Prevalence of chronic kidney disease in HIV positive patients in Lagos, south-west Nigeria

Theophilus Umeizudike,[1] Monica Mabayoje,[2] Charles Okany,[2] Fatima Abdulkareem,[2] Adekunle Adeyomoye,[2] Njideka Okubadejo,[2] Ikechi Okpechi[3]

[1]Nephrology Unit, Department of Medicine, Lagos State University Teaching Hospital, Ikeja; [2]College of Medicine, University of Lagos, Idi-Araba, Lagos State, Nigeria; [3]Division of Nephrology and Hypertension, University of Cape Town, South Africa

Abstract

The human immunodeficiency virus (HIV) pandemic is one of the leading causes of death in the developing world. Chronic kidney disease (CKD) and end-stage renal disease (ESRD) associated with HIV are major causes of morbidity and mortality in HIV-positive patients. This cross-sectional study was conducted to determine the prevalence and risk factors of CKD in HIV-positive, antiretroviral naïve patients at a single HIV clinic in Lagos, Nigeria. Of 402 patients, CKD was observed in 23.5% while among 146 controls, CKD was detected in 5.5% (odds ratio (OR) 5.34 [95% CI 2.4-12.2]; P<0.0001). Macroalbuminuria was seen in 20.1% of patients and 2.1% of controls, (OR 12 [95% CI 3.7-38.5]; P<0.0001). Most of the patients and controls were categorized into CKD stages 1 and 2, none among the control was in stage 4 or 5 CKD, while 2 and 2.2% of patients were in stages 4 and 5, respectively (P=0.005). Macroalbuminuria (P<0.0001) and HIV RNA viral load (P=0.010) correlated with CKD on multivariate linear regression analysis. Macroalbuminuria may, therefore, be a useful marker of degree of CKD in HIV seropositive patients. To reduce the burden of CKD and ESRD in populations with high prevalence of HIV, there is a need for increased screening and surveillance for CKD through performance of simple tests to estimate protein in the urine. One of the limitations of this is in using the abbreviated Modification of Diets in Renal Disease (MDRD) equation for estimating glomerular filtration rate.

Correspondence: Theophilus Umeizudike, Nephrology Unit, Department of Medicine, Lagos State University Teaching Hospital, 1-5 Oba Akinjobi Road, G.R.A. Ikeja, Lagos State Nigeria.
Tel. +234.803.337.3232.
E-mail: theokenny@yahoo.com

Key words: chronic kidney disease, HIV, macroalbuminuria, albumin-creatinine ratio, kidney biopsy.

Conflict of interest: the authors report no conflicts of interest.

Acknowledgments: we thank Mr Bosun Olaleye and Mr Jide Bamiro for their assistance, and in particular in carrying out the laboratory analysis for albumin-creatinine ratio in spot urine.

Received for publication: 23 July 2011.
Revision received: 10 January 2012.
Accepted for publication: 2 February 2012.

Nephrology Reviews 2012; 4:e5
doi:10.4081/nr.2012.e5

Introduction

At the beginning of the new millennium, the prevalence of the human immunodeficiency virus (HIV) had reached a crescendo. The impact of this on various African countries meant that the drive to prevent and treat this infection was paramount. Sub-Saharan Africa (SSA) is home to approximately one-fifth of the world's population and accounts for two-thirds of those infected with HIV. A recent report on the global trends of the HIV epidemic has shown that the incidence of HIV infection has fallen by more than 25% between 2001 and 2009 in 33 countries, 22 of which are in SSA.[1] This trend reflects a combination of factors, including the impact of HIV prevention efforts and the natural course of the HIV epidemic.

HIV associated kidney disease is one of the commonest causes of chronic kidney disease (CKD) in SSA.[2,3] It may be equally ranked in a few countries with hypertension, chronic glomerulonephritis and diabetes mellitus as leading causes of CKD.[3,4] Due to the prohibitive costs of renal replacement therapy, an epidemic of HIV associated kidney disease will further add to the burden of the cost of health care in these countries where there is already a struggle to contain other infectious diseases such as malaria, tuberculosis and diarrhoeal illnesses.

