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Research Paper

The epidemiology of kidney disease in people of African ancestry with HIV in the UK

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ABSTRACT

Background: Chronic kidney disease (CKD) is a leading cause of morbidity and mortality globally. The risk of CKD is increased in people of African ancestry and with Human Immunodeficiency Virus (HIV) infection.
Methods: We conducted a cross-sectional study investigating the relationship between region of ancestry (East, Central, South or West Africa) and kidney disease in people of sub-Saharan African ancestry with HIV in the UK between May 2018 and February 2020. The primary outcome was renal impairment (estimated glomerular filtration rate [eGFR] of $<$60 mL/min/1.73 m^2). Secondary outcomes were stage 5 CKD (eGFR $<$15 ml/min/1.73 m^2, on dialysis for over 3 months or who had received a kidney transplant), proteinuria (urine protein/creatinine ratio $>$50 mg/mmol), and biopsy-confirmed HIV-associated nephropathy (HIVAN), focal segmental glomerulosclerosis (FSGS) or arterionephrosclerosis. Multivariable robust Poisson regression estimated the effect of region of African ancestry on kidney disease outcomes.
Findings: Of the 2468 participants (mean age 48.1 [SD 9.8] years, 62% female), 193 had renal impairment, 87 stage 5 CKD, 126 proteinuria, and 43 HIVAN/FSGS or arterionephrosclerosis. After adjusting for demographic characteristics, HIV and several CKD risk factors and with East African ancestry as referent, West African ancestry was associated with renal impairment (prevalence ratio [PR] 2.06 [95% CI 1.40−3.04]) and stage 5 CKD (PR 2.23 [1.23−4.04]), but not with proteinuria (PR 1.27 [0.78−2.05]). West African ancestry (as compared to East/South African ancestry) was also strongly associated with a diagnosis of HIVAN/FSGS or arterionephrosclerosis on kidney biopsy (PR 6.44 [2.42−17.14]).
Interpretation: Our results indicate that people of West African ancestry with HIV are at increased risk of kidney disease. Although we cannot rule out the possibility of residual confounding, geographical region of origin appears to be a strong independent risk factor for CKD as the association did not appear to be explained by several demographic, HIV or renal risk factors.

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Research in context

Evidence before this study

Chronic kidney disease (CKD) is an important complication of Human Immunodeficiency Virus (HIV) infection, particularly in people of African ancestry. Among African people with HIV, West-Africans appear at greatest risk of kidney disease although CKD estimates are limited by heterogeneity of studies and measures to define CKD, and availability of data on HIV and traditional CKD risk factors.

Added value of the study

We conducted a study in people of African ancestry with HIV in a single healthcare system. We confirmed that West African ancestry was associated with an increased risk of renal impairment (estimated glomerular filtration rate of <60 mL/min/1.73 m^2) and stage 5 CKD (eGFR <15 ml/min/1.73 m^2 or requiring permanent renal replacement therapy), and that this was not explained by differences in several demographic, HIV or traditional CKD risk factors. Moreover, participants of West African ancestry were six-fold more likely to be diagnosed with HIV associated nephropathy (HIVAN), focal segmental glomerulosclerosis (FSGS), or arterionephrosclerosis, glomerular pathologies that have been associated with coding variants of the apolipoprotein L1 *(APOL1)* gene that are highly prevalent in populations of West African ancestry.

Implications of all the available evidence

HIVAN/FSGS disproportionally affects people of West-African ancestry and this may contribute to the high burden of kidney disease in this population. These data suggest that early HIV diagnosis and prompt initiation of ART, already recommended to reduce morbidity and mortality in all people with HIV, may be an important CKD prevention strategy, particularly in populations of West African ancestry.

1. Introduction

Chronic kidney disease (CKD) is a common condition characterized by gradual loss of kidney function over time, leading to increased morbidity and mortality. CKD is ranked as the 12th leading cause of death globally, and is particularly common among people living in sub-Saharan Africa [1]. With a population of over one billion [2], sub-Saharan Africa is a vast and heterogenous region with marked genetic diversity, in which urbanization and economic progress contribute to a rapid transition in disease-burden from communicable diseases and childhood illnesses to chronic, non-communicable diseases, including CKD.

HIV is also highly prevalent in sub-Saharan Africa, with the greatest prevalence in East and Southern Africa [3]. The risk of acute kidney injury and CKD is increased in people with HIV; these conditions frequently have a multifactorial etiology including: chronic immune activation as a direct effect of the HIV virus; drug toxicity from antiretroviral therapy (ART) or agents to treat or prevent opportunistic infections; and age-related comorbid kidney disease due to diabetes, hypertension, and cardiovascular disease for example [4]. In addition, common coding variants of apolipoprotein L1 (*APOL1*) gene were found to be strongly associated with some subsets of CKD in people of African ancestry, especially HIV-associated nephropathy (HIVAN, odds ratio [OR] 29 in African Americans, 89 in South Africans), focal segmental glomerulosclerosis (FSGS, OR 17), and arterionephrosclerosis (OR 2–4) [5–8]. *APOL1* renal risk variants are also associated with steeper decline in estimated glomerular filtration rate (eGFR) [9] and non-diabetic end-stage kidney disease (ESKD, OR 7) [8]. These *APOL1* risk variants are found almost exclusively in people of African ancestry, with the highest frequencies reported in West Africans and the lowest in East Africans [4]. Within West Africa, the frequency of the *APOL1* risk variants is particularly high among the Yoruba and Igbo-Edo speaking populations of Nigeria, and the Asante in Ghana [5,7–9].

There remains a paucity of reliable population-based data on the prevalence of CKD in African people with HIV. A recent systematic review of CKD in Africans with HIV [10] and a study from the UK Collaborative HIV Cohort (UK CHIC) Study [11] reported the highest prevalence of CKD in people from West Africa. However, the systematic review highlighted several weaknesses in the design of the included studies, a lack of standardized measures of eGFR, and differences in the populations studied and HIV care provided. The UK CHIC study was limited by a lack of information on hypertension, diabetes, and cardiovascular disease, all of which are known risk factors for CKD [11].

