Prevalence and correlates of dyslipidemia in HIV positive and negative adults in Western Kenya A cross-sectional study

Medicine

Hailu Tilahun, MD, MSc^{a,*}, Sarah J. Masyuko, MBChB, MPH^{b,c}, Jerusha N. Mogaka, BScN^b, Tecla Temu, MD, PhD^b, John Kinuthia, MMed, MPH^{d,e}, Alfred O. Osoti, MMed PhD^f, Damalie Nakanjako, MBChB, MMed, PhD^f, Carey Farquhar, MD, MPH^g, Stephanie T. Page, MD, PhD^h

Abstract

There is increasing morbidity and mortality from cardiovascular diseases (CVD) in sub-Saharan Africa (SSA). Dyslipidemia is a wellknown CVD risk factor which has been associated with human immunodeficiency virus (HIV) infection and its treatment in highincome countries. Studies in SSA that have examined the relationship between HIV and dyslipidemia have reported mixed results. In this study, we sought to determine the prevalence of dyslipidemia in HIV positive and negative adults (>=30 years old) and evaluate for association in Western Kenya with a higher prevalence expected among HIV positive individuals.

HIV positive adults receiving antiretroviral therapy (ART) and HIV negative individuals seeking HIV testing and counseling services were recruited into a cross-sectional study. Demographic and behavioral data and fasting blood samples were collected. Dyslipidemia was defined according to the National Cholesterol Education Program Adult Treatment Panel III. Associations between baseline demographic and clinical variables and dyslipidemia were analyzed using logistic regression.

A total of 598 participants, 300 HIV positive and 298 HIV negative adults were enrolled. Dyslipidemia data was available for 564 (94%) participants. In total, 267 (47%) had dyslipidemia. This was not significantly different between HIV positive and HIV negative individuals (46% vs 49%, P = .4). In a multivariate analysis including both HIV positive and negative individuals, adults 50 to 59 years of age had a 2-fold increased risk of dyslipidemia (Odds ratio [OR] 2.1, 95% confidence interval (1.2–3.5) when compared to 30 to 39-years-old participants. Abdominal obesity (OR 2.5), being overweight (OR 1.9), and low fruit and vegetable intake (OR 2.2) were significantly associated with dyslipidemia. Among HIV positive participants, time since HIV diagnosis, ART duration, use of (PI) protease inhibitor-based ART, viral load suppression, current cluster of differentiation (CD4) count and nadir CD4 did not have significant associations with dyslipidemia.

The prevalence of dyslipidemia is high in Western Kenya, with nearly half of all participants with lipid abnormalities. Dyslipidemia was not significantly associated with HIV status, or with HIV-specific factors. Older age, being overweight, abdominal obesity, and low fruit and vegetable intake were associated with dyslipidemia and may be targets for public health interventions to lower the prevalence of dyslipidemia and CVD risk in sub-Saharan Africa.

Abbreviations: ART = antiretroviral therapy, BMI = body mass index, CD4 = cluster of differentiation 4, CI = confidence interval, CVD = cardiovascular disease, HDL = high-density lipoprotein, HIV = human immunodeficiency virus, LDL = low-density lipoprotein, OR = odds ratio, PI = protease inhibitor, SSA = sub-Saharan Africa, STEPS = Stepwise Approach to Surveillance, WHO = World Health Organization.

Keywords: cardiovascular risk factors, dyslipidemia, human immunodeficiency virus, Kenya

Editor: Victor Volovici.

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

Received: 6 September 2020 / Received in final form: 1 January 2021 / Accepted: 28 January 2021

http://dx.doi.org/10.1097/MD.00000000024800

This study was supported by National Institutes of Health (NIH) R21TW010459 and Fogarty International Center (FIC) D43 TW009580.

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^a Department of Medicine, Division of Cardiology, ^b Department of Global Health, University of Washington, Seattle, WA, ^c Ministry of Health, ^d Kenyatta National Hospital, ^e University of Nairobi, Nairobi, Kenya, ^f Department of Medicine, School of Medicine, Makerere University College of Health Sciences, Kampala, Uganda, ^g Departments of Global Health, Medicine and Epidemiology, University of Washington, ^h Department of Medicine, Division of Metabolism, Endocrinology and Nutrition, University of Washington, Seattle, WA.

