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Prevalence and factors associated with kidney dysfunction among people living with HIV/AIDS in Northern Tanzania: Retrospective cross-sectional study

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Human Immunodeficiency Virus (PLHIV) and Acquired Immunodeficiency Syndrome (AIDS) patients have increased risk for kidney diseases, including HIV-Associated Nephropathy (HIVAN), non-collapsing focal segmental glomerulosclerosis, immune-complex kidney disease, and comorbid kidney disease, kidney injury following long term use of Highly Active-antiretroviral Therapy (HAART) or opportunistic infections medications. In this population, kidney dysfunction is now an increasingly recognized non-AIDS defining condition, and contributes to the increased morbidity and mortality of PLHIV. The role of HIV-related factors in kidney dysfunction still remains unclear. This hospital-based retrospective cross-sectional study investigates the prevalence and factors associated with kidney dysfunction in HIV people attending Care and Treatment Clinics (CTC) at Kilimanjaro Christian Medical Centre (KCMC) in Northern Tanzania. Clinical records of PLHIV were examined from October 2022 to April 2023. Participants included PLHIV on HAART for above 6 months. Serum creatinine was used to estimate eGFR using the 2021 CKD-EPI equation excluding race. Data were analyzed using STATA 14. Multivariate analysis was conducted and P < 0.05 indicated statistical significance. Among the 331 PLHIV on HAART who met the inclusion criteria, 40(12.1%) had impaired kidney function, based on an estimated glomerular filtration rate of ≤60 mL/min/1.73m2, 32 had an eGFR of 30 to 59 mL/min/1.73 m2, 2 had an eGFR of 15 to 29 mL/min/1.73 m2, and 6 had an eGFR of < 15 mL/min/1.73 m2. Anaemia (adjusted odds ratio [AOR] = 3.37, 95% confidence interval [CI]: 1.35-8.42) and femininity (AOR = 4.18, 95% CI: 1.42-8.19) were independent predictors of renal function impairment. Approximately one tenth of the patients had renal function impairment, with half being anaemic. Anaemia and being a woman correlated with impaired kidney function. For this population, routine screenings are recommended for early detection and treatment of anemia and renal function impairment.

Key words: Kidney dysfunction, renal impairment, HIV positive, people living with HIV, HAART, Kilimanjaro Christian Medical Centre.

INTRODUCTION

People Living with HIV (PLHIV) are at an increased risk for both Acute Kidney Injury (AKI) and Chronic Kidney

Disease (CKD) (Swanepoel et al., 2018). With the prevalent use of Highly Active-antiretroviral Therapy (HAART), HIV-Associated Nephropathy (HIVAN) is now uncommon; nevertheless, the prevalence of other kidney diseases has increased. The lifelong HAART exposure in PLHIV, may potentially cause or exacerbate kidney injury (Swanepoel et al., 2018). Current treatment guidelines recommending earlier initiation of HAART (test and treat strategy) may additionally lower the incidence of HIVAN, but the general risk-benefit for kidney health is unknown (Swanepoel et al., 2018). As the HIV-infected population is aging, the causes of morbidity and mortality among PLHIV are shifting from opportunistic infections to non-infectious disorders such as liver, cardiovascular, and kidney diseases. Kidney dysfunction among HIV patients has been reported to be associated with increased morbidity and mortality. Non-communicable Disease (NCD) is increasing and PLHIV are living longer, which is a burden for them. One of the growing NCD in the globe is kidney dysfunction brought on by kidney diseases; prevalence ranges from 13.9 to 48.5% (Alsaeed et al., 2024; Azagew et al., 2014; Shi et al., 2022; Matłosz et al., 2022; Penner et al., 2023; Kefeni et al., 2021; Fiseha et al., 2021; Mwemezi et al., 2020; Danjuma et al., 2020; Brito et al., 2019; Corona-Villalobos et al., 2017; Cheung et al., 2018; Mapesi et al., 2021; Endris et al., 2020; Nyende et al., 2020). In sub-Saharan Africa (SSA) the prevalence of kidney dysfunction in PLHIV is high, ranging from 25 to 77% (Mapesi et al., 2018). Contributing factors to renal impairment are HIV-Associated Nephropathy (HIVAN) which was largely before the introduction of HAART, the high rate of patients with hypertension and diabetes mellitus, as well as co-infections, and chronic use of nephrotoxic drugs such as Tenofovir Disoproxil Fumarate (TDF), atazanavir/ritonavir (ATV/r), and Lopinavir/ritonavir (LPV/r). In Sub-Saharan Africa (SSA), TDF is widely used as a first-line HAART due to its high efficacy and low side effects (Belay et al., 2023).It is important to determine the burden and factors associated with kidney dysfunction in people living with HIV so as formulate appropriate interventions to improve their health.The aim of this study was to determine the prevalence and factors associated with kidney dysfunction among PLHIV on HAART in Northen Tanzania.

