Original Article

Kidney Impairment in HIV/AIDS Patients Attending Kabutare Level II Teaching Hospital, Southern Province of Rwanda

Augustin Nzitakera[1*], Claudine Muhawenimana[1], Charite Niyikiza[1], Merveille Nzayihimbaza[1], Sandrine Umutoniwase[1], Anathalie Umuhoza[1], Vedaste Nsanzimana[1], Emmanuel Rubayiza[1], Herbert Tendayi Mapira[1], Alphonse Niyodusenga[2], Cuthbert Musarurwa[1]

[1]*Department of Biomedical Laboratory Sciences, School of Health Sciences, College of Medicine and Health Sciences, University of Rwanda, Kigali P.O. Box 3286, Rwanda*
[2]*Department of Clinical Biology, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda, Huye, Rwanda*

***Corresponding authors:** Augustin Nzitakera. Department of Biomedical Laboratory Sciences, School of Health Sciences, College of Medicine and Health Sciences, University of Rwanda, Kigali P.O. Box 3286, Rwanda. Email: naugustin189@gmail.com. ORCID: https://orcid.org/0000-0002-7871-3954

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Abstract

Background
HIV infection itself and antiretroviral therapy (ART) can lead to the impaired kidney function that in turn can significantly impact the quality of life and clinical outcomes in people living with HIV. In this study, we evaluated kidney function status in Rwandan people using serum creatinine levels which were lacking in the existing reports.

Objective
To determine the prevalence and associated risk factors of kidney impairment in patients infected with HIV attending Kabutare level II teaching hospital in southern Rwanda.

Methods
An analytical cross-sectional study was carried out on 179 HIV infected and 179 uninfected patients. Weight and height were measured and a blood sample was drawn from each participant for measurement of serum creatinine. Statistical tools were used to determine the association between kidney impairment and participants characteristics.

Results
Among the 358 participants, 19% HIV positive and 1.7% HIV uninfected participants had GFR impairment. Gender ($x^2 = 4.566$; $p = 0.033$) and advancing age ($x^2 = 24.991$; $p < 0.001$) were identified as independent predictors for kidney impairment.

Conclusion
Patients infected with HIV are at higher risk of developing kidney impairment compared to the HIV uninfected. Routine surveillance of kidney function in patients infected with HIV is paramount.

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Keywords: Kidney impairment, HIV/AIDS, antiretroviral therapy, eGFR, PLWH, Rwanda, Africa

Introduction

Global estimates indicate that over 39.0 million people were living with Human Immunodeficiency Virus (HIV) by 2022 and of these, more than two-thirds were from the WHO African Region.[1] Without treatment, HIV progresses to the acquired immunodeficiency syndrome (AIDS).[2] In Rwanda, HIV/AIDS is among top ten diseases whereby an estimated prevalence of 3.0% are people living with HIV (PLWH) among Rwandans aged 15-64 years.[3] The Rwanda Biomedical Centre (RBC), 2020-2021 report indicated that among 3,348,337 people who were tested across the county, 16,190 people were newly infected with HIV thus, HIV is still a serious public health problem in Rwanda.[3]

HIV impairs the immune system resulting in susceptibility to various infections such as tuberculosis, cryptococcal meningitis among others.[4] According to a UNAIDS report, 690,000 people died from HIV/AIDS-related illnesses globally in 2020.[5] Apart from increased susceptibility to opportunistic infections, HIV infection itself can also directly damage nephrons leading to glomerular impairment and eventually renal failure if there is no intervention.[6] Paradoxically, early initiation of combination antiretroviral therapy (cART) reduces morbidity and mortality and minimises new transmissions but some cART regimens have also been reported to be associated with impaired kidney function.[7,8] It is however, crucial for PLWH to have optimum renal function since kidneys are essential for drug metabolism and excretion of toxins and waste products of metabolism such as urea, creatinine and uric acid).[9] Thus, although, there have been improved clinical outcomes in individuals infected with HIV taking cART, such patients however, have increased odds of developing impaired kidney function due to the nephrotoxic effects of antiretroviral treatment.[10] In addition kidney diseases are associated with blood pressure elevation thus, early detection of kidney impairment in PLWH is very critical in order to reduce the risk of developing associated metabolic complications such hypertension which can in turn exacerbate kidney disease and significantly affect the quality of life and life expectancy of PLWH.[11] Individuals infected with HIV may therefore develop acute kidney injury (AKI), comorbid chronic kidney diseases (CKD) and treatment-related nephrotoxicity. Poorly controlled HIV infections together with hepatitis C virus are among some of the reported predictors of kidney disease in PLWH.[12]

