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Prevalence and Risk Factors of CKD in South Kivu, Democratic Republic of Congo: A Large-Scale Population Study

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Background: The prevalence of chronic kidney disease (CKD) in African American individuals is high but whether this applies to native populations in sub-Saharan Africa is unclear.

Methods: In a cross-sectional study, we assessed the prevalence and risk factors of CKD in rural and urban adults in South Kivu, Democratic Republic of Congo. Glomerular filtration rate (GFR) was estimated using the CKD–Epidemiology Collaboration (CKD-EPI) equations based on serum creatinine (eGFRcr), cystatin C (eGFRcys), or both markers (eGFRcr-cys), without ethnic correction factor. CKD was defined as an eGFR $<$60 ml/min per 1.73 m^2 and/or albuminuria (albumin-to-creatinine ratio $\geq$30 mg/g).

Results: A total of 1317 participants aged 41.1 $\pm$ 17.1 years (730 rural, 587 urban) were enrolled. The prevalence of hypertension (20.2%; 95% confidence interval [CI], 18–22.3), diabetes mellitus (4.3%; 95% CI, 3.2–5.4) and obesity (8.9%; 95% CI, 7.4–10.5) was higher in urban than rural participants (all $P < 0.05$). HIV infection prevalence was 0.41% (95% CI, 0.05–0.78). The prevalence of eGFRcr $<$60 ml/min per 1.73 m^2 was 5.4% (95% CI, 4.2–6.7). The prevalence of albuminuria was 6.6% (95 % CI, 5.1–8.1). The overall prevalence of CKD was 12.2% (95% CI, 10.2–14.2) according to CKD-EPIcr. Factors independently associated with CKD-EPIcr were older age (adjusted odds ratio [aOR], 1.05 [1.04–1.07]), urban residence (aOR 1.86 [1.18–2.95]), female sex (aOR 1.66 [1.04–2.66]), hypertension (aOR 1.90 [1.15–3.12]), diabetes (aOR 2.03 [1.02–4.06]), and HIV infection (10.21 [2.75–37.85]). The results based on eGFRcys or eGFRcr-cys were largely consistent with the preceding.

Conclusion: Overall, the burden of CKD is substantial ($>$11%), predominantly in the urban area, and largely driven by classic risk factors (gender, aging, HIV, hypertension, and diabetes).

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The prevalence of CKD is rising in low- and middle-income countries.[1,2] Potential contributing factors are the persistence of communicable diseases (e.g., HIV infection, schistosomiasis, tuberculosis, malaria) combined with the growing burden of noncommunicable diseases (hypertension, diabetes, and obesity), triggered by rapid urbanization and adoption of Western lifestyle.[3,4] Facing this double burden, most sub-Saharan African (SSA) countries prioritize the fight against communicable diseases; thus, mortality from stage 5 CKD is extremely high because most affected individuals have no access to kidney replacement therapy.[5]

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In this context, screening for CKD and its modifiable risk factors should be prioritized, to implement interventions aiming at reducing incident CKD and slowing down progression of prevalent CKD. However, data on CKD prevalence in SSA are scarce and mostly of low quality, in particular due to the use of convenience samples and unreliable assessments of eGFR and albuminuria. In a recent systematic review and meta-analysis of CKD in SSA, Kaze *et al.*[6] found substantial heterogeneity across studies, especially regarding participant's selection methods and how GFR and albuminuria were estimated or measured. Indeed, the CKD-EPI equation, albeit recommended,[7] was used in only 5 of 25 studies of this meta-analysis. Similarly, the albumin-to-creatinine ratio was used in only 2 SSA population studies from Cameroon and Senegal, respectively.[6] Furthermore, all population-based studies from SSA estimated GFR solely from serum creatinine, which is more prone to bias from non-GFR determinants (muscle mass, physical activity, dietary meat consumption, health status) than cystatin C.[8,9]

Despite the rapid urbanization, African populations are still mostly rural,[10] but few CKD studies (7 of 90 studies [7.7%]) were conducted in rural areas.[11] There is thus a clear need for higher-quality studies on CKD prevalence in SSA across both urban and rural settings.

The aim of the present study was to assess the prevalence of eGFR <60 ml/min per 1.73 m^2 (using either creatinine, or cystatin C, or both markers), albuminuria (albumin-to-creatinine ratio), and CKD and its associated factors in a large sample, representative of urban and rural populations, in the South Kivu, Eastern province of the Democratic Republic of Congo (DRC).

MATERIALS AND METHODS

Study Design and Setting

We conducted a cross-sectional population-based study, between October 2016 and April 2017, in the South Kivu province, in the Eastern part of the DRC. The surface area of South Kivu is 65,070 km^2 with an estimated population of 6,742,196 inhabitants in 2017, distributed across 34 health zones (3 urban and 31 rural zones).[12]

Our study was conducted in 2 health zones (Ibanda and Katana), which served as strata for the sampling scheme. In the Katana rural area, inhabitants (222,491 inhabitants) are mostly farmers, largely from Bashi ethnicity. The Ibanda urban site (446,093 inhabitants) is a cosmopolitan city, inhabited by various ethnic groups originating both from South Kivu and from other DRC provinces.

Study Population and Sampling

Individuals aged $\geq$18 years were eligible to participate in this study. We used a multi-stage cluster sampling stratified by urban and rural status using the STEP-Ssampling.xls tool,[13] as follows: the health area (first stage), the village/street (second stage), and the household (third stage). If the parcel included several households, only 1 was randomly selected. Finally, from each household, a maximum of 2 participants were recruited. Self-declared pregnant women were excluded.

