy (ART), with kidney function being abnormal in up to 30% of HIV-infected patients.[1-3] The causes of renal disease in HIV-infected patients are multifactorial and include HIV infection itself, co-infections, co-morbidities, and their treatments.[4] AIDS-related kidney disease has become a relatively common cause of end-stage renal disease (ESRD) requiring renal replacement therapy, and kidney disease may be associated with progression to AIDS and death.[5,6]

HIV-associated nephropathy (HIVAN) is the most common finding on renal biopsy in HIV-infected black patients and it is also the commonest cause of ESRD in these patients. Early detection of HIVAN may be beneficial in evaluating patients for HIV therapy.[7,8]

The glomerular filtration rate (GFR) is a direct measure of kidney function and reduces before the onset of symptoms of kidney failure, with the decrease in GFR correlating with the severity of kidney disease.[9] One of the ways to estimate GFR is the use of the Cockcroft-Gault equation, which estimates GFR using serum creatinine measurements and anthropometric variables.[10] This method of assessing GFR has been validated among HIV-positive black patients in our environment.[11]

The aim of this study was to investigate the factors associated with impaired renal function among the patients initiating highly active antiretroviral therapy (HAART)

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in the antiretroviral clinic, at the Jos University Teaching Hospital in Jos, Nigeria.

MATERIALS AND METHODS

This was a retrospective study conducted among HIV-1 infected patients attending the antiretroviral clinic of the Jos University Teaching Hospital between November 2005 and November 2007. Cross-sectional data for 491 patients were abstracted for the purpose of this study.

Variables abstracted included age, gender, weight and WHO clinical stage of HIV disease. Blood samples were collected for CD4 count and HIV-1 RNA viral load determination using Cyflow [Partec, Germany] and Roche Ampliclor (version 1.5, Branchburg, NJ, USA), respectively. Additionally, HBsAg and anti-HCV antibody were determined using third-generation enzyme-linked immunosorbent assay (ELISA) kits [BIO-RAD, Marnes-la-Coquette-France and Dia.Pro Diag, Milano-Italy respectively]. The estimated Glomerular Filtration Rates (eGFRs) were calculated from serum creatinine measurements using the Cockcroft Gault equation[10] and graded according to the National Kidney Foundation grading of chronic kidney disease (CKD)[12] as follows: Grade 1, 60-89 mL/min; grade 2, 30-59 mL/min; Grade 3, 15-29 mL/min; and grade 4, <15 mL/min. The Human Research Ethics Committee of the Jos University Teaching Hospital approved the study.

Statistical analysis

The data were analyzed using Epi Info 3.5.1 (CDC, Atlanta, GA, USA). Categorical variables were compared using Chi-square test, group means were compared using the Student's *t*-test, while three or more group means were compared using Analysis of Variance (ANOVA). Mann Whitney test was used to compare variables that did not follow normal distribution (e.g. CD4 counts).

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

RESULTS

Complete data for 491 patients were available for the study [Table 1]. The number of males was 197 (40.1%), with the mean age of the study participants being 38.8 years (±8.8). One hundred and seventeen subjects (23.8%; 95% CI, 20.2-27.9%) had an eGFR <60 mL/min, with disproportionately more females (28.6% vs. 16.8%; *P*=0.02) having an eGFR <60 mL/min. The mean overall eGFR was 76.7 mL/min (±22.8), with females being more likely to have a lower eGFR (females: 74.6±23.10, males: 79.8±22.03; *P*=0.01). Males were more likely to have viral loads >200 copies/mL (*P*=0.006).

Univariate and multivariate analyses showed that age and female sex had significant associations with reduced eGFR. Adjusted odds ratios were 1.07 and 1.96 for age and female sex, respectively [Table 2].

DISCUSSION

Table 1: Characteristics of 491 patients stratified by sex

	Males (*n*=197)	Females (*n*=294)	*P* value
Age (years)	38.2 (±8.6)	39.1 (±9.1)	0.29
Mean CD_4 cells (cells/mm^3)	140 (±98)	153 (±116)	0.46*
CD_4 cells ≤200 cells/mm^3	138 (70.1%)	207 (70.4%)	0.93
Viral load†	4.16 (±0.891)	4.21 (±0.996)	0.59
Viral load >200 copies/mL	185 (93.9%)	253 (86.1%)	0.006
eGFR (mL/min)	79.8 (±22.03)	74.6 (±23.10)	0.01
eGFR grade			0.02
≥90	58 (29.4%)	74 (25.2%)	
60-89	106 (53.8%)	136 (46.2%)	
30-59	30 (15.2%)	80 (27.2%)	
15-29	2 (0.01%)	4 (0.01%)	
<15	1 (0.005%)	0 (0%)	
Hepatitis C	24 (12.2%)	34 (11.6)	0.29
Hepatitis B	34 (17.3%)	38 (12.9%)	0.93
WHO stage			0.16
I	67 (34%)	85 (29%)	
II	92 (46.7%)	131 (44.5%)	
III	29 (14.7%)	62 (21%)	
IV	6 (0.03%)	16 (5.4%)	

