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MAJOR ARTICLE

Prevalence of Cardiometabolic Disease Risk Factors in People With HIV Initiating Antiretroviral Therapy at a High-Volume HIV Clinic in Kampala, Uganda

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Background. Cardiometabolic diseases are a leading cause of HIV-related morbidity and mortality, yet routine screening is not undertaken in high-burden countries. We aimed to assess the prevalence and risk factors of the metabolic syndrome (MetS) and its components in adult Ugandan people with HIV (PWH) initiating dolutegravir-based antiretroviral therapy (ART).

Methods. We conducted a cross-sectional study using baseline sociodemographic and clinical data of PWH aged ≥18 years enrolled in the Glucose metabolism changes in Ugandan HIV patients on Dolutegravir (GLUMED) study from January to October 2021. MetS was defined as having ≥3 of the following: abdominal obesity, hypertension (HTN), hyperglycemia, elevated triglycerides, and low high-density lipoprotein cholesterol. Multiple logistic regression was used to assess associations between potential risk factors and MetS and its components.

Results. Three hundred nine PWH were analyzed (100% ART-naïve, 59.2% female, median age 31 years, and median CD4 count 318 cells/mm^3). The prevalence of MetS was 13.9%. The most common cardiometabolic condition was dyslipidemia (93.6%), followed by abdominal obesity (34.0%), hyperglycemia (18.4%), and HTN (8.1%). In adjusted analysis, MetS was associated with age >40 years (adjusted odds ratio [aOR], 3.33; 95% CI, 1.45–7.67) and CD4 count >200 cells/mm^3 (aOR, 3.79; 95% CI, 1.23–11.63). HTN was associated with age >40 years (aOR, 2.96; 95% CI, 1.32–6.64), and dyslipidemia was associated with urban residence (aOR, 4.99; 95% CI, 1.35–18.53).

Conclusions. Cardiometabolic risk factors were common in this young Ugandan cohort of PWH initiating dolutegravir-based ART, underscoring the need for programmatic implementation of surveillance and management of comorbidities in Uganda and similar settings.

Keywords. ART; HIV; Uganda; metabolic syndrome.

The HIV epidemic remains a major public health problem, with 38 million people infected globally in 2021 [1]. Despite this, increased access to potent combination antiretroviral therapy (ART) has substantially lowered HIV-related morbidity and mortality and prolonged the life expectancy of people with HIV (PWH). This is of utmost relevance in Sub-Saharan Africa (SSA), where the global burden of HIV is highest [2, 3]. Paradoxically, this has resulted in an increase in the burden of noncommunicable diseases (NCDs) among PWH [3–6]. Globally, NCDs cause 41 million deaths annually, with cardiovascular diseases (CVDs) accounting for nearly half (44%) of such deaths [7]. PWH are at a 2-fold higher risk of experiencing myocardial infarction, strokes, and other CVDs due to multiple factors, including having a higher prevalence of traditional CVD risk factors at baseline, ART-associated toxicities, HIV-induced immune activation, and chronic systemic inflammation [8, 9]. With recent modeling studies projecting an excess increase in NCDs among PWH [10, 11], the Joint United Nations Programme on HIV/AIDS (UNAIDS) is advocating for increased surveillance and integration of NCD care in HIV programs [12–14].

Since 2016, the World Health Organization (WHO) has recommended the use of integrase strand transfer inhibitors (INSTIs) as the preferred first- and second-line ARTs [15, 16]. This followed multiple reports of increasing primary HIV drug resistance (HIVDR) to non-nucleoside reverse transcriptase inhibitors (NNRTIs), with many high-burden countries reporting NNRTI HIVDR prevalence rates exceeding the 10%

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recommended threshold [17, 18]. Subsequently, most countries in SSA have adopted dolutegravir (DTG)-based regimens as first-line ART due to their high barrier to resistance, better tolerability, and fewer drug–drug interactions [19–21]. Despite their tolerability profile, however, INSTIs have been consistently linked to excessive weight gain, particularly among women, older individuals, and people of Black or African ancestry [22–24]. Additionally, analyses for insulin resistance trajectories from multiple clinical trial data, for example, SPRING-2 [23], SAILING [24], and VIKING-3, described worsening insulin resistance in PWH after switch to INSTI-based ART [25]. Similarly, multiple case reports and a few cohort studies describing real-world experiences with INSTIs have documented accelerated hyperglycemia in PWH following a switch to INSTI-based ART [26–29]. In 1 such a report from Uganda, there was an observed incidence rate of 4.7 cases of hyperglycemia per 1000 patients in a median duration of 4 months after initiating DGT-based ART, with the majority (15 of 16 cases) presenting with diabetic ketoacidosis [26]. Consequently, the Ugandan Ministry of Health HIV treatment guidelines halted the use of DTG in patients known to have diabetes or at high risk of cardiometabolic diseases [30].

