Contents lists available at ScienceDirect

# Heliyon



journal homepage: www.cell.com/heliyon

Research article

5<sup>©</sup>CelPress

## Prevalence of and factors associated with chronic kidney disease among patients infected with human immunodeficiency virus attending care and treatment centers at tertiary hospitals in dodoma, Tanzania

ABSTRACT

## Mashaka Mwise<sup>a,b,c</sup>, Sarah Magoma<sup>b</sup>, Alfred Meremo<sup>a,b,c,\*</sup>

<sup>a</sup> Department of Internal Medicine, School of Medicine & Dentistry, The University Dodoma, Dodoma, Tanzania

<sup>b</sup> Department of Internal Medicine, The Dodoma Referral Regional Hospital, Dodoma, Tanzania

<sup>c</sup> Department of Internal Medicine, The Benjamin Mkapa Hospital, Dodoma, Tanzania

## ARTICLE INFO

Keywords: Prevalence Factors CKD HIV/AIDS Dodoma Tanzania	<i>Background</i> : The burden and risk of developing chronic kidney disease (CKD) among patients with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is higher than in the general population. This study aimed to determine prevalence of and associated factors with CKD among adults infected with human immunodeficiency virus at tertiary hospitals in Dodoma, Tanzania. <i>Method</i> : ology: A cross-sectional study was carried out between November 2022 to April 2023. Patients' demographic data, and clinical measurements were obtained on the day of the visit. Laboratory investigations were performed as standard of care. Descriptive and inferential ana- lyses were performed, and variables associated with CKD were identified by multivariable logistic regression. <i>Results</i> : A total of 223 patients were enrolled, with a median age of 47 (IQR 38–56) years, and 72.2 % were female. The CKD prevalence was 23.3 % whereby 18.4 % had CKD stage 3a, 4.5 % had CKD stage 3 b, and 0.4 % had CKD stage 4. CKD was observed largely among patients with obesity (34.15 %), anemia (29.41 %), hypertension (45.00 %), and diabetes mellitus (50.00 %). Variables with higher odds for CKD after adjusted analysis were hypertension (OR 3.03, 95 %% CI 1.29–7.11, P = 0.0109), diabetes mellitus (OR 4.50, 95 % CI 1.35–15.03, P = 0.0144), obesity (OR 3.07, 95 % CI 1.11–8.47, P = 0.0301), anaemia (OR 2.42, 95 % CI 1.12–5.26, P = 0.0252) and for each one-unit increase in age (years), there was statistically significant increase in the odds of having CKD by 1.084 folds (OR = 1.084, 95 % CI 1.039–1.131, p = 0.0002). <i>Conclusion</i> : The prevalence of CKD among patients with HIV/AIDS is high. Age, obesity, anaemia, hypertension, and diabetes mellitus were strongly associated with CKD suggesting a need for integrating initiatives for non-communicable disease control in this population.

\* Corresponding author. Department of Internal Medicine, School of Medicine, The University of Dodoma, Tanzania. 2

*E-mail addresses*: cmashaka1@gmail.com (M. Mwise), sarahmagoma.sm@gmail.com (S. Magoma), meremoal@gmail.com, alfred.meremo@udom.ac.tz (A. Meremo).

## https://doi.org/10.1016/j.heliyon.2024.e32994

Received 30 November 2023; Received in revised form 1 May 2024; Accepted 12 June 2024

Available online 14 June 2024

<sup>2405-8440/© 2024</sup> The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

#### 1. Introduction

Chronic kidney disease (CKD), is defined as decreased kidney function identified by glomerular filtration rate (GFR) of less than 60 ml/min per  $1.73 \text{ m}^2$ , or markers of kidney damage, or both, of at least 3 months duration, regardless of the underlying cause [1]. CKD is a global public health issue that has risen from the 27th to 12th most common cause of mortality in the previous two decades [2]. Globally the prevalence of CKD in the general population ranges between 8 and 16 %, while the prevalence of CKD among patients with HIV/AIDS varies geographically between 2.3 and 53.3 % [3]. The burden of HIV infection is highest in Sub-Saharan Africa with 75 % of new infections occurring in this region [4]. According to Samar et al. (2017) meta-analysis, the pooled prevalence of CKD among patients with HIV/AIDS in Africa was 24.7 % [5].

The prevalence of CKD among persons with HIV/AIDS varies across Sub-Saharan Africa, South Africa reported a prevalence of 28.5 %, Ethiopia 16.1 %, rural Tanzania 15.7 %, Nigeria 24.8 % and Cameroon had higher prevalence with 44.4 % affected [6–10]. The delay in diagnosing CKD among patients with HIV/AIDS carries a high mortality, in the study done in Cameroon, mortality due to CKD among patients with HIV/AIDS was 49 % within one year of diagnosis, one of the contributing factors is delayed detection of CKD and late referral to nephrologists [11]. Recent evidence suggests that the prevalence of CKD among patients with HIV/AIDS is rising, including end-stage kidney disease (ESKD), and patients with HIV are more likely than those without HIV to acquire ESKD, with a 2- to 20-fold increased risk compared to the general population [10]. The widespread use of ART has resulted in the decline of the hallmark kidney disease of HIV infection, HIV-associated nephropathy (HIVAN), however, the frequency of CKD among patients with HIV has increased at the same time [12]. Patients with HIV who are receiving ART have increased survival and are subjected to lifetime ART, which has the potential to cause or worsen kidney damage, also with increased survival the patients with HIV are subjected to age-related comorbidities like hypertension and diabetes which are also important risk factors for CKD [13].