^{*} Correspondence: Hailu Tilahun, Department of Medicine, Division of Cardiology, University of Washington, Seattle, WA (e-mail: htilahun1@gmail.com).

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Tilahun H, Masyuko SJ, Mogaka JN, Temu T, Kinuthia J, Osoti AO, Nakanjako D, Farquhar C, Page ST. Prevalence and correlates of dyslipidemia in HIV positive and negative adults in Western Kenya: a cross-sectional study. Medicine 2021;100:10(e24800).

1. Introduction

Sub-Saharan Africa (SSA) countries in this millennium face a double burden of disease with high mortality and morbidity from both communicable and non-communicable diseases. Cardio-vascular diseases (CVD) are the leading cause of mortality from non-communicable diseases and are projected to increase over the next decade.^[1,2] Dyslipidemia is a well-known risk factor for CVD globally and in developing regions such as sub-Saharan Africa.^[3,4] World Health Organization's (WHO) comparative quantification of health risks assessment in 2004 showed that, globally, 4.4 million deaths and 40 million disability-adjusted life years were attributable to elevated cholesterol levels.^[5] More recently, the 2017 Global Burden of Disease Study reported that, compared to 2007, the disability-adjusted life years attributable to elevated low-density lipoprotein (LDL) levels has increased by 17%.^[6]

In some studies, human immunodeficiency virus (HIV) infection has been associated with dyslipidemia and cardiovascular diseases. In both high-income and low and middle income countries, duration of HIV infection, type of antiretroviral regimen (ART), level of immunosuppression, and especially protease-inhibitor (PI) based therapy, and level of immunosuppression have been associated with increased risk of dyslipidemia, however results have not been consistent.^[7–12]

With the increasing burden of cardiovascular diseases in developing countries, and the fact that dyslipidemia is a significant risk factor for developing cardiovascular diseases, it is important to establish the prevalence of dyslipidemia and identify variables associated with dyslipidemia in sub-Saharan African countries, including HIV. This study was a sub-study of a larger study looking at the prevalence of metabolic syndrome and association with 10-year cardiovascular risk.^[13] The goal of this study was to determine the prevalence of dyslipidemia in HIV positive and negative adults in Western Kenya and determine associations between HIV status, demographic, behavioral and clinical variables, and dyslipidemia. A higher prevalence of dyslipidemia was expected in the HIV positive cohort given prior findings in Uganda and South Africa.^[8,14] In addition, for HIV positive participants, we evaluated the relationship between dyslipidemia and HIV specific factors (duration of HIV, duration of ART, use of PI based therapy, low Cluster of Differentiation (CD4) level, high viral load level) which were expected to have a positive association. This study further adds to the literature which has shown somewhat inconsistent associations between HIV status and dyslipidemia prevalence, and HIV specific factors and dyslipidemia.

2. Methods

2.1. Study population and design

This cross-sectional study was conducted at Kisumu County Hospital in Western Kenya between September 2017 and May 2018. A total of 598 participants with equal numbers of men and women were enrolled in the study. 300 participants were HIV positive while 298 were HIV negative. Inclusion and exclusion criteria have been described previously.^[13] HIV positive participants were engaged in care at the HIV Comprehensive Care Clinic at Kisumu County Hospital and consecutively recruited if they had been taking antiretroviral therapy (ART) for a minimum of 6 months. HIV negative participants were consecutively recruited from voluntary and provider-initiated HIV testing and counseling services at Kisumu County Hospital, and through community outreach. Both HIV positive and negative participants needed to be at least 30 years of age and live within a 50 km radius of the hospital to be included in the study.

2.2. Ethics approval

The study was approved by the University of Washington Institutional Review Board and Kenyatta National Hospital and University of Nairobi Ethics Review Committee. All participants provided written informed consent prior to initiation of any study procedures.