In the present study, performed in a setting of universal and free access to healthcare, we sought to further investigate the relationship between region of African ancestry and markers of kidney disease: renal impairment, stage 5 CKD and proteinuria, with adjustment for demographic, HIV, and CKD-associated parameters. As HIVAN is an important cause of CKD in black people with HIV [12], we hypothesized that West African ancestry, a region with the highest prevalence of *APOL1* risk alleles, would be associated with renal impairment (particularly stage 5 CKD), proteinuria and HIVAN/FSGS on kidney biopsy.

2. Methods

2.1. Subject enrolment and demographic data

The genetic markers of kidney disease progression in people of African ancestry (GEN-AFRICA) study is a cross-sectional study designed to investigate genetic factors associated with CKD in the United Kingdom. The GEN-AFRICA study enrolled consenting adults of African ancestry with HIV at 15 HIV clinics and three dialysis/kidney transplantation centers across England between May 2018 and February 2020. There were no exclusion criteria. Demographic data, including country of birth of both parents, clinical information, HIV status and comorbid conditions, were collected from participants using questionnaires and corroborated through review of clinical records. Laboratory data, including nadir and most recent CD4 cell count, viral hepatitis status (hepatitis B surface antigen and anti-hepatitis C antibody) and HIV viral load were obtained from electronic patient records. Renal function, including serum creatinine and urine protein creatinine ratio (uPCR), was measured in local laboratories. If a renal biopsy had ever been performed, a copy of the histopathology report, where available, was obtained. The study was approved by an NHS Research Ethics Committee and Health Research Authority (18/LO/0234 and 239895).

The exposure in the presented analyses was region of sub-Saharan African ancestry (East, South, Central and West Africa) as defined by the African Union [13], with the exception that Angola was included in the Central rather than South region. Participants of Caribbean, North African, or mixed African ancestry were excluded. eGFR was calculated utilizing the CKD Epidemiology Collaboration (CKD-EPI-Cr) equation [14] with and without application of the correction factor for black ethnicity The primary outcome was renal impairment was defined as an eGFR <60 mL/min/1.73 m^2 [15,16]. Participants were stratified by eGFR based on Kidney Disease: Improving Global Outcomes (KDIGO) CKD guidelines [17] and those with eGFR <15 mL/min/1.73 m^2 who were on dialysis for over three months or who had received a kidney transplant were categorized as having

stage 5 CKD. Renal biopsy reports were reviewed and adjudicated by a renal physician (JB) and, in case of discrepancy, a histopathologist to identify cases of HIVAN, (primary) FSGS and arterionephrosclerosis, a common cause of CKD in people of African ancestry [18]. Diabetes mellitus and hypertension were predominantly self-reported diagnoses; medical records were reviewed for those reporting but not on treatment for these conditions to verify the diagnosis. Additionally, diabetes cases were ascertained through review of medical records of those with glycosuria.

2.2. Statistical methods

Baseline characteristics of the study population, stratified by region of ancestry and by eGFR (greater or less than 60 mL/min/1.73m^2), were compared using X^2 for categorical variables, and Kruskal-Wallis tests or ANOVA for continuous variables, as appropriate. Robust Poisson regression was used to quantify the association between each covariate and kidney disease status. It was decided *a priori* that age and sex would be included in the minimally adjusted model, followed by HIV factors (nadir and current CD4 cell count, and prior AIDS). The fully adjusted model also included renal factors (diabetes and cardiovascular disease). As hypertension is on the causal kidney disease pathway, hypertension was excluded as a factor in the primary and secondary outcomes analyses (we conducted sensitivity analyses that included hypertension in the multivariable models). The association between region of ancestry and secondary outcomes: (1) stage 5 CKD, (2) proteinuria (uPCR >50 mg/mmol [approximately 500 mg/g], excluding those with stage 5 CKD) and (3) biopsy-confirmed HIVAN/FSGS/arterionephrosclerosis was also investigated. East African region of ancestry was used as referent for all analyses except for biopsy-confirmed HIVAN/FSGS/arterionephrosclerosis, where East and South African ancestry were combined as referent. As diabetic nephropathy is an important cause of CKD, we performed a further sensitivity analysis excluding participants with diabetes. Finally, interaction analyses were performed to examine whether diabetes, hypertension or cardiovascular disease modified the association between region of African ancestry and renal impairment. All statistical analyses were done using STATA v16 (StataCorp, College Station, Tx). The study was reported according to STROBE guidelines.

2.3. Role of funding sources

This study was supported by the Medical Research Council (UK) Confidence in Concept scheme (MC_PC_17164). The project has been supported in part the National Institutes of Health and the National Cancer Institute Intramural Research Program (CAW).

3. Results

Of the 3026 individuals enrolled in the GEN-AFRICA cohort, 2468 (81.6%) reported sub-Saharan African ancestry with both parents born in the same sub-Saharan region and were included in the current analyses. The characteristics of these participants at the time of enrolment are shown in Table 1. Participants were predominantly women (62%) and had a mean age of 48.1 (SD 9.8) years, and generally long-standing and well-controlled HIV. The prevalence of diabetes, cardiovascular disease and proteinuria was similar across all four sub-Saharan African regions while hypertension was more common among Central and West Africans. Among the 2,281participants with proteinuria data (and no stage 5 CKD), 77.9%, 16.7%, 5.5% had no proteinuria, uPCR 15−49 mg/mmol, and uPCR>50 mg/mmol, respectively. Exposure to antiretroviral drugs was generally similar across all regions (Table S3).

One hundred and ninety-three participants (7.8%) had renal impairment, with the highest prevalence in those of West African ancestry (11.5%) and the lowest in those of South African ancestry (5.3%, Fig. 1). Among participants with renal impairment, 89.1% had hypertension and 26.6% had diabetes. Overall prevalence of hepatitis B (surface antigen) and hepatitis C (anti-HCV) was 6.2% and 1.3% respectively; anti-HCV was more common in those with renal impairment (4.4% vs 1.0%). The characteristics of those with and without renal impairment are shown in Table S2. When stratified by ancestral country, participants with the highest prevalence of renal impairment mostly originated from West Africa, with rates of 13%, 10%, 10% and 9% in those with ancestral roots in Nigeria, Cote d'Ivoire, Ghana and Sierra Leone respectively (Fig. 2, Table S7). Forty-three participants had a biopsy-confirmed diagnosis of HIVAN (N = 36), FSGS (N = 4) or arterionephrosclerosis (N = 3); 1 (2.3%), 6 (14%), 4 (9.3%) and 32 (74.4%) of these occurred in individuals of East, South, Central and West African ancestry (Fig. S1, Table S1).

