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Chronic kidney disease and its predictors among highly active antiretroviral therapy naïve and experienced HIV-infected individuals at the selected hospitals, Southwest Ethiopia: a comparative cross-sectional study

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ABSTRACT

Objective This study aimed to determine the prevalence of chronic kidney disease (CKD) and its predictors among highly active antiretroviral therapy (HAART) naïve and experienced HIV-infected individuals.

Method and analysis Hospital-based comparative cross-sectional study design was used at Mizan-Tepi University Teaching Hospital, Bonga General Hospital and Tepi General Hospital. A total of 616 naïve and experienced HIV-infected individuals participated. A systematic random sampling and consecutive sampling methods were applied to select the HAART experienced and naïve HIV-infected individuals, respectively. Descriptive statistics were used for all study variables. Independent t-test and logistic regression analysis were performed to compare the mean between naïve and experienced patients and to identify its predictor variables considering a <0.05 and 95% CI, respectively.

Results A total of 616 HIV-positive respondents were enrolled in this study. The prevalence of CKD was 41 (29.3%) of 140 and 78 (16.4%) of 476 HAART-naïve and HAART-experienced HIV patients, respectively. Rural residency, being anaemic, being hypertensive, having had a family history of kidney disease and stage IV current WHO) clinical stage were independent risk factors of CKD among naïve HIV patients, whereas, rural residency, utilisation of drinking water per day below the recommended amount, being anaemic, being hypertensive, stage IV current WHO clinical stage and obesity were predictors of CKD among experienced HIV patients. Statistically significant difference was observed between HAART naïve and HAART experienced participants with regard to the mean glomerular filtration rate level (t=−3.987, 95% CI −18.29 to −6.22).

Conclusion CKD was higher among HAART-naïve than HAART-experienced study participants. Therefore, early initiation of antiretroviral therapy (ART) drugs, modification of lifestyles to decrease obesity and early detection and treatment of comorbidities such as anaemia and hypertension may have profound effects in reducing CKD and increasing patients' quality of life.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In low-income and middle-income countries, coinfections and comorbidities associated with HIV/AIDS remain unduly high. HIV-related kidney disease is the main public health problem. Specific types of antiretroviral drugs such as indinavir, atazanavir and tenofovir and ritonavir are known to cause renal toxicity, and therefore, highly active antiretroviral therapy (HAART) experienced patients have been associated with kidney disease.

WHAT THIS STUDY ADDS

⇒ Despite there are different studies claiming that chronic kidney disease (CKD) is higher among HAART experienced patients, in this study, CKD was higher among HAART-naïve than HAART-experienced study participants.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Determining the prevalence and contributing factors for different comorbidities such as CKD is important to improve the quality of life and long-term healthcare management of people living with HIV, especially in low-income countries such as Ethiopia where there are high prevalence of sexually transmitted disease and comorbidities. Moreover, this study gives insight for those practitioners to routinely perform screened for kidney disease before starting antiretroviral treatment and to provide the treatment as per the outcome.

INTRODUCTION

The HIV is a retrovirus that infects cells of the immune system, destroying or damaging their function.[1] By 2022, about 39.0 million people living with HIV (PLHIV), and 1.3 million people were newly infected with HIV. Even

though about 29.8 million of PLHIV received antiretroviral therapy (ART), 630 000 people died of AIDS-related illnesses.[2]

Sub-Saharan Africa (SSA) remains among the hardest hit regions by the pandemic, with nearly 500 000 AIDS-related deaths could be resulted by the end of 2021 after 6 months disruption to medical supplies due to COVID-19 pandemic.[3] In Ethiopia, the annual incidence of HIV among adults (ages 15–64 years) in urban areas was 6000 (0.05%), whereas, the prevalence of HIV among adults in urban Ethiopia was 380 000 (3.0%) where 4.1% were among women and 1.9% were among men as of April 2018.[4]

In low-income and middle-income countries, coinfections and comorbidities associated with HIV/AIDS remain unduly high.[5] The risk of comorbidity increases among HIV patients due to the advanced stage of HIV at ART initiation, antiretroviral toxicity,[6] potential coinfection[7] and different lifestyles (such as alcoholism).[8] Chronic kidney disease (CKD) is among the most common comorbidities,[8] which is defined as kidney damage or reduced renal function that persists for more than 3 months.[9 10] HIV infection may cause renal function impairment, often called, HIV-associated nephropathy (HIVAN). HIVAN is a known cause for CKD and predominantly prevalent in black people especially among the sub-Sahara population.[11–13] Different nephrotic syndrome is also caused by non-HIV-related causes such as different cardiovascular problems: hypertension and atherosclerosis; and metabolic syndrome: diabetes mellitus, dyslipidaemia and others.[14] For instance, >50% of all deaths among individuals with end-stage renal disease (ESRD) are related to a CVD event.[15] Furthermore, different practices such as herbal medicine use in rural community is also contributed for the incidence of CKD. The pooled prevalence of kidney disease among patients with HIV in SSA was 14.6% in 2018.[16]

HIV-related kidney disease becoming the main cause of the ESRD requiring dialytic intervention.[17] CKD becomes increased and progressively high globally which contributes to increased morbidities (bone disease, adverse metabolic and nutritional consequences, infections, and reduced cognitive function) and mortality. As a result of these amplifying effects, there is a profound financial expenditure and medical resources consumed for the management of patients with CKD and also have public health consequences in developing countries.[18 19]

The introduction of highly ART (HAART) has led to a marked reduction in HIV/AIDS-related morbidity and mortality including renal diseases in HIV positive individuals.[20] However, the long-term intake of some HAART has been linked with increased risk of progression to ESRD[21] and some nephrotoxic HAART drugs such as indinavir, atazanavir and tenofovir may cause renal disease.[22] A pooled analysis of 17 studies also showed that there was a significantly greater loss of kidney function among the TDF recipients, compared with control subjects.[23] Moreover, the EuroSIDA, D:A:D: retrospective surveys report indicated that the use of tenofovir together with boosted PIs increased the risk of renal toxicity due to the decline in estimated creatinine clearance, whereas, its risk reduced with coadministration of non-nucleotide reverse transcriptase inhibitor (NNRTI) or raltegravir.[14 24] Dolutegravir (DTG) is also another integrase inhibitor drug, which may inhibit renal creatinine secretion by inhibiting some transporters such as multidrug and toxin extrusion 1.[25] Besides, its inhibition effect on renal creatinine secretion, the use of this drug could increase the serum creatinine (sCr) level.[26] Single-tablet regimen of DTG or its coadminstration with the other ART drug will increase 10%–20% sCr.[27]

WHO recommended the use of DTG as first line treatment, mainly due to its superiority in viral load suppression,[28] following this recommendation, different ART first line regimens such as; TDF+3TC+DTG as a preferred first line and, TDF+3TC+EFV as an alternative first-line treatment, and TDF+3TC+ATV/r as second-line treatment were in use in Ethiopia.[28 29] Moreover, different HAART treatments such as AZT+3TC+NVP, TDF+3TC+NVP and AZT+3TC+EFV were also widely used.[29]

Thus, determining the prevalence and contributing factors for different comorbidities such as CKD is important to improve the quality of life and long-term healthcare management of PLHIV.[30] Despite there are some studies conducted in other parts of Ethiopia,[31–33] still there is a paucity of studies related to CKD and its predictors among HAART naïve and HAART experienced HIV patients in this study area. Therefore, this study aimed to determine the prevalence of CKD and associated factors among HAART naïve and HAART experienced HIV-infected individuals at the selected Hospitals (Bonga G/tsadik Shawo General Hospital, Mizan Tepi University Teaching Hospital (MTUTH) and Tepi General Hospital), Southwest Ethiopia.