2.3. Data collection and definitions

Data was collected using the Kenya/WHO STEP wise Survey for Non-communicable Diseases (STEPS) after it had been modified to include HIV specific variables.^[13,15] Trained personnel interviewed and recorded demographic and behavioral information using the structured survey with pre-specified variables. Anthropometric measurements and venipuncture were performed the same day if participants were fasting longer than 8 hours. If participants were not fasting, they returned the next day for venipuncture. HIV related information including duration of HIV, duration and type of ART, CD4 nadir and viral load suppression status were obtained from the medical record. Starting in 2016, all HIV positive individuals in Kenya were eligible for ART therapy regardless of CD4 level. Proteaseinhibitor based therapy was reserved for second and third line therapy.^[16,17]

All samples for fasting lipids and fasting glucose were processed and stored at the Kenya Medical Research Institute-Centers for Disease Control and Prevention laboratory in Kisumu, Kenya and then shipped to Seattle, USA for testing at a University of Washington Research Testing laboratory using an automated Beckman Coulter AU5812 analyzer with standard reagent disks used for clinical purposes at the University of Washington Medical Center.

The primary outcome, dyslipidemia, was defined as total cholesterol ≥200 mg/dl (5.2 mmol/L) OR high-density lipoprotein <40 mg/dl (1.03 mmol/L) for men or high-density lipoprotein <50 mg/dl (1.3 mmol/L) for women OR triglycerides \geq 150 mg/dl $(1.7 \text{ mmol/L}) \text{ OR low-density lipoprotein (LDL)} \ge 130 \text{ mg/dl} (3.4)$ mmol/L) according to the National Cholesterol Education Program Adult Treatment Panel III.^[18] Participants who met 1 or more of these criteria were categorized as having dyslipidemia. Participants who were on a lipid-lowering agent due to a prior diagnosis of dyslipidemia were also classified as having dyslipidemia. Abdominal obesity was defined as waist circumference >88 cm for women and >94 cm for men per the 2009 consensus criteria.^[19] For self-reported behavioral variables, insufficient fruit and vegetable intake was defined as less than 5 servings per day. Low physical activity was defined as less than 150 minutes per week of moderate activity (at work or sports) or less than 75 minutes of vigorous physical activity (at work or sports) per WHO recommendations or participants who responded no to performing moderate or vigorous work or sports activity.^[20,21] High salt and sugar intake were defined as adding salt/sugar often or always when cooking, or drinking, similar to the Kenya STEPS reporting format.^[15] Current alcohol was defined as alcohol consumption in the last 30 days. A viral

General characteristics of study participants by HIV status (N=564)*.

	Total (N = 564)	HIV +(N=287)	HIV -(N=277)	
	N (%)	N (%)	N (%)	P value
Age				<.001
30–39	201 (35)	68 (24)	133 (48)	
40–49	162 (29)	106 (37)	56 (20)	
50-59	128 (23)	83 (29)	45 (16)	
>=60	73 (13)	30 (10)	43 (16)	
Sex				.90
Male	282 (50)	144 (50)	138 (50)	
Female	282 (50)	143 (50)	139 (50)	
Highest Educational Level	- ()			.01
No Formal Schooling	30 (5)	12 (4)	18 (7)	
Less than Primary School	48 (9)	27 (10)	21 (8)	
Primary School	211 (37)	124 (43)	87 (30)	
At least Secondary School	275 (49)	124 (43)	151 (55)	
Smoker	210 (10)	121 (10)	101 (00)	.20
Current	27 (5)	11 (4)	16 (6)	.20
Previous	43 (7)	27 (9)	16 (6)	
Never	494 (88)	249 (87)	245 (88)	
Alcohol	404 (00)	243 (07)	240 (00)	.30
Current	71 (12)	30 (10)	41 (14)	.00
Ever	116 (21)	62 (22)	54 (20)	
Never		195 (68)		
Body Mass Index	377 (67)	195 (06)	182 (66)	.001
5	E1 (0)	20 (11)	10 (7)	.001
Underweight	51 (9)	32 (11)	19 (7)	
Normal	319 (57)	177 (62)	142 (51)	
Overweight	119 (21)	54 (19)	65 (24)	
Obese	75 (13)	24 (8)	51 (18)	0.1
Abdominal Obesity			01 (00)	.01
Yes	136 (24)	55 (19)	81 (29)	
No	428 (76)	232 (81)	196 (71)	04
Physical Activity				.01
Insufficient	245 (43)	110 (38)	135 (49)	
Recommended	319 (57)	177 (62)	142 (51)	
Salt Intake				.80
High	44 (8)	23 (8)	21 (8)	
Not High	520 (92)	264 (92)	256 (92)	
Sugar Intake				.70
High	288 (51)	144 (50)	144 (52)	
Not High	276 (49)	143 (50)	133 (48)	
Fruit and Vegetable Intake				.80
Low	487 (86)	249 (87)	238 (86)	
Recommended	77 (14)	38 (13)	39 (14)	