Given the well-described metabolic complications associated with INSTIs, their widespread adoption as first- and second-line ARTs in SSA is likely to significantly exacerbate the growing problem of NCDs among PWH in this region. It is therefore essential that HIV treatment programs in SSA implement effective NCD control measures focused on early screening and prevention of comorbidities. However, there are limited studies to inform evidence-based public health policy and clinical practice. In this study, we aimed to assess the prevalence and risk factors associated with metabolic syndrome (MetS) and its components in a cohort of treatment-naïve PWH starting ART at a high-volume HIV clinic in Kampala, Uganda.

METHODS

Study Objective, Design, and Setting

The Glucose metabolism changes in Ugandan HIV patients on Dolutegravir (GLUMED) study was conducted from January to October 2021. This was a prospective cohort study that enrolled newly diagnosed PWH before ART initiation at Kisenyi Health Center HIV Clinic in Kampala, the capital and largest city in Uganda. The primary objective of the GLUMED study was to describe changes in glucose metabolism in Ugandan PWH at study entry and 48 weeks after initiating DTG-based ART. The HIV Clinic is one of the busiest in the country, with about 12 000 active HIV clients enrolled in routine care.

For the present study, we conducted a cross-sectional analysis of baseline sociodemographic and clinical data at entry into the GLUMED study. The objective of this study was to assess the prevalence and factors associated with the MetS, hypertension, hyperlipidemia, and hyperglycemia among PWH before initiation of ART.

Study Participants and Processes

We consecutively screened ART-naïve PWH during the enrollment phase of the GLUMED study. All patients who were age ≥18 years and able to give informed consent were eligible. Pregnant women, sick individuals deemed unable to undergo a 75-g (300-mL) oral glucose tolerance test (OGTT), and individuals unable to provide consent were excluded.

Figure 1 presents a scheme of the screening process. Of 435 PWH screened, 310 patients consented to the oral glucose tolerance test evaluation. The remaining 125 patients were excluded from the study on the basis of the following: 61 preferred to transfer care to other ART clinics, 34 preferred to defer participation, 24 were pregnant, and 6 were ill and unable to perform the OGGT. One patient did not have complete baseline sociodemographic and clinical data, leaving 309 PWH who were included in the final analysis.

Consenting participants underwent an overnight fast of at least 8 hours. About 5 mL of venous blood was collected from each participant into tubes (BD Vacutainer K2 EDTA). After ingesting a 75-g oral glucose solution, repeat 5-mL blood samples were collected from participants at 30, 60, 90, and 120 minutes. Blood glucose was measured at all time points immediately after sample collection (ie, before transfer to vacutainers) using an ACCU-CHECK glucometer (Roche Diagnostics, Manheim, Germany). Individuals found to be euglycemic (ie, fasting blood glucose <126 mg/dL or 2-hour glucose <200 mg/dL) [31] were then enrolled in GLUMED and initiated on a fixed-dose combination of tenofovir/lamivudine/dolutegravir as recommended by the Ugandan National HIV Treatment Guidelines [30]. The venous blood was then spun at 2000*g* for 10 minutes. The plasma was collected into cryogenic vials (Nunc CryoTubes) and stored at −80°C until analysis.

Assessments and Variable Definitions

Baseline sociodemographic and clinical data were collected from consenting participants and recorded in a password-protected spreadsheet accessible only to research team members. All patient identifiers including name and personal identification numbers were removed to ensure confidentiality. Data collected included age, sex, weight, height, marital status, area of residence (urban vs rural), highest level of education attained (none, primary, secondary, or tertiary), religion (Christian vs Muslim), history of smoking, alcohol, level of physical activity, and blood pressure.

HIV status was determined using the rapid test by SD Bioline HIV-1/2 3.0 (Standard Diagnostics Inc., Suwon, Korea). CD4 count was determined using the Alere Pima Analyzer (Abbott, Jena, Germany). Risk of harmful alcohol use was assessed using