METHODOLOGY

Study design

This was a descriptive-analytical, retrospective cross-sectional study, performed on clinical records of PLHIV on HAART.

Study population

The study population was people living with HIV/AIDS attending Kilimanjaro Christian Medical Centre (KCMC) zonal referral hospital Care and Treatment Clinic (CTC) in Northern Tanzania.

Eligibility criteria

Participants included in the study were PLHIV who had complete medical records with at least two measures of serum creatinine laboratory results at an interval of 3 months or more, of both genders, over 18 years old who used HAART for 6 months or longer. Whereas, individuals diagnosed with acute or chronic kidney disease prior to the diagnosis of HIV positive, being on hemodialysis before starting HAART and having stopped the use of anti-retroviral were excluded from the study.

Sample size determination and procedure

The proportion of kidney dysfunction and renal function monitoring of PLHIV on HAART was calculated from the known renal dysfunction prevalence reported by Mwemezi et al. (2020) in Dar es salaam, Tanzania (P=24.7%). Using the Leslie and Kish formula ($n = \frac{Z^2\,P(1-P)}{\varepsilon^2}$), a sample size of 315 people was required as a minimum.

By taking the identification numbers of patients from the appointment book, patients' medical records were located in the service files and the data were extracted until the desired sample size was obtained.

Study area

The study was conducted in one of the country's consultant hospitals which are also a zonal referral hospital in Northern Tanzania, from October 2022 to April 2023. The care and treatment clinic (CTC) for PLHIV in KCMC serves the majority of the population in the Moshi Municipal-Kilimanjaro region, including other neighboring regions. Moshi municipal population was approximately 230,784 people as per 2022 census report. The municipality has a total of 18 health facilities with CTCs. Four out of eighteen CTCs are with high client volume including Kilimanjaro Christian Medical Centre (KCMC). This consultant hospital provides tertiary care medical services to around 6.8 million people living in the Northern zone of Tanzania (Tanga, Kilimanjaro, Arusha and Manyara) and other referrals from nearby health facilities.

Sampling and sampling technique

The calculated minimal sample size was obtained from PLHIV who met the inclusion criteria.

Variables

Kidney dysfunction was a dependent variable, whereas demographic factors such as age, sex, educational status,

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occupation, other factors such as CD4 count, viral load, WHO HIV clinical stage, duration on HAART, body mass index (BMI), the use of other medications to treat opportunistic infections and non-communicable diseases like diabetes mellitus and cardiovascular diseases were independent variables.

Data collection tools, method and study procedures

Data collection tools

Data were collected using structured data extraction sheets. Information about study participants were extracted from patients' CTC-2 files. Demographic, clinical, laboratory, and pharmaceutical data retrospectively were collected and recorded in the data extraction sheet.

The baseline laboratory investigations include CD4 T-cell count, complete blood cell count, aspartate aminotransferase, alanine aminotransferase, serum creatinine in two to three visits, the estimated glomerular filtration rate (eGFR), was calculated using the Chronic Kidney Diseases Epidemiology (CKD-EPI) 2021 formula without considering race. According to "Kidney Disease: Improving Global Outcome" (KDIGO), renal impairment was categorized as either mild (eGFR, 60–89 mL/min/1.73 m2), moderate (eGFR, 30–59 mL/min/1.73 m2) or severe (eGFR < 30 mL/min/1.73 m2).

Data analysis and management

The data collected was cleaned for its consistency, checked for its completeness, coded, and entered to STATA 14.   Univariate analysis followed by multivariate logistic regression analyses were performed using Pearson's correlation coefficient for determining association between dependent and independent variables. The result was presented with odds ratio (O.R) and 95% confidence interval (CI), and P value <0.05 was considered as statistically significant.

Ethical consideration

Ethical approval was obtained from KCMU-College Research Ethical Committee (CRERC), and given research ethical clearance certificate number UG 55/2022. Permission to conduct the study was sought from the executive director of KCMC. Patient informed consent was waived because of the retrospective characteristics of the study. Confidentiality was highly maintained by using patient identification numbers instead of names.