Globally the prevalence of CKD is 8-16%, with about 3.5 to 48% of these occurring in PLWH but as the prevalence of HIV infections varies across the globe, the prevalence of CKD also varies geographically.[13] For instance, in sub-Saharan African countries like South Africa, Nigeria, Côte d'Ivoire, Tanzania, Kenya, Uganda and Zambia, the prevalence varies between 6% in South Africa and 48.5% in Uganda.[14] Kidney diseases are highly prevalent in PLWH as opposed to people uninfected with HIV. The disparity, is more prominent in resource limited countries where ART-induced toxicity follow up is not optimum and resources for screening for kidney diseases are also limited.[15]

In Rwanda (2021) a study that used albuminuria as a marker of kidney impairment reported a high prevalence of impaired kidney function in PLWH compared to a control group.[16] However, the researchers did not measure serum and urine creatinine which are the cornerstone of kidney impairment diagnosis. Another recent underpowered retrospective study conducted at a district hospital in Rwanda, among 98 patients, reported higher levels of serum creatinine at base line in 24.4% of study participants. However, further evaluations at three timepoints : 6, 12 and 18 months post cART initiation, showed higher prevalence of participants with increased levels of serum creatinine at 41.8%, 48.9% and 50.0% respectively.[17] These observed prevalences were significantly higher than the 2.4% previously reported in an earlier prospective study

on 936 Rwandan women.[15] More research on kidney disease in PLWH using adequately powered studies and more appropriate screening tools are therefore required in Rwanda. The aim of the present study was to determine the prevalence and associated risk factors of kidney impairment in PLWH in comparison with HIV negative patients.

Methods

Study design and setting

An analytical cross-sectional study was conducted at Kabutare level II teaching hospital, Huye district which is located in southern province of the republic of Rwanda. This health facility has a bed capacity of 355 and a catchment area of 344, 000 inhabitants.[18] It was chosen due its wide range of services including HIV testing, HIV/AIDS counselling and cART initiation among others. Furthermore, its strategic location in the outskirts of Huye town made it an easy choice for the researchers as it receives both urban and rural residents.

Study population and eligibility criteria

From June 2022 to December 2022, a total number of 179 PLWH and 179 patients uninfected with HIV were recruited. Anthropometric indices such as height and weight were measured as well as serum creatinine levels. The 179 patients uninfected with HIV, who served as a control group, were recruited from among outpatients who independently came to seek medical services for non-renal conditions at the study site and voluntarily agreed to participate in the study. In both groups, study participants aged 18 years and above were recruited consecutively until the sample size was reached. In this study, PLWH on cART for at least 2 years were included but for both groups' participants with preexisting chronic conditions such as diabetes mellitus, hypertension or cardiovascular disease were excluded.

Sample size and sampling technique

Open-Source Epidemiologic Statistics for Public Health (OpenEpi) was used to calculate the sample size based on the following formula:

Sample size = r + 1(p #) (1 - p#) (Zβ + Zα2)2 / r (p1 – p2)2

Where: r = ratio of control in relation to cases, p#: average number of exposed = number of exposed cases + number of controls exposed 2. Zβ = standard normal variate for power = 80%. Zα2= standard normal variate for level of significance. In p 1 – p2, effect size or difference in proportion expected based on previous studies. Furthermore, p1 is proportion in cases and p2 is proportion in control. The outcome was renal dysfunction indicated by impaired eGFR. The ratio of control to cases was 1, hypothetical proportion of exposure in controls was 24%, while the hypothetical proportion of exposure in cases was 38.71 %.[19] The estimated sample size was therefore 179 for cases and 179 for controls. This study was therefore carried out on a total number of 358 participants.