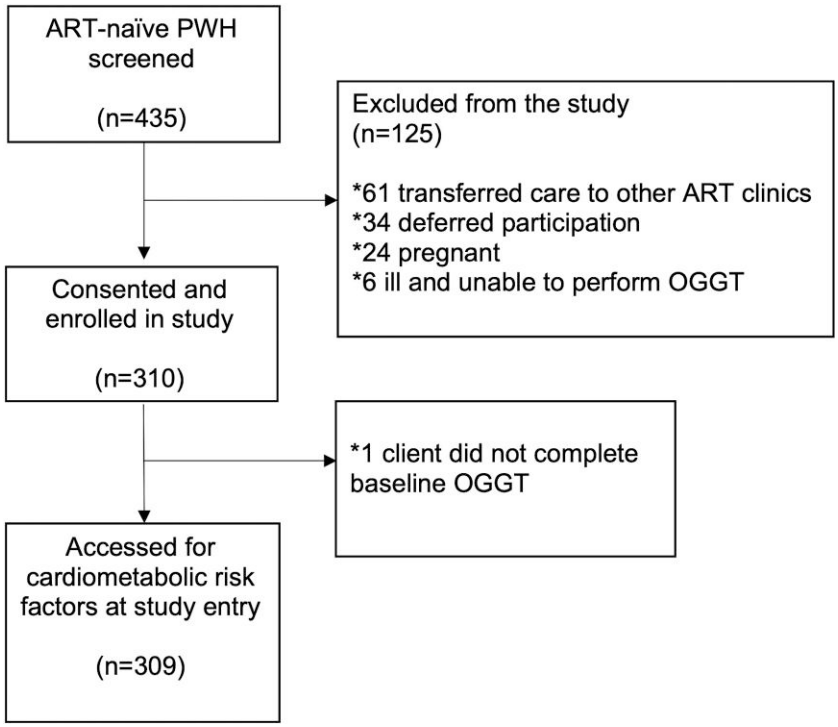

Figure 1. Enrollment schema for the GLUMED study. *Denotes patients excluded from the study. Abbreviations: ART, antiretroviral therapy; GLUMED, Glucose metabolism changes in Ugandan HIV patients on Dolutegravir; OGGT, oral glucose tolerance test; PWH, people with HIV.

the standardized AUDIT questionnaire, with scores ranging 0–7 classified as low risk, 8–15 classified as moderate risk, 16–19 high risk, and ≥20 regarded as addiction [32]. Level of physical activity was assessed by the World Health Organization (WHO) Global Physical Activity Questionnaire, with ≥600 metabolic equivalents (MET) regarded as meeting the minimum daily requirements for physical activity [33]. Laboratory parameters including serum creatine and lipid profiles were determined by the Cobas 6000 Analyzer (Roche Diagnostics, Manheim, Germany). CD4 count was determined by the Alere Pima Analyzer (Abbott Diagnostics, Jena, Germany).

Waist circumference (WC) measurements were used to assess abdominal obesity, and risk of cardiometabolic disease was stratified according to the WHO criteria [34] as follows: (1) not at risk: <95 cm (males) and <81 cm (females); (2) at increased risk: males ≥95 to ≤102 cm and females ≥81 to ≤88 cm; and (3) at substantially increased risk: ≥103 cm (males) and ≥89 cm (females). Body mass index (BMI) was classified based on the US Centers for Disease Control and Prevention criteria as follows: (1) underweight: <18.5 kg/m^2; (2) normal: 18.5–24.9 kg/m^2; (3) overweight: 25–29.9 kg/m^2; and obese: ≥30 kg/m^2 for obesity [35].

Hypertension was assessed as the average of 2 readings or being on antihypertensive treatment and was categorized in accordance with the Joint National Committee 8 (JNC-8) guidelines [36] as follows: (1) normal: systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg; (2) prehypertension: SBP 120–139 mmHg or DBP 80–89 mmHg; and (3) hypertension (HTN): SBP ≥140 mmHg or DBP ≥90 mmHg.

Diabetic status was categorized in accordance with American Diabetes Association criteria [37] as follows: (1) normal: fasting glucose <100 mg/dL or 2-hour OGGT <140 mg/dL; (2) prediabetes: fasting glucose 100–125 mg/dL or 2-hour glucose 140–199 mg/dL; and (3) diabetes: fasting glucose ≥126 mg/dL or 2-hour or glucose ≥200 mg/dL.

Dyslipidemia was defined as having any 1 of the following: (1) hypercholesterolemia, that is, total cholesterol (TC) >200 mg/dL; (2) high-density lipoprotein cholesterol (HDL-C) <40 mg/dL (males) or <50 mg/dL (females); (3) low-density lipoprotein cholesterol (LDL-C) >100 mg/dL; and (4) hypertriglyceridemia, that is, triglycerides (TG) >150 mg/dL [38]. Glomerular filtration rate (eGFR) was estimated using the Modification of Diet in Renal Disease Study equation [39], with renal impairment defined as eGFR <60 mL/min/1.73 m^2. Laboratory-based 10-year CVD (Framingham) risk scores were calculated for participants aged ≥30 years (170/309, 55%) and classified as follows: low risk: <10%; intermediate risk: 10%–20%; and high risk: >20% [40].

Lastly, we used a harmonized definition of the MetS based on diagnostic criteria proposed by the International Diabetes Federation (IDF) Task Force on Epidemiology and Prevention,

the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), and the WHO [41], which requires having at least 3 of the following 5 criteria: (1) WC >94 cm (men) or >81 cm women; (2) TG >150 mg/dL; (3) HDL-C <40 mg/dL (males) or <50 mg/dL (females); (4) fasting glucose >100 mg/dL; and (5) SBP ≥130 mmHg or DBP ≥85 mmHg.

Statistical Analysis

Statistical analyses were performed using SPSS, version 29.0 (IBM Corp, Armonk, NY, USA). Normality of the data was assessed using the Shapiro-Wilk test. Categorical variables were reported as frequencies (percentages), and associations were assessed using the Pearson chi-square or Fisher exact test. Continuous variables were presented as medians (interquartile ranges [IQRs]), and associations were assessed using the nonparametric independent-samples Mann-Whitney *U* test. A logistic regression model was used to identify associations between MetS and each of its components (ie, HTN, dyslipidemia, and hyperglycemia) and established risk factors (age, sex, obesity, smoking, alcohol use, level of physical activity, CD4 count) and potential modifiers of CVD risk (relationship status, educational attainment, religion, employment status, and residence). Only variables that attained a *P* value of <.2 in the univariate analysis were included in the multivariable regression model. Associations were reported as crude odds ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals ($P < .05$ considered statistically significant).