The spectrum of HIV-related kidney disease includes acute kidney injury (from sepsis, hypovolemia, drug-induced tubulointerstitial nephritis) and chronic kidney disease (HIV-associated nephropathy [HIVAN], HIV-associated immune complex glomerulonephritis, HIV-associated thrombotic microangiopathic hemolytic anemia) and several electrolyte/metabolic abnormalities.[5,6]

With the widespread introduction of highly active anti-retroviral therapy (HAART) in 1996, there was a dramatic decline in acquired immune-deficiency state (AIDS)-related deaths in the United States.[7] The proportion of deaths that are attributable to AIDS-defining conditions has continued to decline, with chronic complications, such as liver and kidney disease, becoming increasingly important contributors to mortality in the HAART era.[8] Survival among HIV-infected dialysis patients has also improved in the HAART era, approaching survival rates in the general end stage renal disease (ESRD) population.[9] On the basis of these data and the increasing prevalence of HIV infection among susceptible black individuals, the pool of patients who are at risk for developing HIVAN has expanded dramatically.[10]

In SSA, an estimated 22.5 million people are living with HIV/AIDS;[1] expanding access to HAART will improve survival and may also be accompanied by an epidemic of HIVAN. AIDS-related mortality began to decline in SSA in 2005, coinciding with the dramatically expanded availability of HAART.[1] HIV-associated nephropathy is thought to be the dominant pathology in HIV positive patients and

often is the common pathology leading to ESRD in these patients. Cross-sectional data from South Africa demonstrated albuminuria in 7% of patients, with a surprisingly high prevalence of biopsy-proven HIVAN in patients with micro-albuminuria.[11] In a series of 99 consecutive kidney biopsies in HIV-infected black South Africans, 27% were diagnostic of HIVAN.[3] Another study from Nigeria has reported a high prevalence of renal disease (51.8%) among patients with AIDS compared to 12.2% in a healthy control group.[12] In the present study, glomerular filtration rate was estimated using Modification of Diet in Renal Disease (MDRD) equation; this has, however, not been validated in the HIV population. It is pertinent to note that the Infectious Disease Society of America (IDSA) recommends that MDRD can be used to assess kidney function in HIV positive patients.[5] The MDRD has been validated in African Americans, who might be considered to share some genetic similarity with other Africans, Nigerians included. However, literature is still limited on the prevalence of CKD in HIV positive patients in SSA. This study was carried out to determine the prevalence of CKD in HIV positive, HAART naive patients in Lagos, Nigeria.

Materials and Methods

Study population

Ethical approval was obtained from the ethics committee of the Lagos University Teaching Hospital (LUTH) Lagos, prior to the commencement of the study. This institution serves as a referral center for most of south-west Nigeria. The study was carried out between February and October 2007. The study enrolled consecutive new patients who tested positive for HIV at the HIV clinic of LUTH. The inclusion criteria included people who were at least 18 years of age, HIV sero-positive as confirmed by Western blot, HAART-naïve, non-hypertensive and non-diabetic patients able to provide written informed consent. A group of non-diabetic, non-hypertensive, HIV-negative and otherwise healthy individuals who had come for voluntary counselling and testing, and who consented to participate in this study were chosen as the control group. This was a cross-sectional design study and a questionnaire was administered to all participating patients and controls to document their demographic and clinical details. Blood pressure was measured using a validated Accoson® sphygmanometer. Blood was drawn from all participating subjects to assess: CD4 cell count, HIV RNA viral load, full blood count, serum electrolytes, urea, creatinine, fasting or random blood sugar, hepatitis B virus (HBV) and hepatitis C virus (HCV) serology. A spot-urine sample was used to assess the urine albumin-creatinine ratio (ACR) and macroalbuminuria was defined as ACR over 300mg/g.[5] The estimated glomerular filtration rate (eGFR) was calculated using the abbreviated equation of the Modification of Diet in Renal Disease (MDRD) where:
$186\times(\text{serum creatinine mg/dL})^{-1.154}\times(\text{age in years})^{-0.203}\times 0.742$ (females)$\times 1.210$ (blacks).

