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Burden and Factors Associated with Renal Dysfunction among People Living with HIV in Dar es Salaam, Tanzania

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Abstract

Renal diseases pose a significant burden of morbidity and mortality, particularly among People Living with HIV (PLHIV). The risks are further compounded by drug-induced renal toxicity, and the growing burden of hypertension, diabetes, and Hepatitis C infections. This study assessed the magnitude and factors associated with renal dysfunction among PLHIV attending clinics in Dar es Salaam, Tanzania. A hospital-based cross-sectional study was conducted between January and March 2022 among 331 PLHIV recruited through a multistage sampling. Renal disease was determined through urine analysis and clinical, demographic, and disease-specific data were collected using a structured questionnaire. The analysis, performed in SPSS version 25, involved descriptive analysis, univariate, and multivariable logistic regression to determine the magnitude and predictors of renal dysfunction among PLHIV. Renal dysfunction was observed in 37 (11.1%) participants. Patients with advanced age were 3.89 times more likely to have renal dysfunction (95% CI: 1.56 – 9.72, $p = 0.004$) compared to lower age groups. No statistically significant association was found between renal dysfunction and sex, duration from diagnosis of HIV and on ART, ART-based regimen, HIV viral load, hypertension, or diabetes mellitus. More than one in ten PLHIV in Dar es Salaam, Tanzania, presented with signs of renal dysfunctions, which was more significant among patients aged 55 and older. Routine screening for renal diseases among PLHIV, especially for patients with advanced age is essential to prevent and control for progression to renal failure.

Keywords: Renal dysfunction, proteinuria, ART, People Living with HIV, Dar es Salaam

1. Introduction

The burden of renal diseases is increasing globally, with low- and middle-income countries (LMICs) being the hardest hit, while simultaneously facing a persistent burden of HIV and AIDs (Global Burden of Disease Study 2019). Improved Antiretroviral therapy (ART) has resulted in increased life expectancy for people living with HIV (PLHIV) approaching that of the general population (Jespersen et al., 2021). Consequently, PLHIV are surviving to older ages and thus become more at risk of acquiring and dying from non-communicable diseases (NCDs). (Holmes et al., 2010, Stanifer et al., 2014).

Globally, kidney dysfunction continues to be a significant burden among PLHIV, with prevalence rates ranging between 13.9 to 48.5% (Naicker, 2009; Ekrikpo et al., 2018; Park & Zuniga, 2018). PLHIV have a slightly higher risk of developing chronic kidney disease (CKD) and End Stage Renal Disease (ESRD) than HIV-uninfected patients (Alfano et al., 2019). This increased vulnerability results from several factors, including advanced age, comorbidities such hypertension, diabetes and hepatitis B and C coinfections, HIV-associated nephropathy, HIV immune complex kidney disease, medications for opportunistic infections, and the use of Tenofovir disproxil

fumarate (TDF) based regimen, non-steroidal anti-inflammatory drugs (NSAIDs), and herbal medicines. (Che Awah et al., 2020; NIH.gov, 2021; Mocroft et al., 2010; Flandre et al., 2011; Antonello et al., 2015; Cervantes & Atta, 2023). Studies have shown that patients of African descent have an 18 to 50% higher risk of developing HIV-related ESRD compared to Caucasians. (Alfano et al., 2019). The consequences of renal dysfunction range from acute kidney injury to chronic kidney disease, and end-stage renal disease or death. (Campos, Ortiz, & Soto, 2016).

Globally, the prevalence of end-stage kidney disease and utilization of renal replacement therapies has seen significant increases. Recent reports indicate a rise of 43.1% for end-stage kidney disease and 34.4% for renal replacement therapies (Cockwell & Fisher, 2020). The number of PLHIV on dialysis and dying from ESRD has also increased (Bickel et al., 2013). In Tanzania, around 28% of PLHIV experience renal diseases, contributing to 4.8% of patients on dialysis (Global Burden of Disease, 2017; Barsoum, 2006; Meremo et al., 2018; Cockwell & Fisher, 2020). Further findings have revealed a prevalence of 76% of renal dysfunction among ART-naïve HIV patients in Tanzania (Global Burden of Disease, 2017).