Sample Size Calculation

CKD prevalence was estimated at 12.4 % in adults from Kinshasa, the capital of DRC,[14] and assuming 5% margin of error (e), 5% level of significance, 1.5 for the cluster design effect, 4 age-sex estimates, and 20% of attrition rate, the minimal sample size (N) was calculated as follows: $N = 4^* 1.5 * Z^2 [P (1\text{-}P)] / e^2$.[13] Hence, a minimal sample size of 1200 was required to accurately estimate the prevalence of CKD.

Data Sources and Collection

Trained general physicians and nurse practitioners assisted by community health workers collected data during house-to-house visits. Sociodemographic information (age, sex, marital status, education level, and occupation), personal and family health history (regarding hypertension and diabetes), and lifestyle (smoking and alcohol consumption) of each participant were recorded. Education level was defined as no formal schooling, primary, secondary, and post-secondary (university).[15] Occupation of subjects was recorded as no formal job, business, government, or nongovernmental organization (NGO) job or farming.[16] The use of potentially nephrotoxic substances (nonsteroidal anti-inflammatory drugs and traditional herbal medicine) was also recorded. In all subjects, blood pressure was measured 3 times in the sitting position, using an automated sphygmomanometer (OMRON M6 Comfort; OMRON HealthCare Co., Ltd, Kyoto, Japan). The average of the last 2 measurements was used. Hypertension was defined as systolic blood pressure $\geq$140 mm Hg and/or diastolic blood pressure $\geq$90 mm Hg and/or self-reported use of antihypertensive medications.[17] Body weight and height were measured using standard methods and calibrated devices. Obesity was defined as a body mass index $\geq$30.0 kg/m^2.[18]

Laboratory Measurements

Blood and random spot urine samples were collected at the home for all participants. For capillary glucose, subjects were considered at the time of testing as fasting or nonfasting, based on self-declaration. Diabetes was defined as fasting glucose $\geq$126 mg/dl, postprandial glucose $\geq$200 mg/dl and/or self-declared

diabetes treated with glucose-lowering agent(s).[19] The samples were stored in an ice pack carrier, transported on the same day to the laboratory of Hôpital Provincial Général de Référence de Bukavu, centrifuged as appropriate, and stored at −20 °C. Frozen serum and urine samples were sent to the Clinical Chemistry laboratory of the Cliniques Universitaires Saint-Luc (Brussels, Belgium), where samples were thawed before analysis. Serum creatinine (compensated Jaffé method, IDMS-traceable), urinary albumin, and urinary creatinine were measured with a Roche Cobas analyzer (8000, module c702; Roche Diagnostics, Rotkreuz, Switzerland). Serum cystatin C was measured using a PETIA method on the SPA PLUS analyzer (Binding Site, Birmingham, UK). This method has been standardized according to the reference material ERM-DA471/IFCC. HIV seropositivity was detected by the Elecsys HIV Duo test, on the Roche Cobas analyzer (Roche Diagnostics, 8000, module e602). All HIV-positive or doubtful samples were reanalyzed in the Brussels AIDS Reference Laboratory, with the Vidas HIV DUO Ultra as confirmation test and the Geenius HIV 1/2 confirmatory assay to distinguish HIV-1 from HIV-2 infection.

Assessment of CKD

Glomerular filtration rate was estimated (eGFR) using the 3 CKD-EPI formulae: CKD-EPI-creatinine (eGFRcr), CKD-EPI-cystatin C (eGFRcys), and CKD-EPI-creatinine–cystatin C (eGFRcr-cys),[20] without correction for ethnicity. Recent evidence indeed suggests that it is more appropriate not to use the African American correction factor in SSA populations.[21,22] CKD was classified according to the Kidney Disease: Improving Global Outcomes (KDIGO) guideline, using the combination of eGFR and albuminuria. A low eGFR was defined as eGFR <60 ml/min per 1.73 m^2 based on serum creatinine, cystatin C, or both. CKD was defined by eGFR <60 ml/min per 1.73 m^2 and/or albumin-to-creatinine ratio (ACR) ≥30 mg/g.[7]

Statistical Analyses

All analyses were performed using Stata, version 12.1 (StataCorp LP, College Station, TX). Normally distributed continuous variables are presented as means ± 1 SD, whereas non-normally distributed variables are presented as medians [interquartile range], and qualitative variables as crude counts and percentages. Proportions and means were compared by Pearson's χ^2 test or Student's t test, as appropriate. We estimated the prevalence of CKD according to age, sex, and urban or rural residency.

We carried out univariate and multivariable generalized linear regression models for the binomial family to identify the factors independently associated with albuminuria (ACR ≥30 mg/g), low eGFR (< 60 ml/min per 1.73 m^2) and CKD using the 3 CKD-EPI equations. We used a clustered robust standard error to account for the potential clustering effect in villages or streets. Our initial strategy for selecting variables in multivariate regression models was based on either a $P \leq 0.1$ in univariate analysis or on biological and epidemiological plausibility. We ended up retaining all the key variables examined in univariate regression models. A P value less than 0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the Ethics Committee of the Université Catholique de Bukavu (Commission Institutionnelle d'Ethique, #UCB/CIE/NC/015/2016) and was authorized by the South Kivu Provincial Health Division (#973/CD/DPS-SK/2016). Informed consent was obtained from all participants before enrollment.