Serum creatinine values used were standardized to Cleveland study.[13,14] Chronic kidney disease was classified following K/DOQI guidelines.[15] We classified CKD as being present if eGFR was less than 60 mL/min/1.73 m^2 and/or if patients had persistent macroalbuminuria. Absence of CKD was classified as subjects with e GFR of more than 60 mL/min/1.73 m^2 and absence of persistent macroalbuminuria. HIV positive patients with macroalbuminuria (ACR ≥300mg/g) were requested to have a renal biopsy in order to ascertain the true pathology of renal disease. A radiologist assisted with ultrasound guided kidney biopsy and the kidney tissues were reported by the same pathologist in our institution.

Statistical analysis

Data were analyzed using EPI-INFO software (version 2002). All continuous variables were reported as mean values±standard deviation (SD). Categorical data were reported as frequencies with accompanying percentages in parenthesis. Differences between groups were compared using the χ^2 and Student's t-test for categorical and continuous variables, respectively. Fisher's exact P values are presented for comparison of categorical variables where appropriate. Multivariate linear regression analysis was performed to determine factors associated with CKD. P<0.05 was considered statistically significant. Odds ratio (OR) and 95% confidence interval (CI) were also given where appropriate.

Results

Table 1 shows the demographic and clinical variables of the 402 HIV-positive patients (73.4%) and 146 healthy controls (26.6%) who participated in the study. Age and gender distribution was similar in both groups (P>0.05) while systolic blood pressure (SBP) was significantly lower in HIV-positive patients (P=0.001). Serum creatinine was significantly higher in the HIV-positive group (P=0.001), while serum albumin was significantly higher in the HIV-negative group (P=0.011).

There were 2 and 2.2%, respectively, of HIV positive patients in stages 4 and 5 CKD compared to none in the HIV negative group (P=0.005) (Figure 1). Mean ACR was 255.2 ±400.5 mg/g (ACR in controls=55.5 ±42.3 mg/g; P<0.0001) and 80 HIV-positive patients (20.1%) had macroalbuminuria compared to 3 (2.1%) of controls (OR=12; 95% CI 3.7-38.5; P<0.0001). Chronic kidney disease was present in 95 patients (23.5%) and 8 controls (5.5%), OR=5.34 (95% CI 2.4-12.2; P<0.0001).

A linear relationship between ACR and progressive CKD stage was noted after stage 2 CKD and ACR was observed to have a marked increase in stage 4 CKD (Figure 2).

HIV-positive patients with CKD had significantly lower CD4 count compared to those without CKD (161.5±182.7 cells/mm^3 *vs* 242.6±191.5 cells/ mm^3; P=0.0003) and 69.5% of those with CKD had CD4 count that was lower than 200 cells/mm^3 (Table 2). Chronic kidney disease was statistically significantly higher in those who had CD4 count of 200 and below (P=0.0013).

Mean viral load in patients with CKD was 320112.8 ±301854.4 RNA copies/mL (range 200.0 to-750000.0 RNA copies/mL). Mean viral load for patients without CKD was 224827.8 ±277447.9 RNA copies/mL (range 200.0-

Table 1. Baseline characteristics of the study population.

Variable	HIV positive (n= 02)	HIV negative (n=146)	P
Females	250 (62.2%)	93 (63.7%)	NS
Age (years)	35±8.3	33±7.0	NS
Systolic blood pressure (mmHg)	112.7±14.4	121.6±16.5	0.001
Diastolic blood pressure (mmHg)	71.4±10.8	72.0±11.1	0.06
BMI (Kg/m^2)	22.1±4.2	24.3±4.7	0.07
Mean serum creatinine (µmol/l)	97.4±101.2	87.4±24	0.001
Mean serum albumin (g/dl)	3.7±0.3	3.8±0.3	0.011
Mean ACR (mg/g)	255.2±400.5	55.5±42.3	<0.0001
Mean CD4 count (Cells/mm^3)	223.4±192.3		
Mean viral load (RNA copies/mL)	245102.9±285487.8		

BMI, body mass index; ACR, albumin-to-creatinine ratio; RNA, ribonucleic acid.