In univariable analysis, region of African ancestry, age, female sex, nadir CD4 count, current CD4 count, mode of HIV acquisition, prior AIDS, anti-HCV, hypertension, diabetes, and cardiovascular disease were all associated with renal impairment. In the fully adjusted model, participants of West African ancestry had double the odds (PR 2.06, 95% confidence interval [CI] 1.40 − 3.04) of renal impairment as compared to those of East African ancestry which was quite similar to the univariable estimate. Age, current and nadir CD4 cell count, anti-HCV, prior AIDS, diabetes, and cardiovascular disease also remained associated with renal impairment in these adjusted analyses (Table 2). When hypertension was included in the final model for renal impairment, the association between renal impairment and West African ancestry attenuated but remained significant (PR 1.68, 95% CI 1.16−2.44).

In secondary analyses, West African ancestry was also associated with stage 5 CKD (PR 2.23, 95% CI 1.23−4.04) (Tables 3A and S4) but not with proteinuria (excluding stage 5 CKD, Tables 3A and S5). However, when hypertension was included in the final model for stage 5 CKD, West African ancestry was no longer associated with stage 5 CKD (PR 1.49, 95% CI 0.89−2.52) (Table 3B).

Compared to East and South African ancestry, West African ancestry was also strongly associated with biopsy-confirmed HIVAN/FSGS/arterionephrosclerosis (PR 6.44, 95% CI 2.42−17.14) (Tables 3A and S6). In additional sensitivity analyses, the risk of renal impairment remained similar when correction for ethnicity was excluded in eGFR calculations, and in models that excluded participants with diabetes (Table 3B). There was no evidence of interaction between region of African ancestry and renal impairment with diabetes (p values 0.12−0.87), hypertension (p values 0.25−0.72) or cardiovascular disease (p values 0.09−0.91).

4. Discussion

To our knowledge, GEN-AFRICA is the first pan-African diaspora cohort, allowing for direct comparison of markers of kidney disease, CKD risk factors and a biopsy diagnosis of HIVAN/FSGS and arterionephrosclerosis in the setting of HIV across regions of African ancestry. Consistent with the findings of a recent meta-analysis [10] and the UK CHIC study [11], the highest prevalence of renal impairment was observed in individuals of West African ancestry and the lowest prevalence in those from the South African region. West Africans remained at higher risk of renal impairment and stage 5 CKD after adjusting for demographic, HIV, and CKD risk factors (except for hypertension, which is on the causal pathway for CKD). West African ancestry was also strongly associated with having HIVAN/FSGS and arterionephrosclerosis. By contrast, although proteinuria was common, we observed no association between region of ancestry and proteinuria.

The increased risk of renal impairment in West Africans may relate to the high prevalence of renal risk variants (G1, G2) of the *APOL1* gene that confer protection against trypanosomiasis but increase the risk of glomerular scarring, especially in the setting of

Table 1
Demographic and clinical characteristics of the study participants stratified by African region of ancestry.

			Region of African Ancestry				
		All *N* = 2468	East *N* = 585	South *N* = 810	Central *N* = 168	West *N* = 905	*p* value
Age (years)	Mean (SD)	48.1 (9.8)	49.1 (9.7)	48.3 (9.9)	47.8 (10.2)	47.2 (9.8)	0.002
Female sex	*n* (%)	1531 (62.0)	377 (64.4)	562 (69.4)	95 (56.5)	497 (54.9)	<0.001
Time since HIV diagnosis (years)	Mean (SD)	14.1 (6.3)	16.6 (7.2)	14.9 (5.3)	14.5 (6.3)	11.5 (5.6)	<0.001
Nadir CD4 (cells/mm^3)	Median (IQR)	194 (78–329)	182 (80–319)	200 (85–335)	182 (47–302)	196 (76–351)	0.21
Current CD4 (cells/mm^3)	Median (IQR)	551 (396–719)	534 (376–706)	599 (430–763)	511 (355–645)	531 (390–705)	<0.001
HIV viral load (<200 copies/mL)	*n* (%)	2302 (93.3)	553 (94.5)	766 (94.6)	152 (90.5)	831 (91.8)	0.03
On ART	*n* (%)	2444 (99.0)	581 (99.3)	806 (99.5)	167 (99.4)	890 (98.3)	0.07
Time since ART initiation (years)	median (IQR)	10.9 (6.4–14.9)	12.6 (7.5–18.1)	12.4 (7.5–15.5)	11.4 (6.9–15.8)	9 (5.1–12.6)	<0.001
Mode of HIV acquisition							<0.001
Heterosexual	*n* (%)	2150 (87.1)	484 (82.7)	724 (89.4)	151 (89.9)	791 (87.4)	
MSM	*n* (%)	32 (1.3)	8 (1.4)	7 (0.9)	0 (0.0)	17 (1.9)	
Vertical	*n* (%)	107 (4.3)	26 (4.4)	37 (4.6)	5 (3.0)	39 (4.3)	
Blood products	*n* (%)	20 (0.8)	4 (0.7)	3 (0.4)	1 (0.6)	12 (1.3)	
Unknown	*n* (%)	159 (6.4)	63 (10.8)	39 (4.8)	11 (6.5)	46 (5.1)	
Prior AIDS	*n* (%)	615 (25.7)	169 (29.9)	231 (29.2)	36 (22.0)	179 (20.5)	<0.001
HBsAg positive	*n* (%)	151 (6.2)	25 (4.4)	33 (4.1)	17 (10.2)	76 (8.5)	<0.001
Anti-HCV positive*	*n* (%)	30 (1.3)	4 (0.7)	9 (1.2)	7 (4.3)	10 (1.1)	0.003
Diabetes	*n* (%)	249 (10.2)	63 (10.9)	82 (10.2)	15 (8.9)	89 (9.9)	0.88
Hypertension	*n* (%)	826 (33.5)	184 (31.6)	240 (29.7)	62 (36.9)	340 (37.6)	0.003
Cardiovascular disease[ł]	*n* (%)	109 (4.4)	26 (4.4)	32 (4)	12 (7.2)	29 (4.3)	0.32
BMI (kg/m^2)	Mean (SD)	29.5 (6.2)	29.0 (5.9)	30.7 (6.4)	29.7 (5.7)	29.6 (5.7)	<0.001
eGFR (60 mL/min/1.73m^2**)							<0.001
>90	*n* (%)	1605 (65.0)	410 (70.1)	550 (67.9)	115 (68.5)	530 (58.6)	
60–90	*n* (%)	670 (27.1)	140 (23.9)	217 (26.8)	42 (25.0)	271 (29.9)	
30–59	*n* (%)	92 (3.7)	16 (2.7)	26 (3.2)	4 (2.4)	46 (5.1)	
15–29	*n* (%)	14 (0.6)	3 (0.5)	3 (0.4)	2 (1.2)	6 (0.7)	
<15 (Stage 5 CKD***)	*n* (%)	87 (3.5)	16 (2.7)	14 (1.7)	5 (3.0)	52 (5.7)	
uPCR^ (mg/mmol)							0.90
<15	*n* (%)	1776 (77.9)	429 (77.6)	584 (77.8)	123 (77.9)	640 (78.1)	
15–49	*n* (%)	380 (16.7)	100 (18.1)	120 (16.0)	26 (16.5)	134 (16.4)	
50–99	*n* (%)	65 (2.9)	11 (2.0)	23 (3.1)	5 (3.2)	26 (3.2)	
≥100	*n* (%)	60 (2.6)	13 (2.4)	24 (3.2)	4 (2.5)	19 (2.3)	