RESULTS

Inclusion and General Characteristics of Participants

A total of 1350 subjects were approached by the study staff. Twenty-four subjects were excluded due to ongoing pregnancy and 9 subjects declined to participate. Overall, 1317 of 1350 individuals (730 in the rural site and 587 in the urban site) were included (97.5%). A flow chart of the study population and laboratory measurements is depicted in Figure 1.

Tables 1 and 2 summarize the demographics and clinical characteristics of the study population. The mean age of participants was 41.1 ± 17.1 years, without significant difference by sex. Most participants were women (n = 802; 60.9%). Compared with urban subjects, rural participants were older (44.6 years vs. 36.7 years, $P < 0.001$), less educated, and more frequently farmers. In contrast, urban residents were more likely to use herbal medicines and/or nonsteroidal anti-inflammatory drugs. Furthermore, the overall prevalence of hypertension 20.2% (95% CI, 18.0–22.3), diabetes mellitus 4.3% (95% CI, 3.2–5.4), and obesity 8.9% (95% CI, 7.4–10.5) was higher in individuals living in the urban than rural area (all $P <$ 0.05). The prevalence of hypertension and diabetes did not differ by sex, whereas obesity was more prevalent in women than men (13% vs. 2.4%, $P < 0.001$). The prevalence of HIV infection (hitherto undiagnosed in all 5 subjects) was 0.41% (95% CI, 0.05–0.78), without difference by site or sex.

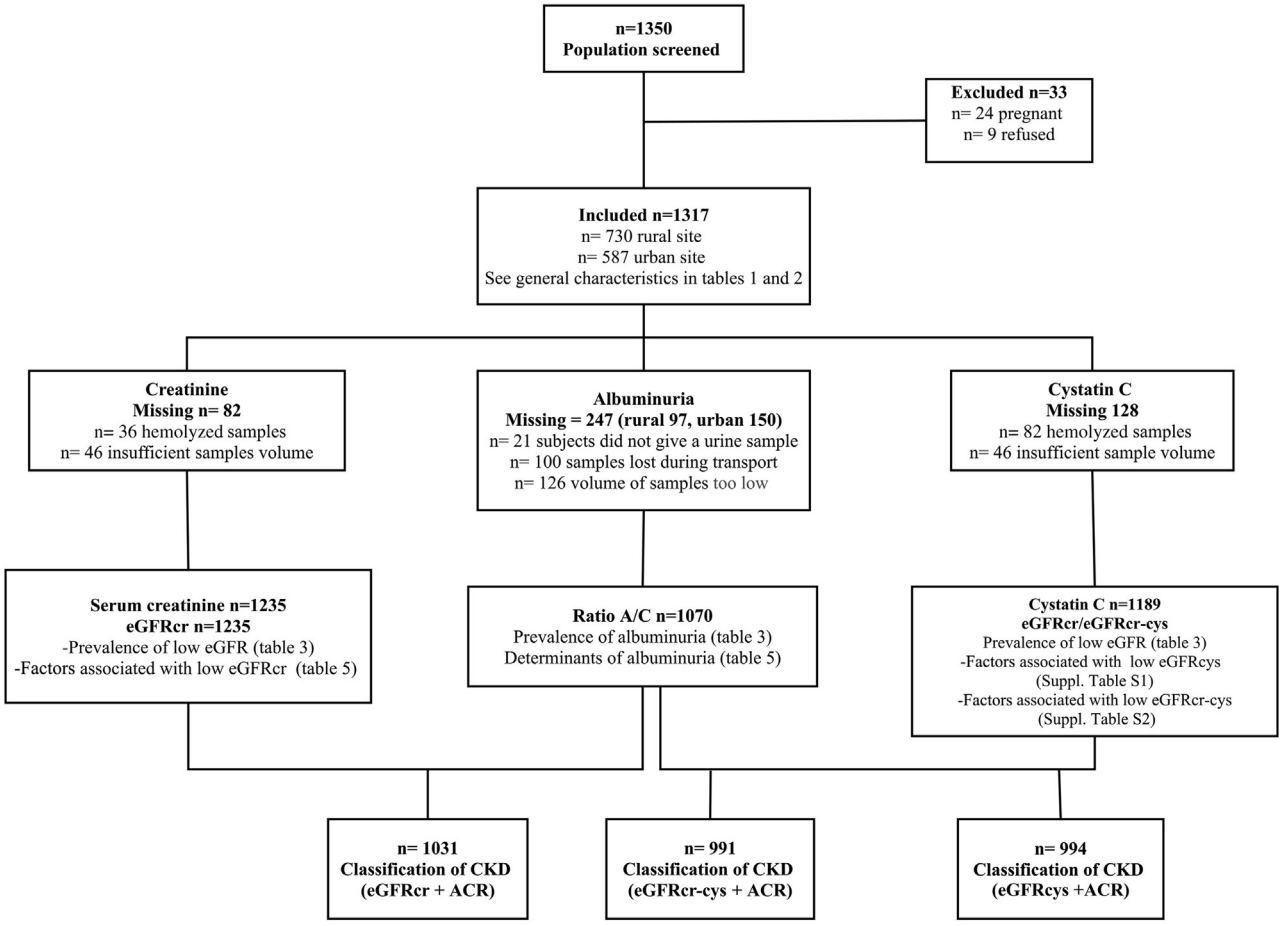

Figure 1. Flow chart of the study population and data availability. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; eGFRcr, eGFR based on serum creatinine; eGFRcys, Cystatin C; eGFRcr-cys, eGFR base on both serum creatinine and Cystatin C.