750000.0 RNA copies/mL) (P=0.0091). On multivariate linear regression analysis to assess for factors associated with CKD, high ACR and HIV RNA viral load were the risk factors associated with CKD (Table 3).

Only 10 patients of all the HIV-positive patients with macroalbuminuria consented to a renal biopsy being performed. Classic HIVAN was found in 50%, HIV-associated immune complex disease was diagnosed in 30% and acute tubulo-interstitial nephritis in 20% (Figure 3).

Discussion

Sub-Saharan Africa has the greatest burden of HIV in the world with an estimated 22 million people living with AIDS. The largest epidemic in west Africa (Nigeria, Africa's most populous country) appears to have stabilized at 3.1% [2.3-3.8%], according to HIV infection trends among women attending antenatal clinics.[1] In South Africa, more than 5.7 million people are infected with HIV with a reported prevalence of 18.8% in economically active adults. The spread of HIV/AIDS in Africa has been reported to be directly related to powerful socio-economic and political factors that include limited availability and access to basic health care facilities, deficient communication and transportation infrastructures, and variable availability and access to HAART.[15]

In HIV positive patients, CKD has been shown to be an important cause of progression to ESRD in patients of African ancestry.[5,16-20] As HIVAN and other forms of kidney diseases associated with HIV are amongst the leading causes of ESRD in many SSA countries, this study adds to our knowledge of the epidemiology of CKD in SSA from two perspectives: i) the prevalence of CKD is high in HIV positive patients not yet on HAART; and ii) macroalbuminuria and HIV viral load are important markers of CKD in HIV positive patients.

The observed frequency of macroalbuminuria in this study (20.1%) is similar to frequencies that have been reported from similar studies conducted in other more homogenous ethnic groups within Nigeria.[12,21] Macroalbuminuria is a well-recognized risk factor for initiation and progression of CKD and may signify advanced (late) presentation in the patients in our study, especially as macroalbuminuria was found to worsen with progressive CKD stage. Late presentation to a nephrologist is common in many parts of SSA and has been shown to be due to the fact that in many countries there are few qualified nephrologists and to the lack of a functioning public health system.[22] The consequences of late presentation are well documented and include higher morbidity and mortality and increased cost to the health care system due to hospitalizations and procedures.[23] Wauters *et al.* have identified 4 reasons why patients with kidney disease often present late to the nephrologist and these include: i) disease-related factors (acute illness or asymptomatic disease); ii) patient-related factors (denial, co-morbid conditions, or low socio-economic status); iii)

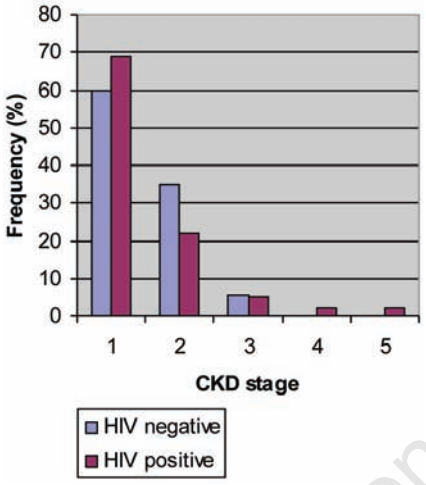

Figure 1. Chronic kidney disease stages in the study population.