The risk of renal diseases is four times higher among PLHV compared to the general population making prevention the best strategy to mitigate the rising burden (Che Awah et al., 2020; Pongpirul et al., 2018). Efforts to identify individuals at risk of renal diseases early on have included continuous health education, screening, and appropriate referral for proper management and to delay complications. However, the management of NCDs in most LMICs faces challenges due to late diagnosis, lack of disease awareness, and limited curative and preventive services, imposing a significant strain on the already weakened health systems (Naicker, 2009; Wouters et al., 2015; Bastos & Kirsztajn, 2011). These findings suggest that there is still a need to determine the burden and characteristics of renal dysfunction among PLHIV in Tanzania. This study, therefore, aimed at assessing the magnitude and factors associated with renal dysfunction among PLHIV in Dar es Salaam Tanzania using routine urine screening, where proteinuria was the biological marker of interest.

2. Methodology

2.1 Study Design and Setting

A hospital-based cross-sectional study was conducted between January and March 2022 at the HIV Care and Treatment Centres (CTC) of three Regional Referral Hospitals in Dar es Salaam: Amana, Temeke, and Mwananyamala. The study sites were selected using purposeful sampling and the criteria for selecting facilities included those with established HIV CTCs providing services to PLHIV.

2.2 Study Population and Sample Size

PLHIV aged 18 years and above attending HIV clinics at the three regional referral hospitals were recruited in the study. A multistage sampling technique was used to obtain study participants. A proportional to population size sampling was done to determine sample distribution for all three facilities in a ratio of 1:1:1, which gave an even distribution of the sample size of at least 110 participants in each study site. PLHIV, who had voluntarily accepted to participate in the study from each study site were conveniently selected to participate in the study. The sample size for the study was calculated using Cochran's formulae based on the prevalence of renal diseases among PLHIV in Tanzania (Fabian & Naicker, 2009), which gave a minimum sample size of 341 participants.

2.3 Variables and Measurements

Proteinuria is a known proxy measure of renal dysfunction (G. Hall & C. M. Wyatt, 2021) and therefore, was used as an outcome variable in this study. Since renal dysfunction risks could also be heightened by factors other than HIV, variables such as diabetes, hypertension, and demographic characteristics were obtained from the participants during data collection and considered as independent variables. The demographic data was collected using a data extraction tool adopted from Kefeni, Hajito and Getnet (2021). Data collected included age, sex, occupation, marital status, and educational status. Clinical data collected included duration since diagnosis of HIV, type, and duration on ART, history of hypertension, and diabetes mellitus. The tool was administered in both Kiswahili (the national language) and English for those who opted to use the English version. Unique identification numbers were used for each participant and the patient's CTC-ID numbers were used to retrieve records from the registry.

Blood pressure was measured in a standard sitting position after a patient had rested for at least five minutes before two measurements were taken. Patients with blood pressure values greater than 140/90 mmHg were considered hypertensive (NHLB, NIH 2023). Low blood pressure was defined as either systolic BP ≤100mmHg or diastolic BP ≤60mmHg. Pre-hypertension was considered when systolic BP values were between 130 and 140 mmHg. Normal blood pressure was the systolic values from 100-120 mmHg and diastolic values of 60-80 mmHg.

Random Blood glucose (RBG) was measured using a Sinocare glucometer with safe AQ smart glucose strips. The

equipment was selected because it requires a small blood sample (approximately 0.6µl), gives accurate results in less than 15 seconds, and is designed to minimize cross-contamination. RBG value between 4-11 mmol/L was considered normal; however, values > 11 mmol/L and < 4 mmol/L were considered hyperglycaemia and hypoglycaemia, respectively (Seery, 2019).

Proteinuria was determined from each participant. Participants were given sterile urine containers and briefed about providing 20 ml of mid-stream urine for determination of the presence of albumin in the urine. Collected urine samples were labelled with corresponding unique identification numbers similar to the individual study questionnaire. The urine sample was stored in a refrigerator at a temperature of between 2-6 ºC before transporting the specimens the same day to the Lancet Laboratory in Dar es Salaam for analysis. Prior to analysis, urine samples were taken from a refrigerator and kept at room temperature for a minimum of 20 mins to attain room temperature, after which urine sample was processed using a URISCAN machine and 10SGL urine strips. A protein level ≥ 30mg/L in a urine sample was considered proteinuria.