Both HIV-related factors and traditional factors are among the risk factors for the development and progression of CKD in patients with HIV [14]. These factors include host genetic susceptibilities such as *APOL*1 gene, sickle cell trait, obesity, older age, black race, illicit drug use, herbal medication, hyperlipidemia, HIV-viremia, long HIV-infection duration, and low CD4 T lymphocyte count [15]. Moreover, it is worth mentioning that anemia and proteinuria are associated with the development and progression of CKD, and also are poor prognostic markers for CKD [16]. Understanding the prevalence and factors associated with CKD among patients with HIV/AIDS in our settings is vital for better treatment interventions and improved outcomes. Thus, this study aimed to assess the prevalence of and factors associated with CKD among patients with HIV/AIDS attending tertiary hospitals in Dodoma, Tanzania.

## 2. Material and methods

## 2.1. Study design, population, and settings

This was a cross-sectional study designed at Care and Treatment Centers [CTCs] in Dodoma Referral Regional Hospital [DRRH] and Benjamin Mkapa Hospital [BMH] in Dodoma, Tanzania conducted from November 2022 to April 2023. The Benjamin Mkapa Hospital and DRRH are tertiary hospitals in Dodoma with a bed capacity of 400 and 420 respectively. Both hospitals are teaching hospitals for the University of Dodoma (UDOM) and provide both specialized and super specialized healthcare to central and nearby zones of Tanzania. The DRRH and BMH have CTCs that serve about 3000 patients with HIV/AIDS per month who have free access to Anti-Retroviral Therapy [ART]. Study participants were adult patients with HIV/AIDS over the age of 18 years who attended CTCs at BMH and DRRH with at least 6 months of ART use, good adherence to ART, and after giving their consent. Adherence was defined as good if it is  $\geq$  95 % (<2 doses of 30 doses or <3 doses of 60 doses is missed) as documented by ART Healthcare [17]. The participants with a history of CKD before the diagnosis of HIV/AIDS and pregnant women were excluded from the study.

## 2.2. Data collection and laboratory procedures

The sample size was obtained using Kish and Leslie's sample size calculation, the minimum required sample size of this study was 203 patients who had HIV/AIDS. Consecutive sampling technique was used whereby every patient who met the inclusion criteria during the study period was enrolled into the study until the last participant. Participants who consented were interviewed utilizing a structured questionnaire, The information on social demographics such as gender, age, level of education, duration since diagnosis of HIV/AIDS, and medical history about co-morbidities such as hypertension and diabetes and presence of other risk factors for CKD such as illicit drugs, herbal medication, nephrotoxic drugs were collected and filed into a questionnaire. The automated digital blood pressure machine of HEM-7360 E of Omron brand was used to measure blood pressure (BP) in each participant. All BP measurements were taken following American Heart Association guideline, Measurement of Blood Pressure in Humans, A Scientific Statement From the American Heart Association, 2019 [18]. Hypertension was defined as an average of two BP measurements (2 min apart) of  $\geq$ 140/90 or a patient who is using antihypertensive medications [19]. The Body weight and height were measured, and the Body Mass Index (BMI) was calculated and classified according to the Report of a WHO Consultation Obesity: Preventing and Managing The Global Epidemic [20], whereby BMI was classified as follows, underweight <18.5, normal 18.5–24.9, overweight 25.0–29.9, obesity >30. The laboratory tests done included HIV-RNA viral load, CD 4 T lymphocyte count, Full Blood Picture, viral hepatitis B infection, viral hepatitis C infection which were performed and analyzed by Cobas 6000 analyzer (Roche Diagnostics, USA). Blood sugar levels (FBG/RBG) were done according to standard operating procedures and urinary protein creatinine ratio (uPCR) was calculated by dividing the amount of protein (g/dl) by the creatinine level (g/dl) in a spot urine test. The serum creatinine was measured by using a well-calibrated Erba XL 200 Automatic Biochemistry Analyzer made by Erba Mannheim company in Germany. The results were

measured in µmol/L and then eGFR was calculated by using CKD-EPI formula 2021 and measured in ml/min/1.73 m<sup>2</sup> [21]. All the laboratory procedures in this study were operated following the standard operating procedures from the Benjamin Mkapa and Dodoma Regional Referral Hospitals accredited laboratories. Based on eGFR the CKD was classified under the KDIGO guideline of 2012 as Stage 3a eGFR from 45 to 59, Stage 3 b eGFR 30–44, Stage 4 eGFR 15–29, Stage 5 EGFR <15 ml/min/1.73 m<sup>2</sup> [22]. HIVAN is defined as a combination of eGFR of < 60 ml/min/1.73 m<sup>2</sup> [13], nephrotic range proteinuria by uPCR  $\geq$ 3.5 g/g [23], CD4-count of <200 cells/mL [24], detectable HIV-RNA viral load and with the pathologic findings of collapsing focal segmental glomerulosclerosis [25].

#### 2.3. Data management and analysis

A statistical software IBM SPSS Statistics version 27, was used for data analysis, and data cleaning was performed before analysis. Descriptive analysis was used to summarize variables whereby, categorical variables were presented as proportions and frequency tables, and continuous variables were reported as medians with interquartile range. Differences between groups of patients with CKD and those without CKD were compared by using the Chi-square test, and the Fishers-exact test was used when more than 20 % of our cell counts had an expected frequency of less than 5. Logistic regression was used to examine the association between variables, and Odds ratios with the 95 % confidence interval (CI) were used to quantify the degree of association between variables and CKD. Variables with a p-value of less than 0.2 on univariate logistic regression models were then fitted into the multivariate logistic regression models, variables with a p-value of less than 0.05 were considered to have significant strength of association.