RESULTS

Socio-demographic characteristics

A total of 345 medical records of PLHIV on various HAART regimens were obtained, carefully analyzed, and data was collected. Among the participants, one hundred and fifteen (33.3%) were men and two hundred and thirty (66.7%) women. The majority (64.1%) of the participants was in the 40- to 59-year-old age range, and the mean age was 47.2 years (SD) 11.7. About 22.0% of people were between the ages of 18 and 39, and 13.9% were over 60 (Table 1).

Clinical characteristics of participant

Forty percent (40.9%) of patients on ART were WHO HIV clinical stage 3, 28.4% patients were WHO HIV clinical stage 4, 16.8% WHO HIV clinical stage 2 and WHO HIV clinical stage 1 accounted for 13.9%.

88% had CD4 levels equal or greater than 350 cells/ml, and about eighty two percent (82%) of participants had achieved viral suppression (VL ≤ 1000 copies/ml). 22.6% of the study participants were hypertensive, and among them not all were on medication. The median BMI was (24.8) kg/m^2 with (49.4%) of participants having a normal BMI (18.5 to 24.9 kg/m^2) as summarized in Table 1.

The mean systolic and diastolic BP was 128.7 ± SD 20.7 and 77.5 ±SD 13.3 respectively. The mean HIV viral load was 92 copies/ml ± SD 38.0.

Prevalence of renal dysfunction

The prevalence of renal dysfunction in this study was 12.1%. Figure 1 shows the renal dysfunction of people living with HIV who are taking HAART at Kilimanjaro Christian Medical Centre, Northern, Tanzania.

Factors associated with kidney dysfunction among PLHIV

Univariate and multivariable analyses

In this study, both univariate and multivariate analyses were conducted to investigate the associations between various independent variables and kidney dysfunction.

In the univariate analysis, each independent variable was examined individually to determine its association with kidney dysfunction. The variables considered in this analysis were age, sex, presence of comorbidity, diabetes mellitus, hypertension, ART regimen, abnormal body mass index, advanced WHO HIV clinical stage, use of other medications, anaemia, duration of taking ARTs, high HIV viral load and low CD4 count. The bivariate analysis, which is a subset of the univariate analysis, assessed the association between each independent variable and kidney dysfunction. The significance level chosen for this analysis was P < 0.25. Based on the bivariate analysis, the variables that showed an association with kidney dysfunction at P < 0.25 were anaemia and the use of other medications. However, it's important to note that the bivariate analysis only considers the relationship between two variables at a time. To further investigate the associations while controlling for possible confounding factors, a multivariate analysis was performed. In the multivariate analysis, the variables that remained statistically significant after controlling for confounders were female and anaemia. The significance level chosen for this analysis was reduced to P < 0.05, indicating a stricter criterion for

Table 1. Patients' characteristics (N= 345).

Characteristic	Percent	Total number (n)
Mean age = 47.2 years, SD = 11.7,		
Age (n=345)		
18-39	22.0	76
40-59	64.1	221
above 60	13.9	48
Sex (n=345)		
Male	33.3	115
Female	66.7	230
Who stage(n=345)		
Stage 1	13.9	48
Stage 2	16.8	58
Stage 3	40.9	141
Stage 4	28.4	98
IPT use (n=345)		
Completed & Continuing	91.9	317
No	8.1	28
BMI (n=340)		
Underweight	4.1	14
Normal	49.4	168
Overweight	25.0	85
Obese	21.5	73
Years on ART (n=344)		
1 - 5	14.2	49
6 - 10	34.9	120
> 10	50.9	175
Use of nephrotoxic drugs (n=345)		
Yes	81.2	280
No	18.8	65
Hypertension (336)		
Yes	22.6	76
No	77.4	260
Viral load (344)		
<1000 cp/ml	82.0	282
≥1000 cp/ml	18.0	62
Cd4 count (n=342)		
≥350	88.6	303
<350	11.4	39
*Other added medication (345)		
No	93.9	324
Yes	6.1	21
Anaemia (310)		
Yes	48.7	151
No	51.3	159

Table 1. Contd.

