Abstract

The burden of Human Immunodeficiency Virus (HIV) infection is highest in sub-Saharan Africa. Increase in numbers of patients with HIV infection coupled with their improved long-term survival has led to increasing prevalence of HIV-associated organ dysfunction, including kidney diseases. Comorbidity of HIV with kidney disease has been associated with faster progression to AIDS and increased mortality. Early detection of kidney disease allows for targeted therapy to delay or prevent development of end stage kidney disease (ESKD). Proteinuria, reduced glomerular filtration rate (GFR), or both, have been utilized to define kidney disease in these patients. Definitive diagnosis by kidney biopsy, when indicated, is critical to optimal management. A wide variety of histopathological lesions have been reported among HIV-infected patients, with the variation attributed to many factors such as geographical and ethnic diversity of the studied population. Kidney diseases such as HIV-associated nephropathy (HIVAN) are commonly known to occur among HIV-infected populations. This lesion has a higher prevalence among individuals of African descent compared to Caucasians and has been associated with rapid progression to ESKD. The possibility of genetic factors contributing to the development of kidney disease among people of African ancestry was supported by findings that variants in the gene located on chromosome 22 which encode for Apolipoprotein L1 (APOL1) have strong association with increased risk of various forms of kidney diseases. Despite the strong association between certain histopathological lesions, such as HIVAN, and African ancestry as described among African-Americans, there is paucity of literature detailing the spectrum of histopathologic lesions among HIV-infected patients with kidney disease in West Africa. Not many studies were reported on the APOL1 variants and kidney diseases among native Africans. The present study conducted in Northern Nigeria explored the prevalence and

outcomes of chronic kidney disease (CKD) in a cohort of antiretroviral therapy (ART)-naive HIV-infected patients, evaluated the histopathologic patterns among those that had biopsy and determined the frequencies of APOL1 genotypes among them in comparison to those with no evidence of kidney disease.

Methods

This cross-sectional study was conducted at the dedicated HIV clinic of Aminu Kano Teaching Hospital (AKTH), which is one of the approved United State President's Emergency Plan for AIDS Relief (PEPFAR) centres in Nigeria. Following ethical approval, consecutive treatment naïve HIV patients were evaluated clinically and screened for the presence of CKD defined as persistent proteinuria and/ or reduced eGFR confirmed after three months, and were followed up every month for the first 3 months and subsequently every 3 months for 12 months. Those with CKD and no contraindication to kidney biopsy and had given consent to participate, had a kidney biopsy following established unit protocols. DNA samples obtained from the whole blood of 142 participants were genotyped for *APOL1* G1 and G2 variants after initial baseline investigations including assessment of kidney function. They comprised of 50 HIV positive patients with no evidence of kidney disease, 52 HIV negative individuals with no kidney disease and 40 HIV positive patients with CKD.

Results

Nine hundred patients were studied; 63% were females with mean age of 34.17±10 years and mean CD4 count of 238 ±210 cells/ml. CKD prevalence was 22.8% using the CKD-EPI equation (without the race factor) with the majority 146 (71.21%) having stage 3 CKD. Multivariable analysis identified age, CD4 count <200 cells/mL, low body mass index (BMI) and a history of use of traditional medications as being independently associated with CKD. Fourteen patients

with stage 5 CKD were followed up at the Nephrology Clinic for the first year and eight of them were dialysis-requiring within the first 6 months of follow up. Two were lost to follow up and the remaining 4 died of other complications within the follow up period. Among those with CKD, 53 had kidney biopsy and the commonest histological type was focal segmental glomerulosclerosis (FSGS) present in 20 patients (37.7%), followed by HIVAN in 17 (32.1 %) patients, and chronic interstitial nephritis in 7 patients (13.2%) among others. Compared to non-HIVAN patients, HIVAN patients tended to have higher serum creatinine levels (p= 0.005); lower eGFR (p= 0.030) and higher urine protein to creatinine ratio (uPCR; p= 0.020).

The prevalence of the individual risk alleles was 26.1% for G1 and 19.0% for G2. The frequency of the High Risk Genotype (HRG) was 12.5% among those with CKD, compared to 5.8% in the HIV negative group. Having the HRG was associated with a higher odds for developing HIVAN (2 vs 0 risk alleles: OR 10.83, 95% CI 1.38 - 84.52; p= 0.023). The presence HRG was also associated with higher odds for FSGS (2 vs 0 risk alleles: OR 13.0, 95% CI 2.06 - 81.91; p=0.006) when compared to the control group.

Conclusions

There was a high prevalence of CKD and its risk factors in this cohort of HIV- infected and treatment naïve patients, which has implications for overall organisation of HIV care in this environment. It calls for the incorporation of screening for CKD and its risk factors, and implementation of strategies targeted at early detection, and institution of therapies to reduce and slow progression of CKD to ESKD. Kidney involvement is a common form of presentation among these patients, with FSGS and HIVAN being the most common histologic types especially among those carrying two copies of the HRG. There was high frequency of the high risk APOL1 genes among HIV-positive CKD patients compared to those without CKD.