ART=antiretroviral therapy; MSM=men who have sex with men; AIDS=acquired immunodeficiency syndrome; HBsAg=hepatitis B surface antigen; Anti-HCV=hepatitis C virus antibody; BMI=body mass index; uPCR=urine protein/creatinine ratio; SD=standard deviation; IQR=interquartile range.
There are no missing data for age, sex, mode of HIV acquisition, ART and eGFR; 0.2% of participants lack data for time since HIV diagnosis, 0.3% for current CD4 cell count, 5.5% for nadir CD4 cell count, 8.9% for time since ART initiation, 3% of for prior AIDS, 0.9% for diabetes, 0.2% for hypertension, 1.4% for HBsAg, 2.8% for anti-HCV, and 5% for uPCR (mainly those with stage 5 CKD).
ŀCardiovascular disease = composite of any previous history of myocardial infarction, coronary artery disease, peripheral vascular disease, stroke, heart failure and cardiomyopathy.
* Hepatitis C RNA: detectable *N* = 4, undetectable *N* = 24, not available *N* = 2.
** estimated glomerular filtration rate calculated with CKD EPI formula with correction of black ethnicity included.
*** Stage 5 CKD=eGFR <15 mL/min/1.73m^2 and those on dialysis for over three months or had a kidney transplant.
^ uPCR does not include participants with stage 5 CKD (eGFR <15 mL/min/1.73m^2 and those on dialysis or had a kidney transplant).

viral infections such as HIV [6]. As Nigerian ancestry was predominant among the West Africans enrolled in our cohort, the observed increased risk of renal impairment among West Africans may relate to the high prevalence of *APOL1* G1/G2 variants in this population. Indeed, a majority (over 70%) of HIVAN/FSGS/arterionephrosclerosis, each of which has been associated with *APOL1* high risk genotypes, was diagnosed in West Africans, mostly of Nigerian ancestry. The greater burden of renal impairment and stage 5 CKD in those of West African ancestry may, at least in part, be due to HIVAN/FSGS. As ART, a higher CD4 cell count and suppressed HIV viral load have all been associated with a reduced incidence of HIVAN [18,19], our findings suggest that early HIV diagnosis followed by prompt initiation of fully suppressive ART may be an important CKD prevention strategy.

Contrasting with our findings, a recent study of kidney disease in predominantly HIV negative Africans found the lowest prevalence of CKD, defined as an eGFR <60 mL/min/1.73 m^2 and/or albuminuria >3 mg/mmol, in West Africans and highest prevalence in South Africans [20]. This was a large population-based study of CKD prevalence (AWI-Gen study) conducted in six discrete locations in East, South and West Africa. The AWI-Gen study recruited from two rural areas in West Africa: Burkina Faso (Nanoro) and Ghana (Navrango), each with a known low prevalence of HIV, CKD and *APOL1* risk variants [5,21]. This study is therefore unable to account for differences in CKD prevalence in relation to regional variability in the prevalence of *APOL1* risk variants. Rather, the higher prevalence of CKD in the South African sites may reflect a different stage of epidemiological transition from rural to urban lifestyle; the South African sites in AWI-Gen were semi-rural to urban areas with higher prevalence of CKD risk factors including diabetes and hypertension.

Proteinuria was not associated with region of African ancestry. This finding was surprising given that studies have shown *APOL1* renal risk genotypes to be associated with more frequent and earlier onset of proteinuria [22–25]. Proteinuria is an important risk factor for CKD progression with a higher prevalence generally among people of African ancestry [26,27] and it is likely that participants with severe proteinuria have progressed to stage 5 CKD in our study. As we excluded participants with Stage 5 CKD from the proteinuria analyses, this may explain the lack of association with region of African ancestry. As most participants had well controlled HIV, it is possible that the lack of association between proteinuria and CKD is due to past rather than current renal injury (e.g. prior to HIV diagnosis/control). It is also possible that the HIV virus itself, exposure to ART or