Adherence to medications (345)		
Good	96.5	333
Poor	3.5	12

*Other added medication: Nifedipine, captopril, furosemide, atorvastatin, cotrimoxazole.
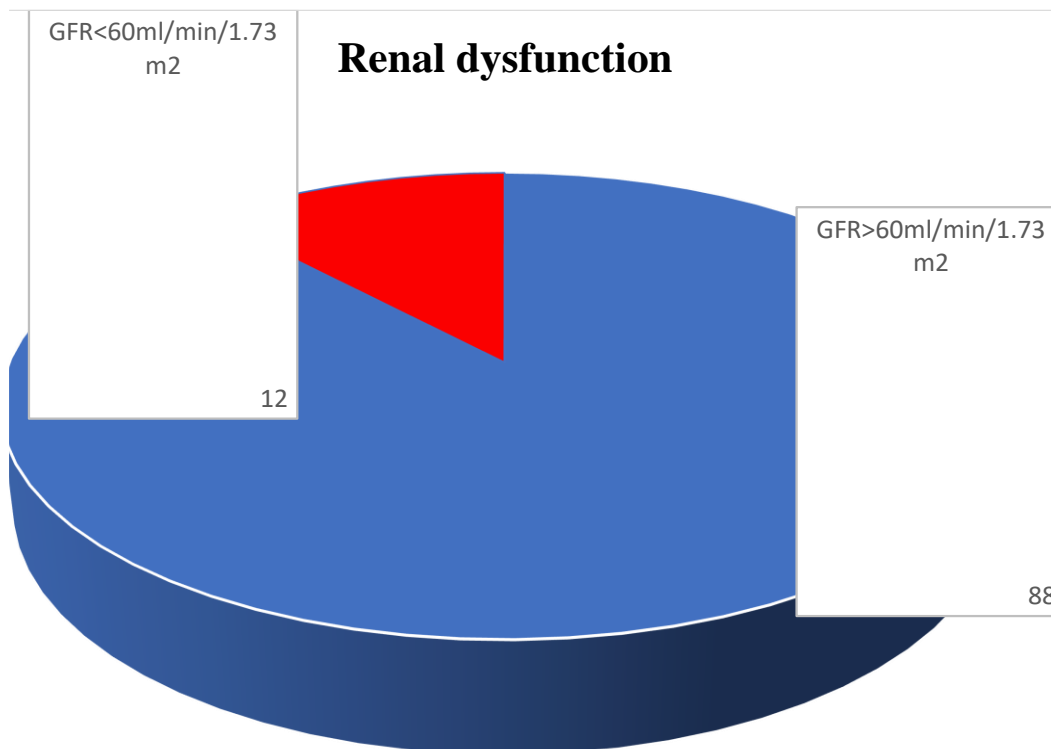

Figure 1. Renal dysfunction of people living with HIV who are taking HAART at Kilimanjaro Christian Medical Centre, Northern, Tanzania.

determining statistical significance.

Accordingly, the multivariate analysis revealed that kidney disfunction was statistically significantly associated with female (adjusted odds ratio [AOR] = 4.18, 95% confidence interval [CI]: (1.42 to 8.19) and anaemia (AOR = 3.37, 95% CI: (1.35-8.42). These findings indicate that these factors have a significant impact on the likelihood of experiencing kidney dysfunction after accounting for potential confounders. The adjusted odds ratios provide estimates of the strength of association between each independent variable and kidney dysfunction, while the 95% confidence intervals indicate the range of plausible values for these odds ratios (Table 2).

DISCUSSION

Renal dysfunction is a not uncommon complication of HIV infection and may be induced by HIV itself, antiretroviral medications, or medications used to treat certain opportunistic infections. In our study, the prevalence of renal impairment, defined by our operational definition as eGFR < 60 mL/min/1.73 m², among HIV patients was found to be 12.1% (40/331) using the CKD EPI equation (2021). This finding is slightly lower than studies conducted in the Lake Zone and Eastern Tanzania at Bugando Medical Centre and Dar es Salaam at Muhimbili National Hospital, which reported a prevalence of 24.5 and 24.7%, respectively (Mwemezi et al., 2020; Mapesi et al., 2018). Similarly, studies in West Africa, Ethiopia, Australia, and the USA have reported prevalence rates ranging from as low as 0.5% to as high as 35%, with prevalence rates of 12.7 and 7.4% reported in rural Morogoro, Tanzania (Mapesi et al., 2018).

The explanation for the lower prevalence observed in

Table 2. Prevalence of Kidney dysfunction among HIV patients at KCMC (N=331).