METHODS AND MATERIALS

Study design, period and setting

A hospital-based comparative cross-sectional study with secondary data review was conducted from February 2020 to September 2020 to assess the prevalence of CKD and its predictors among HAART naïve and HAART experienced HIV-infected individuals attending ART clinics of the selected Hospitals. These hospitals are Bonga G/tsadik Shawo General Hospital, MTUTH and Tepi General Hospital. Bonga G/tsadik Shawo General Hospital has located in Bonga 464 km and 739 km far from Addis Ababa and Hawassa, respectively. MTUTH has located in Mizan Aman 585 km and 844 km far from Addis Ababa and Hawassa, respectively. Tepi General Hospital has located in Tepi 644 km and 914 km far from Addis Ababa and Hawassa, respectively. These three hospitals are hospitals located in the southwest region of Ethiopia. In 2019, the ART clinics in each hospital provide a service for a total of 4992 HIV-infected individuals on HAART, where 1733 in MTUTH, 1409 in Bonga G/tsadik Shawo

General Hospital and 1850 in Tepi general hospital (unpublished report).

Study participants

All HIV-infected HAART naïve and HAART experienced individuals who visit ART clinics of the selected hospitals were the source populations, whereas, all HIV-infected HAART naïve and HAART experienced individuals who visited the hospital during the study period and fulfil the eligibility criteria were the study populations. All HIV-infected adults (≥18 years old) who were HAART naïve and HAART experienced (who were on follow-up for ≥6 months on HAART) were included, whereas, those severely ill patients (unable to speak, admitted patients), pregnant women, and amputees were excluded from the study.

Sample size determination

The sample size was determined using double population proportion formula by taking two different proportions of chronic renal disease (3.6%) for HAART naïve and (11.7%) for HAART experienced participants from the study done in the northwest of Ethiopia,[33] taking a critical value at 95% confidence level, the level of significance 0.05 and power (1–β) =80. Then the calculated sample size using online Epi-Tools epidemiological calculators[34] was 439 for HAART experienced, and 135 for HAART naive groups. By assuming a 10% non-respondent rate, the final sample size was 483 for HAART experienced and 149 for HAART naïve HIV patients. Finally, the total sample size was 632.

Sampling procedure

HAART naïve HIV patients were selected consecutively. A consecutive sampling method was applied because we were unable to determine the sampling frame for HAART naïve HIV patients as these patients did not start HAART at the time of the survey. HAART experienced HIV patients were selected using a systematic random sampling method. First, the past 1-year report of HAART experienced patients was taken. Then, we divide by twelve to find the average numbers of HAART-experienced HIV patients on monthly follow-up. Finally, the 5 monthly reports of HAART experienced patients from each hospital were taken as the sampling frame. Then, using this sampling frame, the sample size was proportionally allocated to each selected public hospital. Then, the sampling fraction was determined by dividing the total HAART experienced HIV patients during the study period at each hospital by the allocated sample. Finally, the HAART experienced HIV patients at each hospital were selected using a systematic sampling method with sampling interval of K=4 (figure 1). The first HAART experienced HIV patients were considered as a starting point and then the next eligible participant will be interviewed every fourth individual. Then, using this sampling fraction; interviews, record review using the checklist, and blood and urine specimen collection for chemistry analysis and urine dipstick, respectively were conducted. All HAART naïve HIV patients who visited the selected hospital HIV care unit were selected consecutively from the three hospitals until the desired sample size was achieved.

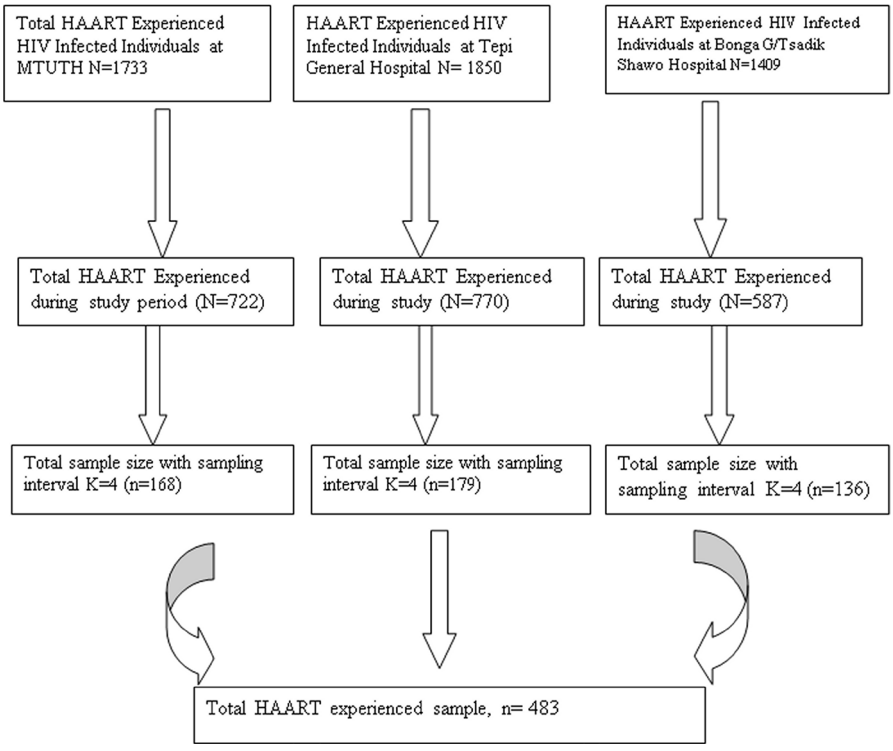

Figure 1 Schematic representation of the sampling procedure of HAART experienced HIV-infected Individuals at the selected Hospitals from February 2020 to September 2020. HAART, highly active antiretroviral therapy; MTUTH, Mizan Tepi University Teaching Hospital.

Data collection tool, procedures and quality control

An interview-administered structured questioner was adapted from reviewing different literatures (online supplemental file 1).[31 35–38] Before the actual data collection, a pretest was conducted among 5% of the study participants at Bachuma primary hospital for its accuracy and consistency prior to the actual data collection. Three days of training was given for data collectors about the objectivity and relevance of the study, confidentiality issues, study participants' rights, consenting, techniques of interview, and regarding laboratory test procedures and their quality control. Then, sociodemographic data, anthropometric data (weight and height) and clinical data (blood pressure (BP) and waist circumference (WC)) were collected by three trained nurses, the specimen was collected by three lab technologists and supervised by three trained nurses during the first and second visit.

To address the potential sources of bias (ie, recall bias), a review of records was also conducted using the checklist. Height and weight were measured using Seca 761 wt scales with a height ruler calibrated with a metre reading attached to it (made in Germany). Generally, to maintain the quality of the result, 3 days of training, pretest, close supervision of data collection, analysis of samples following standard operating procedures and double-entry of data were done. Moreover, to improve the quality of reporting of observational studies and facilitate critical appraisal and interpretation of this study by reviewers, journal editors and readers; a STrengthening the Reporting of OBservational studies in Epidemiology: cross-sectional study reporting checklist was used.[39]

Specimen collection and laboratory procedure

A 3 mL of venous blood sample was collected with EDTA tube for haematological analysis and 5 mL of venous blood sample was collected in a gel containing serum separator test tube for blood chemistry. Then, serum was separated after the sample was collected and centrifuged by trained laboratory technologists. Biochemical analysis of serum was done using Mindray BS-200 chemistry analyzer (Shenzhen Mindray Bio-Medical Electronics, China) for creatinine level determination. For the fast blood glucose (FBG) test, the participants were appointed to come the next day after an overnight fast and then each selected participant was tested for their fasting blood glucose level using (Dr. Trust (USA) Fully Automatic Blood Sugar Testing Glucometer) under the standard operating procedure.