Prevalence of Albuminuria, eGFR <60 ml/min per 1.73 m^2, and CKD

As shown in Table 3, the prevalence of albuminuria was 6.6 % (95% CI, 5.1–8.1) without difference by site or sex. eGFR was similar in rural and urban subjects using all equations except for eGFRcys, which was higher in urban than rural subjects (94.1 ± 21.1 vs. 91.5 ± 21.1, $P = 0.03$). In addition, eGFRcr was higher in men (97.3 ± 22.2) than women (92.8 ± 22.9, $P < 0.001$).

The overall prevalence of CKD was 12.2% (95% CI, 10.2–14.2), 13.8% (95% CI, 11.6–15.9), and 11.5% (95% CI, 9.5–13.4), based on the eGFRcr, eGFRcys and eGFRcr-cys CKD-EPI equations, respectively. Independently of the equation used, the overall prevalence of CKD did not differ by site. Similarly, the prevalence of CKD did not differ by sex, except for eGFRcr. In that case, CKD was more frequent in women than men (14.3% vs. 8.2%, $P < 0.001$).

Stratified by age groups of 18 to 35, 36 to 45, 46 to 55, 56 to 65, and >65 years, CKD prevalence (or low eGFR) increased with age group regardless of the eGFR equation used (Figures 2 and 3).

The classification of patients by CKD stage (G1 to G5) using the CKD-EPIcr equation showed the following: G1, 3%; G2, 2.8%; G3a, 4.1%; G3b, 0.6%; G4, 0.3%; and G5, 0.2%; respectively. Compared with CKD-EPIcr (4.7%), the prevalence of CKD stage 3 was 6.0% and 4.1% with CKD-EPIcys and CKDcr-cys, respectively (Table 4).

Predictors of eGFR <60 ml/min per 1.73 m^2, Albuminuria and CKD By Logistic Regression

In univariate regression analysis, older age (uOR, 1.08 [1.06–1.11]), female sex (uOR, 1.99 [1.14–3.50]), hypertension (uOR, 6.46 [3.84–10.70]), and diabetes (uOR, 3.10 [1.43–6.99]) were significantly associated with an eGFRcr <60 ml/min per 1.73 m^2. Furthermore, older age (uOR, 1.02 [1.01–1.03]), hypertension (uOR, 2.57 [1.55–4.28]), diabetes (uOR, 5.20 [2.51–10.78]), and HIV infection (uOR, 14.27 [1.9–102.9]) were significantly associated with albuminuria (Supplementary Table S1).

In multivariable regression, diabetes (aOR, 4.20 [1.85–9.51]) and HIV infection (aOR, 19.4 [4.16–89.44]) were the main predictors of albuminuria, whereas the aOR of low eGFRcr was significant for age (aOR, 1.09 [1.06–1.11]), sex (aOR, 1.97 [1.05–3.69]), urban resi-

Table 1. General characteristics of the study population stratified by site and sex

Characteristics	Overall $n = 1317$	Rural $n = 730$	Urban $n = 587$	*P* value	Male $n = 515$	Female $n = 802$	*P* value
Age, y	41.1 ± 17.1	44.6 ± 17	36.7 ± 16.4	<0.001	40.4 ± 17	42.1 ± 17.3	0.07
Female, *n* (%)	802 (60.9)	432 (59.3)	370 (63.3)	0.15			
Professional, *n* (%)				<0.05			<0.05
Gov.employ./NGOs	123 (9.3)	57 (7.8)	66 (12.2)		86 (16.7)	37 (4.6)	
Farming	526 (40)	519 (71.1)	7 (1.2)		178 (34.6)	348 (43.4)	
Business	128 (9.8)	45 (6.2)	83 (14.2)		63 (12.2)	65 (8.1)	
None	540 (40)	109 (14.9)	431 (73.4)		188 (36.5)	352 (43.9)	
Education level, *n* (%)				<0.05			<0.05
None	483 (36.7)	395 (54.1)	88 (15)		125 (24.3)	358 (44.6)	
Primary	280 (21.3)	194 (26.6)	86 (14.7)		130 (25.2)	150 (18.7)	
Secondary	420 (31.9)	132 (18.1)	288 (49.1)		184 (35.7)	236 (29.4)	
Post-secondary	134 (10.2)	9 (1.2)	125 (21.3)		76 (14.8)	58 (7.2)	
Marital status, *n* (%)				<0.05			
Married	938 (71.2)	576 (78.9)	362 (61.7)		387 (75.1)	551 (68.7)	<0.05
Single	238 (18.1)	57(7.8)	181 (30. 8)		106 (20.6)	132 (16.5)	NS
Divorced/Widowed	125 (9.5)	84 (11.5)	41 (7)		11 (2.1)	114 (14.2)	<0.05
Current smoking	71 (5.4)	53 (7.3)	18 (3.1)	<0.05	47 (9.1)	24 (3)	<0.05
Alcohol consumption	562 (42.7)	344 (47.1)	218 (37.1)	<0.05	305 (59.2)	257 (32)	<0.05
Use of medicinal plants	293 (22.2)	121 (16.6)	172 (29.3)	<0.05	118 (22.9)	175 (21.8)	NS
Use of NSAIDs	435 (33)	212 (29)	223 (38)	<0.05	166 (32.2)	269 (33.5)	NS
Family history, *n* (%)							
Diabetes	177 (13.4)	25 (3.4)	152 (25.9)	< 0.001	68 (13.2)	109 (13.5)	NS
Hypertension	347 (26.3)	109 (14.2)	238 (40.5)	< 0.001	116 (22.5)	231 (28.8)	0.012
Personal history, *n* (%)							
Hypertension	148 (11.2)	90 (12.3)	58(9.9)	0.17	39 (7.6)	109 (13.6)	0.001
Diabetes	36 (2.7)	8 (1.1)	28 (4.8)	< 0.001	16 (3.1)	20 (2.5)	NS

Gov.employ., government employment; NGOs, nongovernment organizations; NS, not significant; NSAIDs, nonsteroidal anti-inflammatory drugs.

dency (aOR, 2.34 [1.35–4.07]), and hypertension (aOR, 2.35 [1.09–5.04]), but not for diabetes (Table 5). However, only age (aOR, 1.12 [1.10–1.15]) was independently associated with low eGFRcys.