Characteristic	Kidney dysfunction (%)	Total (N)	Kidney dysfunction Prevalence (95 % CI)
Overall	**40 (12.1)**	**331**	**12.1 (9.0-16.1)**
Age			
18-39	7(10.1)	69	10.1 (4.9-19.8)
40-59	25(11.6)	215	11.6 (8.0-16.7)
above 60	8(17.0)	47	17.0 (8.7-30.6)
Sex			
male	8	109	7.3 (3.7-14.0)
female	32	222	14.4 (10.4-19.7)
Who stage			
Stage 1	6	47	12.8 (5.8-25.7)
Stage 2	6	54	11.1 (5.1-22.7)
Stage 3	14	136	10.3 (6.2-16.7)
Stage 4	14	94	14.9 (9.0-23.6)
IPT use			
Yes	37	306	12.1 (8.9-16.3)
No	3	25	12.0 (3.9-31.4)
BMI			
Underweight	2	13	15.4 (3.8-45.2)
Normal	17	158	10.8 (6.8-16.7)
Overweight	8	82	9.8 (4.9-18.4)
Obese	12	73	16.4 (9.6-26.8)
Years on ART			
1 - 5	5	45	11.1 (4.7-24.1)
6 - 10	18	114	15.8 (10.2-23.7)
> 10	17	171	9.9 (6.3-15.4)
**Use of nephrotoxic drugs			
Yes	34	267	12.7 (9.2-17.3)
No	6	64	9.4 (4.3-19.4)
Hypertension			
Yes	13	75	17.3 (10.3-27.7)
No	26	249	10.4 (7.2-14.9)
Viral load (cp/ml)			
<1000	32	271	11.8 (8.5-16.2)
≥1000	7	59	11.7 (5.7-22.9)
Cd4 count			
≥350	33	290	11.4 (8.2-15.6)
<350	7	38	18.4 (9.0-34.0)
Other added medication			
Yes	34	310	11.0 (7.9-15.0)
No	6	21	28.6 (13.4-50.9)

Table 2. Contd.

Anaemia			
Yes	23	142	16.2 (11.0-23.2)
No	11	154	7.1 (4.0-12.5)
Adherence to medications			
Good	38	320	11.9 (8.7-15.9)
Poor	2	11	18.2 (4.5-50.9)

eGFR, Estimated glomerular filtration rate; BMI, body mass index; WHO, World Health Organization; IQR, inter quartile range; ART, antiretroviral treatment; AZT, zidovudine; 3TC, lamivudine; NVP, nevirapine; EFV, efavirenz; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; ABC, abacavir. **nephrotoxic drugs: Tenofovir Disoproxil Fumarate (TDF), Atazanavir (ATV), Lopinavir enhanced with Ritonavir (LPV/r), and Indinavir (IDV).

our study may be attributed to the fact that most of our study participants had high CD4 cell counts, undetectable HIV viral loads, and a relatively young population with a mean age of 47.2 years (SD 11.7). In contrast, previous research often found a higher prevalence among individuals with advanced HIV disease (WHO stages III or IV), higher HIV viral loads, and lower CD4 cell counts.

Additionally, our study found that gender is statistically significantly associated with renal impairment, with females being at increased risk of developing renal dysfunction. This finding is consistent with the results reported by other studies (Cristelli et al., 2018).

In this study, it was found that low Haemoglobin level (Hb) was associated with renal function impairment in PLHIV; even after a multivariate linear regression showed that low Hb was an independent predictor of renal function impairment in this population. This agreed with the report of a study in which low Hb was found to be a predictor of renal dysfunction (Reid et al., 2008) (24). However, anaemia may also be secondary to renal dysfunction. Contrary to several studies, in which a low CD4 cells count and a high HIV viral load were reported to predict renal dysfunction in HIV (Fiseha et al., 2021; Joshi et al., 2018; Kaboré et al., 2019; Yazie et al., 2019) our study did not find a significant association between CD4 cells count, HIV viral load and renal dysfunction. Age, WHO clinical stages, BMI, Hypertension was not statistically associated with renal dysfunction in this study (Table 3). Some studies have reported that age, WHO clinical stages, BMI, and hypertension are well- documented risk factors for renal impairment. This suggests that individuals with later stages may have a higher likelihood of experiencing renal impairment compared to those at earlier stages (Mapesi et al., 2021; Cristelli et al., 2018; Joshi et al., 2018; Kaboré et al., 2019; Mwanjala et al., 2022). The variance could be accounted by difference in population characteristics. The study population consisted of majority of clinically stable clients.

CONCLUSION AND RECOMMENDATIONS

These findings indicate that renal dysfunction is a

prevalent issue among people living with HIV (PLHIV), with at least one in ten individuals affected. Additionally, half of PLHIV in Northern Tanzania were found to have anemia. Our study revealed that anemia and female sex were associated with the development of kidney dysfunction among PLHIV.