## 2.4. Ethical issues

Before the conduction of this study ethical approval was obtained from the University of Dodoma Ethical Committee (Institutional



Fig. 1. Patients' enrolment and categorization flow chart.

Research Review Ethical Committee-IRREC), Reference number MA.84/261/63/103 prior conduction of this study. Written informed consent was obtained from each of the participants before embarking on data collection.

## 3. Results

In this study 236 participants were assessed for eligibility according to inclusion and exclusion criteria, 13 participants were excluded, of which 11 declined to participate and 2 were pregnant. Therefore 223 patients were enrolled in this study, The overall prevalence of CKD (eGFR <60 ml/min/ $1.72 \text{ m}^2$ ) by CKD-EPI (2021) was 52 (23.3.%), while one subject 1 (0.45 %) had HIVAN (Fig. 1).

## 3.1. Socio-demographic and clinical characteristics of the study participants

Table 1

Of the 223 study participants, (72.2 %) were female, and the mean age of the participants was 47 (38–56) years. The majority of the participants (59.6 %) had a primary level of education and a few (9.4 %) had tertiary level education. Almost half (49.3 %) of the participants were married, 20.2 % were single, and 15.2 % were divorced or were widows/widowers. The median Body Mass Index was 24.78(IQR 22.43–28.60) kg/m<sup>2</sup>, median systolic blood pressure 126(IQR 115–136) mmHg, median diastolic blood pressure 70 (IQR 65–85) mmHg, median duration of HIV infection was 7 (3–11) years. The median CD 4 T lymphocyte count was 588(IQR 358–761) cells/mL, median serum creatinine level 91(IQR 72–105)  $\mu$ mol/L, median eGFR was 74(IQR 61–95) ml/min/1.73 m<sup>2</sup>, median uPCR was 0.13(IQR 0.12–0.14) g/g and median hemoglobin level 12.2 (IQR 11–13.2) g/dL. Furthermore, 60 (26.91 %) were hypertensive, 20 (8.97 %) had diabetes mellitus, 9 (4.04 %) had Chronic hepatitis B and 3 (1.35 %) had hepatitis C. Almost half (42.2

Socio-demographic and	clinical	characteristics	of 223	patients.

Characteristics	N (%) or Median (IQR)
Age	47 (38–56)
Sex	
Male	62 (27.80)
Female	161 (72.20)
Education Level	
No formal education	17 (7.62)
Primary Education	133 (59.64)
Secondary Education	52 (23.32)
Tertiary Education	21 (9.42)
Marital Status	
Single	45 (20.18)
Married	110 (49.33)
Divorced	34 (15.25
Widow/Widower	34 (15.25)
ART regimen	
TLD	223 (100)
Other	0 (0.00)
BMI (kg/m <sup>2</sup> )	24.78 (22.43-28.60)
Systolic blood pressure (mmHg)	126 (115–136)
Diastolic blood pressure (mmHg)	70 (65–85)
Duration of HIV infection (years)	7 (3–11)
CD4-lymphocyte count (cells/mL)	588 (358–761)
Serum creatinine (µmol/L)	91 (72–105)
eGFR (ml/min/1.73m <sup>2</sup> )	74 (61–95)
uPCR (g/g)	0.13 (0.12-0.14)
Hb level (g/dL)	12.1 (11–13.2)
Diagnosis of hypertension	60 (26.91 %)
Duration of hypertension (years)	1 (0–3)
Diagnosis of diabetes	20 (8.97 %)
Duration of diabetes mellitus (years)	3.5 (2–5)
Hepatitis B infection	9 (4.04 %)
Hepatitis C infection	3 (1.35 %)
HIV-RNA viral load	
< 50 (copies/mL)	213 (95.5 %)
<b>50</b> + (copies/mL)	10 (4.5 %)
WHO HIV Clinical stage	
I	32 (14.35)
Ш	59 (26.46)
III	94 (42.15)
IV	38 (17.04)

Abbreviations, IQR, interquartile range, BMI, body mass index; uPCR, urine protein creatinine ratio; eGFR, estimated glomerular filtration rate; CD4, cluster of differentiation 4; Hb, Hemoglobin; HIV, human immunodeficiency virus; WHO, World Health Organization; HIV, human immunodeficiency virus; RNA, Ribonucleic acid. %) of the patients with HIV/AIDS were in WHO stage III, 26.5 % of the patients were in WHO stage II, 17.0 % of the patients were in WHO stage IV and 14.4 % were in WHO HIV/AIDS clinical stage I. The majority (95.5 %) of the patients had HIV-RNA viral load of <50 copies/mL with very few 10 (4.5 %) having $\geq$  50 copies/mL (Table 1).

#### 3.2. Clinical pattern of CKD among patients with HIV/AIDS

Of 223 participants 41 (18.39 %) had CKD stage 3a, 10 (4.48 %) had CKD stage 3 b, and 1 (0.45 %) subject had CKD stage 4 (eGFR of 28 ml/min/1.73 m<sup>2</sup>) with nephrotic range proteinuria by uPCR (6.2 g/g), CD4 T-lymphocyte count of 105 cells/mL and viral load of 1003 copies/mL. Of all 223 participants, 36 (16 %) had Moderate to severe (A2 and A3) proteinuria by uPCR as per KDIGO classification, while participants with CKD stage 3 consist majority 24 (66.7 %) of the population with proteinuria (Table 2).