HIV Viral load (HVL) test determines the number of copies of HIV RNA present per millilitre of serum or plasma, and is expressed as copies/mL or in log scale. High HIV viral load indicates viral replication and is often conducted to monitor progress of antiretroviral therapy. In this study, HVL was extracted from the database. The success of antiretroviral therapy is measured both clinically and by suppression of viraemia below 50 copies/mL in two successive measurements (https://shop.elsevier.com/books/clinical-chemistry-immunology-and-laboratory/). Viral load (VL) values above 1000 copies/l were considered high, and VL <1000 copies/liter were considered low. Safety precaution and infection prevention and control (IPC) was observed throughout by wearing of protective gears such as gloves, safety boxes and appropriate disposing bins were used to dispose hazardous waste when measuring blood glucose and during collection and processing urine sample.

2.4 Data Management and Analysis

Data was collected using a developed Google form questionnaire, which was then exported in an Excel sheet. Data cleaning and management were done by checking for the correctness of the recorded values and correcting typing errors. Continuous variables such as age, HVL, duration with HIV, and duration on ART were categorized into groups. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 25. Variables were summarized as means and standard deviation for normally distributed data, and categorical variables were summarized as frequencies and percentages and presented in tables. The prevalence of renal dysfunction was determined by using the frequency and percentage of participants with proteinuria ≥30 mg/l. Demographic and clinical characteristics of the study participants were analysed by descriptive statistics. We computed the Pearson chi-square (X^2) test and univariate regression to determine the factors associated with renal dysfunction. Variables included in the multivariable regression were chosen using the purposeful selection method; independent variables with p-value <0.2 on univariate regression were included in the multivariable model.

2.5 Ethical Consideration

This study carried minimum pain from blood and urine sample collection. The collection of blood could, in some individuals cause pain and skin irritation, and the collection of urine samples could elicit anxiety in some individuals. In order to minimize these, prior to the interviews, the methods and purpose of the study, the benefits and risks were clearly explained to each participant. In addition, all participants were informed that participation in the study was voluntary and participants were free to withdraw from the study at any stage without compromising their rights to receive services from the health facilities. Upon comprehension, each participant was then asked to consent in writing. Ethical approval was obtained from Hubert Kairuki Memorial University (Ref. HK/MD/17/1743, dated 27th September 2021). Letters of introduction and permission to carry out the study in the respective hospitals were presented to the Hospital Administrators. Only authorized personnel had access to the data.

3. Results

A total of 332 participants were recruited: 113 from Mwananyamala RRH, 109 from Amana RRH, and 110 from Temeke RRH. The majority of the participants, 254 (76.6%) were female with a mean age of 43.78 ± 11.58 and an age range of 18-78 years. Among the study participants, 246 (73.7%) had primary education, and 134 (40.1%) were either married or living with partners (Table 1).

Table 1. Demographic characteristics of study participants attending health care at three regional referral hospitals in Dar es Salaam, Tanzania

Variable	n	%
Gender		
Male	78	23.4
Female	254	76.6
Age (years)		
18- 34	65	19.6
35-54	225	67.8
≥ 55	42	12.6
(mean ± SD)	43.78 ± 11.58	
Education level		
No formal education	4	1.2
Primary level	246	73.7
Secondary level	71	21.3
College education	11	3.3
Marital status		
Single	119	35.6
Married/cohabiting	134	40.1
Divorced/separated	41	12.3
Widow/widower	38	11.4

3.1 Clinical Findings

Data on clinical findings are presented in Table 2. In this study, a total of 37 (11.1%) participants had proteinuria an indicator of potential renal dysfunction. Approximately two-thirds (66.3%) of participants had lived with HIV for five years, while 61.1% had been on ART for the same period. Hypertension was prevalent in 73 (21.9%) participants. A total of 212 (63.5%) participants had normal blood pressure, and 83 (24.9%) had hypertension; among them, 26 (35.6%) were known to have hypertension. The mean systolic and diastolic blood pressure (BP) were 127.18 ± 21.7 mmHg and 80.52 ± 14.99 mmHg, respectively. Thirteen participants (3.9%) had diabetes mellitus (known with DM). Regarding ART regimens, most participants (95.03%) were on a tenofovir-based ART regimen, and 263 (93.6%) had low HVL (<1000 copies), with 207 (75.8%) showing complete viral suppression, as presented in Table 2.