^{*} Excludes 34 participants without blood samples who were not included in the dyslipidemia analysis.

load of less than 1000 copies/ml was defined as suppressed, consistent with the Kenya ART guidelines. ^[16]

2.4. Statistical analysis

Baseline demographic, behavioral, and anthropometric variables were compared by HIV status using Chi-Squared test for statistical analysis. HIV-specific baseline variables were described using median and interquartile ranges, or proportions. The prevalence of the primary outcome, dyslipidemia, and its components were described using proportions and compared by HIV status using Chi-Squared test. Univariate and multivariate logistic regression were used to identify association between demographic, behavioral, anthropometric, clinical variables, and dyslipidemia. A two-sided test with a *P* value <.05 was considered significant. This study had 80% power to detect an

effect size of 15% in the prevalence of dyslipidemia. All analyses were done using STATA version 13 (Stata Corp. College Station, TX).

3. Result

3

3.1. Baseline characteristics

Of a total of 598 participants enrolled in the study, blood samples for 564 individuals were available and these individuals were included in this analysis. Table 1 shows the baseline demographic, behavioral, and anthropometric variables for the 564 participants compared by HIV status. Overall, about two-thirds of patients were 30 to 50 years of age. HIV negative participants were younger with 133 (48%) between the ages of 30 and 40 years, while only 68 (24%) HIV positive participants were 30

Table 2	
HIV-specific baseline variable	es [*] .

	HIV positive (N = 287) [*] N (%) or Median (IQR ⁺)
HIV duration since diagnosis, years	9 (5, 11)
ART duration, years	8 (4,10)
Current CD4, cells/mm3	512 (364, 666)
Nadir CD4 [‡] , cells/mm3	365 (213, 571)
Suppressed Viral Load, <1000 copies/ml	275 (96)
ART Regimen	
PI-based	36 (13)
Non-PI based	251 (87)

 * Excludes 13 participants not included in dyslipidemia analysis since no blood sample available. † IQR = interquartile range.

[‡]N=271.

to 40 years old (P < .001). About half of the participants completed at least secondary school, which was significantly greater for HIV negative (55%) vs positive (43%) participants (P = .01).

Most participants reported never smoking (88%) or drinking alcohol (67%). This was not significantly different by HIV status. About one-third of participants (34%) were either overweight or obese. HIV negative participants were significantly more likely to be overweight (body mass index (BMI) 18.5-24.9) or obese (BMI >=25) compared to HIV positive ones (42% vs 27%, P=.001). They were also more likely to have abdominal obesity (29% vs 19%, P=.01). Forty-three percent of study participants had insufficient physical activity, 51% had high sugar intake and 86% had low fruit and vegetable intake. More HIV positive patients reported recommended physical activity levels compared to HIV negative patients (62% vs 51%, P=.01). Salt intake, sugar intake and fruit and vegetable intake were not significantly different by HIV status. In summary, HIV negative individuals were younger, had less physical activity, more abdominal obesity, and a higher BMI.

3.2. HIV specific variables

Table 3

Table 2 shows HIV-specific baseline variables. The median time since HIV diagnosis and ART duration were 9 and 8 years, respectively. The median nadir CD4 was 365 cells/mm³ while the

current median CD4 was 512 cells/mm³. Ninety six percent of participants had suppressed viral load. Only 13% of HIV positive participants were on protease-inhibitor based ART therapy.

3.3. Prevalence of dyslipidemia and individual components

The prevalence of dyslipidemia (meeting 1 or more criteria for dyslipidemia) in the study population (n=564) was 47% (Table 3). The prevalence of dyslipidemia did not differ based on HIV status (HIV positive 49% vs HIV negative 46%, P=.4). Among the components of dyslipidemia, low high-density Lipoprotein, (HDL) had the highest prevalence overall for both HIV positive and negative cohorts, followed by elevated total cholesterol, elevated LDL, and elevated triglycerides. The prevalence of hypertriglyceridemia was higher for HIV positive participants but this was not significant (10.5 vs 6.5%, P=.09). The prevalence of low HDL tended to be higher for HIV negative participants but was not significant (33% vs 26%, P=.07).