Concerning age, a large proportion of CKD was observed among patients aged 40 years and above 51 (32.68 %%), With respect to BMI, a significant proportion of CKD was observed among patients with obesity 14 (34.15 %), Regarding co-morbidities, a large proportion of those with CKD was observed among patients with hypertension 27 (45.00 %), diabetes mellitus 10 (50.00 %) and anemia 35 (29.41 %). Furthermore, a large proportion of those with CKD was observed among patients with more than 10 years of HIV-infection diagnosis (39.66 %) (Table 3).

#### 3.3. Factors associated with CKD among patients with HIV/AIDS

We divided the patients into two subgroups according to CKD status [ CKD (eGFR <60 ml/min/1.73 m<sup>2</sup>) vs. No CKD (eGFR  $\ge 60$  ml/min/1.73 m<sup>2</sup>)], seven potential variables were identified after performing univariate logistic regression analyses. Backward elimination reduced this to 5 parameters; Variables with higher odds for CKD after multivariable logistic regression analysis hypertension (OR 3.03, 95 %% CI 1.29–7.11, P = 0.0109), diabetes mellitus (OR 4.50, 95 % CI 1.35–15.03, P = 0.0144), Obesity (OR 3.07, 95 % CI 1.11–8.47, P = 0.0301), anemia (OR 2.42, 95 % CI 1.12–5.26, P = 0.0252) and for each one-unit increase in age (years), there was statistically significant increase in the odds of having CKD by 1.084 folds (OR = 1.084, 95 % CI 1.039–1.131, p = 0.0002) (Table 4).

#### 4. Discussion

This study assessed the prevalence, clinical pattern, and risk factors for CKD among patients with HIV/AIDS attending CTCs in tertiary hospitals in Dodoma, Tanzania. The overall prevalence of CKD among patients with HIV/AIDS is 23.3 %, a large proportion of patients with CKD were older than 40 years of age, had obesity, anemia, hypertension, diabetes mellitus, and had a duration of HIV infection since diagnosis of more than 10 years. Furthermore, in multivariable analysis age, obesity, anemia, hypertension, and diabetes mellitus were significantly associated with the likelihood of having CKD, while duration of HIV infection did not show significant association with the development of CKD.

The prevalence of CKD in patients with HIV/AIDS in our study is higher (23.3 %) than in a study that was done in Morogoro Tanzania 15.7 %, a study done in Ethiopia 16.1 %, in Mexico 15.8 % and Spain 4.9 % [26–29]. Our findings are also comparable to a report of a systematic review on CKD in persons living with HIV, which showed a prevalence of CKD range of 2.3 %–53.3 % [3]. Some studies done in Nigeria and Cameroon showed a higher prevalence of CKD in patients with HIV/AIDS, 26 % and 44.4 % respectively [30,31]. These observed differences could be due to differences in the characteristics of study participants, such as age, race, and geographical location. Furthermore, variations in risk factors such as the prevalence of diabetes and hypertension in the sample population could affect the results. Some studies excluded patients with diabetes mellitus and hypertension, other studies recruited participants as young as 15 years old.

Our findings indicate that 51 (22.9 %) out of 52 (23.3 %) had CKD stage 3 and 1 (0.45 %) had an eGFR of 28 ml/min/1.73 m<sup>2</sup>, with very severely increased proteinuria, low CD4 T-lymphocyte count and detectable viral load. This is similar to findings from other studies where the majority of patients with HIV/AIDS had CKD stage 3 [32,33]. It was observed in other studies that with the use of effective combination ART, the prevalence of severe forms of HIV/AIDS has largely declined, the patients' survival has been prolonged and the spectrum of renal diseases has shifted, whereby, traditional risk factors such as co-morbidities like hypertension and diabetes

#### Table 2

Pattern of proteinuria by uPCR across eGFR categories by CKD-EPI (2021).

2	Proteinuria categories (expressed as g protein/g creatinine in urine)				
eGFR categories (expressed as mL/min/1.73m <sup>2</sup> )	A1 (<0.150 g/g) N (%)	A2 (0.150–0.499 g/g) N (%)	A3 (≥0.5 g/g) N (%)	Total	
Stage 1 (≥90)	60 (32.09)	4 (17.39)	0 (0.00)	64 (28.70)	
Stage 2 (60-89)	100 (53.46)	5 (21.74)	2 (15.38)	107 (47.98)	
Stage 3a (45–59)	22 (11.76))	11 (47.82)	8 (61.54)	41 (18.39)	
Stage 3 b [30-44]	5 (2.67)	3 (13.04)	2 (15.38)	10 (4.5)	
Stage 4 [15-29]	0 (0.00)	0 (0.00)	1 (7.69)	1 (0.45)	
Stage 5 (<15)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	
Total	187	23	13	223	

The table demonstrates the number of individuals (%) that belong to each stage of CKD according to both proteinuria level and estimated glomerular filtration rate by CKD -EP1(2021).

#### Table 3

Clinical pattern of CKD among patients with HIV/AIDS.