Participant Consent

Ethical approval to perform the study was obtained from The AIDS Support Organization (TASO) Institutional Review Board (registration number: TASOREC/051/2020-UG-REC-009) and the Uganda National Council for Science and technology (registration number: HS1032ES). All participants signed informed consent before enrollment in the study.

RESULTS

Baseline Characteristics of Study Participants

A total of 309 PWH were enrolled in the study, and the majority (59.2%, 183/309) were female. The median age (IQR) was 31 (27–39) years, with males being older than females (median age, 34 years vs 30 years; $P < .001$). Most were single (57.6%, 178/309), had attained primary education or higher (98.7%, 305/309), were Christian (79.3%, 245/309), resided in urban areas (92.2%, 285/309), and were employed (81.9%, 253/309). Of the 259 PWH with available data, the median CD4 count (IQR) was 318 (163–550) cells/mm^3 at enrollment (Table 1).

Prevalence of Cardiometabolic Risk Factors

The overall proportion of participants with a history of smoking and harmful alcohol use (AUDIT ≥16) was low at 4.9% (15/309) and 6.5% (20/309), respectively. The majority (78.0%, 241/309) met the WHO daily goals for physical activity.

The median BMI (IQR) was 22.2 (19.7–25.6) kg/m^2, with women more likely to have higher median BMIs compared with their male counterparts ($P < .001$). Overall, 21.7% (67/30) were classified as overweight (pre-obesity, BMI 25–29.9 kg/m^2), while 8.1% (25/309) were classified as obese (BMI ≥30 kg/m^2). Based on the WC measurements, 18.4% (57/309) of participants were at increased risk of cardiometabolic disease, while 15.5% (48/309) were at a substantially higher risk. There were sex differences observed, with women more likely to have higher WC measurements ($P < .001$). The overall prevalence of abdominal obesity was 34.0% (105/309).

A substantial proportion of study participants had prehypertension (16.8%, 52/309), while 8.1% (25/309) had HTN. The prevalence of overt diabetes was low at 0.3% (1/309); however, 18.1% (56/309) had prediabetes. Of those with available testing for kidney function, the median serum creatinine (IQR) was 0.80 (0.68–0.93) mg/dL, with only a small proportion of study

Table 1. Baseline Characteristics of Study Participants by Sex (N = 309)

Characteristics	All PWH	Male	Female	*P* Value
Total	309	126	183	
Age, y				
Median (IQR)	31 (27–39)	34 (28–40)	30 (26–37)	<.001
<30	122 (39.5)	35 (27.8)	87 (47.5)	.002
30–39	121 (39.2)	57 (45.2)	64 (35.0)	
40–49	57 (18.4)	31 (24.6)	26 (14.2)	
≥50	9 (2.9)	3 (2.4)	6 (3.3)	
Relationship status				
Single	178 (57.6)	62 (49.2)	116 (63.4)	.013
Married	131 (42.4)	64 (50.8)	67 (36.6)	
Education				
None	4 (1.3)	0	4 (2.2)	.015
Primary	166 (53.7)	74 (58.7)	92 (50.3)	
Secondary	126 (40.8)	43 (34.2)	83 (45.4)	
Tertiary	13 (4.2)	9 (7.1)	4 (2.1)	
Religion				
Christian	245 (79.3)	102 (81.0)	143 (78.1)	.549
Muslim	64 (20.7)	24 (19.0)	40 (21.9)	
Residence				
Urban	285 (92.2)	120 (95.2)	165 (90.2)	.101
Rural	24 (7.8)	6 (4.8)	18 (9.8)	
Employment				
Yes	253 (81.9)	120 (95.2)	133 (72.7)	<.001
No	56 (18.1)	6 (4.8)	50 (27.3)	
Baseline CD4 count, cells/mm^3 (n = 259)				
Median (IQR)	318 (163–550)	251 (123–382)	399 (238–6510)	<.001
≤99	36 (13.9)	21 (20.4)	15 (9.6)	<.001
100–199	37 (14.3)	21 (20.4)	16 (10.3)	
200–349	66 (25.5)	31 (30.1)	35 (22.4)	
≥350	120 (46.3)	30 (29.1)	90 (57.7)	

Abbreviations: IQR, interquartile range; CD4, cluster of differentiation 4; PWH, people with HIV.

participants (1.4%, 4/282) having impaired renal function (eGFR <60 mL/min/1.73m^2).