3.4. Associations of dyslipidemia

Table 4 shows the univariate and multivariate logistic regression analysis for the association between demographic, behavioral, anthropometric, and clinical variables and dyslipidemia among all participants (n = 564). The univariate analysis included all the variables shown in Table 4. The multivariate model included the following variables; HIV status, age group, sex, smoking status, alcohol drinking status, abdominal obesity, BMI, physical activity, sugar intake, salt intake and fruits and vegetable intake with dietary intake dichotomized as shown in Table 1. In a multivariate analysis including age and other variables as indicated above, HIV status did not have a significant association with dyslipidemia (OR 0.9, P = .6). There was an increased risk of dyslipidemia with older age, abdominal obesity, overweight status, and low fruit and vegetable intake across the study cohort. There was a 2.1-fold increased risk (OR = 2.1) for age group 50 to 59 years compared to 30 to 39 years, 1.9-fold for overweight vs normal BMI, 2.5-fold for abdominal obesity vs none, and 2.2fold for low fruit and vegetable intake vs recommended intake. Insufficient physical activity tended to be associated with higher prevalence of dyslipidemia (OR 1.5), but did not reach significance (P=.08). In addition, smoking status, alcohol use

	Total			
	N = 564	HIV+ N=287	HIV – N = 277	
	N (%)	N (%)	N (%)	P value
Total Cholesterol				
>=200 mg/dl	97 (17)	52 (18)	45 (16)	.60
Triglycerides				
>=150 mg/dl	48 (9)	30 (11)	18 (7)	.09
Low-density Lipoprotein				
>= 130 mg/dl	75 (13)	36 (13)	39 (14)	.60
High-density Lipoprotein				
<40 mg/dl Male	167 (30)	75 (26)	92 (33)	.07
<50 mg/dl Female				
Dyslipidemia				
Any of the above	267 (47)	131 (46)	136 (49)	.40

^{*} Excludes 34 participants without blood samples who were not included in the dyslipidemia analysis.

Table 4

Associations with dyslipidemia^{*}, univariate, and multivariate logistic regression (N=564)[†].

	Univariate ana	lysis	Multivariate and	
	OR[§] (95% CI[¶])	P	OR [§] (95% Cl [¶])	P
HIV		.40		
Negative	Ref [#]		Ref [#]	
Positive	0.9 (0.8, 1.2)		0.9 (0.6, 1.3)	.60
Age (years)		.12		
30-39	Ref		Ref	
40-49	1.3 (0.8, 1.9)		1.5 (0.9, 2.4)	.10
50-59	1.7 (1.1, 2.7)		2.1 (1.2, 3.5)	.01
>=60	1.3 (0.7, 2.2)		1.4 (0.8, 2.6)	.30
Sex		.001	() -)	
Female	Ref		Ref	
Male	0.5 (0.3, 0.7)		0.6 (0.4, 1.0)	.06
Highest Educational Level		.60		100
No Formal Schooling	Ref	100		
Less than Primary School	0.8 (0.3, 2.1)			
Primary School	0.6 (0.3, 1.4)			
At least Secondary School	0.7 (0.3, 1.4)			
Smoker	0.0, 1.17	.30		
Never	Ref	.00	Ref	
Previous	1.0 (0.6, 1.9)		1.7 (0.8, 3.5)	.20
Current	0.5 (0.2, 1.2)		0.9 (0.3, 2.2)	.80
Alcohol	0.0 (0.2, 1.2)	.07	0.0 (0.0, 2.2)	.00
Never	Ref	.07	Ref	
Past	0.6 (0.4, 1.0)		0.7 (0.4, 1.1)	.20
Current	0.7 (0.4, 1.2)		1.1 (0.6, 1.9)	.80
Abdominal Obesity	0.7 (0.4, 1.2)	.001	1.1 (0.0, 1.9)	.00
No	Ref	.001	Ref	
Yes	3.8 (2.5, 5.7)		2.5 (1.3, 4.8)	.01
Body Mass Index	5.0 (2.5, 5.7)	.001	2.5 (1.5, 4.6)	.01
Normal	Ref	.001	Ref	
Underweight	0.7 (0.4, 1.3)		.7 (0.4, 1.4)	.30
-				
Overweight	3.0 (1.9, 4.6)		1.9 (1.1, 3.2)	.02 .90
Obese	2.8 (1.6, 4.7)	00	1.1 (0.5, 2.3)	.90
Physical Activity Recommended	Ref	.06	Ref	
				00
Insufficient	1.4 (1.0, 1.9)	40	1.5 (0.9, 2.2)	.08
Salt Intake	Def	.40	Def	
Not High	Ref		Ref	
High	0.8 (0.4, 1.4)	70	0.9 (0.5, 1.9)	.80
Sugar Intake	D (.70		
Not High	Ref		Ref	
High	1.1 (0.8, 1.5)	0-	1.3 (0.9, 2.0)	.20
Fruit and Vegetable Intake		.02		
Recommended	Ref		Ref	
Low	1.8 (1.1, 3.0)		2.2 (1.3, 3.8)	.01