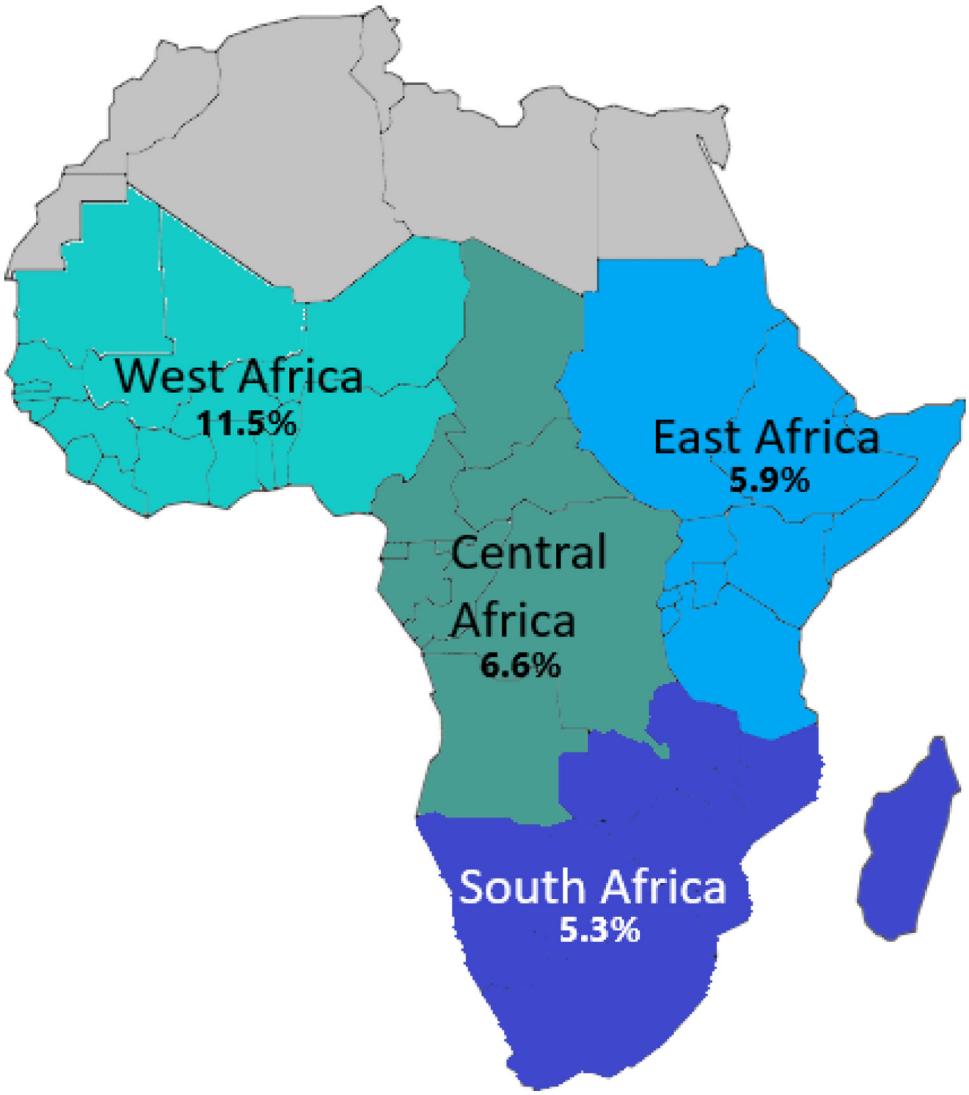

Fig. 1. Regions of sub-Saharan Africa (East, Central, West, South) and prevalence of renal impairment (eGFR <60 ml/min/1.73m^2) by region of ancestry of the study participants.

other medications, or traditional CKD risk factors such as diabetes and hypertension were the predominant causes of proteinuria rather than *APOL1*-associated glomerular disease.

The strengths of this study include the large number of participants who are representative of people of African ancestry currently living with HIV in the UK. In addition, our study included a substantial number (n = 87) of people with stage 5 CKD who, in the absence of renal replacement therapy, would be missing from most studies conducted in Africa. Consistent with other studies from sub-Saharan Africa, our study included a higher proportion of females (by contrast, most US studies have a predominance of African American males). The limitations include the cross-sectional design and use of a single creatinine time point to calculate eGFR which may not accurately reflect CKD status; however, as almost all participants were clinically well and recruited during routine outpatient visits, it is likely that most had stable kidney function. The CKD-EPI equation, which is a creatinine-based equation, has not been widely validated in African populations, and the use of the adjustment for ethnicity, while arguable given the high BMI of our participants, remains contentious [27]; this issue is currently being investigated by the African Research into Kidney Diseases (ARK) study [28]. However, in our study, analyses of stage 5 CKD support the findings of the primary outcome suggesting that the association between region of ancestry and renal impairment is real. We did not investigate the associations between specific ART medications and CKD as tenofovir disoproxil fumarate (TDF), atazanavir and lopinavir are generally avoided in people with CKD [11,29], and have no information on markers of renal tubular (dys)function, hence we are unable to account for the effects of some ART medications that may lead to reduced tubular creatinine secretion [30]. We also have incomplete data on anti-hypertensive medications and are unable to exclude that differential use of angiotensin converting enzyme inhibitors or angiotensin II receptor antagonist may have affected the severity of proteinuria in different regions.

We lacked information on other factors that may contribute to renal impairment in Africa including infections such as malaria and schistosomiasis, environmental exposure to heavy metals, or data on current use of non-steroidal anti-inflammatory drugs and prior use of antimicrobial treatments and prophylaxis. A small number of recruitment centers were renal centers, and thus our sample includes a higher proportion of people with stage 5 CKD, meaning our study is unable to provide true prevalence estimates. Finally, although we had a sizeable cohort with broad representation from across sub-Saharan Africa, the Central African cohort was small, the East, South and West African regions were over-represented by people of