About 93.6% (264/282) of study participants had dyslipidemia. The prevalence of hypercholesterolemia was low at 5.3% (15/282). Of the individual components of the lipid panel, 88.3% (249/282) had low HDL-C, 20.9% (59/282) had elevated LDL-C, while 13.1% (37/282) had elevated triglycerides. Women had higher median total cholesterolemia (138 mg/dL vs 125 mg/dL; $P = .002$), HDL-C (34 mg/dL vs 27 mg/dL; $P < .001$), and LDL-C (78 mg/dL vs 66 mg/dL; $P = .007$); however, there was no statistically significant difference in median serum triglyceride levels between women and men (86 mg/dL vs 93 mg/dL; $P = .058$). Overall, 13.9% (43/309) of study participants met the criteria for metabolic syndrome, without sex differences ($P = .129$). Despite this, only a small proportion (1.8%, 3/170) had a 10-year CVD risk >10% (Table 2).

Associated Risk Factors of MetS and its Components

In adjusted multivariable logistic regression analysis, individuals aged >40 years were 3.33 times more likely (95% CI, 1.47–7.67) to have MetS and 2.96 times more likely (95% CI, 1.32–6.64) compared with individuals 40 years or younger. Similarly, PWH with a CD4 count >200 cells/mm^3 were 3.79 times more likely (95% CI, 1.23–11.63) to have MetS compared with individuals with CD4 <200 cells/mm^3. Additionally, PWH residing in urban areas had 4.99 higher odds (95% CI, 1.35–18.53) of dyslipidemia compared with PWH living in rural areas. However, there were no independent predictors for hyperglycemia (Table 3).

DISCUSSION

In this study of treatment-naïve adult PWH initiating ART in Uganda, we estimated the baseline prevalence of MetS and key CVD risk factors with the aim of enhancing early screening and timely prevention of NCDs among Ugandan PWH. The prevalence of MetS was 13.9%. Of the individual components of the MetS, dyslipidemia was the most prevalent in our cohort (93.5%), followed by abdominal obesity (34.0%), hyperglycemia (18.4%), and HTN (8.1%). These findings are consistent with findings from mixed-population studies, where HIV-positive status has consistently conferred higher risk of MetS and its components [42]. This underscores the necessity for preemptive screening for MetS both at baseline and prospectively while on ART.

Despite being a relatively young cohort (median age, 31 years), the prevalence of MetS was substantial, affecting about 1 in 7 PWH. While several studies have assessed the prevalence of MetS among PWH in SSA, few have incorporated metabolic profiling at ART initiation. Estimates of the prevalence of MetS among PWH in SSA have generally been reported to be higher than our estimate, ranging from 20% to 58% [42–46]. This is likely a reflection of the fact that in most of these studies, participants were older and had a history of exposure to early ART-era protease inhibitors (PIs) and nucleoside reverse transcriptase inhibitors, which have been associated with higher rates of disturbances in lipid and glucose metabolism [47–50].

Dyslipidemia was the most common CVD risk factor in our cohort, affecting about 93.6% of PWH. Of these, low HDL-C was by far the most important risk factor and was present in 88.6% (or nearly 9 in 10 PWH). Few studies from SSA have documented the lipid profile of PWH pre-ART, as most reports have focused largely on ART-exposed individuals. In 5 cross-sectional studies of ART-exposed PWH from Malawi, Nigeria, Ethiopia, and Cameroon, the prevalence of low HDL-C, elevated LDL-C, TG, and TC was 34%–63%, 17%–21%, 9%, and 11%–24%, respectively; these rates were lower than our findings [51–54]. In these and other studies from SSA, advanced age, duration on ART, increased waist-to-hip ratio, high BMI, and a sedentary lifestyle have been identified as risk factors of dyslipidemia [51–59]. We did not detect any statistically significant associations between these traditional risk factors and dyslipidemia in our cohort; however, urban residence conferred a 5-fold higher risk of dyslipidemia. Plausible explanations for this finding include a higher prevalence of traditional CVD risk factors among urban dwellers compared with their rural counterparts, such as unhealthy dietary habits, a more sedentary lifestyle, and greater levels of exposure to environmental pollutants among urban dwellers (eg, emissions from fossil fuel combustion and industrial processes). Careful studies are needed to confirm these hypotheses.

Hypertension is a common comorbidity among PWH and was estimated to affect 24% of PWH globally in recent meta-analysis by Bigna et al. [60]. In this and other studies, geographic variations in the prevalence of hypertension among PWH have been reported, with countries in SSA being disproportionately affected [61–67]. Despite the prevalence of hypertension being lower in our study (8.1%), a substantial proportion (17%) of participants were prehypertensive and at risk of progressing to hypertension. Similarly, the prevalence of diabetes mellitus in our study was very low (0.3%), while prediabetes was higher (18.1%). The link between diabetes and HIV is controversial, with some studies suggesting that HIV is an independent risk factor of diabetes [68, 69], while others have failed to establish a clear link [70, 71]. However, as previously discussed, PWH exposed to ART (especially INTSI-based regimens) are at risk of metabolic complications including weight gain, increased insulin resistance, and metabolic syndrome [22–30]. Thus, the identification of prehypertension and prediabetes before ART exposure offers opportunities to intervene early with nonpharmacological risk-reduction strategies (eg, smoking cessation, increased physical exercise, weight loss, and reduced salt intake) to lower overall CVD risk.