After collecting 5 mL of freshly voided urine by clean and dry container, urine chemistry (urine dipstick) such as protein and haematuria were determined according to manufacturer instruction. Initially, all patients were determined for their creatinine and proteinuria, and then those with positive proteinuria (+1 to +4) were checked for creatinine and proteinuria for the second time after 3 months. Then, those with consecutive proteinuria were considered as having CKD and then their stages were determined by using the estimate glomerular filtration rate (eGFR). Since this study was conducted among black races and many of the studies supported that sCr is usually higher among black people due to increased muscle mass, justifying the addition of race adjustment in creatinine-based formulas to eGFR. Therefore, for this study, the eGFR was estimated by using the CKD Epidemiology Collaboration (2009 CKD-EPI) equation than (2021 CKD-EPI) equation: $eGFR=141\times\min(S_{cr}/\kappa, 1)^{\alpha}\times\max(S_{cr}/\kappa, 1)^{-1.209}\times0.993^{age}$ 1.018 (if female)×1.159 (if black)[40] by using eGFR online calculator,[41] where: S_{cr} is sCr in mg/dL, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of S_{cr}/κ or 1, and max indicates the maximum of S_{cr}/κ or 1,[40] because the (2021 CKD-EPI) equation does not consider race adjustment which can contribute to an overestimated diagnosis which leads to the unnecessary management. In addition to proteinuria, the other clinical characteristics such as creatinine, CD4 count, viral load, adherence, WHO stage were also repeated after 3 months.

Measurements

Chronic kidney disease is defined as the presence of persistent proteinuria and abnormal creatinine level (above 1.2 mg/dL, for males and above 1.0 mg/dL for females)[42] for at least 3 or more months, and the stages were classified based on the levels of eGFR category.[43]

- Stage 1: persistent proteinuria with eGFR≥90 mL/min/1.73 m^2.
- Stage 2: persistent proteinuria with eGFR of 60–89.9 mL/min/1.73 m^2.
- Stage 3: eGFR 30–59.9 mL/min/1.73 m^2 with or without proteinuria.
  - 3A (eGFR 45–59.9 mL/min/1.73 m^2).
  - 3B (eGFR 30–44.9 mL/min/1.73 m^2).
- Stage 4: eGFR 15–29.9 mL/min/1.73 m^2 with or without proteinuria.
- Stage 5: (kidney failure), eGFR<15 mL/min/1.73 m^2 with or without proteinuria.

HAART experienced is defined as those participants who were taking HAART for more than 6 months which is composed of two nucleoside/NRTIs plus an NNRTI.[44]

HAART-naïve is defined as those patients who were screened and resulted positive but not on HAART treatment.[44]

Underweight, normal weight, overweight and obesity were defined as a body mass index (BMI) of<18.5 kg/m^2, 18.5–24.9 kg/m^2, 25–29.9 kg/m^2 and ≥30 kg/m^2, respectively.[45]

Fasting blood sugar test: It is a test after an overnight fast. A fasting blood sugar level of less than 100 mg/dL (5.6 mmol/L) is normal. A fasting blood sugar level from 100 to 125 mg/dL (5.6–6.9 mmol/L) is considered as pre-diabetes. If a fasting blood sugar level is 126 mg/dL (7 mmol/L) or higher on two separate tests, it is considered as diabetes.[46]

Hypertension is a diagnosis of high BP based on the average of three readings taken on separate occasions. According to 2020 international society of hypertension global hypertension practice guidelines, hypertension is classified as normal if BP is <130/85, high normal or prehypertension (130–139/85–89), grade 1 hypertension (140–159/90–99) and grade 2 hypertension (≥160/100).[47]

Waist circumference: High risk (abnormal WC) is defined by a WC>40 inches (102 cm) for men and >35 inches (88 cm) for women.[48]

Recommended amount of water to drink: The WHO recommends taking at least 2 L/day and 3 L/day for females and males, respectively.[49]

Anaemia: If a non-pregnant woman whose age is 15 years and above and haemoglobin level of less than 12.0 g/dL and men whose age is 15 years and above and haemoglobin level of less than 13 g/dL were considered as anaemic. Anaemia, further classified as mild (11–12.9 for males and 11–11.9 g/dL for females) moderate (8–11 g/dL), and severe (<8 g/dL).[50]

Data processing and analysis

The data were checked for their completeness and then the data were entered to Epi-Data Manager V.4.2 and then transferred to SPSS V.21 for analysis. Descriptive statistics (frequency, percentage, mean and SD) were used to describe the sociodemographic variables, exercise and behavioural related variables, chronic medical illnesses, and clinical and anthropometric measurements.

Multicollinearity among independent predictors was checked; a predictor with a variance inflation factor of >2 was dropped from the analysis. An independent t-test was used to determine the mean differences of variables between outcome variables (HAAR naïve and HAART experienced). Then, the statistically significant difference in the mean of GFR, creatinine level, WC, FBG level, BMI and current cluster of differentiation 4 (CD4) count between HAART naïve and HAART experienced patents were determined at a p<0.05 and 95% CI.

Binary logistic regression analysis was done to see the significant association between each predictor (sex, occupational status, educational status, residence, age of participant, current ARV regimens, viral load, $CD4^+$ T-cell count, BMI, duration of ART (in years), WHO clinical stage, family history of kidney disease, status of diabetic mellitus, status of hypertension, status of anaemia, consumption of drinking water per day, and among others) with CKD. Then, predictors with a p<0.05 were included in a multivariable logistic regression model to control all possible confounders and to identify the strong predictors significantly associated with CKD. The model fitness was checked using the Hosmer-Lemeshow goodness of fit test and a p>0.05 considered as a good fit. Then, after computing for the measure of association both before and after adjusting for potential confounding factors and if there is a 10% or more difference between the two measures of association, the predictor is considered as a confounder. Finally, significant predictors associated with CKD were determined at a p <0.05 and a 95% CI.

Patient and public involvement

Patients and/or the public were not involved in the design or conduct or reporting or dissemination plans of this research.

RESULTS

Sociodemographic characteristics of the respondents

A total of 616 HIV-positive respondents where 140 (22.7%) of them were naïve and 476 (77.3%) were experienced HIV patients with a 97.5% response rate were enrolled in this study. Sixteen study participants declined to participate in the study. The median (IQR) age of the study participants was 38[13] years with most 228 (37.0 %) of participants were in the age range of 30–39 years. Almost half 307 (49.8%) of the participants were married. Regarding their ethnicity, 124 (20.1%) of them were Kaffa followed by Amhara 103 (16.7%). Nearly one-third of the participants, 184 (29.9%) could n't read and write (table 1).

Exercise and other behavioural related characteristics of respondents

From the total participants who were involved in either moderate, vigorous or combinations of both, the majority 148 (85.5%) of them met the WHO recommendations of physical activity per week. The majority 538 (87.3%) of the respondents did not drink the recommended amount of drinking water per day. About 49 (8.0%) of the participants ever smoked cigarettes, whereas about 249 (40.4%) of the total ever consumed different alcohols. About 279 (45.3%) of the participants ever drink chemo (table 2).

Current status of CKD and other chronic medical illnesses of respondents

The overall prevalence of CKD among HAART naïve and experienced HIV patients was 119 (19.3%) with 95% CI (16.2 to 22.4). The prevalence of CKD was 41 (29.3%) with 95% C.I (21.7 to 36.9) and 78 (16.4%) with 95% C.I (13.1 to 19.7) among the total HAART naïve and HAART experienced HIV patients, respectively. More than half 63 (52.9%) of the HAART naïve and experienced HIV patients were at stage 1 of CKD with the mean (±SD) of GFR of 127.4±32.4. During data collection time, 105 (17.0%) of the respondents were anaemic with the mean (±SD) of Hgb level 14.1±1.9 (table 3).

Clinical and anthropometric measurements of respondents

Of the total HAART naïve and experienced HIV patients, most 355 (57.6%) of the respondents had normal weight with a BMI range of 18.5–24.9 kg/m^2, followed by underweight (BMI<18.5 kg/m^2) which accounted for 138 (22.4%) of the total respondents with a mean (±SD) of BMI of participants was 21.9±4.9 (table 4).