Data collection

Collection of socio-demographic data and medical history

A semi-structured questionnaire adapted from the one used by Kefeni et al.[9] and face to face interviews were applied for collecting sociodemographic data and medical history from the study participants. The questionnaire elicited information about participants' address, age, gender, education level, occupation, residence (urban, or rural area), duration of HIV infection, cART adherence and cART regimen type. Questionnaires were designed in English and Kinyarwanda and were administered in the language in which participants were more conversant.

Serum creatinine measurement

Serum creatinine was measured by Cobas C311 (Roche Diagnostics International AG Rotkreuz, Switzerland) using the modified Jaffee reaction.[20] This method is a fixed time kinetic method whereby in an alkaline medium, creatinine in serum reacted with picric acid to give a red-orange colored Janovsky complex, whose absorbance was measured at 520 nm spectrophotometrically.

The intensity of the red-orange color is directly proportional to the amount of creatinine present within the sample.[20]

Determination of body mass index (BMI)

For the purpose of calculating the body mass index, height in kilograms (kg) and weight in metres (m) for each study participant were measured. The two measurements were done using a dual reading beam scale known as DETECTO's eye level weighbeam scales (DETECTO, Missouri, USA), with participants standing upright without shoes. The BMI was calculated as BMI = weight (kg) / height (m)2.[21] "BMI categories were defined as Underweight < 18.5, Normal weight: 18.5-25; Overweight; 25.1-30 and Obese > 30".[22]

Determination of the estimated glomerular filtration rate (eGFR)

The eGFR was calculated using the Cockcroft-Gault (CG) formula,[23] based on serum creatinine levels, body weight, age and gender. The eGFR (in ml/min) based on the CG formula is calculated as follow: "{(140 - age in years) × weight (Kg) / (72 × serum creatinine level in mg/dL} adjusted by sex (× 0.85 (if female) and then adjusted for body surface area". A low GFR indicating impaired kidney function was defined as eGFR < 60mls / minute.[24]

Validity and reliability of the questionnaire

The quality of the data collection tools was ensured by pre-testing the questionnaire among few members of the sampling frame before the actual data collection process.

Statistical analysis and data management

Data were collected using hard copies of data collection sheets and when completed such sheets were kept in locked cabinets to maintain participant confidentiality.From the hard copies, data were entered onto a password protected Excel database, cleaned and exported to the Statistical Software for Social Sciences (SPSS) for statistical analysis version 29.0 (SPSS Inc., Chicago, IL, USA). Confidentiality was also maintained by assigning each participant a unique study identification number.

Mean and standard deviation (SD) were used to present parametric numerical data whilst the median and interquartile range (IQR) were used to summarise non-parametric numerical data. Categorical data were summarized as count and proportion. Pearson's chi-squared test was used to determine whether there was an association between kidney impairment and clinical and sociodemographic characteristics among the study participants. To assess the nature of the association, univariate and multiple logistic regression analysis were used for factors revealed by Chi-squared tests. The t-test or non-parametric equivalent Wilcoxan tests were used to compare means and medians respectively. For all statistical comparisons, the level of significance was set at $p < 0.05$.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board (IRB) of the University of Rwanda College of Medicine and Health Sciences (Approval notice Ref: CMHS/IRB/435/2022. Permission to carry out the study was also requested from the Kabutare Hospital authority (Ref No: 473/11/Hosp. Kab/2022). All study participants were informed of the purpose of the study and voluntarily signed a written informed consent form before participating in this study.

Results

Demographic and clinical characteristics of study participants

The majority of the study participants were female with n = 108 (60.3%) for the PLWH and n = 129 (72.1%) for the comparison group and the proportions according to sex were significantly different between the two groups, ($x^2 = 5.505$; $p = 0.019$). The mean (SD) age of 50.1 (11.7) years for the PLWH group was significantly higher compared to 38.6 (SD = 14.4) years for the control group, ($x^2 = 96.237$; $p < 0.001$).The median (IQR) duration on cART was 15 (11, 17) years. The majority of PLWH, 171 (95.5%) were receiving the combination of tenofovir (TDF),