Of the traditional CVD risk factors that were assessed in our study, increasing age (>40 years) and higher CD4 count (≥200

Table 2. Cardiometabolic Risk Factors of Study Participants by Sex

Risk Factors	All PWH	Male	Female	*P* Value
Total	309	126	183	
Active or past smoking				
Yes	15 (4.9)	9 (7.1)	6 (3.3)	.120
No	294 (95.1)	117 (92.9)	177 (96.7)	
Alcohol use (AUDIT scores)				
0–7 (low risk)	263 (85.1)	97 (77.0)	166 (90.7)	.011
8–15 (at risk)	26 (8.4)	16 (12.7)	10 (5.5)	
16–19 (high risk)	12 (3.9)	8 (6.3)	4 (2.2)	
≥20 (addiction)	8 (2.6)	5 (4.0)	3 (1.6)	
Level of physical activity				
<600 MET (does not meet WHO goals)	68 (22.0)	22 (17.5)	46 (25.1)	.109
≥600 MET (meets WHO goals)	241 (78.0)	104 (82.5)	137 (74.9)	
Body mass index, kg/m^2				
Median (IQR)	22.2 (19.7–25.6)	21.1 (19.2–22.9)	23.4 (20.7–27.6)	<.001
<18.5 (underweight)	32 (10.4)	16 (12.7)	16 (8.78)	<.001
18.5–24.9 (normal)	185 (59.9)	96 (76.2)	89 (48.6)	
25.0–29.9 (pre-obesity)	67 (21.7)	10 (7.9)	57 (31.1)	
≥30 (obese)	25 (8.1)	4 (3.2)	21 (11.5)	
Waist circumference, cm				
Median (IQR)	79.0 (75.0–86.0)	79.0 (75.0–83.0)	81.0 (74.0–88.0)	.153
Not at risk (males: <95 cm and females: <81 cm)	204 (66.0)	115 (91.3)	89 (48.6)	<.001
Increased risk (males: ≥95 to ≤102 cm and females: ≥81 to ≤88 cm)	57 (18.4)	8 (6.3)	49 (26.8)	
Substantially increased risk (males: ≥103 cm and females: ≥89 cm)	48 (15.5)	3 (2.4)	45 (24.6)	
Blood pressure, mmHg				
Normal (<120/80 mmHg)	232 (75.1)	92 (73.0)	140 (76.5)	.115
Prehypertension (120–139/80–89 mmHg)	52 (16.8)	19 (15.1)	33 (18.0)	
Hypertension (≥140/90 mmHg)	25 (8.1)	15 (11.9)	10 (5.5)	
Laboratory-based CVD risk score[a] (n = 170)				
<5%	149 (87.6)	67 (79.8)	82 (95.3)	.007
5%–10%	18 (10.6)	15 (17.9)	3 (3.5)	
>10%	3 (1.8)	2 (2.4)	1 (1.2)	
Blood glucose, mg/dL				
Normal (fasting <100 mg/dL or 2-h OGGT <140 mg/dL)	252 (81.6)	98 (77.8)	154 (84.2)	.150
Prediabetes (fasting 100–125 mg/dL or 2-h glucose 140–199 mg/dL)	56 (18.1)	27 (21.4)	29 (15.8)	
Diabetes (fasting ≥126 mg/dL or 2-h or glucose ≥200 mg/dL)	1 (0.3)	1 (0.8)	0 (0)	
Serum creatinine, mg/dL (n = 281)				
Median (IQR)	0.80 (0.68–0.93)	0.89 (0.77–1.01)	0.76 (0.64–0.84)	<.001
eGFR, mL/min/1.73m^2 (n = 281)				
Median (IQR)	111 (96–129)	118 (99–135)	106 (94–122)	.231
≥90 (Stage 1)	230 (81.9)	101 (86.3)	129 (78.7)	
60–89 (Stage 2)	47 (16.7)	14 (12.0)	33 (20.1)	
45–59 (Stage 3a)	2 (0.7)	1 (0.9)	1 (0.6)	
30–44 (Stage 3b)	2 (0.7)	1(0.9)	1 (0.6)	
29–15 (Stage 4)	0 (0)	0 (0)	0 (0)	
<15 (Stage 5)	0 (0)	0 (0)	0 (0)	
Total cholesterol, mg/dL (n = 282)				
Median (IQR)	132 (112–157)	125 (106–147)	138 (115–163)	.002
TC >200 mg/dL	15 (5.3)	4 (3.4)	11 (6.7)	.288
HDL-C, mg/dL (n = 282)				
Median (IQR)	31 (24–38)	27 (22–36)	34 (26–41)	<.001
HDL-C <40 mg/dL (men) or <50 mg/dL (women)	249 (88.3)	101 (86.3)	148 (89.7)	.385
LDL-C, mg/dL (n = 282)				
Median (IQR)	73 (53–93)	66 (50–88)	78 (56–100)	.007
LDL-C >100 mg/dL	59 (20.9)	14 (12.0)	45 (27.3)	.002

