IJKD KIDNEY DISEASES

Prevalence and Associated Factors of Chronic Kidney Disease Among Patients Infected With Human Immunodeficiency Virus in Cameroon

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Introduction. Chronic kidney disease (CKD) is frequent amongst human immunodeficiency virus (HIV)-positive patients, and screening is not routinely performed in Sub-Saharan Africa due to resource constraints. We aimed to determine the prevalence of CKD and associated factors in HIV-infected patients in Cameroon.
Materials and Methods. A cross-sectional study in Northern Cameroon included HIV-positive patients who attended the HIV clinic. Patients with an estimated glomerular filtration rate less than 60 mL/min/1.73 m² or urinary abnormalities underwent a second measurement 3 months later. Glomerular filtration rate was estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. Logistic regression was used to identify factors associated with CKD.
Results. We included 709 participants. The median CD4 count was 219 cells/mL. Proteinuria accounted for 34.4%; leukocyturia, 6.9%; and hematuria, 6.1%. Prevalence of CKD was 44.4% (CKD-EPI) and 47.2% (MDRD). Stages 3 to 5 of CKD were documented in 11.6% using the CKD-EPI and 7.5% using the MDRD. Factors associated with CKD were an age greater than 35 years (odds ratio [OR], 104; 95% confidence interval [CI], 1.02 to 1.06), longer duration of HIV (OR, 2.60; 95% CI, 1.53 to 3.95), history of hepatitis B (OR, 3.04; 95% CI, 1.08 to 8.54), and CD4 cells less than 200 cells/mL (OR, 3.64; 95% CI, 2.55 to 5.21).
Conclusions. The prevalence of CKD is high among HIV patients in Cameroon. There is a need of implementing measures to encourage early detection of kidney disease in these patients.

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INTRODUCTION

Chronic Kidney Disease (CKD) is a major complication in patients infected with human immunodeficiency virus (HIV).[1] This is mainly due to the infection of renal cells by the virus itself; antiretroviral (ARV) medications and presence of others risk factors such as diabetes mellitus, hypertension, hepatitis C virus; and illicit drug use.[2-4] The risk of progression to end stage kidney disease (ESKD) is 2- to 20-fold greater in HIV patients compared to the general population. People of African descent borne the higher risk, with HIV-associated nephropathy being the most common and severe disease.[5] Guidelines recommend the evaluation of kidney function prior to initiation of ARV treatment, and during

follow-up in patients with risk factors,[6] but due to resources constraints, these recommendations are poorly applied in most low-income countries such as the sub-Saharan Africa (SSA). The HIV pandemic touched approximately 25 million people in SSA, and CKD with its silent course affects mostly young adults in their productive years.[7]

Few data exist on the epidemiology of CKD among HIV-infected patients, and the reported prevalence in Africa ranged from 6% to 48.5%.[8-10] This wide variation is due to the differences in study design, populations studied, and most of all definitions of CKD used. In most studies, kidney disease was defined as the presence of albuminuria or low estimated glomerular filtration rate (GFR) on a single measurement, and some studies did not perform serum creatinine measurements and others measured proteinuria only by dipstick. Reported potential factors associated with an increased risk of CKD in HIV-infected individuals include older age, black race, female sex, diabetes mellitus, hypertension, low CD4 cell count, high viral load, co-infection with hepatitis C virus, and specific antiretroviral drugs.[11,12]

Considering the extent of HIV epidemic, the resource limitations in SSA, the high cost of renal replacement therapy, and the growing number of people with ESKD, early detection and treatment of CKD is a priority. In Cameroon, a country in SSA, CKD and HIV are major public health problems affecting approximately 10% and 4.3% of the population, respectively.[13,14] Infection with HIV is the 4th leading etiology of ESKD among patients on hemodialysis.[15] Little is known about kidney disease among HIV patients in this resource-limited country, where kidney function is not routinely examined. A single cross-sectional study including 104 HIV patients naive to ARV treatment who underwent a single measurement of creatinine and urine analysis, reported a high prevalence of renal abnormalities.[16] The aim of the present study was to determine the prevalence of CKD and associated risk factors in HIV patients in Cameroon, in order to enable early treatment and delay progression to ESKD among these patients.

MATERIALS AND METHODS

Study Setting and Design

This was a cross-sectional study carried out from January to September 2014 at the HIV clinic of the Garoua Regional Hospital in the northern region of Cameroon. Garoua is the capital city of the region with 1 687 959 inhabitants.[17] The HIV clinic was established in 2003 and is the only center for the care of HIV patients in the city. A total of 3785 patients were registered in January 2014 and about 60 new patients were diagnosed monthly. In Cameroon, all patients have free access to ARV drugs since 2007 included in the national health program. This study was approved by the Institutional Ethics Committee of the Douala University, and authorization was obtained from the regional delegation of public health. Abnormal results were forwarded to the physician in charge of kidney disease in the hospital, such that appropriate decisions could be taken.