lamivudine (3TC) and dolutegravir (DTG) as first-line cART regimen. Overall, most participants lived in a rural area with 140 (78.2%) for PLWH and 129 (72.1%) for the comparison group but there was no significant difference between the two groups, (x^2 = 3.268; p = 0.071). The highest education level for the majority of PLWH was primary school level n = 117 (65.4%) whilst for the comparison group, the highest level of education was predominantly secondary school level n = 62 (34.6%), the level of educational attainment was unequally distributed among the two groups (x^2 = 43.580; p < 0.001) (Table 1). However, the level of educational attainment was not significantly associated with kidney impairment in both groups (HIV-infected, x^2 = 2.708; p = 0.258) and HIV-uninfected, x^2 = 3.142; p = 0.534) (Table 2). In both groups, farming was the most predominant occupation with 126 (70.4%) among PLWH and 77 (43.0%) in the comparison group and the occupational status also varied significantly between the two groups (x^2 = 37.964; p < 0.001) (Table 1).

Table 1. The distribution of socio-clinic-demographic characteristics among study participants

	HIV status (n = 179 in each category)		
Characteristics	**Infected**	**Uninfected**	χ^2 (***p* value**)
Age			96.237 (< 0.001*)
Mean	50.1	38.6	
Std. Deviation	11.7	14.4	
Minimum	20	18	
Maximum	73	78	
Range	53	60	
	n (%)	**n (%)**	
Gender			5.505 (0.019*)
Female	108 (60.3)	129 (72.1)	
Male	71 (39.7)	50 (27.9)	
Area of residence			3.268 (0.071)
Rural	140 (78.2)	125 (69.8)	
Urban	39 (21.8)	54 (30.2)	
Educational level			43.580 (< 0.001*)
Illiterate	23 (12.8)	47 (26.3)	
Primary	117 (65.4)	59 (33.0)	
Secondary	39 (21.8)	62 (34.6)	
University	0	10 (5.6)	
Masters	0	1 (0.6)	
Occupation			37.964 (< 0.001*)
Farmers	126 (70.4)	77 (43.0)	
Formally employed	11 (6.1)	47 (26.3)	
Self-employed	23 (12.8)	22 (12.3)	
Unemployed	19 (10.6)	33 (18.4)	

Keys: *p values from Pearson Chi-square (x^2) tests, significant at p ≤ 0.05. HIV: Human immunodeficiency virus; cART: combination antiretroviral therapy; NA: not applicable, BMI: Body Mass Index, eGFR: Estimated glomerular filtration rate. Age comparisons computed by use of the student's t-test and differences in proportions were computed using Pearson Chi-square tests. Level of significance set at < 0.05 in all comparisons.

Table 1. Continued

	HIV status (n = 179 in each category)		
Characteristics	**Infected**	**Uninfected**	x^2 (***p* value**)
	n (%)	**n (%)**	
Unemployed	19 (10.6)	33 (18.4)	
BMI range			75.643 (< 0.001*)
less than 18.5	44 (24.6)	0 (0.0)	
18.5-25	106 (59.2)	115 (64.2)	
25.001-30	19 (10.6)	63 (35.2)	
30.001-35	5 (2.8)	1 (0.6)	
35.001-40	4 (2.2)	0 (0.0)	
above 40	1 (0.6)	0 (0.0)	
eGFR level			28.967 (< 0.001*)
< 60mL/min	34 (19.0)	3 (1.7)	
≥ 60mL/min	145 (81.0)	176 (98.3)	
ART regimen			
AZT/3TC/ATV/r	7 (3.9)	NA	
TDF/3TC/DTG	172 (96.1)	NA	
ART duration			
< 5	12 (6.7)	NA	
5-9	21 (11.7)	NA	
10-14	42 (23.5)	NA	
15-19	94 (52.5)	NA	
20-24	9 (5.0)	NA	
> 25	1 (0.6)	NA	
ART adherence			
Good	175 (97.8)	NA	
Poor	4 (2.2)	NA	

Keys: *p values from Pearson Chi-square (x^2) tests, significant at $p \leq 0.05$. HIV: Human immunodeficiency virus; cART: combination antiretroviral therapy; NA: not applicable, BMI: Body Mass Index, eGFR: Estimated glomerular filtration rate. Age comparisons computed by use of the student's t-test and differences in proportions were computed using Pearson Chi-square tests. Level of significance set at < 0.05 in all comparisons.