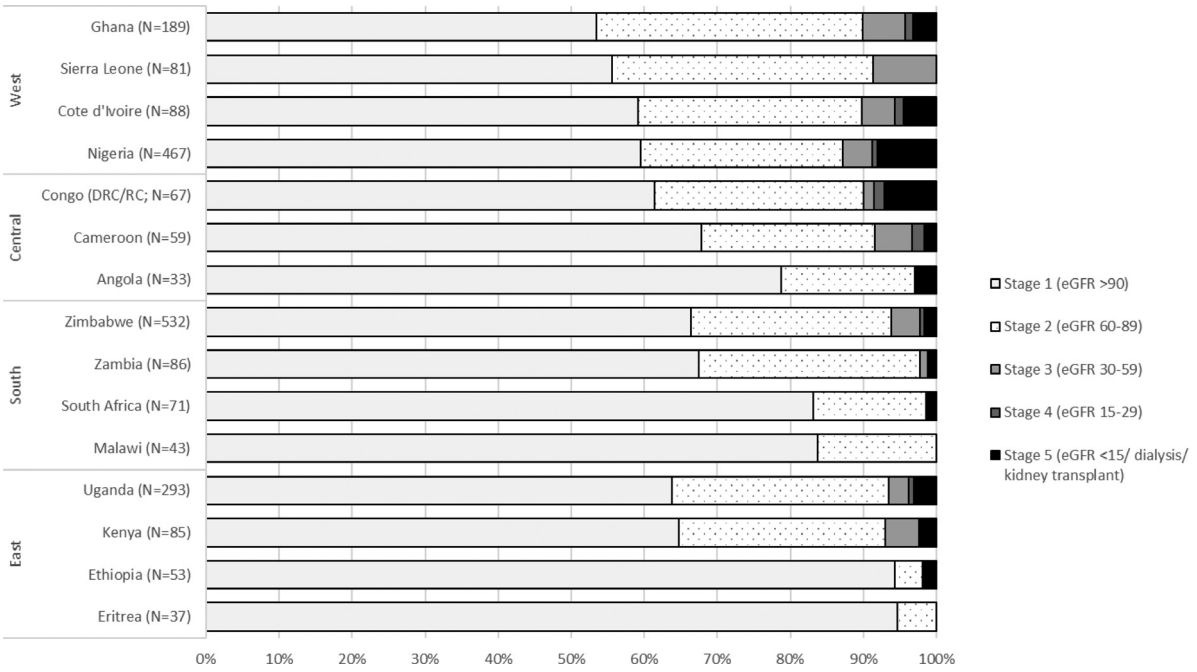

Fig. 2. Proportion of participants with eGFR stages 1–5, by country of ancestry

Proportion of participants in each country of ancestry with estimated glomerular filtration rate >90, 60–89, 30–59, 15–29 and <15 mLmin/1.73 m^2. Data are restricted to participants with both parents born in the same country, and to countries with at least *N* = 10 individuals.

Ugandan, Zimbabwean and Nigerian ancestry, and there was substantial heterogeneity in prevalence of renal impairment and stage 5 CKD within regions. Our data show that in a setting where healthcare is universally accessible, there was an increased burden of kidney disease among those of West African ancestry. Consistent with the known distribution of *APOL1* risk alleles, we observed a particularly strong association between West African ancestry and HIVAN/FSGS and arterionephrosclerosis. Genetic analyses in the GEN-AFRICA cohort are currently being undertaken; if these confirm that *APOL1* high risk genotypes are a major driver of the increased risk of kidney

Table 2
Factors associated with renal impairment (eGFR <60 mL/min/1.73m^2), *n* = 193.

	Univariate			Adjusted for age and sex			Adjusted for HIV factors			Adjusted for renal factors		
	PR	95% CI	*p* value	PR	95% CI	*p* value	PR	95% CI	*p* value	PR	95% CI	*p* value
African Region of Ancestry			<0.001			<0.001			<0.001			<0.001
East	1			1			1			1		
South	0.89	0.58–1.37	0.59	0.94	0.61–1.44	0.76	0.87	0.54–1.41	0.58	0.90	0.56–1.44	0.67
Central	1.09	0.57–2.11	0.79	1.10	0.58–2.10	0.76	0.85	0.40–1.82	0.68	0.69	0.29–1.68	0.41
West	1.92	1.33–2.78	0.001	2.04	1.12–2.93	<0.001	2.00	1.35–2.96	0.001	2.06	1.40–3.04	<0.001
Age (per 1 year increment)	1.05	1.04–1.07	<0.001	1.05	1.04–1.07	<0.001	1.05	1.03–1.06	<0.001	1.04	1.02–1.06	<0.001
Sex (Female vs. male)	0.62	0.47–0.81	<0.001	0.77	0.53–1.01	0.06	0.97	0.71–1.31	0.83	0.97	0.72–1.32	0.87
Time since HIV diagnosis (5 years increments)	1.05	0.95–1.17	0.31									
Nadir CD4 (50 cell/mm^3 increment)	0.88	0.8/3–0.93	<0.001				0.94	0.89–0.99	0.03	0.95	0.90–1.00	0.05
Current CD4 (50 cell/mm^3 increment)	0.93	0.90–0.97	<0.001				0.96	0.92–1.00	0.06	0.95	0.92–0.99	0.007
On ART	0.62	0.21–1.81	0.38									
HIV viral load (<200 copies/mL)	1.09	0.62–1.91	0.77									
Mode of HIV Acquisition			0.26									
Heterosexual	1											
MSM	1.61	0.64–4.07	0.32									
Vertical	0.48	0.19–1.27	0.14									
Blood products	1.93	0.67–5.54	0.22									
Unknown	1.21	0.73–2.01	0.45									
Prior AIDS	1.76	1.33–2.32	<0.001				1.66	1.19–2.29	0.003	1.52	1.09–2.11	0.01
HBsAg (positive)	0.96	0.53–1.73	0.89									
Anti-HCV (Positive)	3.63	1.97–6.69	<0.001				3.48	1.84–6.57	<0.001	2.97	1.44–6.14	0.003
Diabetes	3.20	2.38–4.30	<0.001							2.15	1.52–3.03	<0.001
Hypertension	16.24	10.40–25.35	<0.001									
Cardiovascular disease	3.83	2.71–5.40	<0.001							2.94	1.98–4.35	<0.001
BMI (kg/m^2)												
<18.5	1.64	0.44–6.12	0.46									
18.5–24.99	1											
25–30	0.82	0.56–1.91	0.30									
>=30	0.84	0.59–1.20	0.34									

ART=antiretroviral therapy; MSM=men who have sex with men; AIDS=acquired immunodeficiency syndrome; HBsAg=hepatitis B surface antigen; Anti-HCV=hepatitis C virus antibody; BMI=body mass index; PR=prevalence ratio; CI=confidence interval.

Table 3
Secondary outcomes (A) and sensitivity analyses (B).