^{*} Dyslipidemia defined as total cholesterol ≥200 mg/dl (5.2 mmol/L) or high-density lipoprotein <40 mg/dl (1.03 mmol/L) for men or high-density lipoprotein <50 mg/dL (1.3 mmol/L) for women or triglycerides ≥150 mg/dL (1.7 mmol/L) or low-density lipoprotein (LDL) ≥ 130 mg/dl (3.4 mmol/L).

[†]N=564, excludes 34 participants without blood samples who were not included in the dyslipidemia analysis.

* The multivariate model included the variables; HIV status, age group, sex, smoking status, drinking status, abdominal obesity, BMI, physical activity, sugar intake, salt intake and fruits and vegetable intake. § OR = odds ratio.

|| P = P value.

 $^{\$}$ CI = confidence interval.

[#]Ref = reference variable.

history, salt intake and sugar intake were not associated with increased risk of dyslipidemia.

obesity, BMI, physical activity, salt intake, sugar intake, and fruit and vegetable intake.

Among HIV positive participants, the HIV-specific variables; HIV duration, ART duration, PI-based ART therapy vs non-PI based therapy, viral load suppression, current CD4, nadir CD4 did not have a significant association with dyslipidemia (Table 5). In addition to the variables shown in Table 5, the association was also adjusted for age, sex, smoking, alcohol drinking, abdominal

4. Discussion

In this cohort of HIV positive adults on ART and HIV negative adults living in Western Kenya, about half of the participants had dyslipidemia (47%) without a difference in prevalence associated

Table 5

Association between HIV-specific factors and dyslipidemia^{*} in HIV-positive participants, multivariate logistic regression (N = 271)[†].

	Multivariate Analysis [‡]		
	OR^* (95% $Cl^{ }$)	P value	
ART Regimen			
Non-PI Based	Ref [¶]		
PI Based	1.1 (0.5, 2.6)	.90	
Viral Load			
Non-suppressed	Ref		
Suppressed (<1000 cells/ml)	0.5 (0.1, 2.4)	.40	
Current CD4			
>=500 cells/mm ³	Ref		
<500 cells/mm ³	0.7 (0.4, 1.3)	.30	
Nadir CD4			
$>=200 \text{ cells/mm}^3$	Ref		
<200 cells/mm ³	0.5 (0.3, 1.1)	.10	
HIV Duration, years	1.0 (0.9, 1.1)	.70	
ART Duration, years	1.0 (0.9, 1.1)	.80	

^{*} Dyslipidemia defined as total cholesterol ≥200 mg/dl (5.2 mmol/L) or high-density lipoprotein <40 mg/dl (1.03 mmol/L) for men or high-density lipoprotein <50 mg/dl (1.3 mmol/L) for women or triglycerides ≥150 mg/dl (1.7 mmol/L) or low-density lipoprotein (LDL) ≥ 130 mg/dl (3.4 mmol/L).</p>
[†] Excludes 13 participants without blood samples who were not included in the dyslipidemia analysis and 16 patients missing CD4 data.

* In addition to the variables shown in Table 5, the association was also adjusted for age, sex, smoking, alcohol drinking, abdominal obesity, BMI, physical activity, salt intake, sugar intake, and fruit and vegetable intake.

§ OR = odds ratio.

|| CI = confidence interval.