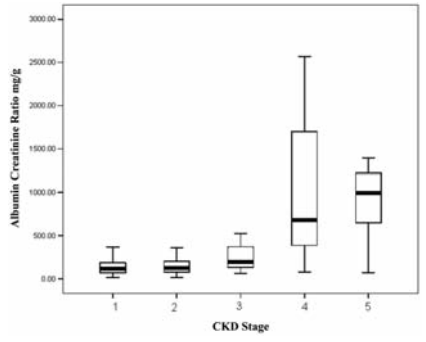

Figure 2. Relationship between stages of CKD and level of albuminuria.

Table 2. Relationship between CKD and CD4 count in HIV positive patients.

CD4 category	CKD absent** n (%)	CKD present* n (%)
CD4≥200 cells/mm^3 (n=178)	149 (83.7)	29 (16.3)
CD4<200 cells/mm^3 (n=224)	158 (70.5)	66 (29.5)

CKD, chronic kidney disease; χ^2=8.8, P=0.001; *CKD present if eGFR was <60 ml/min and/or there was persistent macroalbuminuria; **CKD absent if eGFR was >60 ml/min and/or no persistent macroalbuminuria.

Table 3. Multiple linear regression analysis of predictors of CKD in HIV positive patients.

Parameter	Odds ratio (OR)	95% CI	P
Viral load (copies/mL)	0.17	0.042- 0.29	0.010
CD4 cell count (cells/mm^3)	1.64	3.54- 25.93	0.09
Albumin creatinine ratio (mg/g)	6.25	5.37- 7.15	0.0001

Generalized linear model (with model-based estimation) using CKD as dependent variable, covariates/main effects explored (viral load, CD4 cell count and ACR).

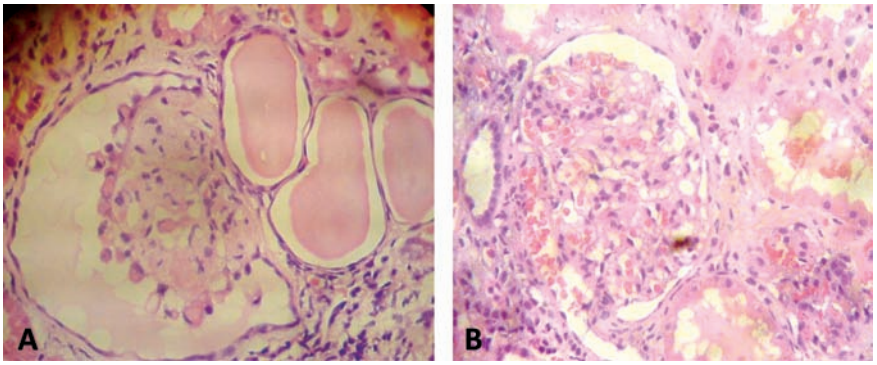

Figure 3. Biopsy in HIV-positive patients showing classic HIVAN (panel A) and acute tubulo-interstitial nephritis. A) collapsing glomerulopathy, epithelial cell hypertrophy and proliferation and microcystic dilatation of the tubules; B) interstitial infiltration with inflammatory cells, cast (debris) in the tubular lumen and normal glomerulus.

physician-related factors (primary care physician-related or policy of renal unit); and iv) health care system-related (limited access to care or limited access to specialized care).[24] A study on renal disease in anti-retroviral naïve patients in western Kenya have similarly reported worsening of proteinuria with progressive stages of CKD.[25] Together, this all suggests that simple and cheap methods of assessing for renal function, such as dipstick testing for proteinuria (or albumin-creatinine ratio in spot urine, where this is affordable), can be a useful tool to screen for renal disease in many parts of SSA where poverty is still a major factor affecting health care delivery. The ability to regularly perform such tests will allow for early identification of patients with renal disease (or worsening renal disease) and for appropriate treatment strategies to be initiated. Msango *et al.* found a CKD prevalence of 25% among similar group of HIV positive patients in Tanzania; this compares with the 23.5% seen in our study.[26]