	Univariate			Multivariable [X]		
	PR	95% CI	*p* value	PR	95% CI	*p* value
A. Secondary Analyses						
Stage 5 CKD[*] (*n* = 87)						
African Region of Ancestry			<0.001			0.001
East	1			1		
South	0.63	0.31–1.28	0.21	0.69	0.31–1.54	0.36
Central	1.09	0.40–2.93	0.87	1.03	0.34–3.13	0.96
West	2.11	1.21–3.64	0.01	2.23	1.23–4.04	0.009
Biopsy-confirmed HIVAN/FSGS and arterionephrosclerosis (*n* = 43)						
African Region of Ancestry			<0.001			0.001
East/South	1			1		
Central	4.74	1.40–16.04	0.01	4.47	1.20–16.69	0.03
West	7.05	3.12–15.90	<0.001	6.44	2.42–17.14	<0.001
Proteinuria[†] (*n* = 126)						
African Region of Ancestry			0.47			
East		1				
South	1.43	0.91–2.37	0.11			
Central	1.31	0.62–2.77	0.48			
West	1.27	0.78–2.05	0.34			
B. Sensitivity Analyses						
eGFR<60 ml/min/1.72m^2 with additional adjustment for hypertension (*n* = 193)						
African Region of Ancestry			<0.001			<0.001
East	1			1		
South	0.89	0.58–1.37	0.59	0.93	0.59–1.47	0.76
Central	1.09	0.57–2.11	0.79	0.67	0.30–1.47	0.32
West	1.92	1.33–2.78	0.001	1.68	1.16–2.44	0.006
Stage 5 CKD[*] with additional adjustment for hypertension (*n* = 87)						
African Region of Ancestry			<0.001			0.03
East	1			1		
South	0.63	0.31–1.28	0.21	0.59	0.28–1.27	0.18
Central	1.09	0.40–2.93	0.87	0.73	0.26–2.05	0.55
West	2.11	1.21–3.64	0.01	1.49	0.89–2.52	0.13
eGFR without correction for ethnicity [K] (*n* = 193)						
African Region of Ancestry			<0.001			<0.001
East	1			1		
South	1.12	0.80–1.57	0.51	1.10	0.77–1.58	0.60
Central	1.16	0.69–1.96	0.58	1.01	0.56–1.82	0.98
West	1.89	1.40–2.55	<0.001	2.03	1.49–2.75	<0.001
Participants without diabetes (*n* = 2197)						
African Region of Ancestry			<0.001			<0.001
East	1			1		
South	0.87	0.51–1.47	0.6	0.87	0.49–1.54	0.64
Central	1.42	0.70–2.91	0.34	1.08	0.49–2.38	0.85
West	2.13	1.37–3.32	0.001	2.11	1.32–3.36	0.002

ART=antiretroviral therapy; MSM=men who have sex with men; AIDS=acquired immunodeficiency syndrome; HBsAg=hepatitis B surface antigen; Anti-HCV=hepatitis C virus antibody; BMI=body mass index; PR=prevalence ratio; CI=confidence interval.

[K] eGFR based on CKD-EPI equation, excluding correction for African American ethnicity.

[X] Multivariable model for Stage 5 CKD and for eGFR without correction for ethnicity adjusted for age, sex, nadir CD4, current CD4, diabetes, cardiovascular disease and hepatitis C virus antibody; multivariable model for biopsy-confirmed HIVAN/FSGS and arterionephrosclerosis adjusted for age, sex, nadir CD4, current CD4, cardiovascular disease and hepatitis C virus antibody; multivariable model for eGFR<60 ml/min/1.72m^2 with adjusting for hypertension adjusted for age, sex, nadir CD4, current CD4, prior AIDS, diabetes, hypertension, cardiovascular disease and hepatitis C virus antibody; multivariable model for individuals without diabetes adjusted for age, sex, nadir CD4, current CD4, prior AIDS, cardiovascular disease and hepatitis C virus antibody.

[*] Stage 5 CKD=eGFR <15 mL/min/1.73 m^2 and those on dialysis for over three months or had a kidney transplant.

[†] Proteinuria=uPCR >50 mg/mmol [approximately 500 mg/g] (excluding those with Stage 5 CKD).

disease in West Africans with HIV, early HIV diagnosis and prompt initiation of ART will be even more important CKD prevention strategies. This cohort is well placed to help further examine the complex interactions between genes and the environment that ultimately promote the development of CKD.

Contributors

The study was designed by FAP. LH, JF, JB, AC, RV, RJ, DP, MH, RH, JB and FAP were site principal investigators and coordinated recruitment and data collection at their sites. BSS, EBR and LC assisted with logistic and governance aspects. JB preformed a review of all kidney biopsy reports with assistance from Catherine Horsfield. RH and FAP performed the analyses with input from CAS and CAW. RH, KB, CAS, CAW and FAP interpreted the findings. RH wrote the first draft of the manuscript with input from CAS, CAW and FAP. RH and FP verified the underlying data. All authors revised and approved the final version of the manuscript.

Data sharing statement

The database contains personal and sensitive information and is therefore not publicly available. Access to the study data and/or samples is governed by the National Health Service data access policy

and those of King's College Hospital NHS Foundation Trust, the study sponsor. The Gen-AFRICA cohort is open to collaborations, and all requests from researchers who meet the criteria for access to fully anonymized patient level data will be considered. Concepts can be submitted for review to the principal investigator (Prof. Frank Post; email: frank.post@kcl.ac.uk).

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Declaration of Competing Interest

Dr Hung has nothing to disclose.
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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.101006.

Appendix

Genetic markers of chronic kidney disease in people of African ancestry with HIV (GEN-AFRICA) Study Group

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References

[1] Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the global burden of disease study 2017. The Lancet 2018;392(10159):1736–88. doi: 10.1016/S0140-6736(18)32203-7.
[2] Population, total - Sub-Saharan Africa | Data. Accessed December 4, 2020. https://data.worldbank.org/indicator/SP.POP.TOTL?locations=ZG
[3] Dwyer-Lindgren L, Cork MA, Sligar A, et al. Mapping HIV prevalence in sub-Saharan Africa between 2000 and 2017. Nature 2019;570(7760):189–93. doi: 10.1038/s41586-019-1200-9.
[4] Swanepoel CR, Atta MG, D'Agati VD, et al. Kidney disease in the setting of HIV infection: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. Kidney Int 2018;93(3):545–59. doi: 10.1016/j.kint.2017.11.007.