Table 2. Clinical findings among PLHIV participants attending health care at three referral hospitals in Dar es Salaam Region, Tanzania the study

Variables	N	%
Years after HIV diagnosis (n = 332)		
≤ 5 years	112	33.7
> 5 years	220	66.3
ART regimen *(n=301)*		
Tenofovir-based ART regimens	287	95.03
Non-tenofovir-based ART regimens	14	4.6
Tenofovir disproxil fumarate (TDF) therapy	276	91.4
Duration on ART		
≤ 5 years	129	38.9
>5 years	203	61.1
HIV Viral load (n=281)		
Low HV	263	93.6
High HVL	18	6.4
Viral load (mean ± SD)	14752 ± 144799	
Hypertensive (Known Hypertensive)	73	21.9
Measured BP		
Low BP	9	2.7
Normal BP	212	63.5
Pre-Hypertensive	28	8.4
Hypertensive	83	24.9
Systolic blood pressure (mean ± SD)	127.18 ± 21.76	
Diastolic blood pressure (mean ± SD)	80.52 ± 14.99	
Patient with Diabetes Mellitus	13	3.9
Measured Blood glucose		
Hypoglycaemia	13	3.9
Normal BG	207	91.9
Hyperglycaemia	12	3.6
Blood glucose (mean ± SD)	5.9 ± 2.60	
Proteinuria		
Yes	37	11.1
No	295	88.9

3.2 Renal Dysfunction

Renal dysfunction was observed in 12 (15.8%) male participants and 10 (23.8%) participants aged 55 years and older. Renal dysfunction was more prevalent in participants who lived with HIV for more than five years, with 25 (11.4%) showing signs of renal dysfunction. Similarly, 24 (11.8%) participants on ART for more than five years and 31 (10.8%) participants on tenofovir-based regimens exhibited renal dysfunction. On the contrary, renal dysfunction was less prevalent among participants with diabetes (n=1, 7.1%), and those who had high HVL (n=1, 5.6%). (Table 3).

Table 3. Association of the demographic, clinical characteristics with renal dysfunction (proteinuria) among PLHIV participants attending health care at the regional referral hospitals in Dar es Salaam, Tanzania

Variables	Proteinuria			
	Yes (%)	No (%)	Chi square (X^2)	P-Value
Age (years)				
18-34	8 (12.3)	57 (87.7)		
35-54	19 (8.4)	206 (91.6)	8.55	0.014
≥ 55	10 (23.8)	32 (76.2)		
Gender				
Male	12 (15.4)	66 (84.6)	1.851	0.174
Female	25 (9.8)	229 (90.2)		
Education level				
No formal education	0	4 (100)		
Primary level	28 (11.4)	218 (88.6)	3.925	0.27
Secondary level	6 (8.5)	65 (91.5)		
College education	3 (27.3)	8 (72.7)		
Marital status				
Single	10 (8.4)	109 (91.6)		
Married/cohabiting	16 (11.9)	118 (88.1)	1.868	0.76
Divorced/separated	5 (12.2)	36 (87.8)		
Widow/widower	6 (15.8)	32 (84.2)		
ART regimen (n=301)				
Tenofovir based	31 (10.8)	256 (89.2)	0.17	0.68
Non-tenofovir based	2 (14.3)	12 (85.7)		
Duration on ART (years)				
≤ 5 years	13 (10.1)	116 (89.9)	0.776	0.678
>5 years	24 (11.8)	179 (88.2)		
Duration since HIV diagnosis (year)				
≤ 5 years	12 (10.7)	100 (89.3)	0.638	0.727
>5 years	25 (11.4)	195 (88.6)		
HIV Viral Load (n=281)				
High HVL	1 (5.6)	17 (94.4)	0.427	0.492
Low HVL	28 (10.6)	235 (89.4)		
Diabetes Mellitus				
Yes	1 (7.1)	13 (92.9)	0.236	0.627
No	36 (11.3)	282 (88.7)		
Hypertension				
Yes	10 (13.7)	63 (86.3)	0.616	0.432
No	27 (10.4)	232 (89.6)		