Study Participants

All consenting HIV-positive patients older than 16 years who attended the clinic during the study period were included and those with the following conditions were excluded: any acute or febrile illness, decompensated diabetes mellitus, pregnancy or menstruations, and leucocytes associated with nitrites on dipstick. Ethics approval was obtained from the ethics board of the Douala University and all of the participants signed a consent form.

Data Collection

Data were collected using patient's records and interview by a final-year medical student in the routine outpatient consultation. Variables collected were sociodemographics (age, sex, profession, and marital status), history of HIV infection (duration, ARV treatment, CD4 count), comorbidities (diabetes mellitus, hypertension, and hepatitis B and C), and use of nephrotoxic medications. For each patient, a sample of morning urine was collected before 9.0 AM in a sterile vial for dipstick analysis using a Combi Screen 10SL (Roche, Germany), and 3 mL of blood for standardized creatinine dosage using a compact automatic biochemistry analyzer ABX Pentra 400 (Chicago, USA). All patients with an estimated GFR less than or equal to 60 mL/min/1.73 m^2 or urinary abnormalities underwent a second urinalysis, blood analysis, or both, 3 months later.

Definitions of Operational Terms and Calculations

Glomerular filtration rate was estimated using

the 4-variable Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. The definition and classification of CKD were based on the Kidney Disease Improving Global Outcomes (2012).[18] Accordingly, CKD was defined as a GFR less than 60 mL/min/1.73 m^2 or urinary abnormality persistent for 3 months. Urinary abnormality was defined as isolated proteinuria (≥ 1+), hematuria (≥ 1+), or leukocyturia (≥ 1+). Chronic Kidney Disease was then classified in 5 stages.

Statistical Analysis

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, IL, USA). Qualitative and quantitative data were represented as percentage and mean ± standard deviation, respectively. The chi-square test and the 1-way analysis of variance were used to compare proportions and means between groups. Logistic regression was used to identify factors associated with CKD. A *P* value less than .05 was considered significant.

RESULTS

A total of 709 patients were included, 519 of whom (73.3%) were female. Baseline data are provided in Table 1. The mean age of the participants was 37.09 ± 10.18 years. The median CD4 count was 219 cells/mL (interquartile range, 128 cells/mL to 369 cells/mL). Three hundred and eleven patients (56.1%) were on ARV treatment with 196 (63%) of them including tenofovir. Ten patients (1.4%) had a history of hypertension and diabetes mellitus, respectively, 19 (2.7%) were co-infected with hepatitis B virus, and 85 (12%) were using traditional herbs. The mean estimated GFR (CKD-EPI) was 90.92 ± 25.82 mL/ min/1.73 m^2. A total of 244 patients (34.4%) had proteinuria, 43 (6.1%) had hematuria, and 49 (6.9%) had leukocyturia.

The overall prevalence of CKD was 44.4% according to the CKD-EPI and 47.2% according to the MDRD (Table 2). Patients with CKD stages 3 to 5 (GFR < 60 mL/min) accounted for 7.5% (54 patients) using the MDRD equation and 11.6% (83 patients) using the CKD-EPI, with 8 patients (1.1%) at stage 5.

In the multivariate analysis (Table 3), factors associated with CKD were an age greater than 35 years (odds ratio [OR], 104; 95% confidence interval [CI], 1.02 to 1.06), longer duration of HIV (OR, 2.60; 95% CI, 1.53 to 3.95), history of hepatitis B (OR, 3.04; 95% CI, 1.08 to 8.54), and CD4 cells less than 200 cells/mL (OR,3.64; 95% CI, 2.55 to 5.21).

Table 1. Baseline Characteristics of the Study Participants*

Characteristic	Value
Sex	
Female	520 (73.3)
Male	189 (26.7)
Age, y	37.09 ± 10.18 (16 to 69)
Matrimonial status	
Married	355 (50.4)
Non married	350 (49.6)
Education level	
None	370 (52.2)
Primary	202 (28.5)
Secondary	123 (17.3)
University	14 (2.0)
Profession	
Farmers and related	78 (11)
Officials	33 (4.7)
Students	19 (2.7)
Informal	161 (22.7)
Health care providers	6 (0.8)
Unemployed	412 (58.1)
History of diabetes	10 (1.4)
History of hypertension	10 (1.4)
Hepatitis B	19 (2.7)
Using traditional herbs	85 (12)
Nonsteroid anti-inflammatroy drugs	17 (2.5)
Using HAART	311 (43.9)
Protocols with tenofovir disoproxil fumarate	196 (63.0)
Clinical and biological data	
Systolic blood pressure, mm Hg	118.15 ± 17.66
Diastolic blood pressure, mm Hg	76.13 ± 10.69
Body mass index, kg/m^2	20.29 ± 3.22
CD4 cells, cells/mL	219 (128 to 369)
Creatinine, mg/L	9.83 ± 6.63
Hemoglobin, g/dL	10.92 ± 1.70
Glomerular filtration rate, mL/min/1.73 m^2	
MDRD	105.72 ± 34.47
CKD-EPI	90.92 ± 25.82
Proteinuria	244 (34.4)
Leukocyturia	49(6.9)
Hematuria	43 (6.1)