Table 2. Continued

Risk Factors	All PWH	Male	Female	*P* Value
Triglycerides mg/dL (n = 282)				
Median (IQR)	89 (62–118)	93 (70–124)	86 (59–116)	.058
TG >150 mg/dL	37 (13.1)	19 (16.2)	18 (10.9)	.191
Dyslipidemia (any 1 of the following: elevated TC,[b] low HDL-C,[c] elevated LDL-C[d] or elevated TG[e]; n = 282)				
Yes	264 (93.6)	106 (90.6)	158 (95.8)	.081
No	18 (6.4)	11 (9.4)	7 (4.2)	
Metabolic syndrome (any 3 of the following: central obesity,[f] impaired fasting glucose,[g] HTN,[h] low HDL-C,[d] or elevated TG[f])				
Yes	43 (13.9)	13 (10.3)	30 (16.4)	.129
No	266 (86.1)	113 (89.7)	153 (3.6)	

Abbreviations: AUDIT, Alcohol Identification Disorder Test; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HTN, hypertension; HDL-C, high-density lipoprotein; IQR, interquartile range; MET, metabolic equivalent; LDH-C, low-density lipoprotein; OGGT, Oral Glucose Tolerance Test; PWH, people with HIV; TC, total cholesterol; TG, serum triglycerides; WHO, World Health Organization.

[a]Laboratory-based Framingham cardiovascular risk score.

[b]TC >200 mg/dL.

[c]HDL-C <40 mg/dL (men) or <50 mg/dL (women).

[d]LDL-C >100 mg/dL.

[e]TG >150 mg/dL.

[f]Central obesity, defined as waist circumference ≥95 cm (males) or ≥81 cm (females).

[g]Impaired fasting glucose, defined as fasting glucose ≥126 mg/dL or 2-hour glucose ≥200 mg/dL.

[h]HTN, defined as systolic blood pressure ≥130 mmHg and ≥85 mmHg.

cells/mm^3) were associated with a higher risk of both MetS and HTN. The latter finding is consistent with previous studies, which have shown that higher CD4 cell count is an independent predictor of the development of MetS, which is largely attributed to the increased nutritional intake, weight gain, and energy conservation associated with ART initiation [72–74]. However, our cohort was entirely ART-naïve. The underlying pathophysiologic mechanisms linking high CD4 count, MetS, and HTN in ART-naïve PWH have not been elucidated. It is plausible that in ART-naïve subjects, multiple factors are at play, with HIV-specific factors such as immune activation and chronic inflammation acting in synergy with traditional risk factors (eg, smoking, poor diet, and a sedentary lifestyle) to drive MetS and its components in aging PWH [8, 9, 75]. Further studies are needed to explore this assertion.

We used laboratory-based Framingham scores to estimate 10-year CVD risk for study participants aged >30 years (50% of enrolled participants) and determined that the majority had low 10-year CVD risk. In 3 studies from Cameroon and South Africa, 50% to 93% of PWH had a 10-year CVD risk of <5% [76–78], compared with 87% of participants in our study. Most CVD risk calculators, including the Framingham score that we used in our study, tend to underestimate the 10-year CVD risk, as they do not take into account other participant characteristics such as the inherent effect of HIV itself, systemic inflammation, and infectious and noncommunicable comorbidities [79]. This may explain the possible underestimation of risk in the studies cited above, involving much older PWH on ART, a known risk factor for both micro- and macrovascular disease [47]. Despite the reported low 10-year risk of CVD in our study population, we demonstrated that this is a population with a high prevalence of CVD risk factors, and therefore hypothesize that their actual CVD risk may be much higher than the calculated risk.

Another noteworthy finding of our study was that although women had a higher prevalence of individual CVD risk factors (eg, higher BMI, waist circumference, higher LDL, and TG) compared with their male counterparts, there was no sex difference in the overall prevalence of MetS. Sex differences are known to influence the occurrence of MetS across different age groups in the general population [80]. A large part of this difference has been attributed to the cardioprotective effects of estrogen and other hormones on glucose and lipid metabolism in women [76, 80]. Similar to our study, most studies that have reported on the prevalence of MetS in SSA have been in ART-exposed PWH and have not shown a sex differential effect [44, 81].

Our study had several limitations worthy of discussion. First, the definition of MetS and its key components is based on models developed in high-income countries and may not be applicable to populations in SSA, which may exhibit significant phenotypic and genotypic differences. Second, this was a single-center study in an urban setting; hence the findings may not be generalizable to the wider Ugandan PWH population. Third, based on study inclusion criteria, sicker patients were excluded due to their inability to undergo a 2-hour OGTT, which would have resulted in underestimation of the prevalence of MetS and its components. Despite these