Body Mass Index in PLWH and HIV negative participants

Overall, the majority of the participants had a normal BMI in the range of 18.5-25 comprising 59.2% and 64.4% for PLWH and the comparison group respectively. Among the 179 PLWH, 44 (24.6%) were underweight with BMI less than 18.5 whereas in the same group 29 (16.3%) were overweight with BMI greater than 25. In the comparison group, 63 (35.2%) were overweight. There was a statistically significant difference in body weight distribution between the two groups, (x^2 = 75.643; $p <$ 0.001) (Table 1).

eGFR in both HIV positive and HIV negative participants

Our study indicated that 34 (19.0%) (95% CI: 13.6 -25.6%) of HIV infected participants had kidney impairment while in HIV negative participants, only 3 (1.7%) (95%CI: 0.3-4.9%) had kidney impairment and this difference was statistically significant, (x^2 = 28.967 $p < 0.001$) (Table 1).

Factors associated with the impaired EGFR in the study participants

Table 2. Association of eGFR with demographical characteristics of study participants

HIV status		Infected			Uninfected		
eGFR in mL/min		< 60	≥ 60		< 60	≥ 60	
		n (%)	n (%)	x^2 (p*)	n (%)	n (%)	x^2 (p*)
Gender				4.566 (0.033*)			0.044 (0.833)
	Female	26 (76.5)	82 (56.6)		2 (66.7)	127 (72.2)	
	Male	8 (23.5)	63 (43.4)		1 (33.3)	49 (27.8)	
Age groups				24.991 (< 0.001*)			5.274 (0.383)
	18-29	0 (0.0)	15 (10.3)		0 (0.0)	53 (30.1)	
	30-39	2 (5.9)	12 (8.3)		1 (33.3)	62 (35.2)	
	40-49	2 (5.9)	45 (31)		0 (0.0)	23 (13.1)	
	50-59	13 (38.2)	50 (34.5)		1 (33.3)	15 (8.5)	
	60-69	15 (44.1)	21 (14.5)		1 (33.3)	16 (9.1)	
	70-	2 (5.9)	2 (1.4)		0 (0.0)	7 (4.0)	
Area of residence				6.231 (0.013*)			1.318 (0.251)
	Rural	32 (94.1)	108 (74.5)		3 (100)	122 (69.3)	
	Urban	2 (5.9)	37 (25.5)		0 (0)	54 (30.7)	
Educational level				2.708 (0.258)			3.142 (0.534)
	Illiterate	2 (5.9)	21 (14.5)		2 (66.7)	45 (25.6)	
	Primary	26 (76.5)	91 (62.8)		1 (33.3)	58 (33.0)	
	Secondary	6 (17.6)	33 (22.8)		0 (0.0)	62 (35.2)	
	University	0 (0.0)	0 (0.0)		0 (0.0)	10 (5.7)	
	Masters	0 (0.0)	0 (0.0)		0 (0.0)	1 (0.6)	
Occupation				6.949 (0.074)			1.940 (0.534)
	Farmers	30 (88.2)	96 (66.2)		2 (66.7)	75 (42.6)	
	Formally employed	0 (0.0)	11 (7.6)		0 (0.0)	47 (26.7)	
	Self-employed	2 (5.9)	21 (14.5)		0 (0.0)	22 (12.5)	
	Unemployed	2 (5.9)	17 (11.7)		1 (33.3)	32 (18.2)	
BMI range				8.212 (0.145)			0.023 (0.989)
	less than 18.5	14 (41.2)	30 (20.7)		0 (0)	0 (0)	
	18.5-25	18 (52.9)	88 (60.7)		2 (66.7)	113 (64.2)	
	25.001-30	2 (5.9)	17 (11.7)		1 (33.3)	62 (35.2)	
	30.001-35	0 (0.0)	5 (3.4)		0 (0.0)	1 (0.6)	
	35.001-40	0 (0.0)	4 (2.8)		0 (0.0)	0 (0.0)	
	above 40	0 (0.0)	1 (0.7)		0 (0.0)	0 (0.0)	
ART regimen				0.105 (0.746)			NA
	AZT/3TC/ATV/r	1 (2.9)	6 (4.1)		NA	NA	
	TDF/3TC/DTG	33 (97.1)	139 (95.9)		NA	NA	
ART duration				4.895 (0.429)			NA
	< 5	1 (2.9)	12 (8.3)		NA	NA	
	5-9	1 (2.9)	18 (12.4)		NA	NA	
	10-14	8 (23.5)	35 (24.1)		NA	NA	
	15-19	22 (64.7)	72 (49.7)		NA	NA	
	20-24	2 (5.9)	7 (4.8)		NA	NA	
	> 25	0 (0.0)	1 (0.7)		NA	NA	
ART adherence				0.959 (0.0327)			NA
	Good	34 (100.0)	141 (97.2)		NA	NA	
	Poor	0 (0.0)	4 (2.8)		NA	NA	