In addition, in multivariable analysis, independent predictors of CKDcr were older age (aOR, 1.05 [1.04–1.07]), urban residence (aOR, 1.86 [1.18–2.95]), female sex (aOR, 1.66 [1.04–2.66]), hypertension (aOR, 1.90 [1.15–3.12]), diabetes (aOR, 2.03 [1.02–4.06]), and HIV infection (10.21 [2.75–37.85]). Using CKDcys or CKDcr-cys, CKD was more prevalent in older participants, urban residents, diabetic individuals, and HIV-positive patients (Supplementary Tables S2 and S3). Subjects who did not use medicinal plants had significantly higher odds of having albuminuria (aOR, 4.62 [2.03–10.50], $P = 0.001$) and CKD, but not of having eGFR <60 ml/min per 1.73 m^2 whatever the equation used.

DISCUSSION

To the best of our knowledge, this is the first study of CKD prevalence in a large population from SSA, covering both rural and urban settings, and using the best routinely available markers.

The overall prevalence of CKD was 12.2% by CKD-EPIcr, 13.8% by CKD-EPIcys, and 11.5% by CKD-EPIcr-cys, respectively. In addition, the prevalence of low eGFR (<60 ml/min per 1.73 m^2) was 5.4% by CKD-EPIcr, 6.7 % by CKD-EPIcys, and 4.7 % by CKD-EPIcr-cys, respectively. CKD was independently

Table 2. Clinical characteristics of the study population stratified by site and sex

Characteristics	Overall $n = 1317$	Rural $n = 730$	Urban $n = 587$	*P* value	Male $n = 515$	Female $n = 802$	*P* value
Weight, kg	59.7 ± 12.4	56.1 ± 9.8	64.0 ± 13.9	<0.001	59.9 ± 10.1	59.5 ± 13.7	0.57
Height, cm	160.2 ± 8.5	159.6 ± 8.4	160.9 ± 8.6	0.03	165.5 ± 8	157.0 ± 7.2	<0.001
Body mass index, kg/m^2	23.3 ± 4.3	22.1 ± 3.4	24.8 ± 4.9	<0.001	22 ± 3	24.1 ± 4.8	<0.001
Systolic blood pressure, mm Hg	122 ± 20.7	121.5 ± 20.5	123.3 ± 21.0	0.28	124.3 ± 18.4	120.6 ± 22	0.002
Diastolic blood pressure, mm Hg	78.8 ± 11.8	77.5 ± 11.6	80.4 ± 12.0	<0.001	78.9 ± 11.4	78.7 ± 12.2	0.78
Obesity, *n* (%)	115 (8. 9)	21 (3)	94 (16.3)	<0.001	12 (2.4)	103 (13)	<0.001
Hypertension, *n* (%)	266 (20.2)	134 (18.4)	132 (22.5)	0.06	102 (19.8)	164 (20.4)	0.77
Diabetes, *n* (%)	57 (4.3)	21 (2.9)	36 (6.1)	0.004	24 (4.7)	33 (4.1)	0.67
HIV infection, *n* (%)	5 (0.4)	1 (0.1)	4 (0.8)	0.96	3 (0.6)	2 (0.3)	0.34

Table 3. Biological characteristics of the study population stratified by site and sex

Characteristics	Overall $n = 1317$	Rural $n = 730$	Urban $n = 587$	*P* value	Male $n = 515$	Female $n = 802$	*P* value
Kidney markers							
Creatinine, mg/dl	0.89 ± 0.49	0.87 ± 0.49	0.92 ± 0.49	0.07	0.98 ± 0.51	0.83 ± 0.46	<0.001
Cystatin C, mg/l	0.93 ± 0.28	0.93 ± 0.28	0.93 ± 0.29	0.49	0.96 ± 0.31	0.90 ± 0.27	<0.001
eGFR, ml/min per 1.73 m^2							
CKD-EPI creatinine	94.6 ± 22.7	94.8 ± 22.8	94.4 ± 22.7	0.77	97.3 ± 22.2	92.8 ± 22.9	<0.001
CKD-EPI cystatin C	92.6 ± 21.1	91.5 ± 21.1	94.1 ± 21.1	0.03	92.1 ± 21.1	92.9 ± 21.1	0.541
CKD-EPI combined	100.4 ± 21.6	100.1 ± 21.7	100.9 ± 21.6	0.51	101.9 ± 21.2	99.4 ± 21.9	0.052
Urinalysis, *n* (%)							
ACR ≥ 30 mg/g, $n = 1070$	71 (6.6)	38 (6)	33 (7.6)	0.31	25 (5.9)	46 (7.1)	0.431
CKD prevalence							
Stages 3–5 (eGFR <60 ml/1.73 m^2), *n* (%)							
CKD-EPI creatinine, $n = 1235$	67 (5.4)	34 (4.9)	33 (6.1)	0.34	17 (3.5)	50 (6.7)	0.014
CKD-EPI cystatin C, $n = 1189$	80 (6.7)	48 (7.1)	32 (6.3)	0.55	30 (6.4)	50 (6.9)	0.736
CKD-EPI combined, $n = 1186$	56 (4.7)	27 (4)	29 (5.7)	0.26	18 (3.9)	38 (5.3)	0.256
Overall (eGFR <60 and/or ACR ≥ 30)							
CKD-EPI creatinine, $n = 1046$	128 (12.2)	67 (10.9)	61 (14.1)	0.11	38 (8.2)	90 (14.3)	0.011
CKD-EPI cystatin C, $n = 1009$	139 (13.8)	82 (13.6)	57 (14.1)	0.82	50 (12.5)	89 (14.6)	0.341
CKD-EPI combined, $n = 1002$	115 (11.5)	61 (10.2)	54 (13.4)	0.11	38 (9.5)	77 (12.8)	0.110