*Values are mean ± standard deviation (range) or frequency (percentage). CKD-EPI indicates Chronic Kidney Disease Epidemiology; HAART, highly active antiretroviral treatment; and MDRD, Modification of Diet in Renal Disease.

DISCUSSION

This study carried out in Northern Cameroon showed that HIV-infected outpatients were young

Table 2. Prevalence of Chronic Kidney Disease (CKD) According to Chronic Kidney Disease Epidemiology (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Equations

CKD Stage	Glomerular Filtration Rate, mL/min/1.73 m^2	MDRD	CKD-EPI
No CKD	≥ 90, without urine dipstick abnormality	374 (52.8)	366 (51.6)
1	≥ 90, with urine dipstick abnormality	173 (24.4)	154 (21.7)
2	60 to 89, with urine dipstick abnormality	108 (15.2)	106 (15)
3	30 to 59, with or without urine dipstick abnormality	40 (5.6)	69 (9.7)
4	15 to 29, with or without urine dipstick abnormality	6 (0.8)	6 (0.8)
5	< 15, with or without urine dipstick abnormality	8 (1.1)	8 (1.1)
Total CKD	…	335 (47.2)	343 (44.4)

Table 3. Associated Risk Factors of Chronic Kidney Disease (CKD) According to Chronic Kidney Disease Epidemiology (CKD-EPI) Equation

Factor	No CKD (n = 366)	CKD (n = 343)	Univariable Analysis		Multivariable Analysis	
			Odds Ratio (95% Confidence Interval)	*P*	Odds Ratio (95% Confidence Interval)	*P*
Age ≥ 35 years	156 (42.6)	206 (60.1)	2.02 (1.50 to 2.73)	< .001	1.04 (1.02 to 1.06)	< .001
Male sex	82 (22.4)	113 (32.9)	1.70 (1.22 to 2.37)	.002	1.35 (0.93 to 1.95)	.12
Hypertension	2 (0.5)	8 (2.3)	4.35 (0.92 to 20.61)	.06	2.47 (0.50 to 12.23)	.27
Diabetes mellitus	0	13 (3.8)	…	…	…	…
Hepatitis B	6 (1.6)	13 (3.8)	2.36 (0.88 to 6.29)	.09	3.04 (1.08 to 8.54)	.04
History of tuberculosis	53 (14.5)	65 (19.0)	1.38 (0.93 to 2.05)	.11	…	…
Use of traditional herbs	36 (10.0)	49 (14.3)	1.53 (0.97 to 2.42)	.07	1.38 (0.84 to 2.27)	.21
CD4 < 200 cells/mL	116 (31.7)	189 (55.1)	2.65 (1.95 to 3.59)	< .001	3.64 (2.55 to 5.21)	.001
Being on highly active antiretroviral treatment	146 (39.9)	165 (48.1)	1.40 (1.04 to 1.88)	.03	1.12 (0.70 to 1.81)	.63
Use of tenofovir	100 (27.3)	96 (28)	1.03 (0.74 to 1.43)	.84	…	…
Being on cotrimoxazole	58 (15.8)	62 (18.1)	1.17 (0.79 to 1.73)	.43	…	…
Duration of HIV ≥ 1 year	141 (38.5)	181 (52.8)	1.78 (1.32 to 2.40)	< .001	2.46 (1.53 to 3.95)	.001

adults with 3 quarters of them being females. The overall prevalence of CKD was 44.4% using the CKD-EPI, and 47.2% with the MDRD. The prevalence of CKD stages 3 to 5 was 11.6% with the CKD-EPI, and 1.1% of the patients were at stage 5. Factors associated with CKD were older age, history of hepatitis B, duration of HIV infection, and decreased CD4 cells.