[¶]Ref = reference variable.

with HIV status in univariate analysis and after adjusting for other factors in multivariate analyses. There was also no significant difference in each of the components of dyslipidemia based on HIV status, although there was a trend towards elevated triglyceride levels in the HIV positive and a higher proportion of low HDL levels in the HIV negative groups. The prevalence of dyslipidemia and each of its components in this study are comparable to findings from other sub-Saharan African countries though there is a wide range of dyslipidemia prevalence reported in the literature.^[22-25] Prior studies analyzing the association of HIV with dyslipidemia in both low-income and high-income countries have reported mixed results. In a study of HIV negative and HIV positive individuals in the United States, where most participants were receiving ART (about a third on PI therapy), HIV positive status was associated with increased prevalence of elevated triglycerides and low HDL.^[10] When ART naïve HIV positive people were compared to HIV negative participants in South Africa, the prevalence of low HDL was significantly higher in the HIV positive group.^[14] However, in a Ugandan study including HIV positive participants on ART, ART naïve HIV positive participants, and HIV negative participants, there was no statistically significant difference in low HDL based on HIV status.^[8] A recent Kenyan study based in the capital city, Nairobi, did not find significant differences in elevated total cholesterol or low HDL levels comparing ART naïve HIV positive individuals with HIV negative participants.^[26] In our study, there was no difference in the prevalence of dyslipidemia or its components based on HIV status.

In multivariate analysis, there was a statistically significant association between older age, abdominal obesity, being overweight, low fruit and vegetable intake, and dyslipidemia. This finding might potentially explain why there is considerable variation among observational studies analyzing the association of HIV with dyslipidemia. The varying prevalence of these behavioral and anthropometric factors in the different study populations might have impacted the association of HIV with dyslipidemia. Our findings highlight the importance of modifiable factors such as physical activity, fruit and vegetable intake and abdominal obesity in the etiology of dyslipidemia in SSA. These factors are potential targets for interventions that can lower the risk of dyslipidemia, especially given the high prevalence of low physical activity (43%), low fruit and vegetable intake (86%), abdominal obesity (24%) and overweight/obesity (34%) we observed. Public health interventions with exercise programs in other sub-Saharan African countries such as South Africa and Ghana have been associated with improvement in lipid abnormalities.^[27,28] Since the diet and exercise data was selfreported and retrospective in nature, further longitudinal studies specifically designed with detailed, validated instruments to analyze the association of diet and exercise with dyslipidemia will be important to validate these findings.

The use of protease-inhibitor based ART, ART duration, low CD4 count and unsuppressed viral load have been associated with increased prevalence of dyslipidemia in prior studies.^[7,9,26,29] Among ART experienced HIV positive individuals in this study, in a multivariate analysis, PI-based ART, ART duration, CD4 nadir count, current CD4 count and viral load >1000 copies/ml did not have a statistically significant association with dyslipidemia after accounting for other demographic, behavioral, and anthropometric factors. The assessment of the association between PI-based therapy, viral load suppression status and dyslipidemia was limited by the low proportion of patients on PI-based ART (13%) and those who have unsuppressed viral load (4%), leading to loss of statistical power. The low use of PI-based therapy in SSA may in part explain the lack of association between HIV and dyslipidemia in SSA compared to other regions.

In this study, HIV negative participants were less physically active and had a higher proportion of abdominal obesity and body mass index (BMI) which were all found to be associated with dyslipidemia. Findings from prior studies comparing anthroprometric variables among HIV positive and negative individuals have not been consistent. When ART naïve HIV positive participants in South Africa and Kenya were compared with HIV negative participants, there was no significant difference in waist circumference or BMI.^[14,26] In contrast to those results but similar to what we observed in this cohort, HIV negative participants in a US study had higher BMI and waist circumference when compared with HIV positive individuals receiving ART.^[10] These findings might be a result of greater engagement with the healthcare system among HIV positive individuals and highlight the need to ensure both HIV positive and negative people have access to preventive care and education.

This study has some limitations. Given the cross-sectional design, we were only able to determine associations between baseline variables and dyslipidemia, without knowledge of their temporal relationships. Baseline behavioral variables were self-reported, potentially leading to misclassification, but this was somewhat mitigated given trained local research personnel administered the questionnaire using a validated WHO STEPS survey format. Lastly, the study was likely underpowered to detect associations between dyslipidemia and use of PI based therapy or viral suppression status since use of PIs was extremely low and viral suppression exceptionally high in this cohort.