Table 1 Sociodemographic characteristics of respondents (n=616) in Selected Public Hospitals, South West Ethiopia, 2020

Variables		HAART naïve n (%)	HAART experienced n (%)	Total n (%)
Place of residence				
	Urban	91 (65.0)	301 (63.2)	392 (63.6)
	Rural	49 (35.0)	175 (36.8)	224 (36.4)
Sex				
	Female	90 (64.3)	311 (65.3)	401 (65.1)
	Male	50 (35.7)	165 (34.7)	215 (34.9)
Age of participants				
	18–29	36 (25.7)	72 (15.1)	108 (17.5)
	30–39	52 (37.1)	176 (37.0)	228 (37.0)
	40–49	41 (29.3)	162 (34.0)	203 (33.0)
	≥50	11 (7.9)	66 (13.9)	77 (12.5)
Marital status				
	Single	34 (24.3)	88 (18.5)	122 (19.8)
	Married	68 (48.6)	239 (50.2)	307 (49.8)
	Divorced	21 (15.0)	73 (15.3)	94 (15.3)
	Widowed	17 (12.1)	76 (16.0)	93 (15.1)
Ethnicity				
	Kaffa	34 (24.3)	90 (18.9)	124 (20.1)
	Amhara	16 (11.4)	87 (18.3)	103 (16.7)
	Oromo	18 (12.9)	82 (17.2)	100 (16.2)
	Bench	21 (15.0)	75 (15.8)	96 (15.6)
	Sheka	19 (13.6)	74 (15.5)	93 (15.1)
	Tigre	24 (17.1)	45 (9.5)	69 (11.2)
	Other*	8 (5.7)	23 (4.8)	31 (5.0)
Respondent's educational status				
	Cannot read and write	41 (29.3)	143 (30.0)	184 (29.9)
	Primary	41 (29.3)	138 (29.0)	179 (29.1)
	Secondary	39 (27.9)	151 (31.7)	190 (30.8)
	Certificate and above	19 (13.6)	44 (9.2)	63 (10.2)
Respondent's occupational status				
	Housewife	24 (17.1)	122 (25.6)	146 (23.7)
	Merchant	22 (15.7)	86 (18.1)	108 (17.5)
	Daily labourer	31 (22.1)	95 (20.0)	126 (20.5)
	Farmer	28 (20.0)	73 (15.3)	101 (16.4)
	Government employee	19 (13.6)	63 (13.2)	82 (13.3)
	Student	16 (11.4)	37 (7.8)	53 (8.6)
Monthly income (US dollars US$))				
	Mean±SD			52.1±52.7

*Silte, Gurage, Hadiya and Wolayita.

Factors associated with the overall CKD among all HIV-infected individual

Both binary and multiple logistic regression analysis were performed to identify the risk factors of CKD among all HAART naïve and HAART experienced HIV positive participants. The variables; age, residence, educational status, ever use of chemo, current status of anaemia, current status of hypertension, current status of diabetic mellitus, family history of kidney disease, baseline WHO clinical stage and BMI were included in the analysis. After adjusting for these factors in a multiple logistic regression analysis; residence, educational status, current status of anaemia, current status of hypertension, current status of diabetic mellitus, family history of kidney disease, baseline WHO clinical stage and BMI were significantly associated with CKD. The Hosmer-Lemeshow test of this model is p=0.890, so a p>0.05 considered as a good fit. The area under the curve is 0.698 with 95% CI (0.637 to 759). Also,

Table 2 Exercise and other behavioural related characteristics of respondents in Selected Public Hospitals, South West Ethiopia, 2020

Variables	HAART naïve n (%)	HAART experienced n (%)	Total n (%)
Engaged in vigorous-intensity exercises			
No	118 (84.3)	409 (85.9)	527 (85.6)
Yes	22 (15.7)	67 (14.1)	89 (14.4)
Involved in moderate-intensity exercises			
No	98 (70.0)	359 (75.4)	457 (74.2)
Yes	42 (30.0)	117 (24.6)	159 (25.8)
WHO recommended physical activity per a week			
No	13 (28.2)	12 (9.4)	25 (14.5)
Yes	33 (71.7)	115 (90.6)	148 (5.5)
Herbal medicine use			
No	120 (85.7)	424 (89.1)	544 (88.3)
Yes	20 (14.3)	52 (10.9)	72 (11.7)
Over-the-counter NSAIDs drugs use			
No	120 (85.7)	437 (91.8)	557 (90.4)
Yes	20 (14.3)	39 (8.2)	59 (9.6)
Source of drinking water			
Pipe	89 (63.6)	293 (61.6)	382 (62.0)
Spring	29 (20.7)	99 (20.8)	128 (20.8)
Well	22 (15.7)	84 (17.6)	106 (17.2)
Utilisation of drinking water per day			
Used below recommended amount	122 (87.1)	416 (87.4)	538 (87.3)
Used recommended amount	18 (12.9)	60 (12.6)	78 (12.7)
Ever smoke cigarette			
No	125 (89.3)	442 (92.9)	567 (92.0)
Yes	15 (10.7)	34 (7.1)	49 (8.0)
Ever consumed of any alcohol (beer, wine, 'tela', 'areki' and others)			
No	75 (53.6)	292 (61.3)	367 (59.6)
Yes	65 (46.4)	184 (38.7)	249 (40.4)
Ever drink of chemo			
No	67 (47.9)	270 (56.7)	337 (54.7)
Yes	73 (52.1)	206 (43.3)	279 (45.3)
Ever use of canned foods			
No	127 (90.7)	444 (93.3)	571 (92.7)
Yes	13 (9.3)	32 (6.7)	45(.3)

Tela and areki: these are locally made alcoholic drinks.
Chemo: it is a locally made non-alcoholic hot drink which is made up of salt, coffee leaves and other spices.
HAART, highly active antiretroviral therapy; NSAID, non-steroidal anti-inflammatory drug.

the area under the curve is significantly different from 0.5 since p value is 0.000 meaning that there is a higher overall accuracy of the test (table 5).

Factors associated with CKD among naïve HIV-infected individuals

In bivariate logistic regression analysis, predictor variables such as; the age of participant, residence, consumption of drinking water per day, current status of anaemia, the current status of hypertension, the current status of diabetic mellitus, family history of kidney disease, the current WHO clinical stage, BMI and WC were found to be significantly associated with CKD among naïve HIV-infected Individuals. The Hosmer-Lemeshow test of this model is p=0.5, so a p>0.05 considered as a good fit. The area under the curve is 0.910 with 95% CI (0.864 to 957). Also, the area under the curve is significantly different from 0.5 since p value is 0.000 meaning that there is a higher overall accuracy of the test.

These eligible predictors were adjusted for possible confounding using multivariate logistic regression

Table 3 Current status of CKD and other chronic medical illnesses of respondents in Selected Public Hospitals, South West Ethiopia, 2020

Variables		HAART naïve n (%)	HAART experienced n (%)	Total n (%)
Current status of CKD (n=616)				
	No	99 (70.7)	398 (83.6)	497 (80.7)
	Yes	41 (29.3)	78 (16.4)	119 (19.3)
Stages of chronic kidney disease (n=119)				
	Stage 1—eGFR≥90 mL/min/1.73 m^2	13 (31.7)	50 (64.1)	63 (52.9)
	Stage 2—eGFR of 60–89.9 mL/min/1.73 m^2	25 (61.0)	24 (30.8)	49 (41.2)
	Stage 3—eGFR 30–59.9 mL/min/1.73 m^2	2 (4.9)	1 (1.3)	3 (2.5)
	Stage 4—eGFR 15–29.9 mL/min/1.73 m^2	1 (2.4)	0 (0.0)	1(.8)
	Stage 5—eGFR<15 mL/min/1.73 m^2	0 (0.0)	3 (3.8)	3 (2.5)
	eGFR mean±SD		127.4±32.4	
Current status of anaemia				
	Yes	20 (14.3)	85 (17.9)	105 (17.0)
	No	120 (85.7)	391 (82.1)	511 (83.0)
	Mean±SD of Hgb		14.1±1.9	
Ever history of heart disease				
	No	128 (91.4)	440 (92.4)	568 (92.2)
	Yes	12 (8.6)	36 (7.6)	48 (7.8)
Current status of hypertension				
	No	123 (87.9)	417 (87.6)	540 (87.7)
	Yes	17 (12.1)	59 (12.4)	76 (12.3)
Stages of hypertension				
	Normal	114 (81.4)	393 (82.6)	507 (82.3)
	High normal or prehypertension	9 (6.4)	24 (5.0)	33 (5.4)
	Grade 1 hypertension	12 (8.6)	46 (9.7)	58 (9.4)
	Grade 2 hypertension	5 (3.6)	13 (2.7)	18 (2.9)
Current status of diabetes mellitus				
	No	125 (89.3)	427 (89.7)	552 (89.6)
	Yes	15 (10.7)	49 (10.3)	64 (10.4)
	Mean±SD of FBG	90.1±25.9		
Family history of kidney disease				
	No	99 (70.7)	369 (77.5)	468 (76.0)
	Yes	41 (29.3)	107 (22.5)	148 (24.0)
History of kidney stone				
	No	132 (94.3)	455 (95.6)	587 (95.3
	Yes	8 (5.7)	21 (4.4)	29 (4.7)
Current WHO clinical stage				
	Stage I	57 (40.7)	139 (29.2)	196 (31.8)
	Stage II	31 (22.1)	100 (21.0)	131 (21.3)
	Stage III	41 (29.3)	189 (39.7)	230 (37.3)
	Stage IV	11 (7.9)	48 (10.1)	59 (9.6)
Duration of ARV treatment (in years)				
	≤6	140 (100.0)	90 (18.9)	230 (37.3)
	>6	0 (0.0)	386 (81.1)	386 (62.7)
	Mean±SD	6.3±4.2		
ARV regimens				
	First line	–	454 (73.7)	454 (73.7)