Therefore, aggressive management of anemia should be considered in this population. We recommend that all Care and Treatment Centers (CTCs) be equipped with laboratories capable of assessing kidney function as part of routine follow-up for PLHIV. For stable clients on Highly Active Antiretroviral Therapy (HAART), annual monitoring of kidney function seems appropriate. However, for those with or at increased risk of kidney dysfunction, more frequent monitoring, typically 2 to 4 times per year depending on risk factors, is recommended. Furthermore, kidney function should be carefully monitored during hospitalization. Prospective studies are needed to establish a causal relationship.

Study limitations

The non-experimental design of the study made it difficult to establish a causal relationship. Additionally, reliance on secondary data presented limitations, notably incomplete records due to improper handling of patient documentation. Furthermore, missing data, such as body weight and height measurements for accurate BMI estimation, blood pressure readings, and serum creatinine tests, further compounded the challenges encountered during the study.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

Table 3. Predictors of Kidney dysfunction among HIV patients at KCMC.

Characteristic	Kidney dysfunction n(%)	Normal kidney function n(%)	OR (95% CI)	aOR (95% CI)
Age				
18-39	7 (17.5)	62 (21.3)		
40-59	25 (62.5)	190 (65.3)	1.17 (0.48-2.83)	0.98 (0.35-2.70)
above 60	8 (20.0)	39 (13.4)	1.82 (0.61-5.41)	2.02 (0.50-8.19)
Sex				
Male	8 (20.0)	101 (34.7)		
Female	32 (80.0)	190 (65.3)	2.13 (0.94-4.79)	4.18 (1.42-8.19)
Who stage				
Stage 1	6 (15.0)	41 (14.1)		
Stage 2	6 (15.0)	48 (16.5)	0.85 (0.26-2.85)	0.86 (0.20-3.74)
Stage 3	14 (35.0)	122 (41.9)	0.78 (0.28-2.17)	0.66(0.17-2.51)
Stage 4	14 (35.0)	80 (27.5)	1.20 (0.43-3.34)	1.41 (0.38-5.20)
IPT use				
Yes	37 (92.5)	269 (92.4)		
No	3 (7.50)	22 (7.6)	0.99 (0.28-3.48)	0.78 (0.17-3.50)
BMI				
Underweight	2 (5.1)	11 (3.8)		
Normal	17 (43.6)	141 (49.1)	0.66 (0.14-3.25)	1.20 (0.16-8.59)
Overweight	8 (20.5)	74 (25.8)	0.59 (0.11-3.17)	0.82 (0.10-6.50)
Obese	12 (30.8)	61 (21.3)	1.08 (0.21-5.52)	2.26 ((0.27-18.87)
Years on ART				
1 - 5	5 (12.5)	40 (13.8)		
6 - 10	18 (45.0)	96 (33.1)	1.5 (0.52-4.32)	1.38 (0.36-5.29)
> 10	17 (42.5)	154 (53.1)	0.88 (0.31-2.54)	0.82 (0.21-3.26)
Use of nephrotoxic drugs				
Yes	34 (85.0)	233 (80.1)		
No	6 (15.0)	58 (19.9)	0.71 (0.28-1.77)	0.53 (0.14-1.98)
Hypertension				
Yes	13 (33.3)	62 (21.8)		
No	26 (66.7)	223 (78.3)	0.56 (0.27-1.15)	1.04 (0.39-2.81)
Viral load (cp/ml)				
<1000	32 (82.1)	239 (82.1)		
≥1000	7 (18.0)	52 (17.9)	1.01 (0.42-2.41)	0.51 (0.13-1.95)
Cd4 count				
≥350	33 (82.50)	257 (89.2)		
<350	7 (17.5)	31 (10.8)	1.76 (0.71-4.33)	1.71 (0.47-6.18)
Other added medication				
Yes	6 (15.0)	15 (5.2)		
No	34 (85.0)	276 (94.9)	*0.31 (0.11-0.86)	0.26 (0.06-1.16)
Anaemia				
No	23 (67.7)	119 (45.4)		
Yes	11 (32.4)	143 (54.6)	*2.51 (1.17-5.41)	3.37 (1.35-8.42)

Table 3. Contd.

Adherence to medications				
Good	38 (95.0)	282 (96.9)		
Poor	2 (5.0)	9 (3.1)	1.65 (0.34-7.95)	1.88 (0.23-15.59)

*Statistically significant at P < 0.25, other medications; Nifedipine, captopril, furosemide, atorvastatin, cotrimoxazole.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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