Characteristic	All N (%)	No CKD N (%)	CKD N (%)	Chi-Square	P-Value
	223	171 (76.68)	52 (23.32)		
Age (vears)	-			22 6266	< 0.0001
18-39	62 (27 80)	61 (98 39)	1 (0.02)	22.0200	< 0.0001
40+	161 (72.20)	110 (68.32)	51 (31.68)		
Sex	101 (72.20)	110 (00.02)	01 (01.00)	0.0261	0.8716
Male	62 (27 80)	48 (77 42)	14 (22 58)	0.0201	0.0710
Female	161 (72 20)	123 (76 40)	38 (23.60)		
BMI	101 (72.20)	120 (70.10)	30 (20.00)	10 1474	0.0174
Underweight	7 (3.14)	5 (71.43)	2 (28.57)		
Normal	107 (47.98)	92 (85.98)	15 (14.02)		
Overweight	68 (30.49)	47 (69.12)	21 (30.88)		
Obesity	41 (18.39)	27 (65.85)	14 (34.15)		
Hepatitis B infection		_, (00100)	- ( (		0.2185*
Negative	214 (95.96)	166 (77.57)	48 (22,43)		
Positive	9 (4.04)	5 (55.56)	4 (44.44)		
Hepatitis C infection					1.000*
Negative	220 (98.65)	168 (76.36)	52 (23.64)		
Positive	3 (1.35)	3 (100)	0 (0.00)		
Anaemia**				5.2984	0.0213
No	167 (74.89)	87 (83.65)	17 (16.35)		
Yes	56 (25.11)	84 (70.59)	35 (29.41)		
Hypertension				21.5805	< 0.0001
No	163 (73.09)	138 (84.66)	25 (15.34)		
Yes	60 (26.91)	33 (55.00)	27 (45.00)		
Diabetes mellitus		. ,			0.0096*
No	203 (91.03)	161 (79.31)	42 (20.69)		
Yes	20 (8.97)	10 (50.00)	10 (50.00)		
HIV-RNA viral load					1.000*
<50 (copies/mL)	213 (95.52)	163 (76.53)	50 (23.47)		
50+(copies/mL)	10 (4.48)	8 (80.00)	2 (20.00)		
CD4 T-lymphocyte count				1.4531	0.2280
<500 cells/mL	87 (39.01)	63 (72.41)	24 (27.59)		
500+ cells/mL	136 (60.99)	108 (79.41)	28 (20.59)		
WHO HIV clinical stage				1.5184	0.6780
I	32 (14.35)	24 (75.00)	8 (25.00)		
П	59 (26.46)	45 (76.27)	14 (22.73)		
III	94 (42.15)	70 (74.47)	24 (25.53)		
IV	38 (17.04)	32 (84.21)	6 (15.79)		
Duration of HIV infection(years)				14.0890	0.0009
0-5	92 (41.26)	80 (86.96)	12 (13.04)		
6-10	73 (32.74)	56 (76.71)	17 (23.29)		
11-24	58 (26.01)	35 (60.34)	23 (39.66)		

The clinical pattern was based on the Chi-square test, \*Fisher exact was used; \*\*Anemia defined as female Hemoglobin level <11.9, Male <13.6. Abbreviations; BMI, Body mass index; HIV-RNA, human immunodeficiency virus ribonucleic acid; WHO, World Health Organization; CD-cluster of differentiation.

play a greater role in the development of CKD among patients with HIV/AIDS [13,34]. Our study suggested a similar observation, whereby a large proportion of CKD was observed among patients who had hypertension and those patients who had diabetes mellitus. It is unquestionably established that persistently elevated blood pressure leads chronic kidney damage by hypertensive arteriolar nephrosclerosis, while diabetes mellitus leads to diabetic nephropathy which progresses from glomerulobasement membrane thickening, to mesangial expansion, nodular glomerulosclerosis, and global glomerulosclerosis [35,36]. In this study, both hypertension and diabetes mellitus were significantly associated with the likelihood of having CKD whereby, in adjusted analysis those with hypertension had 3.03-fold increased risk and people with diabetes mellitus had a 4.5-fold higher likelihood of developing CKD.

Studies have shown that age is an important risk factor for the development of CKD among patients with HIV/AIDS [13,37]. It is established that, due to physiological changes in each decade after the age of 40 years, there is a progressive decline of eGFR by 8 ml/min/1.73 m<sup>2</sup> [38]. In our study a large proportion of CKD patients was observed among patients with age >40 years. In multivariable analysis, age was significantly associated with the development of CKD, for each unit increase in age (years), there was statistically significant increase in the odds of having CKD by 1.084-fold. However other studies did suggest that age was not significantly associated with the development of CKD [39,40]. A possible explanation could be the fact that the majority of the study participants in these studies were younger.

A significant proportion of CKD was observed in patients with obesity in this study, obesity has been mentioned as a risk factor for the development of CKD in several studies [41,42]. A compensatory hyperfiltration takes place in obese people to meet the higher metabolic needs of their increased body weight, chronically increased intraglomerular pressure can harm the kidneys and increase the

#### Table 4

Factors associated with CKD among patients with HIV/AIDS.

Characteristic	unadjusted		adjusted	adjusted	
	OR [95 % CI]	P-value	AOR [95 % CI]	P-value	
Age	1.098 [1.061,1.137]	< 0.0001	1.084 [1.039,1.131]	0.0002	
BMI					
Normal	Ref		Ref		
Underweight	2.453 [0.436,13.814]	0.3088	3.961 [0.479,32.742]	0.2015	
Overweight	2.740 [1.294,5.801]	0.0084	1.744 [0.712,4.268]	0.2235	
Obesity	3.180 [1.386,7.406]	0.0073	3.073 [1.114,8.472]	0.0301	
Anaemia					
No	Ref		Ref		
Yes	2.132 [1.111,4.094]	0.0229	2.424 [1.116,5.263]	0.0252	
Hypertension					
No	Ref		Ref		
Yes	4.516 [2.326,8.769]	< 0.0001	3.029 [1.291,7.105]	0.0109	
Duration of hypertension (years)	1.336 [0.974,1.832]	0.0725			
Diabetes mellitus					
No	Ref		Ref		
Yes	3.833 [1.497,9.813]	0.0051	4.502 [1.349,15.025]	0.0144	
Duration of diabetes mellitus (years)	1.022 [0.654,1.599]	0.9234			
Duration of HIV infection (years)					
0-5	Ref		Ref		
6-10	2.024 [0.897,4.568]	0.0896	0.834 [0.313,2.219]	0.7156	
11-24	4.381 [1.962,9.780]	0.0003	1.019 [0.374,2.777]	0.9710	