Continued

Table 3 Continued

Variables	HAART naïve n (%)	HAART experienced n (%)	Total n (%)
Second line	–	22 (3.6)	22 (3.6)
Regimen type of HAART			
AZT+3TC+NVP	–	147 (23.9)	147 (23.9)
TDF+3TC+EFV	–	122 (19.8)	122 (19.8)
TDF+3TC+DTG	–	70 (11.4)	70 (11.4)
TDF+3TC+NVP	–	63 (10.2)	63 (10.2)
AZT+3TC+EFV	–	49(8)	49(8)
AZT+3TC+LPV/r	–	9 (1.5)	9 (1.5)
AZT+3TC+ATV/r	–	4 (0.6)	4 (0.6)
TDF+3TC+ATV/r	–	4 (0.6)	4 (0.6)
ABC+3TC+LPV/r	–	4 (0.6)	4 (0.6)
ABC+3TC+NVP	–	3 (0.5)	3 (0.5)
TDF+3TC+ATV/r	–	1 (0.2)	1 (0.2)

ABC, abacavir; ARV, antiretroviral; ATV/r, atazanavir/ritonavir; AZT, zidovudine; CKD, chronic kidney disease; DTG, dolutegravir; EFV, efavirenz; eGFR, estimated glomerular filtration rate; FBG, fast blood glucose; HAART, highly active antiretroviral therapy; Hgb, haemoglobin; LPV/R, lopinavir/ritonavir; NVP, nevirapine; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.

analysis. Variables such as rural residency (adjusted OR, AOR 6.44, 95% CI 1.72 to 24.05), being anaemic (AOR 14.47, 95% CI 2.04 to 102.39), being hypertensive (AOR 18.54, 95% CI 3.48 to 98.88), having had family history of kidney disease (AOR 3.78, 95% CI 1.05 to 13.57), stage IV current WHO clinical stage (AOR 11.13, 95% CI 1.03 to 120.69) and abnormal WC (AOR 11.72, 95% CI 2.67 to 51.38) were 6.44, 14.47, 18.54, 3.78, 11.13 and 11.72 times more likely to have CKD among naïve HIV patients compared with their comparison group urban residency, being not anaemic, being not hypertensive, no family history of kidney disease, stage I current WHO clinical stage and normal WC, respectively (table 6).

Factors associated with CKD among HAART experienced HIV patients

In bivariate logistic regression analysis, the association of different predictors related to; sociodemographic characteristics, exercise and behavioural characteristics, chronic medical illnesses, and clinical and anthropometric measurements with CKD among HAART experienced HIV-infected individuals were checked. Then, predictor variables such as age of participant, residence, educational status, consumption of drinking water per day, current status of anaemia, current status of hypertension, current status of diabetes mellitus, family history of kidney disease, current WHO clinical stage, duration of ART treatment, BMI and WC were found to be significantly associated with CKD among HAART experienced HIV-infected individuals. The Hosmer-Lemeshow test of this model is p=0.629, so a p>0.05 considered as a good fit. The area under the curve is 0.856 with 95% CI (0.813 to 898). Also, the area under the curve is significantly different from 0.5 since p value is 0.000 meaning that there is a higher overall accuracy of the test.

These eligible predictors were adjusted for possible confounding using multivariate logistic regression analysis. Variables such as rural residency (AOR 4.11, 95% CI 2.18 to 7.75), consumption of drinking water per day below recommended amount (AOR 6.01, 95% CI 1.58 to 22.79), being anaemic (AOR 2.41, 95% CI 1.16 to 5.02), being hypertensive (AOR 3.79, 95% CI 1.66 to 8.64), stage IV current WHO clinical stage (AOR 4.62, 95% CI 1.44 o 14.78), BMI of obesity (AOR 4.21, 95% CI 1.29 to 13.67) and abnormal WC (AOR 5.92, 95% CI 2.94 to 11.92) were 4.11, 6.01, 2.41, 3.79, 4.62, 4.21 and 5.92 times more likely to have CKD among experienced HIV patients compared with their comparison group (table 7).

Comparison of HAART naïve and experienced HIV patients

The mean (±SD) of eGFR in HAART naïve and HAART experienced participants was 117.97±33.29 mL/min/1.73 m^2 and 130.22±31.56 mL/min/1.73 m^2, respectively. Statistically significant difference was observed between HAART naïve and HAART experienced participants with regard to the mean GFR level (t=−3.99, 95% CI −18.29 to −6.22). There was also a significant difference in the mean value of current $CD4^+$ T-cell count (cells/mm^3) between HAART naïve and HAART experienced participants (p<0.05) (table 8).

DISCUSSION

General finding

In this study, the overall prevalence of CKD among HAART naïve and experienced HIV patients was 19.3%. The prevalence of CKD was 29.3% and 16.4% among the total HAART naïve and HAART experienced HIV patients, respectively. Predictor variables such as rural residency, being anaemic, being hypertensive, family

Table 4 Clinical and anthropometric measurements of respondents in selected Public Hospitals, South West Ethiopia, 2020

Variables		HAART naïve n (%)	HAART experienced n (%)	Total n (%)
BMI				
	Underweight (BMI<18.5 kg/m^2)	32 (22.9)	106 (22.3)	138 (22.4)
	Normal weight (18.5–24.9 kg/m^2)	80 (57.1)	275 (57.8)	355 (57.6)
	Overweight (25–29.9 kg/m^2)	20 (14.3)	58 (12.2)	78 (12.7)
	Obesity (≥30 kg/m^2)	8 (5.7)	37 (7.8)	45 (7.3)
	Mean±SD		21.9±4.9	
Waist circumference				
	Normal	115 (82.1)	394 (82.8)	509 (82.6)
	Abnormal	25 (17.9)	82 (17.2)	107 (17.4)
	Mean±SD		75.5±17.0	
First protein urea				
	Positive	64 (45.7)	115 (24.2)	179 (29.1)
	Negative	76 (54.3)	361 (75.8)	437 (70.9)
Second protein urea				
	Negative	23 (35.9)	37 (32.2)	60 (33.5)
	Positive	41 (64.1)	78 (67.8)	119 (66.5)
Current viral load (cells/mm^3)				
	Undetected	55 (39.3)	168 (35.3)	223 (36.2)
	<20	2 (1.4)	12 (2.5)	14 (2.3)
	20–999	53 (37.9)	226 (47.5)	279 (45.3)
	≥1000	30 (21.4)	70 (14.7)	100 (16.2)
	Mean±SD		3467±17 953	
Current CD4$^+$ T-cell count (cells/mm^3)				
	≤199	26 (18.6)	34 (7.1)	60 (9.7)
	200–349	28 (20.0)	99 (20.8)	127 (20.6)
	350–499	34 (24.3)	114 (23.9)	148 (24.0)
	≥500	52 (37.1)	229 (48.1)	281 (45.6)
	Mean±SD		506±268	

BMI, body mass index; HAART, highly active antiretroviral therapy.

history of kidney disease and stage IV current WHO clinical stage were significantly associated with CKD among HAART naïve study participants. Rural residency, utilisation of drinking water per day below recommended amount, being anaemic, being hypertensive, advanced WHO clinical stage and obesity were significantly associated with CKD among HAART experienced HIV positive study participants.