Key: x^2 : Chi-square value, p* p values from chi-square test, the significant value was set at $p \leq 0.05$, BMI: Body Mass Index, ART: antiretroviral therapy, eGFR: Estimated glomerular filtration rate

From our findings, there was a statistically significant association between gender, age and area of residence with low levels of eGFR in PLWH, all p < 0.05 (Table 2). A total of 26 (76.5%) females had eGFR less than 60mL/min compared to 8 (23.5%) males indicating that significantly more females were susceptible to kidney impairment among PLWH. Pearson's correlation between age and eGFR levels show a negative correlation between the two factors in both HIV infected (r = - 0.339, p < 0.001) and uninfected patients (r = - 0. 437, p < 0.001), implying that eGFR levels decreased as the age of patients increased. This trend was observed in both categories of participants but was more prominent in PLWH in whom 19.0% had eGFR levels less than 60mL/min compared to only 1.7% in uninfected (Figure 1). Of the 34 patients with eGFR < 60mls/minute in PLWH, the majority 32(97.1%) resided in a rural area compared to only 2 (2.9%) residing in an urban area, p = 0.013.

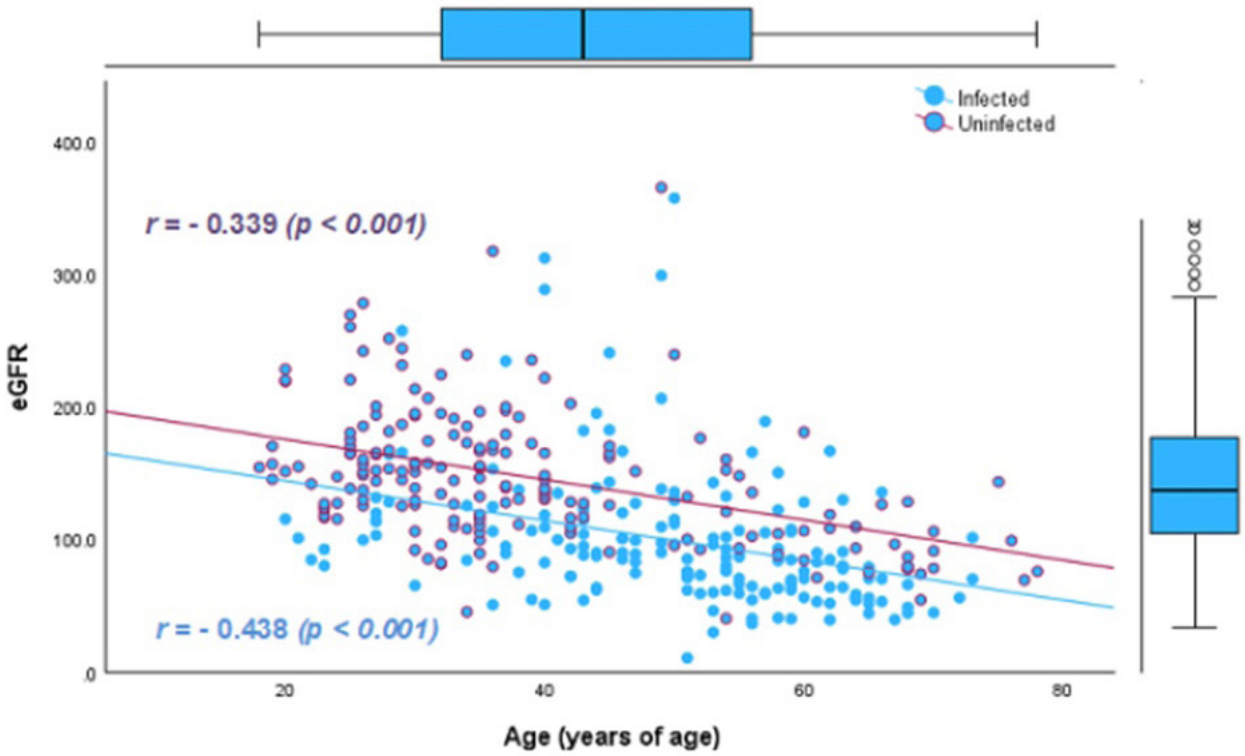

Figure 1. Plot of eGFR with age and HIV status

The data from the scatter plot show a downhill pattern as you move from left to right, this indicates a negative relationship between age and eGFR. As the age increases (move right) the eGFR values tend to decrease (move down). The results from the linear regression analysis showed that an increase in one year of age would result in eGFR levels decreased by 0.339 (p < 0.001, CI: -2.114, -0.882) in HIV infected and by 0.437 (p < 0.001, CI: -1.983, -1.056) in uninfected.

On bivariate logistic regression analysis (Table 3), gender, age and residing in a rural area were significantly predictive of impaired GFR; gender (OR = 0.400; 95%CI = 0.170, 0.944; p = 0.037), age (OR = -0.339; 95%CI = -2.114, -0.882; p < 0.001), and residing in a rural area (OR = 0.0.182; 95%CI = 0.042, 0.799; p = 0.024). After multivariable logistic regression analysis in PLWH, age and gender remained significant predictors of the odds of kidney impairments. Living in a rural area was associated with low levels of eGFR in PLWH, but the strength of the association was not statistically significant after multiple regression analysis (adjusted OR = 0.261; 95%CI = 0.056, 1.209; p = 0.086).