In our study we also observed that CKD significantly correlated with low CD4 count (<200 cells/mm^3) and high HIV RNA viral load; both factors which have been previously reported from other studies and have been shown to be markers of untreated HIV or late presentation of disease.[11,21,25,27] That CKD was associated with a significantly higher viral load in our HIV positive CKD population may suggest that CKD in HIV infection is more likely a direct effect of viral replication in the kidneys, as earlier reported by other authors.[28-30] Szczech *et al.* reported a lower CD4 count and higher viral load among patients with proteinuria compared to others with microalbuminuria and no urinary abnormality.[31] In a study of 3,976 HIV positive patients designed to assess temporal changes in the incidence of HIVAN and the association with use of HAART, Lucas *et al.* reported a 60% (95% CI, -30 to -80%) reduced risk of HIVAN with no patient developing HIVAN following treatment with HAART.[32] Hence, early initiation of HAART in HIV positive patients could have a significant impact in the prevention and, possibly, recovery of renal function due to HIV infection.

Renal biopsy which is often necessary to determine the exact histology of renal disease in HIV positive patients could only be performed in 10 patients due to economic reasons (patients were required to pay for this in advance before the procedure was performed). Although the discussion on how poverty affects health care may be beyond the scope of this study, it must, however, be said that in order to reduce the burden of CKD and ESRD amongst Africans, socio-economic factors that impact negatively on health care will have to be addressed and it will be necessary to sustain HAART with measures that ensure regular monitoring of patients.

Limitations in this study include its cross-sectional design that meant only one screening test for albuminuria was used. Also the use of MDRD equation for eGFR that may have underestimated the GFR, as this equation was derived from a CKD population. The MDRD has not been validated in HIV patients and Nigerians. Finally, a renal biopsy could only be performed in a few patients due to economic factors. If more patients had been biopsied, the exact types of HIV renal disease (other than HIVAN) would have been determined.

Conclusion

There is clearly need for more epidemiological studies on the prevalence of CKD in many developing countries. As the prevalence of HIV-related kidney disease has been shown from several studies to be high in HIV positive patients, there is the need for increased screening and surveillance in this group of patients to ensure early detection of disease and institution of measures to slow progression of CKD. Although CKD is more common in patients with low CD4 count, severity of immunosuppression is not an independent risk factor for developing CKD in HIV infected subjects. HIV RNA viral load may be a useful surrogate marker for CKD as high viral load is an independent risk factor for developing CKD. Measures that increase awareness of HIV, and that encourage people to be tested and started on therapy, need to continue if countries in SSA are to contain the burden of ESRD.

References

1. Global report: UNAIDS report on Global AIDS Epidemic 2010. ''UNAIDS/10.11EJC 1958E''. Available from: http://www.unaids.org/globalreport/
2. Okpechi IG, Rayner BL, Swanepoel CR. Nephrotic Syndrome in Adult Black South Africans: HIVAN as the main culprit. J Natl Med Assoc 2010;102:1193-7.
3. Gernholtz TE, Goetsch SJW, Katz I. HIV–related nephropathy: A South African perspective. Kidney Int 2006; 69:1885-91.
4. Okpechi IG, Swanepoel CR, Rayner BL, et al. Patterns of Renal Disease in Cape Town South Africa: A 10-Year Review of a Single Centre Renal Biopsy Database. Nephrol Dial Transplant 2011;26:1853-61.
5. Gupta SK, Eustace JA, Winston JA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2005;40:1559-85.
6. Weiner NJ, Goodman JW and Kimmel PL. The HIV-associated renal diseases: Current insight into pathogenesis and treatment. Kidney Int 2003;63:1618-31.
7. Palella FJ, Delaney KM, Moorman AC, et al: Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998;26:853-60.
8. Selik RM, Byers RH Jr, Dworkin MS. Trends in diseases reported on US death certificates that mentioned HIV infection, 1987-1999. J Acquir Immune Defic Syndr 2002;29:378-87.
9. Abbott KC, Hypolite I, Welch PG, et al. Human immunodeficiency virus/acquired immunodeficiency syndrome-associated nephropathy at end-stage renal disease in the United States: Patient characteristics and survival in the pre highly active antiretroviral therapy era. J Nephrol 2001;14: 377-83.
10. Wyatt CM, Klotman PE. HIV-1 and HIV-Associated Nephropathy 25 Years Later. Clin J Am Soc Nephrol 2007;2:S20-4.
11. Han TM, Naicker S, Ramdial PK, et al. A cross-sectional study of HIV-seropositive patients with varying degrees of proteinuria in South Africa. Kidney Int 2006;69: 2243-50.
12. Agaba EI, Agaba PA, Sirisena ND, et al. Renal Disease in the Acquired Immunodeficiency Syndrome in North Central Nigeria. Nig J Med 2003;12:120-5.
13. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145: 247-54.
14. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-70.
15. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Am J Kidney Dis 2002;39:S1-S266.
16. Eggers PW, Kimmel PL. Is there an epidemic of HIV infection in the US ESRD program? J Am Soc Nephrol 2004;15:2477-85.
17. US Renal Data System (USRDS). USRDS 2005 Annual data report: atlas of end-stage renal disease in the United States. Bethesda, MD, National Institute of Diabetes and Digestive and Kidney Diseases, 2005.
18. Choi AI, Rodriguez RA, Bacchetti P, et al. Racial Differences in End-Stage Renal