Comparison with similar studies

According to this study, the overall prevalence of CKD among HAART naïve and experienced HIV patients was 119 (19.3%) with 95% C.I (16.2 to 22.4). This finding was found to be consistent with different studies conducted in Queen Elizabeth Hospital, the tertiary referral centre in Hong Kong, China (16.8%),[51] Gondar (16.1%)[31] and Jimma (18.2%).[35] However, the prevalence of CKD in this study was lower as compared with different studies conducted in Nigeria (38%),[52] Côte d'Ivoire (26%),[53] Zambia (33.5%)[54] and Kenya (25%).[55] In contrast to this, the result was higher as compared with the report from Belgium (3.0%),[56] Brazil (8.4%)[57] and Ghana (10.8%).[58] This discrepancy might be due to different populations, study designs, variation in sample size, a definition used to define CKD and use different estimating formulas of GFR may contribute to the differences observed.

In this study, the prevalence of CKD among HAART naïve HIV patients was (29.3%) with 95%CI (21.65 to 36.92). It is comparable to different studies conducted in Tanzania (25%),[59] Blantyre, Malawi 23%[60] and in different parts of Ethiopia; (31.1%) in Felege Hiwot Referral Hospital[61] and 28.7% in Jimma University Specialised Hospital (JUSH).[35] However, the prevalence of this study was higher than different studies conducted in other African countries; 20% in Uganda,[62] 8% in Lusaka, Zambia[63] and 3% in Cameroon.[64] This variation might be due to the difference in the study setting, inclusion and exclusion criteria of the study participants, sample size, the definition used to define CKD and formulas used to

Table 5 Independent factors associated with current CD4+T cell count among all HIV-infected patients in selected Public Hospitals, South West Ethiopia, 2020

Variables		Chronic kidney disease		Logistic regression analysis	
		No n (%)	Yes n (%)	COR (95% CI)*	AOR (95% CI)†
Age of participant					
	18–29	98 (19.7)	10 (8.4)	1.00‡	1.00‡
	30–39	185 (37.2)	43 (36.1)	0.29 (0.13, 0.66)§	0.63 (0.23, 1.70)
	40–49	157 (31.6)	46 (38.7)	0.66 (0.36, 1.22)	1.14 (0.53, 2.483)
	≥50	57 (11.5)	20 (16.8)	83 (0.45, 1.53)	1.08 (0.50, 2.342)
Residence					
	Urban	347 (69.8)	45 (37.8)	1.00‡	1.00‡
	Rural	150 (30.2)	74 (62.2)	3.80 (2.51, 5.77)§	3.82 (2.34, 6.226)§
Educational status					
	Cannot read and write	134 (27.0)	50 (42.0)	1.00‡	1.00‡
	Primary	143 (28.8)	36 (30.3)	0.67 (0.41, 1.10)	3.09 (1.09, 8.770)§
	Secondary	164 (33.0)	26 (21.8)	0.43 (0.25, 0.72)	2.21 (0.77, 6.326)
	Certificate and above	56 (11.3)	7 (5.9)	0.33 (0.14, 0.78)§	1.75 (0.60, 5.14)
Use of chemo					
	No	290 (58.4)	47 (39.5)	0.46 (0.31, 0.70)§	0.62 (0.37, 1.03)
	Yes	207 (41.6)	72 (60.5)	1.00‡	1.00‡
Current status of anaemia					
	Yes	67 (13.5)	38 (31.9)	3.01 (1.89, 4.78)§	2.68 (1.48, 4.87)§
	No	430 (86.5)	81 (68.1)	1.00‡	1.00‡
Current status of hypertension					
	No	453 (91.1)	87 (73.1)	1.00‡	1.00‡
	Yes	44 (8.9)	32 (26.9)	3.78 (2.27, 6.31)§	4.22 (2.21, 8.05)§
Current status of diabetic mellitus					
	No	458 (92.2)	94 (79.0)	1.00‡	1.00‡
	Yes	39 (7.8)	25 (21.0)	3.12 (1.80, 5.41)§	1.49 (0.73, 3.05)
Family history of kidney disease					
	No	404 (81.3)	64 (53.8)	1.00‡	1.00‡
	Yes	93 (18.7)	55 (46.2)	3.73 (2.44, 5.71)§	3.15 (1.84, 5.37)§
Baseline WHO clinical stage					
	Stage I	176 (35.4)	20 (16.8)	1.00‡	1.00‡
	Stage II	104 (20.9)	27 (22.7)	2.28 (1.22, 4.27)	2.75 (1.29, 5.86)
	Stage III	176 (35.4)	54 (45.4)	2.70 (1.55, 4.69)	2.92 (1.47, 5.77)
	Stage IV	41 (8.2)	18 (15.1)	3.86 (1.87, 7.95)§	4.41 (1.85, 10.52)§
BMI					
	Underweight	117 (23.5)	21 (17.6)	1.00‡	1.00‡
	Normal weight	305 (61.4)	50 (42.0)	0.91 (0.52, 1.58)	1.14 (0.60, 2.18)
	Overweight	50 (10.1)	28 (23.5)	3.12 (1.62, 6.01)	3.21 (1.44, 7.13)
	Obesity	25 (5.0)	20 (16.8)	4.45 (2.11, 9.43)§	3.06 (1.21, 7.77)§

*Significant variables determined using bivariate logistic regression analysis.
†Predictors identified using multivariate logistic regression analysis.
‡Reference category.
§Adjusted for all significant variables at p<0.05.
AOR, adjusted OR; COR, crude OR.

Table 6 Independent factors associated with current CD4+ T-cell count among naïve HIV-infected patients in selected Public Hospitals, South West Ethiopia, 2020

Variables	Chronic kidney disease		Logistic regression analysis	
	No n (%)	Yes n (%)	COR (95% CI)†	AOR (95% CI)‡
Age of participant				
18–29	31 (31.3)	5 (12.2)	1.00*	1.00*
30–39	35 (35.4)	17 (41.5)	3.01 (.99 to 9.12)	1.45 (.27 to 7.65)
40–49	27 (27.3)	14 (34.1)	3.22 (1.02 to 10.09)§	.79 (.13 to 4.73)
≥50	6 (6.1)	5 (12.2)	5.17 (1.13 to 23.55)§	2.46(.23 to 26.53)
Residence				
Urban	73 (73.7)	18 (43.9)	1.00*	1.00*
Rural	26 (26.3)	23 (56.1)	3.59 (1.67 to 7.69)§	6.44 (1.72 to 24.05)§
Utilisation of drinking water per day				
Used below recommended amount	82 (82.8)	40 (97.6)	8.29 (1.07 to 64.5)§	2.81(.24 to 33.11)
Used recommended amount	17 (17.2)	1 (2.4)	1.00*	1.00*
Current status of anaemia				
Yes	8 (8.1)	12 (29.3)	4.71 (1.75 to 12.64)§	14.47 (2.04 to 102.39)§
No	91 (91.9)	29 (70.7)	1.00*	1.00*
Current status of hypertension				
No	92 (92.9)	31 (75.6)	1.00*	1.00*
Yes	7 (7.1)	10 (24.4)	4.24 (1.49 to 12.09)§	18.54 (3.48 to 98.88)§
Current status of diabetes mellitus				
No	92 (92.9)	33 (80.5)	1.00*	1.00*
Yes	7 (7.1)	8 (19.5)	3.19 (1.07 to 9.47)§	2.72 (.42 to 17.84)
Family history of kidney disease				
No	79 (79.8)	20 (48.8)	1.00*	1.00*
Yes	20 (20.2)	21 (51.2)	4.15 (1.89 to 9.09)§	3.782 (1.05 to 13.57)§
Current WHO clinical stage				
Stage I	50 (50.5)	7 (17.1)	1.00*	1.00*
Stage II	21 (21.2)	10 (24.4)	3.40 (1.14 to 10.14)§	3.39(.59 to 19.48)
Stage III	23 (23.2)	18 (43.9)	5.59 (2.05 to 15.24)§	10.51 (1.89 to 58.49)§
Stage IV	5 (5.1)	6 (14.6)	8.57 (2.06 to 35.68)§	11.13 (1.03 to 120.69)§
BMI				
Underweight	25 (25.3)	7 (17.1)	1.00*	1.00*
Normal weight	61 (61.6)	19 (46.3)	1.11 (.42 to 2.98)	1.81 (.34 to 9.70)
Overweight	10 (10.1)	10 (24.4)	3.57 (1.06 to 12.01)§	3.56 (.48 to 26.28)
Obesity	3 (3.0)	5 (12.2)	5.95 (1.13 to 31.26)§	3.60 (.293 to 44.32)