Table 3. Regression analysis of demographic factors associated with eGFR levels on Chi-square analysis in PLWH

Statistic	Bivariate logistic regression		Multivariable logistic regression	
	OR (95%CI)	*p* value	OR (95%CI)	*p* value
Gender	0.400 (0.170,0.944)	0.037	0.389 (0.150, 1.004)	0.05
Age	-0.339 (-2.114, -0.882)	< 0.001	0.906 (0.863, 0.952)	0.001
Area of residence	0.182 (0.042, 0.799)	0.024	0.261 (0.056, 1.209)	0.086

Key: OR = odds ratio, CI = confidence interval

Discussion

In the present study 19.0% of PLWH had kidney impairment as suggested by eGFR < 60mls/minute while in HIV negative participants, only 1.9% had kidney impairment. The higher prevalence of kidney impairment in PLWH compared to the uninfected, might be a consequence of HIV-associated nephropathy (HIVAN) which leads to the injury of nephrons. The damage to the nephrons may be partly due to renal endothelial injury by circulating viral proteins combined with other factors like proinflammatory molecules,[25] anti-HIV antibodies can also form immune complex in kidney and this may result in glomerulonephritis.[26] Although the mechanism remains unclear, there are reports that direct infection by HIV of renal tubule cells which is thought to be mediated via transfer from leukocytes,[27] phagocytosis of apoptotic CD4+ T cells by macrophages in renal compartments could also be another possible way through which HIV accesses renal cells.[27] As reported in studies carried out in Nigeria by Ibrahim et al [28] and Alfano et al,[29] AKI or CKD may occur in HIV infection and manifest as HIVAN or AKI both of which may eventually lead to CKD.

In this study, female participants had significantly higher odds of developing kidney impairment compared to males. This suggests that females living with HIV are more likely to have kidney impairment compared to males of the same status. Several reasons may explain this: studies have identified sex differences in prior AIDS events indicating more advanced stages of HIV-infection at diagnosis in females than males.[30,31] Furthermore, women have been found to be more susceptible than men to developing cART-associated toxicities as there are sex differences in the antiretroviral pharmacokinetic parameters.[32]