Table 3. Predictors of the Metabolic Syndrome and its Components

	Metabolic Syndrome		Hypertension		Dyslipidemia		Hyperglycemia	
Risk Factors	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Gender								
Male	**Ref**	Ref	**Ref**	Ref	**Ref**	Ref	Ref	…
Female	**1.70 (0.85–3.41)**	1.44 (0.64–3.25)	**0.61 (0.33–1.11)**	0.58 (0.24–1.41)	**2.34 (0.88–6.25)**	1.56 (0.51–4.77)	0.76 (0.36–1.58)	…
Age, y								
<40	**Ref**	**Ref**	**Ref**	**Ref**	Ref	…	**Ref**	Ref
≥40	**3.27 (1.65–6.47)**	**3.33 (1.45–7.67)****	**2.67 (1.39–5.10)**	**2.96 (1.32–6.64)*****	0.96 (0.31–3.04)	…	**1.79 (0.80–4.00)**	1.59 (0.70–3.59)
Relationship status								
Single	Ref	…	Ref	…	Ref	**…**	Ref	…
Married	1.35 (0.71–2.58)	…	1.25 (0.69–2.29)	…	0.57 (0.22–1.49)	…	0.92 (0.44–1.94)	…
Education								
None or primary	Ref	…	**Ref**	Ref	Ref	**…**	Ref	…
Secondary or tertiary	1.07 (0.56–2.05)	…	**1.62 (0.87–3.02)**	1.61 (0.77–3.33)	1.01 (0.39–2.64)	…	1.41 (0.66–2.99)	…
Religion								
Christian	1.40 (0.59–3.32)	…	1.49 (0.66–3.35)	…	0.46 (0.10–2.08)	…	0.76 (0.32–1.78)	…
Muslim	Ref	…	Ref	…	Ref	…	Ref	…
Residence								
Urban	1.14 (0.33–4.01)	…	0.73 (0.26–2.06)	…	**4.43 (1.31–15.01)**	**4.99 (1.35–18.53)*****	0.79 (0.22–2.82)	…
Rural	Ref	…	Ref	…	**Ref**	**Ref**	Ref	…
Employment								
Yes	1.43 (0.57–3.57)	…	**2.27 (0.86–5.99)**	1.41 (0.49–4.08)	**0.25 (0.03–1.94)**	0.31 (0.04–2.62)	**3.63 (0.84–15.67)**	3.55 (0.81–15.51)
No	Ref	…	**Ref**	Ref	**Ref**	Ref	**Ref**	Ref
Smoking								
Yes	1.59 (0.43–5.87)	…	1.28 (0.35-4.71)	…	0.74 (0.09–6.07)	…	…	…
No	Ref	…	Ref	…	Ref	…	…	…
Alcohol use (AUDIT scores)								
Low–moderate	Ref	…	Ref	…	Ref	…	Ref	…
High risk	0.67 (0.15–3.01)	…	0.54 (0.12–2.42)	…	0.59 (0.13–2.75)	…	0.96 (0.21–4.34)	…
Physical activity								
High	Ref	…	Ref	…	Ref	…	Ref	…
Low	0.92 (0.43–1.98)	…	0.90 (0.44–1.83)	…	1.44 (0.40–5.14)	…	1.45 (0.64–3.29)	…
Body mass index, kg/m^2								
<25	**…**	**…**	**Ref**	Ref	**Ref**	Ref	**Ref**	Ref
≥25	**…**	**…**	**2.25 (1.21–4.17)**	2.94 (0.83–10.43)	**7.93 (1.04–60.61)**	6.29 (0.48–81.57)	**1.72 (0.81–3.68)**	1.78 (0.83–3.81)
Waist circumference								
Normal	**…**	**…**	**Ref**	Ref	**Ref**	Ref	Ref	…
Increased	**…**	**…**	**1.57 (0.85–2.90)**	1.16 (0.32–4.35)	**4.63 (1.05–20.64)**	1.03 (0.14–7.45)	1.00 (0.46–2.17)	…
CD4 count, cells/mm^3								
<200	**Ref**	**Ref**	**Ref**	**Ref**	Ref	…	Ref	…
≥200	**3.32 (1.13–9.78)**	**3.79 (1.23–11.63)*****	**2.50 (1.00–6.23)**	**2.90 (1.09–7.73)****	0.62 (0.17–2.26)	…	1.01 (0.40–2.53)	…

Variables that were found to be significant (<.20 univariable, <.05 multivariable) are marked in bold.

Abbreviations: aOR, adjusted odds ratio; AUDIT, Alcohol Identification Disorder Test; CD4, cluster of differentiation; OR, odds ratio.

Significance *P* levels: ** $P < .05$; *** $P < 0.01$.

limitations, while most studies have described prevalence rates of CVD risk factors in PWH on ART, our study described the metabolic profiles of ART-naïve Ugandan PWH at ART initiation, thus offering an opportunity to improve prevention strategies in a population with a high CVD risk.

CONCLUSIONS

In summary, we demonstrated that despite being a relatively young population, MetS and other cardiometabolic risk factors including HTN, hyperlipidemia, and hyperglycemia were common among Ugandan PWH initiating DTG-based ART, underscoring the need for programmatic implementation of surveillance and management of NCD comorbidities among PWH initiating ART in Uganda and similar settings.

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Data availability. The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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