ACR, albumin-to-creatinine ratio; CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration equation; eGFR, estimated glomerular filtration rate.

associated with urban residence, older age, female sex, hypertension, diabetes, and HIV infection.

Our overall CKD prevalence estimate is lower than the 17.7% reported in a recent meta-analysis of CKD in SSA.[6] Nevertheless, the comparison of our robust estimate with previous studies is hampered by limitations in the methods previously used to estimate GFR. We reported eGFR prevalence using the CKD-EPI creatinine equations while omitting the ethnic African American correction factor, as recent evidence showed that this equation best matches (albeit still imperfectly) the gold (GFR) standard in SSA.[21,22] It is known that using this ethnic coefficient systematically overestimates eGFR in the general population and prevalence rates calculated with ethnic correction are lower.[23] For example, in rural Ghanaians, Eastwood *et al.*[24] found that CKD prevalence increased from 1.7% to 4.7% when the ethnic factor was omitted in the CKD-EPI equation. Therefore, if previous estimates of CKD prevalence in SSA were revised by omitting this correction factor, the burden of CKD (especially of low eGFRcr) in SSA would be reevaluated upward. Besides the ethnic

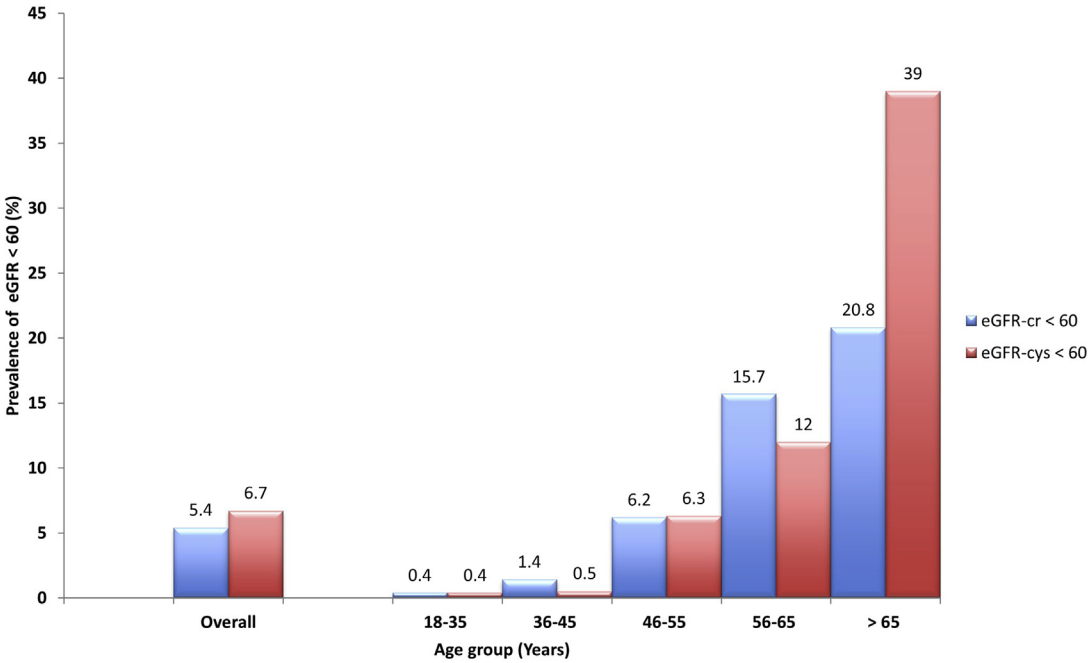

Figure 2. Prevalence of low estimated glomerular filtration rate (eGFR) by age group (using Chronic Kidney Disease–Epidemiology Collaboration serum creatinine [CKD-EPIcr] and CKD-EPI Cystatin C [CKD-EPIcys]).