Infection with HIV is epidemic in SSA and is a well-established risk factor for CKD. Guidelines recommend screening for CKD in HIV-infected patients before initiation of ARV treatment and during the follow-up.[6] In Cameroon, as in most countries in SSA, despite the recommendations, screening the kidney disease is not routinely performed. This study showed an overall prevalence of CKD among HIV-positive outpatients in the north region of Cameroon of at least 44%. Reported prevalence of CKD in HIV patients in Africa is variable ranging from 6 to 48% %, due to differences in study design, the type of participants and especially the heterogeneity in CKD diagnostic criteria.[8-10,19,20] Studies using the Kidney Disease Improving Global Outcomes definition as in the present study are scanty in SSA. A study by Cailhol and colleagues in Burundi using the same definition and same population as in this study had a similar result with an overall CKD prevalence of 45.7% (using MDRD) among 300 HIV patients.[8] This prevalence is one of the highest in the literature. Emem and coworkers in Nigeria had a prevalence of 38%, and this rate was 28.4% by Janaby and associates in Tanzania and 24% in the United States by Fernando and colleagues.[19,21,22] The high prevalence in our study can be explained by the fact that the majority of our patients were severely immunodepressed with a median CD4 count of 219 cells/mL. Studies have shown that kidney dysfunction increases with the severity of the HIV infection,[23,24] and also the presence of others CKD risk factor such as hypertension, diabetes mellitus and hepatitis among our study population could contribute to this high prevalence.

Early identification of kidney disease gives a

chance to implement treatments and prevent the kidney from further disease progression.[25] In the present study, patients with a GFR less than 60 mL/min/1.73 m^2 accounted for 11.6% of our sample using the CKD-EPI, and 7.5% with the MDRD. This is higher compared to the findings of Cailhol and colleagues in Burundi who had a prevalence of 2% with the MDRD and 4.9% with Cockroft-Gault. Also in Kenya, the rate was 4.8 % with the MDRD.[8] However, our result is in the range with the report of Sorli and coworkers in Spain (7.6%).[26] The prevalence of CKD stage 3 in this study was 7.6% using the MDRD, with 8 patients (1.1%) at stage 5. It is known that kidney function impairment is associated with increased risk of mortality, and dose adjustment of ARV treatment and other nephrotoxic drugs are necessary.[27] Identification and additional monitoring of this group of patients is primordial in our setting where the majority of patients are referred late to renal physician.

As the 4th leading cause of ESKD, HIV is associated with mortality of patients on hemodialysis.[28,29] Studies have shown that proteinuria, an early sign of kidney disease, is common in HIV-infected patients, and is associated with faster progression of HIV infection to AIDS and death.[30] Early detection of proteinuria in such a population is therefore primordial, but neglected in our setting. In the present study, 34.4% of participants had a persistent proteinuria of 1+ or more and this is in the range reported in the literature in Africa.[6,16] Nonetheless, this result is higher compared to the rate found in Burundi and Brazil.[6,31] This high prevalence can be the expression of HIV-associated nephropathy, a disease predominantly found in black population. Albuminuria is an independent risk factor of a poor prognosis among HIV-infected individuals and early detection could help with implementing measures to slow disease progression and improve outcome of these patients.[32]

Other urine abnormalities found in this study were hematuria (6.1%) and leukocyturia (6.9%). This prevalence is lower compared to other studies and can be explain by the presence of confounding factors such as the use of nonsteriod anti-inflammatory drugs, tuberculosis, and urologic abnormalities.[6,16,33]

As reported elsewhere, older age, longer duration of the HIV infection, history of hepatitis B, and low CD4 count were factors independently associated to kidney disease in this study.[34,35] Patients with HIV infection are at risk of developing nephrotoxicity in response to ARV drugs; in early reports protease inhibitors and tenofovir were associated to CKD.[11,12,36] In the present study, we found no association with tenofovir, probably because of the limited statistical power as only few patients were on that drug.

We acknowledge some limitations to this study: we did not assess for microalbuminuria in patient with normal dipstick although it has been shown to be the earliest marker of kidney disease, especially HIV-associated nephropathy.[37] Furthermore, estimation of estimated GFR and creatinine clearance can be affected by various factors that we did not explore such as medications, diet, and protein intake, but the confirmation of the persistent abnormality after 3 months reduces the risk of false positive. Given the high prevalence of CKD found in our setting, we believe these results should help to raise awareness on CKD among HIV-infected patients in this context and the need of strict application of recommended guidelines.

CONCLUSIONS

Despite recommendations, screening for kidney disease among patients with HIV is a neglected clinical goal in our setting and nephrologists deal with patients at advanced CKD stage. The prevalence of CKD in HIV-infected patients in this study was one of the highest in the literature, and potential risk factors are in accordance with others reports. This suggests a need of implementing measures to encourage early detection of kidney disease before initiation of ARVT and during follow-up. This may help to do dose adjustment of drugs, to institute measures to delay the progression of the kidney disease, and to reduce the rate of patients with ESKD.

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CONFLICT OF INTEREST

None declared.

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