likelihood of CKD development [43]. In this study patients with obesity were 3.07-fold more likely to have CKD than those with normal body weight. One study done in rural Tanzania demonstrated that obesity was not associated with the development of CKD among people with HIV/AIDS [28]. This is possible because the prevalence of obesity is higher in urban areas than in rural areas [44]. Anaemia is associated with the development of CKD and End-Stage Renal Disease [45]. Among patients with CKD anemia was observed in few patients and when compared to those patients with normal hemoglobin, those with anemia had a 2.42-fold more likely to have CKD.

Studies have reported that HIV-related risk factors for the development of CKD are high HIV-RNA viral load, low CD4 T-lymphocyte count, longer HIV infection duration, and advanced WHO HIV clinical stage [46]. It is established that HIV- viremia causes kidney damage in different ways, including replication within renal epithelia causing cellular apoptosis and dedifferentiation, furthermore low CD4-T lymphocyte count is associated with increased susceptibility to infections, immune response dysregulation, and heightened chronic inflammatory state which may lead to the development of the CKD [47]. Our study has shown there was no significant difference in the proportion of patients with CKD and those with no CKD regarding these factors. However, few patients among those with CKD had HIV-infection duration of more than 10 years. It was observed that as the duration of illness since diagnosis increased, the likelihood of having CKD also increased, although these findings were not statistically significant. A study done in Mexico suggested that low CD4 count of <200 cells/mL, HIV-RNA viral load  $\geq$ 100,000 copies/mL, and advanced clinical stage of HIV were significantly associated with CKD among HIV-infected persons, furthermore, in Zambian study a CD 4 T lymphocyte count of <350 cells/mL was significantly associated with CKD in Patients with HIV [29,40,48]. These differences could be accounted by the fact that in this study participants were on ART  $\geq$ 6 months, the majority had undetectable HIV-RNA viral load and higher median CD 4 T lymphocyte counts contrary to the participants of mentioned studies which included naïve Patients with HIV, majority had lower CD4-count and higher HIV-RNA viral load with advanced WHO HIV/AIDS clinical stage.

The limitations of this study include: being a cross sectional study rather than interventional or prospective. Also, this study was conducted in two tertiary hospitals in Dodoma thus restricting its generalizability to the entire Tanzania. Despite these limitations, this study reports a high prevalence of CKD among people living with HIV/AIDS from a treatment and health care resource perspective.

## 5. Conclusion

The prevalence of CKD among people living with HIV/AIDS is high. Age, obesity, anaemia, hypertension, and diabetes mellitus are strongly associated with the development of CKD. The study recommends the importance of surveillance and prompt management of modifiable risk factors such as hypertension, diabetes mellitus, obesity, and anaemia among HIV-infected patients to delay the development and progression of CKD. There is need for more emphasis on integrating non-communicable diseases control initiatives in our HIV programs.

## 6. Data availability statement

Data will be made available on request.

#### CRediT authorship contribution statement

Mashaka Mwise: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Sarah Magoma: Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization. Alfred Meremo: Writing – review & editing, Writing – original draft, Supervision, Project administration, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgments

I would like to express my deepest gratitude to all patients who were willing to participate in this study, to the staff of the Care and Treatment Centers [CTC] in Dodoma Referral Regional Hospital [DRRH] and Benjamin Mkapa Hospital [BMH] and hospitals' administrations for permission to conduct this study. Many thanks to the laboratory staff of DRRH and BMH for their hard work and patience. I thank the University of Dodoma for providing support and a favorable atmosphere for my training.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32994.

#### References

- W.C. Winkelmayer, P.E. Stevens, C. Participants, Harmonizing acute and chronic kidney disease de fi nition and classi fi cation: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference, 2021, pp. 1–11.
- [2] C.P. Kovesdy, Epidemiology of chronic kidney disease: an update 2022, Kidney Int Suppl [Internet] 12 (1) (2022) 7–11, https://doi.org/10.1016/j. kisu.2021.11.003.
- [3] J. Park, J.A. Zuñiga, Chronic kidney disease in persons living with HIV: a systematic review, J. Assoc. Nurses AIDS Care 29 (5) (2018 Sep 1) 655-666.
- [4] L Dwyer-lindgren, MA Cork, A Sligar, KM Steuben, KF Wilson, NR Provost, et al., Mapping HIV prevalence in sub-Saharan Africa between 2000 and 2017,

Nature 570 (7760) (2019 Jun) 189–193.