The overall observation in our dataset is that, the older the individuals are the more likely they would be to have a lower eGFR. It is hypothesized that the older the person is, the longer the duration since HIV-infection and therefore the more pronounced the HIV/cART effects will be [33,34] While this logic is respected in both HIV infected and uninfected participants, current results reveal a pattern whereby 17/34 PLWH who had low eGFR (< 60mL/min) were less than 60 years of age. Toyama T et al, reported an association between increasing age and eGFR impairment.[35] Furthermore, physiological, GFR declines with age by approximately 1 ml/min/m2 per year beginning in the third decade of life.[36] However, the findings from this study suggest that kidney impairment is not uncommon in younger individual who are infected with HIV. This is supported by a study done in Tanzania on abnormalities of renal function in children infected with HIV.[37] Overall, this underscores the role of screening HIV infected children for renal complications as well before starting ART.

In this study, the observation that a significantly higher proportion of participants with lower eGFR resided in a rural setting compared to those residing in an urban environment is a cause of concern.

This finding suggests that individuals infected with HIV residing in rural areas may be more susceptible to impaired eGFR due to life styles which may expose them to other environmental risk factors other than just the HIV infection.[38] This is possibly coupled with limited access to essential health care services in rural areas compared to urban areas.[39] In Rwanda, the exact cause of this difference remains unclear given the significant effort deployed by the government in quality health care services at the community level through community health workers.[40,41] In a cross-sectional study conducted in Malawi by Nakanga W. P et al [42] it was also concluded that people who live in rural areas tended to have higher prevalence of impaired eGFR compared to the urban-dwelling ones.[42]

The relatively higher proportion of participants with low eGFR in patients under TDF/3TC/DTG regimen compared to AZT/3TC/ATV/r is in line with findings that were observed in a study conducted in Yaoundé, Cameroon, which reported no effect of tenofovir based cART regimen on eGFR impairment, although some cART regimens containing Lamivudine (3TC) and some other cART combinations were reported to be nephroprotective.[43] In contrast, in a cross-sectional study done at Mulago Hospital, Uganda on the prevalence of renal dysfunction among PLWH taking tenofovir-based cART regimen, the prevalence of kidney impairment was 2.4% and an association between tenofovir and kidney impairment was reported.[44] Even though the clinical impact of cART regimen on kidney function was not statistically significant in our study, this finding does not preclude the possibility of some negative impact given that after stratification by cART regimen, our study might have been underpowered to detect any underlying difference.[45,46]

The lack of a significant association between the duration on cART and decreased eGFR is in contrast with a cohort study conducted in Asia, which indicated that long-term exposure to cART increases the risk of eGFR impairment.[47] However, it is also worth noting that the role of cART in improving renal function tests in patients infected with HIV has been highlighted when compared to patients with HIV but who are cART naive.[48] It is therefore important for individuals to know their HIV status, since it not only minimises transmission to others but also provides the lifetime opportunity to start cART for individuals whose HIV test would be positive.[49] In the present study, occupation was not associated with eGFR impairment. However discordant observations were reported by Sponholtz et al [50] who reported occupation as a risk factor of eGFR impairment, but mainly due to the exposure of study participants to industrial toxins and endotoxins since they worked in industrial settings[50] in contrast to our study participants who were mostly farmers.

This study highlighted the need to give greater importance to the renal function assessment on a routine basis due to changes in renal function as a result of HIV infections. The higher proportion of PLWH participants with reduced eGFR compared to HIV negative participants , strongly allude to the increasing need for HIV testing in order for individuals to know their HIV status thus prevent or delay the development of complications related to HIV infection including renal function disorders. A limitation of the present study however, is our inability to differentiate whether the kidney impairment observed was caused by HIV itself or as a result of cART usage.

Conclusion

Findings from this study indicated that prevalence of impaired GFR in HIV infected participants was 19% and 1.7% in HIV negative participants. Our findings corroborate the need for routine monitoring of serum creatinine and BMI among PLWH and formulation of policy on health education to minimize exposure to other risk factors.

Availability of data and materials
Available from the corresponding authors on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
AN study design, study conception, drafted the manuscript. CM, CN, MN, SU Study conception, Study design, performed experiment. AU, VN provided technical assistance regarding creatinine measurement. ER, HTM, CM data curation, review and editing of the manuscript. AN coordinated the study design, supervision and editing the manuscript. All authors have read and approved the final manuscript.

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