3.3 Factors Associated with Renal Dysfunction among PLHIV

On bivariate analysis, only age was associated with renal dysfunction (Table 3). Among the participants, those

aged 55 years and older were almost four times more likely to develop renal dysfunction compared to participants of younger age (aOR 3.89, 95% CI [1.56, 9.72], $p = 0.004$). However, other factors such as gender, duration since HIV diagnosis, duration on ART, specific ART regimen, HIV viral load, hypertension, and diabetes mellitus did not show a statistically significant association with the occurrence of renal dysfunction among the study participants both on bivariate and multivariable analysis (Table 4).

Table 4. Factors associated with renal dysfunction among PLHIV in three regional referral hospitals in Dar es Salaam, Tanzania

Characteristics	Univariate analysis			Multivariable analysis		
	cOR	95% CI	p-Value	aOR	95% CI	p-Value
Age (years)						
18-34	1					
35-54	0.45	0.16, 1.25	0.126	2.23	0.73, 6.84	0.160
55+	0.30	0.13, 0.69	0.005	3.89	1.56, 9.72	0.004
Sex						
Male	1			1		
Female	1.67	0.29, 1.26	0.180	1.73	0.74, 4.01	0.210
Duration with HIV (year)						
≤ 5 years	1			1		
> 5 years	0.84	0.41, 1.71	0.620	0.79	0.09, 7.03	0.830
Duration on ART (years)						
≤ 5 years	1			1		
>5 years	0.94	0.45,1.94	0.860	1.55	0.18, 12.9	0.690
ART regimen (n=301)						
Non-tenofovir based	1			1		
Tenofovir based	1.38	0.29, 6.44	0.685	0.64	0.13, 3.18	0.590
HIV Viral Load (n=281)						
Low HVL	1			1		
High HVL	2.03	0.26, 15.81	0.50	1.30	0.16, 10.7	0.810
Hypertension						
No	1			1		
Yes	0.73	0.34, 1.40	0.434	1.32	0.52, 3.36	0.570
Diabetes Mellitus						
No	1			1		
Yes	1.67	0.21, 13.06	0.63	0.72	0.08, 6.65	0.770

4. Discussion

Renal dysfunction was prevalent among 11.1% of PLHIV attending care and treatment at the three regional referral hospitals in Dar es Salaam, Tanzania. This study shows a higher than 6.4% global prevalence reported among PLHIV (Ekrikpo et al., 2018) and is within the prevalence range in other countries in the Saharan (Fabian & Naicker, 2009). Previous studies in the country have indicated varying prevalences of renal dysfunction as determined by proteinuria. While a study at the Muhimbili National Hospital in Dar es Salaam reported a prevalence of 24.7% (Mwenezi et al., 2020), another study conducted in southern highlands revealed a prevalence of 20.7% among PLHIV (Mwanjala, Orio, & Mtebe, 2022). These previous findings are higher than the results in this study and the difference could be explained by differences in the study setting and the characteristics of the

study participants. The previous studies were carried out on patients attending tertiary hospitals which mostly attend to referred patients with comorbidities, including kidney impairment for further management and specialized services. We carried out this study at CTCs, which attend to patients routinely for monitoring and HIV care where the majority of the patients are stable and have no known severe diseases that require specialized care. The relatively lower prevalence of renal dysfunction observed in this study suggests improvement in the quality of services offered at the CTCs on PLHIV and adherence to ART. Our results are supported by previous studies which have reported that adherence to ART results in low viremia and reduced risk of renal dysfunction among PLHIV. (Alfano et al., 2019; Lucas et al., 2014). Compared to previous studies, results of the duration of ART and the type of ART regimen in this study did not significantly associate with renal dysfunction. However, evidence indicates that ARTs, especially Tenofovir Disoproxil Fumarate have a significant impact on the development of renal diseases. (Flandre et al., 2011; Antonello, Antonello, Herrmann, & Tov, 2015; Kefeni, Hajito, & Getnet, 2021). In addition, as renal dysfunction results from viral infestation on the renal parenchyma, therefore, low-level viremia reduces the risk of renal damage (Chou & Chen, 2021). Similarly, our findings concur with the findings in a cohort study in Mwanza **(**Mpondo et al., 2014), but differs from the report of the study in the southern highlands part of Tanzania (Mwanjala, Urio, & Mtebe, 2022).