Disease Rates in HIV Infection versus Diabetes .J Am Soc Nephrol 2007;18:2968-74.
19. Freedman BI, Soucie JM, Stone SM, et al. Familial clustering of end-stage renal disease in blacks with HIV-associated nephropathy. Am J Kidney Dis 1999;34: 254-8.
20. Martins D, Tareen N, Norris KC. The epidemiology of end-stage renal disease among African Americans. Am J Med Sci 2002;323:65-71.
21. Emem CP, Arogundade F, Sanusi A, et al. Renal Disease in HIV-Seropositive Patients in Nigeria: an Assessment of Prevalence, Clinical Features and Risk Factors. Nephrol Dial Transplant 2008;23:741-6.
22. Katz IJ, Gerntholtz T, Naicker S. Africa and Nephrology: The Forgotten Continent. Nephron Clin Pract 2011;117:320-7.
23. Schmidt RJ, Domico JR, Sorkin MI, et al. Early referral and its impact on emergent first dialyses, health care costs, and outcome. Am J Kidney Dis 1998;32:278-83.
24. Wauters JP, Lameire N, Davison A, et al. Why patients with progressing kidney disease are referred late to the nephrologist: on causes and proposals for improvement. Nephrol Dial Transplant 2005;20:490-6.
25. Wools-Kaloustian K, Gupta SK, Muloma E, et al. Renal disease in an antiretroviral-naïve HIV-infected outpatient population in Western Kenya. Nephrol Dial Transplant 2007;22:2208-12.
26. Msango L, Downs JA, Kalluvya SE, et al. Renal dysfunction among HIV-infected patients starting antiretroviral therapy. AIDS 2011;25:1421-5.
27. Winston JA, Klotman ME, Klotman PE. HIV-associated nephropathy is a late, not early, manifestation of HIV-1 infection. Kidney Int 1999;55:1036-40.
28. Bruggeman LA, Ross MD, Tanji N, et al. Renal epithelium is a previously unrecognized site of HIV-1 infection. J Am Soc Nephrol 2000;11:2079-87.
29. D'Agati V, Appel G.B. HIV infection and the kidney. J Am Soc Nephrol 1997;8:138-52.
30. Winston JA, Bruggeman LA, Ross MD, et al. Nephropathy and establishment of a renal reservoir of HIV type 1 during primary infection. N Engl J Med 2001;344: 1979-84.
31. Szczech LA, Menezes P, Quinlivan EB, et al. Microalbuminaria predicts overt proteinuria among patients with HIV infection. HIV Med 2010;11:419-26.
32. Lucas GM, Eustace JA, Sozio S, et al. Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. AIDS 2004; 18:541-6.