- [5] S.A. Elhafeez, D. Bolignano, G.D. Arrigo, E. Dounousi, G. Tripepi, C. Zoccali, Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa : a systematic review, BMJ Open 8 (1) (2018 Jan 10) e015069.
- [6] H. Mapesi, A.V. Kalinjuma, A. Ngerecha, F. Franzeck, C. Hatz, M. Tanner, et al., Prevalence and evolution of renal impairment in people living with HIV in rural Tanzania. Cdci) (2016) 1–8.
- [7] S.Y. Lokpo, W. Owiredu, J. Osei-yeboah, G.K. Norgbe, L.E. Kuatsienu, M.T. Anim, et al., Chronic kidney disease among Ghanaian HIV individuals on haart in the Ho municipality: a single-center descriptive cross-sectional, Study 5 (2018) 1–10. November 2017.
- [8] N.D. Madala, G.P. Thusi, A.G.H. Assounga, S. Naicker, Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study (2014) 1–9.
- [9] M.O. Ogiator, J.E. Ojobi, P. Asor, Predictors of renal dysfunction among patients with human immunodeficiency virus seen at benue state university teaching 19 (2) (2020) 31–34.
- [10] J.E. Heron, C.I. Bagnis, D.M. Gracey, Contemporary issues and new challenges in chronic kidney disease amongst people living with HIV, AIDS Res. Ther. 17 (1) (2020) 1–13, 171, https://aidsrestherapy.biomedcentral.com/articles/10.1186/s12981-020-00266-3.
- [11] M.P. Halle, N. Essomba, H. Djantio, G. Tsele, H. Fouda, N.H. Luma, et al., Clinical characteristics and outcome of HIV infected patients with chronic kidney disease in Sub Saharan Africa: an example from in Cameroon, BMC Nephrol. 20 (1) (2019) 1–11.
- [12] N.E. Diana, S. Naicker, Update on Current Management of Chronic Kidney Disease in Patients with HIV Infection Update on Current Management of Chronic Kidney Disease in Patients with HIV Infection, 2022.
- [13] J. Gameiro, S. Jorge, J.A. Lopes, HIV and renal disease: a contemporary review, Int. J. STD AIDS 29 (7) (2018 Jun 1) 714-719.
- [14] G. Alfano, G. Cappelli, F. Fontana, L. Di Lullo, B. Di Iorio, A. Bellasi, et al., Kidney disease in HIV infection, J. Clin. Med. 8 (2019) 1254 [Internet]. 2019 Aug 19 [cited 2022 Mar 8];8(8):1254, https://www.mdpi.com/2077-0383/8/8/1254/htm.
- [15] C.R. Swanepoel, M.G. Atta, V.D. D'Agati, M.M. Estrella, A.B. Fogo, S. Naicker, et al., Kidney disease in the setting of HIV infection: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference, Kidney Int. 93 (3) (2018 Mar 1) 545–559.
- [16] L. Schaefer, M. Xiao, B.N. Bohnert, D. Essigke, M. Wo, J.M. Beirne, et al., Proteinuric Chronic Kidney Diesease Is Associated with Altered Red Blood Cell Lifespan, Deformability and Metabolism, 2021, pp. 1227–1239.
- [17] A Tesfaye, TA Legesse, MA Reta, North-Eastern Ethiopia : A Cross-Sectional Study, Ethiop J. Health Sci. 29 (3) (2019 May) 299–308.
- [18] P. Muntner, D. Shimbo, R.M. Carey, J.B. Charleston, T. Gaillard, S. Misra, et al., Measurement of Blood Pressure in Humans, 2019, pp. 1–32.
- [19] P. Geldsetzer, J. Manne-goehler, M. Marcus, C. Ebert, Z. Zhumadilov, C.S. Wesseh, et al., Articles the state of hypertension care in 44 low-income and middleincome countries : a cross-sectional study of nationally representative individual-level data from 1 · 1 million adults, Lancet (2019) 1–11.
- [20] L. Uccioli, G. Monticone, F. Russo, F. Mormile, L. Durola, G. Mennuni, et al., Autonomic neuropathy and transcutaneous oxymetry in diabetic lower extremities, Diabetol. Metab. Syndrome 37 (10) (2003) 1051–1055.
- [21] W.G. Miller, H.W. Kaufman, A.S. Levey, J.A. Straseski, K.W. Wilhelms, H.Y.E. Yu, et al., National kidney foundation laboratory engagement working group recommendations for implementing the CKD-EPI 2021 race-free equations for estimated glomerular filtration rate: practical guidance for clinical laboratories, Clin. Chem. 68 (4) (2022) 511–520.
- [22] M. Murton, D. Goff-Leggett, A. Bobrowska, J.J. Garcia Sanchez, G. James, E. Wittbrodt, et al., Burden of chronic kidney disease by KDIGO categories of glomerular filtration rate and albuminuria: a systematic review, Adv. Ther. 38 (1) (2021) 180–200.
- [23] G. Hall, C.M. Wyatt, Mechanisms of proteinuria in HIV, Front. Med. 8 (October) (2021) 1-7.
- [24] F.X. Lescure, C. Flateau, J. Pacanowski, I. Brocheriou, E. Rondeau, P.M. Girard, et al., HIV-associated kidney glomerular diseases: changes with time and HAART, Nephrol. Dial. Transplant. 27 (6) (2012) 2349–2355.