We observed that older age increases the risk of developing renal dysfunction among PLHIV. Although differences can be found between individuals, it is highly likely that organ functioning, including structural and functional changes of the renal parenchyma and vascular changes among PLHIV contribute to renal diseases. Additionally, the presence of comorbidities with aging likely exacerbates renal dysfunction among PLHIV (Mallappallil et al., 2014; M. E. Hall & J. E. Hall, 2018).

Unlike the reports (Meremo et al., 2018; Mwemezi et al., 2020), the current study did not find a statistically significant association between renal dysfunction and viral load, diabetes mellitus, and hypertension. Renal dysfunction could be attributed to a complex interplay of genetic and environmental factors that influence intrarenal, neurohormonal, immune and inflammatory systems (Desormais et al., 2019). In many instances, abnormal kidney function is obscured by compensatory changes that permit the kidneys to maintain salt and water balance. Such compensatory mechanisms could have been initiated and the use of ART could be contributing to the maintenance of improved renal function in these patients.

Hypertension is a public health issue in Africa that is largely underdiagnosed (Pilleron et al., 2017; WHO, 2018), and studies in sub-Saharan Africa have presented the highest prevalence of hypertension. (Ferdinand, 2020; Masenga et al., 2019). HIV-infected patients may have additional risk factors related to endothelial dysfunction and the metabolic effects of antiretroviral drugs such as dyslipidaemias or insulin resistance. The chronic inflammation induced by HIV can heighten HIV-infected patients' predisposition to CVDs. In general, the prevalence of hypertension in PLHIV on ART and ART-naive PLHIV have ranged from 6 to 50% and 2 to 41%, respectively. (Kamdem et al., 2018). We found a 24.9% prevalence of hypertension among PLHIV on ART of which only 26 (35.6%) were known hypertensives. This observation raises concerns because the assessment of blood pressure is among the routine measurements in PLHV on ART, and patients have the right to know their status. This finding supports previous observations in Africa that hypertension is largely underdiagnosed (Pilleron et al., 2017) which could have partly contributed to increased renal dysfunction even among PLHIV on ART.

These study findings also highlight policy implications for addressing NCDs in Tanzania. The findings report of high prevalence of renal dysfunction among PLHIV as well as an increased risk of renal dysfunction among the elderly. Further, we have observed a persistent trend of underdiagnosis of hypertension including PLHIV. Although there are standing national guidelines on NCD management in the general population and specific populations such as PLHIV. Reports and anecdotal findings suggest low compliance with guidelines in several health facilities in the country, this being influenced by inadequate resources. There is also a need for improved screening and early detection of renal dysfunction among PLHIV to mitigate progression to severe kidney disease. Therefore, further studies to review health facility practice and to understand the factors contributing to below standard of practice need to be conducted in order to improve the policies on NCD management and control.

5. Conclusion and Recommendation

Renal dysfunction was prevalent among 11.1% of PLHIV attending HIV care and treatment facilities in Dar es Salaam, Tanzania. The burden is higher than the global burden among people of the same risk. Within the same population, age was an independent factor associated with renal dysfunction, and awareness of the hypertension status was low. This calls for regular screening and follow-up of renal functions and measurement of blood pressure among PLHIV with advanced age during routine care. Further studies should be carried out to include PLHIV in rural areas to determine the general prevalence of renal dysfunction in Tanzania.

6. Limitations

The findings in this study are useful and provide insight into a public health problem that needs to be addressed by raising awareness of the magnitude and impact of the consequences of renal dysfunction in terms of livelihoods and economic development. The study is limited to a small number of patients in the Dar es Salaam region. Further studies are needed to include people in rural areas.

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Authors Contribution

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The data that support the findings of this study are available on request.

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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