*Reference category.
†Significant variables determined using bivariate logistic regression analysis.
‡Predictors identified using multivariate logistic regression analysis.
§Adjusted for all significant variables at p<0.05.
AOR, adjusted OR; BMI, body mass index; COR, crude OR.

eGFR. For instance, in Kenya, participants with known sickle cell disease, acute infection, previously diagnosed diabetes, marked hypertension or renal disease were excluded, and in Lusaka, Zambia the renal function was calculated using Cockcroft Gault formula, and only patients initiated on tenofovir containing drugs were included.

The prevalence of CKD among HAART experienced HIV patients was 78 (16.4%) with 95% CI (13.1 to 19.7). This study was comparable with the study conducted in Ghana (14.5%).[58] However, this study finding is higher as compared with studies reported in Tanzania (1.1%),[65] Uganda (6%),[62] in the University of Gondar Hospital, Ethiopia (11.7%),[33] in JUSH, Ethiopia, (7.6%),[35] in Felege Hiwot Referral Hospital, Ethiopia (12.1%).[61] This wide variation could be attributed to the differences in the HAART regimen, and the method used to eGFR. For instance, in Tanzania, adjusted the Cockroft-Gault equation was used to calculate eGFRs, and may contribute

Table 7 Independent factors associated with current CD4+T cell count among HAART experienced HIV patients in Selected Public Hospitals, South West Ethiopia, 2020

Variables	Chronic kidney disease		Logistic regression analysis	
	No **n (%)**	Yes **n (%)**	**COR (95% CI)***	**AOR (95% CI)†**
Age of participant				
18–29	67 (16.8)	5 (6.4)	1.00‡	1.00‡
30–39	150 (37.7)	26 (33.3)	2.32 (.86 to 6.31)	2.56 (.79 to 8.27)
40–49	130 (32.7)	32 (41.0)	3.29 (1.23 to 8.86)§	2.85 (.89 to 9.17)
≥50	51 (12.8)	15 (19.2)	3.94 (1.34 to 11.56)§	2.84 (.74 to 10.89)
Residence				
Urban	274 (68.8)	27 (34.6)	1.00‡	1.00‡
Rural	124 (31.2)	51 (65.4)	4.17 (2.50 to 6.97)§	4.11 (2.18 to 7.75)§
Educational status				
Cannot read and write	111 (27.9)	32 (41.0)	1.00‡	1.00‡
Primary	115 (28.9)	23 (29.5)	.69 (.38 to 1.26)	.73 (.33 to 1.59)
Secondary	132 (33.2)	19 (24.4)	.49 (.27 to .93)§	.91 (.40 to 2.05)
Certificate and above	40 (10.1)	4 (5.1)	.35(.12 to 1.04)	.39 (.09 to 1.71)
Consumption of drinking water per day				
Used below recommended amount	342 (85.9)	74 (94.9)	3.03 (1.07 to 8.61)§	6.01 (1.58 to 22.79)§
Used recommended amount	56 (14.1)	4 (5.1)	1.00‡	1.00‡
Current status of anaemia				
Yes	59 (14.8)	26 (33.3)	2.87 (1.66 to 4.96)§	2.41 (1.16 to 5.02)§
No	339 (85.2)	52 (66.7)	1.00‡	1.00‡
Current status of hypertension				
No	361 (90.7)	56 (71.8)	1.00‡	1.00‡
Yes	37 (9.3)	22 (28.2)	3.83 (2.11 to 6.97)§	3.79 (1.658 to 8.64)§
Current status of diabetes mellitus				
No	366 (92.0)	61 (78.2)	1.00‡	1.00‡
Yes	32 (8.0)	17 (21.8)	3.19 (1.67 to 6.09)§	1.27 (.49 to 3.29)
Family history of kidney disease				
No	325 (81.7)	44 (56.4)	1.00‡	1.00‡
Yes	73 (18.3)	34 (43.6)	3.44 (2.06 to 5.76)§	1.94 (.971 to 3.87)
Baseline WHO clinical stage				
Stage I	126 (31.7)	13 (16.7)	1.00‡	1.00‡
Stage II	83 (20.9)	17 (21.8)	1.99 (.92 to 4.30)	4.23 (1.46 to 12.29)§
Stage III	153 (38.4)	36 (46.2)	2.28 (1.16 to 4.49)§	3.67 (1.44 to 9.36)§
Stage IV	36 (9.0)	12 (15.4)	3.23 (1.36 to 7.69)§	4.62 (1.44 to 14.78)§
Duration of ART (in years)				
≤6	82 (20.6)	8 (10.3)	1.00‡	1.00‡
>6	316 (79.4)	70 (89.7)	2.27 (1.05 to 4.91)§	1.93 (.72 to 5.23)
BMI				
Underweight	92 (23.1)	14 (17.9)	1.00‡	1.00‡
Normal weight	244 (61.3)	31 (39.7)	.84 (.43 to 1.64)	1.28 (.55 to 2.98)
Overweight	40 (10.1)	18 (23.1)	2.96 (1.34 to 6.52)§	2.47 (.85 to 7.15)
Obesity	22 (5.5)	15 (19.2)	4.48 (1.89 to 10.63)§	4.21 (1.29 to 13.67)§

*Significant variables determined using bivariate logistic regression analysis.
†Predictors identified using multivariate logistic regression analysis.
‡Reference category.
§Adjusted for all significant variables p<0.05.
AOR, adjusted OR; ART, antiretroviral therapy; BMI, body mass index; COR, crude OR; HAART, highly active antiretroviral therapy.

Table 8 The mean values of clinical and anthropometric parameters of HAART naïve and experienced HIV positive patients in Selected Public Hospitals, South West Ethiopia, 2020

Parameters	HIV patients		P value	T-value (95% CI)*
	HAART naïve HIV patients (mean±SD)	HAART experienced HIV patients (mean±SD)		
eGFR	117.97±33.29	130.22±31.56	0.000	−3.99 (−18.29 to 6.22)†
Creatinine level	0.77±0.37	0.70±0.77	0.283	1.07 (−0.06 to 0.20)
Waist circumference	76.76±16.95	74.93±17.06	0.264	1.12 (−1.39 to 5.05)
FBG level	87.95±23.63	90.76±26.52	0.259	−1.13 (−7.70 to 2.07)
BMI	21.45±4.14	22.03±5.06	0.213	−1.25 (−1.50 to .34)
Current $CD4^+$ T-cell count	443±262	525±267	0.001	−3.22 (−132.54 to 32.13)†

*Mean difference analysed using independent t-test.
†Statistically significant mean difference at p<0.05.
BMI, body mass index; CD4, cluster of differentiation 4; FBG, fast blood glucose; GFR, glomerular filtration rate; HAART, highly active antiretroviral therapy.

to the differences observed. But in our study, eGFR was calculated using the CKD-EPI equation which is the most accurate for the staging of CKD at all levels of eGFR.[17]

The prevalence of CKD was significantly higher in naive study participants than HAART experienced study participants. This finding is supported by researches done in Nigeria,[66] Jimma[35] and Bahir Dar Ethiopia.[61] The finding of lower CKD prevalence in HAART experienced study participants may be due to the improvement in renal function because of HAART drugs. In the current study, different predictors were found to be significantly associated with both CKD among HAART naïve and CKD among HAART experienced HIV patients.