*Mann–Whitney test; †Log_{10} viral copies/mL

Table 2: Characteristics of 491 patients stratified by reduced eGFR

	<60 mL/min (*n*=117)	≥60 mL/min (*n*=374)	*P* value	Adjusted OR (95% CI)
Age (years)	42.9 (±10.01)	37.5 (±8.07)	<0.0001*	1.07 (1.04, 1.10)
Female	84 (71.8%)	210 (56.1%)	0.003	1.96 (1.23, 3.12)
CD_4 cells (cells/μL)	156.6 (±113.97)	145.0 (±108.65)	0.32	-
CD_4 cells ≤200 cells/mL	82 (70.1%)	263 (70.3%)	0.96	-
Viral load†	4.22 (±0.997)	4.18 (±0.940)	0.66	-
Viral load >200 copies/mL	103 (88.0%)	335 (89.6%)	0.64	-
Hepatitis C	16 (13.7%)	42 (11.2%)	0.47	-
Hepatitis B	16 (13.7%)	56 (15.0%)	0.73	-
WHO stage				-
1	35 (30%)	117 (31.2%)	0.1	
2	54 (46.1%)	169 (45.1%)		
3	27 (23%)	64 (17.1%)		
4	1 (0.9%)	21 (5.6%)		

*Mann–Whitney; †Log_{10} viral copies/mL

This study demonstrates older age and female sex to be independent predictors of impaired renal function in HIV-1 infected patients commencing HAART in Nigeria. This finding is at variance with that reported by the Development of Antiretroviral Therapy (DART) Trial group;[14] they reported a younger age, male sex and a lower systolic blood pressure (BP) to be predictors of reduced renal function at initiation of ART in their cohort. This difference could be as a result of the differences in characteristics between the study populations, as the DART trial recruited over 3000 participants from three centers in two East African countries. The DART trial patients also had more severe immune deficiency than our patients (mean CD4 cells of 86 cells/mm^3 and 146 cells/mm^3, respectively), though the age and sex distribution of both study populations were similar (37 years in DART as against 38.8 years in our cohort; 65% of DART patients were females and 60% were females in our cohort). Renal function is known to decline with age. Hence, this finding is consistent with what is expected and reported widely. However, unlike in other similar studies, we did not find an association between CD4 counts, viral load, HCV infection and reduced eGFR.[1,6,13] This difference could be explained in part by the difference in study design, as one of these studies used MDRD equation to estimate the eGFR. Also, the patients in that study were already on HAART.[13] These studies and others have shown that CD4 counts of <200 cells/μL were predictive of impaired renal function and that HIV patients with this severe immune deficiency were more likely to develop CKD, particularly if the viral load was >100,000 copies/mL and were not on HAART.[14]

This study also showed that 23.8% of the patients had reduced renal function. This is higher than what was reported by the DART trial group.[15] They reported that 7% of their participants had mild reduction of eGFR (<60 mL/min) at initiation of HAART. This may suggest that our patients had more severe renal impairment at the time of initiation of HAART. However, in a recent study from this center, Chukwuonye *et al*. reported that 50% of HIV-infected patients had mild reduction in eGFR.[16] This is higher than what we have reported, although the fact that they used creatinine clearance to estimate the GFR could be a contributory factor. Other studies in Kenya and Uganda have also reported a mild reduction in eGFR of patients at initiation of HAART.[17,18]

It is important that HIV-infected patients with impaired renal function be identified before initiation of therapy as the eGFR will determine the dosing of their antiretroviral medications. Also, early initiation of ART should be instituted for these patients in line with the new WHO guidelines for initiation of ART.

There is a need for further studies to investigate renal function in HIV-infected individuals, the impact of ART on renal disease as well as to evaluate how well creatinine-based equations estimate renal function in HIV-1 infected individuals in Africa.

This study is limited by the fact that only a single measurement of serum creatinine was done, hence spurious results were not excluded. Also, the fact that the study is a retrospective study is another limitation. In addition, there was no assessment for proteinuria; however, this was the standard of care in the center as at the time of this study.

We therefore conclude that older age and female sex are independently associated with a higher likelihood of having lower GFRs at initiation of HAART among our study population. This study highlights the need for an increased awareness of CKD in HIV-positive individuals among clinicians in order to identify those patients at risk for renal disease and implement potentially preventative and therapeutic strategies.

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