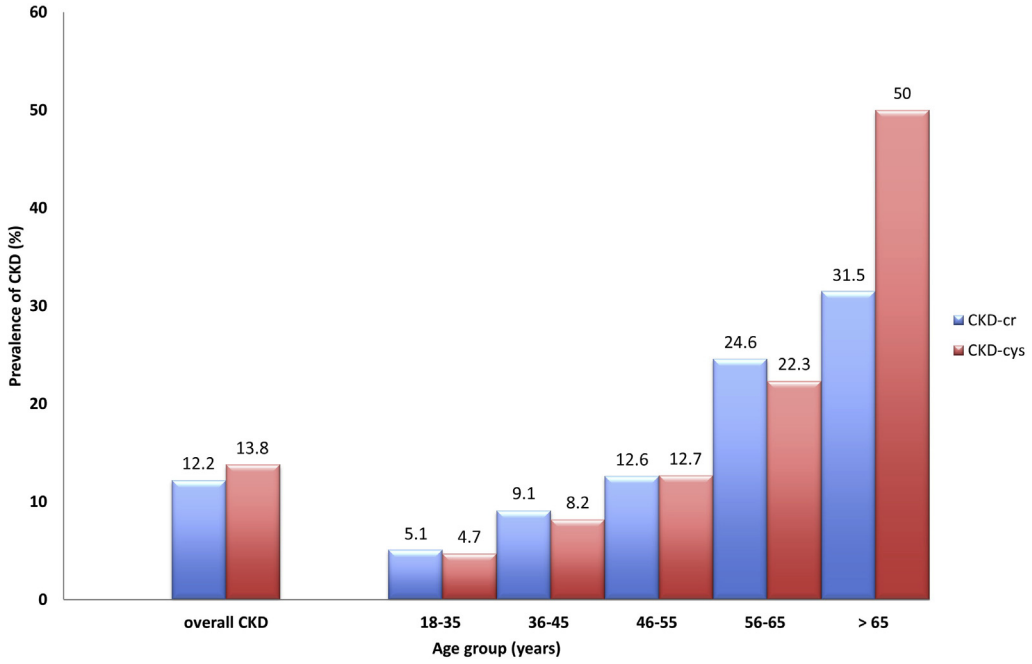

Figure 3. Prevalence of chronic kidney disease (CKD) by age group (using Chronic Kidney Disease–Epidemiology Collaboration serum creatinine [CKD-EPIcr] and CKD-EPI Cystatin C [CKD-EPIcys]).

coefficient factor, other issues including the lack of calibration of creatinine measurement, the choice of older eGFR equations (Cockcroft-Gault, Modification of Diet in Renal Disease), and the dearth of studies using ACR strikingly limit the accuracy of most previous studies of CKD prevalence in SSA.[6,11]

We further estimated GFR using CKD-EPI cystatin C and combined creatinine–cystatin C equations. This is a major strength of this study, as differences in muscle mass, dietary habits, and nutritional status, which impact creatinine generation, may differ between urban versus rural settings.[9] The respective performance of the 3 equations was beyond the scope of this study, as GFR was not measured. However, recent evidence in a cohort from Kinshasa showed similar (good) performance of the CKD-EPIcr and CKD-EPIcys equations, both without ethnic factor.[22] Interestingly after adjustment for age, sex, and other risk factors, living in an urban setting was independently associated with CKD by all 3 eGFR equations. Our findings are in line with studies performed in Tanzania[25] and Ghana,[26] but contrast with a study conducted in Cameroon, reporting CKD to be more prevalent (14.1% vs. 10.9%) in rural vs urban populations.[27]

In the present study, hypertension and diabetes were associated with CKD as in Kinshasa, the capital of DRC. However, the prevalence of hypertension and diabetes was lower in our study than the 27.7% (hypertension) and 11.7% (diabetes) prevalence reported by Sumaili *et al.*[14] in an urban population from Kinshasa. It should be noted that some studies found no association between hypertension or diabetes and CKD in SSA,[28,29] suggesting that additional specific causes of CKD may be at play in SSA, especially genetic factors (such as *APOL1* genetic variants) and communicable diseases (e.g., HIV infection, schistosomiasis, malaria, tuberculosis).[28,30–32] Our prevalence estimate of HIV infection (0.41%) is low compared with the 1.2% to 1.8% previously reported in the DRC, often obtained from women attending prenatal consultation services.[33] Our result highlights the importance of general population surveys to assess the exact magnitude of HIV prevalence in developing countries.

The decline of kidney function observed with aging with all 3 equations confirms many previous studies from the United States[34] and Europe.[35] It is noteworthy that in our SSA study, the prevalence of CKD rises sharply in the 40 to 69 age category, highlighting the need for additional studies to assess the causes of this finding.

Table 4. CKD stages distribution using 3 CKD-EPI equations

CKD stage	CKD-EPI creatinine *n* = 1031	CKD-EPI cystatin C *n* = 994	CKD-EPI combined *n* = 991
1	31 (3)	31(3.1)	32 (3.2)
2	29 (2.8)	28 (2.8)	27 (2.7)
3a	42 (4.1)	49 (4.9)	36 (3.6)
3b	6 (0.6)	11(1.1)	5 (0.5)
4	3 (0.3)	3 (0.3)	2 (0.2)
5	2 (0.2)	2 (0.2)	2 (0.2)

ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration equation.
Values are expressed as absolute *n* (%). The numbers of subjects staged for CKD may be variable in each column, as staging was performed only in individuals with both ACR and the mentioned GFR marker(s).