[5] Limou S, Nelson GW, Kopp JB, Winkler CA. APOL1 kidney risk alleles: population genetics and disease associations. Adv Chronic Kidney Dis 2014;21(5):426–33.
[6] Kasembeli AN, Duarte R, Ramsay M, et al. APOL1 risk variants are strongly associated with HIV-associated nephropathy in black South Africans. J Am Soc Nephrol 2015;26(11):2882–90. doi: 10.1681/asn.2014050469.
[7] Kopp JB, Nelson GW, Sampath K, et al. APOL1 genetic variants in focal segmental glomerulosclerosis and HIV-associated nephropathy. J Am Soc Nephrol 2011;22 (11):2129–37. doi: 10.1681/asn.2011040388.
[8] Genovese G, Friedman DJ, Ross MD, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. Science 2010;329(5993):841–5. doi: 10.1126/science.1193032.
[9] Parsa A, Kao WHL, Xie D, et al. APOL1 risk variants, race, and progression of chronic kidney disease. N Engl J Med 2013;369(23):2183–96.
[10] Ekrikpo UE, Kengne AP, Bello AK, et al. Chronic kidney disease in the global adult HIV-infected population: a systematic review and meta-analysis Reboldi G, ed. PLoS ONE 2018;13(4):e0195443. doi: 10.1371/journal.pone.0195443.
[11] Jose S, Hamzah L, Jones R, et al. Chronic kidney disease risk in African and Caribbean populations with HIV. J Infect Dis 2018;218(11):1767–72. doi: 10.1093/infdis/jiy397.
[12] Bansi L, Hughes A, Bhagani S, et al. Clinical epidemiology of HIV-associated end-stage renal failure in the UK. Aids 2009;23(18):2517–21. doi: 10.1097/QAD.0b013e3283320e12.
[13] The six regions of the African Union | West Africa Gateway | Portail de l'Afrique de l'Ouest. Accessed August 4, 2020. http://www.west-africa-brief.org/content/en/six-regions-african-union
[14] Levey AS, Stevens LA. Estimating GFR using the CKD epidemiology collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. Am J Kidney Dis 2010;55(4):622–7. doi: 10.1053/j.ajkd.2010.02.337.
[15] Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med 2013;158(11):825–30. doi: 10.7326/0003-4819-158-11-201306040-00007.
[16] Levey AS, Coresh J, Balk E, et al. National kidney foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139(2):137–47. doi: 10.7326/0003-4819-139-2-200307150-00013.
[17] Official JOurnal Of the InternatiOnal SOciety Of NephrOlOgy KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.
[18] Booth JW, Hamzah L, Jose S, et al. Clinical characteristics and outcomes of HIV-associated immune complex kidney disease. Nephrol Dial Transplant 2016;31 (12):2099–107. doi: 10.1093/ndt/gfv436.
[19] Lucas GM, Eustace JA, Sozio S, Mentari EK, Appiah KA, Moore RD. Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. AIDS 2004;18(3):541–6. doi: 10.1097/00002030-200402200-00022.
[20] George JA, Brandenburg JT, Fabian J, et al. Kidney damage and associated risk factors in rural and urban sub-Saharan Africa (AWI-Gen): a cross-sectional population study. Lancet Glob Health 2019;7(12):e1632–43. doi: 10.1016/S2214-109X(19)30443-7.
[21] Kaboré NF, Poda A, Zoungrana J, et al. Chronic kidney disease and HIV in the era of antiretroviral treatment: findings from a 10-year cohort study in a west African setting. BMC Nephrol 2019;20(1). doi: 10.1186/s12882-019-1335-9.
[22] Chen TK, Tin A, Peralta CA, et al. APOL1 risk variants, incident proteinuria, and subsequent eGFR decline in blacks with hypertension-attributed CKD. Clin J Am Soc Nephrol 2017;12(11):1771–7. doi: 10.2215/CJN.01180117.
[23] Lipkowitz MS, Freedman BI, Langefeld CD, et al. Apolipoprotein L1 gene variants associate with hypertension-attributed nephropathy and the rate of kidney function decline in African Americans. Kidney Int 2013;83(1):114–20.
[24] Estrella MM, Wyatt CM, Pearce CL, et al. Host APOL1 genotype is independently associated with proteinuria in HIV infection. Kidney Int 2013;84(4):834–40. doi: 10.1038/ki.2013.203.
[25] Peralta CA, Bibbins-Domingo K, Vittinghoff E, et al. APOL1 genotype and race differences in incident albuminuria and renal function decline. J Am Soc Nephrol 2016;27(3):887–93. doi: 10.1681/ASN.2015020124.
[26] Mathur R, Dreyer G, Yaqoob MM, Hull SA. Ethnic differences in the progression of chronic kidney disease and risk of death in a UK diabetic population: an observational cohort study. BMJ Open 2018;8:20145. doi: 10.1136/bmjopen-2017-020145.
[27] Delanaye P, Mariat C, Maillard N, Jean-Marie K, Cavalier E. Are the creatinine-based equations accurate to estimate glomerular filtration rate in African American populations? Clin J Am Soc Nephrol 2011;6(4):906–12. doi: 10.2215/CJN.10931210.
[28] Kalyesubula R, Fabian J, Nakanga W, et al. How to estimate glomerular filtration rate in sub-Saharan Africa: design and methods of the African Research into kidney diseases (ARK) study. BMC Nephrol 2020;21(1):20. doi: 10.1186/s12882-020-1688-0.
[29] Mocroft A, Kirk O, Reiss P, et al. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. AIDS 2010;24 (11):1667–78. doi: 10.1097/QAD.0b013e328339fe53.
[30] Yombi J, Jones R, Pozniak A, Hougardy J-M, Post F. Monitoring of kidney function in HIV-positive patients. HIV Med 2015;16(8):457–67. doi: 10.1111/hiv.12249.