- [25] L. Palau, S. Menez, J. Rodriguez-Sanchez, T. Novick, M. Delsante, B.A. McMahon, et al., HIV-associated nephropathy: links, risks and management, HIV AIDS Res. Palliat. Care 10 (2018) 73–81.
- [26] A. Bonjoch, E. Negredo, B. Bayes, J. Bonet, B. Clotet, R. Romero, Prevalence, Evolution, and Related Risk Factors of Kidney Disease Among Spanish HIV-Infected Individuals, 2017.
- [27] G.A. Manaye, D.D. Abateneh, W. Niguse, Chronic Kidney Disease and Associated Factors Chronic Kidney Disease and Associated Factors Among HIV/AIDS Patients on HAART in Ethiopia, 2022.
- [28] H. Mapesi, A.V. Kalinjuma, A. Ngerecha, F. Franzeck, C. Hatz, M. Tanner, et al., Prevalence and evolution of renal impairment in people living with HIV in rural Tanzania, Open Forum Infect. Dis. 5 (4) (2018) 1–8.
- [29] V. Valdivia-Cerda, M. Alvarez-Zavala, K. Sánchez-Reyes, R.I. Cabrera-Silva, V.V. Ruiz-Herrera, A.D. Loza-Salazar, et al., Prevalence and risk factors of chronic kidney disease in an HIV positive Mexican cohort, BMC Nephrol. 22 (1) (2021) 1–7, https://doi.org/10.1186/s12882-021-02526-4 [Internet].
- [30] H.M. Patrice, O. Moussa, K.F. François, M. Yacouba, M. Ngahane, B. Hugo, et al., Prevalence and associated factors of chronic kidney disease among patients infected with human immunodeficiency virus in Cameroon 12 (5) (2018) 268–274.
- [31] A.M. Nalado, A. Kano, T. Hospital, A. Abdu, B. Adamu, M.H. Aliyu, Prevalence of chronic kidney disease markers in Kumbotso, rural Northern Prevlaence of chronic kidney disease markers in Kumbotso, rural Northern Nigeria, Afr J Med Med Sci. 45 (1) (2016 May) 61–65.
- [32] R.M. Brito, D.T. Nguyen, J.R. Johnson, E.J. Lai, R.E. Castro, A.M.A. Id, et al., Chronic Kidney Disease in Patients Infected with Human Immunodeficiency Virus (HIV) in an Urban Cohort, 2019, pp. 1–14.
- [33] U.E. Ekrikpo, A.P. Kengne, A.K. Bello, E.E. Effa, J.J. Noubiap, B.L. Salako, et al., Chronic kidney disease in the global adult HIV-infected population: a systematic review and meta-analysis, PLoS ONE, Public Library of Science 13 (2018).
- [34] A. Bertoldi, E De Crignis, A. Miserocchi, I. Bon, G. Musumeci, HIV and Kidney: A Dangerous Liaison, 2017 (June 2020.
- [35] V.V. Costantino, A. Fernanda, G. Lorenzo, V. Bocanegra, P.G. Vall, Molecular Mechanisms of Hypertensive Nephropathy : Renoprotective Effect of Losartan through Hsp 70, 2021.
- [36] R. Agarwal, Pathogenesis of Diabetic Nephropathy, vols. 2-7, 2020.
- [37] A. Bertoldi, E De Crignis, A. Miserocchi, I. Bon, G. Musumeci, HIV and Kidney: A Dangerous Liaison, 2017 (January.
- [38] Z. Karam, J. Tuazon, Anatomic and physiologic changes of the aging kidney, Clin Geriatr Med [Internet] 29 (3) (2013) 555–564, https://doi.org/10.1016/j. cger.2013.05.006.
- [39] L. Frigati, S. Mahtab, P. Nourse, P. Ray, S. Perrazzo, T. Machemedze, et al., Prevalence of Risk Factors for Chronic Kidney Disease in South African Youth with Perinatally Acquired HIV, 2018.
- [40] E.E. Abene, Z.M. Gimba, O.O. Agbaji, E.I. Agaba, Prevalence of Chronic Kidney Disease Among Antiretroviral Naïve Human Immunodeficiency Virus Infected Patients, 2018, pp. 42–46.
- [41] V.A. Luyckx, K.R. Tuttle, G. Garcia-garcia, Z.A. Massy, O. Moe, R.G. Nelson, et al., Reducing major risk factors for chronic kidney disease, Kidney Int Suppl [Internet] 7 (2) (2017) 71–87, https://doi.org/10.1016/j.kisu.2017.07.003.
- [42] H. Knobel, P. Domingo, I. Suarez-Jozano, F. Gutierrez, V. Estrada, Rate of cardiovascular, renal and bone disease and their major risks factors in HIV-infected individuals on antiretroviral therapy in Spain, Enferm Infecc Microbiol Clin [Internet] 37 (6) (2019) 373–379, https://doi.org/10.1016/j.eimce.2018.09.005.
  [43] C.P. Kovesdy, S. Furth, C. Zoccali, Obesity and Kidney Disease: Hidden Consequences of the Epidemic, 2017, pp. 281–291.
- [44] I.O. Ajayi, C. Adebamowo, H. Adami, S. Dalal, M.B. Diamond, F. Bajunirwe, et al., Urban rural and geographic differences in overweight and obesity in four sub-Saharan African adult populations : a multi-country cross-sectional study, BMC Publ. Health (2016) 1–13, https://doi.org/10.1186/s12889-016-3789-z [Internet]
- [45] Sang-wook Yi, S.J. Moon, J. Yi, Low-normal Hemoglobin Levels and Anemia Are Associated with Increased Risk of End- Stage Renal Disease in General Populations : A Prospective Cohort Study, 75, 2019, pp. 1–12.
- [46] L. Palau, S. Menez, J. Rodriguez-Sanchez, T. Novick, M. Delsante, B.A. McMahon, et al., HIV-associated nephropathy: links, risks and management, HIV AIDS Res. Palliat. Care 10 (2018) 73-81.
- [47] S. Naicker, S. Naicker, S. Rahmanian, J.B. Kopp, HIV and Chronic Kidney Disease, 2015.
- [48] E. Wantakisha, C. G, M.C. D, M. Renal, Dysfunction Among HIV-Infected Patients on Tenofovir-Based AIDS & Clinical Research Renal Dysfunction Among HIV-Infected Patients on Tenofovir-Based Antiretroviral Therapy at Ronald Ross Hospital in Zambia, 2017.