The rural residency was found to be a strong predictor variable for both CKD among HAART naïve and CKD among HAART experienced HIV patients. This is supported by the study conducted in SSA,[67] and other low-income and middle-income countries.[68] This is due to the fact that the use of herbal medicines is commonly practiced in rural communities of both Africa and Asia which can also act as nephrotoxins, thus increasing the risk of CKD progression.[69] Moreover, in low-income and middle-income countries, most populations are rural residing communities where awareness of CKD remains low and also recognising problems associated with CKD are ill-equipped particularly during the early asymptomatic stages of the disease.[70] Worldwide, only one-third of people with CKD are diagnosed in rural communities and are more prone to develop different complications due to unavailability and unaffordability of health services like laboratory investigations and different treatments.[71] Furthermore, this might be due to the burden of travelling long distances to access health services, costs of accommodation and perceived lack of education regarding their kidney disease and treatment options.[72] Moreover, associated with the unavailability of health services in rural community, the low provision of drugs and poor adherence check-up will contribute for CKD to appear more common in rural community.

In this study, being anaemic was also significantly associated with both CKD among HAART naïve and CKD among HAART experienced HIV patients. Similarly, this finding was supported by the study conducted in Nigeria.[52] Anaemia occurs commonly in CKD among HIV patients as the result of decreased production of erythropoietin which is responsible for the production of red blood cells[73] either due to functional or absolute iron deficiencies.[74] Moreover, anaemia in CKD among HIV patients has been associated with opportunistic infections and inflammation,[75] micronutrient deficiencies, medication-induced and neoplastic diseases.[76]

Similarly, this study revealed that being hypertensive and advanced WHO clinical stage were also significantly associated with both CKD among HAART naïve and CKD among HAART experienced HIV patients, respectively. This finding was corroborated by studies conducted in Brazil[57] and Nigeria.[77] Previous study report by Ibrahim *et al* confirmed that the likelihood of developing kidney disease among hypertensive patients on HAART was almost fivefold,[78] where hypertension inhibits the immune status of patients with HIV which in turn may increase in viral load and renal dysfunction.[79] Similarly, patients with late-stage of HIV diagnosis were at risk of high viral load which in turn may affect the renal function.[9]

Consumption of drinking water per day below recommended amount was an important factor which determines CKD among HAART experienced HIV patients. Similarly, this finding was supported by a study conducted in Ontario, Canada.[80] This is due to the fact that lower levels of water intake cause decreased urine output which may increase the supersaturation of calcium phosphate, calcium oxalate and uric acid, which finally increases the risk of stone formation and eventually predisposes to CKD.[81]

Obesity was also another factor significantly associated with CKD among HAART-experienced HIV patients. This finding was supported by a study conducted in China.[82] This is explained by the fact that traditional risk

factors like obesity, diabetes and hypertension are global contributing factors for CKD.[83] This is because, in obese individuals, there is an increased metabolic demand of the increased body weight, resulting in glomerular hyperfiltration, hypertrophy and intraglomerular pressure, subsequently predisposed to CKD.[84]

Furthermore, having a family history of kidney disease was also another factor significantly associated with CKD among HAART naïve HIV patients. This finding was in line with the study in the Netherlands.[85] This might be because of some hereditary kidney diseases like autosomal-dominant polycystic kidney disease which is caused by genetic changes of PKD1 gene located on chromosome 16 encoding membrane protein polycystin which is responsible for maintaining of renal epithelial differentiation and organisation, where this function is disrupted by mutations in PKD1 which probably leads to abnormal differentiation of tubular cells and cyst formation. Therefore, this mutated gene can be inherited by family members and causes enormous kidney problems.[86 87]

However, in this study, the current status of DM remains insignificant among HAART naïve, HAART experienced, and overall all HIV patients, the study conducted in Jordan revealed that being diabetic was the strong significant factor for CKD due to the reason that DM cause long-term microvascular and macrovascular complications, contributing to the increased morbidity of CKD.[88] This discrepancy might be due to the reason that in this study, the total numbers of diabetic participants who developed CKD are very rare, and this could contribute for this variable to remain insignificant when adjusted. Moreover, since the average time of onset of kidney impairment in patients with diabetes is about 7–10 years, in this study, patients with diabetes might not be chronically ill for such duration of time. Furthermore, this discrepancy could also be due to the difference in; the follow-up time, severity of DM, the timing of initiation of treatment, treatment options, early recognition of risk factors and symptoms, and availability of health services.[89]

Statistically significant difference was observed in the mean value of GFR level between HAART naïve and HAART experienced HIV patients, where the mean value of GFR level among HAART experienced HIV patients exceeds the mean value of GFR level among HAART naïve HIV patients. This is due to the fact that the HAART regimen has a positive impact on the increment of GFR level. In contrast to this, the GFR level among HAART naïve was decreased. This might be explained by the fact that HAART naïve HIV patients are commonly at risk of advanced HIV disease where high viral load is common, and this will contribute to the decrement of GFR which turns to cause severe stage of CKD. As to the researchers' knowledge, no comparative study was done to discuss.

Similarly, there was also a statistically significant difference in the mean value of Current $CD4^+$ T-cell count (cells/mm^3) between HAART naïve and HAART experienced HIV patients. This is due to the reason that HAART naïve patients are affected by the high viral load which depletes the level of $CD4^+$ T-cell count.

This study was conducted in the three hospitals and increases the probability of generalisability of CKD among HIV patients. However, this study has its own limitation. First, since this study was the cross-sectional study, it did not show the cause and effect relationship of variables. Second, there will be lower risk prediction due to the reason that some biomarker like cystatin C was not tested to estimation of GFR. Third, there will be poor sensitivity and high false-discovery rates due to the reason that proteinuria was assessed using dipstick not the albumin-creatinine ratio. Therefore, this study results should be interpreted with caution.

Policy implication and future research

Despite major progress that have been made by the Ethiopian Ministry of Health to reduce the burden of non-communicable diseases (NCDs), (NCDs) estimated to account for 46% of all deaths in Ethiopia and also causes for an estimated cost of 31.3 billion birrs (US$1.1 billion) per year.[90] CKD is also one of the NCDs which also cause different complications like dyslipidaemia, hyperkalaemia, metabolic acidosis, anaemia and bone and mineral disorders. In this study, CKD was also found to be prevalent among HIV patients. Therefore, early initiation of ART drugs, modification of lifestyles to decrease obesity and or abnormal WC, and early detection and treatment of comorbidities such as; anaemia and hypertension have profound effects in reducing CKD among HIV patients and increase their quality of life. Furthermore, researchers need to do researches on the complications associated with CKD among HIV patients considering a strong study design. Moreover, the specific impact of HAART regimen to the clinical parameters such as creatinine, GFR and others should be further investigated.

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Ethics approval This study was conducted in accordance with the Declaration of Helsinki and after ethical clearance was obtained from the research directorate office of Mizan Tepi University (Ref No: MTU/CHS/16/1221/27/12). Written consent was obtained from each study participant after explaining the purpose and objectives of the study. For those participants who were illiterate, a fingerprint was used as a signature after trained interviewers have carefully explained the purpose, benefits and potential risks before consent was obtained. The interview with study participants was conducted with strict privacy and confidentiality. The test was also performed following the manufacturer's instructions and interpreted accordingly. Then, all necessary information and the results of each study participant were communicated with their physicians for further investigations and management.

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