Table 5. Multivariable logistic regression of factors associated with albuminuria, eGFRcr < 60 ml/min per 1.73 m^2 and CKDcr (eGFR <60 ml/1.73 m^2 and/or ACR ≥30 mg/g)

	Albuminuria aOR (95% CI)	*P* value	eGFR < 60 ml/min per 1.73 m^2 aOR (95% CI)	*P* value	CKD aOR (95% CI)	*P* value
Age, y	1.02 (1.00–1.03)	0.04	1.09 (1.06–1.11)	<0.001	1.05 (1.04–1.07)	<0.001
Sex (female)	1.23 (0.68–2.20)	0.48	1.97 (1.05–3.69)	0.03	1.66 (1.04–2.66)	0.03
Site (urban)	1.35 (0.72–2.53)	0.34	2.34 (1.35–4.07)	0.002	1.86 (1.18–2.95)	0.007
Smoking	1.89 (0.70–5.10)	0.21	0.58 (0.10–3.58)	0.56	1.35 (0.53–3.43)	0.53
Alcohol	1.09 (0.58–1.98)	0.78	1.75 (0.92–3.32)	0.08	1.30 (0.82–2.05)	0.26
NSAIDs	1.04 (0.62–1.73)	0.88	0.86 (0.48–1.34)	0.61	0.92 (0.59–1.43)	0.72
No use of medicinal plants	4.62 (2.03–10.50)	0.001	2.09 (0.98–4.47)	0.06	2.65 (1.46–4.82)	0.001
Obesity	1.15 (0.51–2.60)	0.99	0.70 (0.29–1.70)	0.44	0.94 (0.46–1.92)	0.87
Hypertension	1.60 (0.83–3.06)	0.16	2.35 (1.09–5.04)	<0.01	1.90 (1.15–3.12)	0.012
Diabetes	4.20 (1.85–9.51)	0.001	0.77 (0.32–1.81)	0.55	2.03 (1.02–4.06)	0.04
HIV	19.4(4.16–89.44)	0.001	NA		10.21 (2.75–37.85)	0.001

ACR, albumin-to-creatinine ratio; aOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; CKDcr, CKD creatinine; eGFR, estimated glomerular filtration rate; eGFRcr, eGFR creatinine; NA, not applicable (no subject with HIV infection had a low eGFR); NSAID, nonsteroidal anti-inflammatory drug.

In this study, CKD was more prevalent in women than men, in agreement with most population-based studies.[3,36] This is generally ascribed to the longer life expectancy of women than men and/or to the normalization of eGFR by a constant body surface area in men and women.[36]

In the current study, herbal medicinal plants were much more regularly used by the urban than rural population (29.2% vs. 16.6%) and rather surprisingly; not using medicinal plants was associated with CKD (although the association was accounted for albuminuria, and not by low eGFR). The self-declared use of herbal remedies in this survey was lower than the 80% reported by Stanifer *et al.*[11] in SSA. The use of herbal medicinal plants has previously been linked to 35% of all new cases of acute kidney injury in SSA.[11] Our finding of an apparent protective role of herbal derivatives against albuminuria should be interpreted with caution, given the cross-sectional study design. Indeed, the temporal relationship and the biological mechanisms if any linking the exposure with outcome cannot be established.

Study Strengths and Limitations

The present study has many strengths, including a population-based design, a large sample size, and stratification by urban and rural residence. It is the first study assessing the prevalence of CKD using serum cystatin C in a representative population from SSA. Furthermore, in contrast to most previous studies in SSA,[6] ACR was measured and measurements of both creatinine and cystatin C were traceable to the international standard reference material. In addition, our statistical analysis accounted for the potentially clustered nature of the data by village or street.

Our study has limitations. First, the estimates were based on single-time measurements rather than on abnormalities for 3 or more months, as recommended by the Kidney Disease: Improving Global Outcomes guidelines.[7] This limitation is, however, the rule in other large-sized cross-sectional studies. Second, similarly to all previous studies of CKD prevalence in SSA, we did not directly measure GFR. Third, the cross-sectional nature limits causal inferences. Fourth, the study was conducted in only 2 of the 34 health zones of the South Kivu Province, although we included both a rural and an urban area. Therefore, our findings may not be generalizable to the entire South Kivu province nor the wider sub-Saharan region. Finally, there were some missing data for albuminuria, creatinine, and cystatin C, preventing CKD classification in a minority of subjects. Participants with missing data for albuminuria or creatinine were mostly urban residents and obese, but other characteristics (such as age, sex, existing diabetes or hypertension) did not differ between those with and without missing data (Supplementary Tables S4, S5). Fortunately, our sample size remained large enough (≈1000 subjects) to draw reliable conclusions on CKD prevalence by using complete case analyses, as recommended for handling missing data.[37]

This study also highlights the feasibility, albeit with some challenges, of research in SSA, particularly with respect to funding, complex access to rural areas, logistics, and clinical laboratory facilities. For the latter, we and others used the sole alternative, that is, to ship samples overseas,[14,22,31] after careful storage and continued compliance with refrigeration conditions.

CONCLUSIONS

This high CKD prevalence (>11%) represents a substantial health burden in young adults from South Kivu, DRC. It is largely driven by classic risk factors (age, gender, HIV, diabetes, and hypertension). Our observations suggest a major impact of the epidemiological transition in the DRC, and call for an aggressive

primary care management of hypertension and diabetes, given the unaffordable cost of kidney replacement therapy for most individuals in the DRC.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

MIM, MJ, and EKS conceived and designed the study. MIM, EKS, PW, EBM, MPH, WD, CAW, SL, and MJ analyzed the data and/or interpreted the results. PW and CF supervised laboratory analyses. MIM drafted the manuscript. All authors revised the manuscript and approved the final version.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Univariate regression analysis of factors associated with albuminuria (ACR >30 mg/g) and eGFR <60 ml/min per 1.73 m^2 (CKD-EPIcr).

Table S2. Multivariable logistic regression of factors associated with eGFRcys <60 ml/min per 1.73 m^2 and CKDcys.

Table S3. Multivariable logistic regression of factors associated with eGFRcr-cys <60 ml/min per 1.73 m^2 and CKDcr-cys.

Table S4. Distribution of subjects with missing albuminuria.

Table S5. Distribution of subjects with missing creatinine.

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