5. Conclusion

In this cohort of HIV positive adults on ART and HIV negative participants from the same community in Western Kenya, the prevalence of dyslipidemia was high. Dyslipidemia did not have a significant association with HIV status, HIV duration since diagnosis, ART duration, CD4 level, protease-inhibitor therapy and viral load suppression. Modifiable factors such as low physical activity and low fruit and vegetable intake and being overweight were significantly associated with dyslipidemia across this cohort. This study identifies these potential targets for interventions to reduce the prevalence of dyslipidemia, which subsequently may lead to a lower burden of cardiovascular diseases and the associated morbidity and mortality.

Acknowledgments

We wish to thank all the volunteers and staff at Kisumu County Hospital for their participation in this project.

Author contributions

Conceptualization: Sarah J. Masyuko, Damalie Nakanjako, Carey Farquhar, Stephanie T. Page.

- Data curation: Hailu Tilahun, Sarah J. Masyuko, Jerusha N. Mogaka.
- Formal analysis: Hailu Tilahun, Sarah J. Masyuko, Tecla Temu, John Kinuthia, Alfred O. Osoti.
- Investigation: Sarah J. Masyuko.
- Methodology: Hailu Tilahun, Sarah J. Masyuko, Tecla Temu, Damalie Nakanjako, Carey Farquhar, Stephanie T. Page.

Supervision: Carey Farquhar, Stephanie T. Page.

- Writing original draft: Hailu Tilahun.
- Writing review & editing: Hailu Tilahun, Sarah J. Masyuko, Jerusha N. Mogaka, Tecla Temu, John Kinuthia, Alfred O. Osoti, Damalie Nakanjako, Carey Farquhar, Stephanie T. Page.

References

- Collaborators GCoD. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017. Lancet 2018;392:1736–88.
- [2] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442.
- [3] Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/ AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. Rep Am Coll Cardiol/Am Heart AssociatTask Force on Clin Pract Guidel 2019;73:e285–350.
- [4] Steyn K, Sliwa K, Hawken S, et al. Risk factors associated with myocardial infarction in Africa: the INTERHEART Africa study. Circulation 2005;112:3554–61.
- [5] Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors /edited by Majid Ezzati [et al.]. World Health Organization. 2004. Cited 19 June 2020. Available from: https://apps.who.int/iris/handle/10665/42770
- [6] Collaborators GRFGlobal, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1923–94.
- [7] Holmberg SD, Moorman AC, Williamson JM, et al. Protease inhibitors and cardiovascular outcomes in patients with HIV-1. Lancet 2002; 360:1747–8.
- [8] Asiki G, Murphy GA, Baisley K, et al. Prevalence of dyslipidaemia and associated risk factors in a rural population in South-Western Uganda: a community based survey. PLoS One 2015;10:e0126166.

- [9] Kazooba P, Kasamba I, Mayanja BN, et al. Cardiometabolic risk among HIV-POSITIVE Ugandan adults: prevalence, predictors and effect of long-term antiretroviral therapy. Pan Afr Med J 2017;27:40.
- [10] Mondy K, Overton ET, Grubb J, et al. Metabolic syndrome in HIVinfected patients from an urban, midwestern US outpatient population. Clin Infect Dis 2007;44:726–34.
- [11] Friis-Møller N, Sabin CA, Weber R, et al. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 2003;349:1993–2003.
- [12] Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med 2013;173: 614–22.
- [13] Masyuko SJ, Page ST, Kinuthia J, et al. Metabolic syndrome and 10-year cardiovascular risk among HIV-positive and HIV-negative adults: a cross-sectional study. Medicine 2020;99:e20845.
- [14] Fourie CM, Van Rooyen JM, Kruger A, et al. Lipid abnormalities in a never-treated HIV-1 subtype C-infected African population. Lipids 2010;45:73–80.
- [15] Ministry of Health. Director of Non-communicable Diseases. Kenya STEPwise survey for non-communicable diseases risk factors 2015 report. 2015. Cited 19 June 2020. Available from: https://www.who.int/ ncds/surveillance/steps/Kenya_2015_STEPS_Report.pdf
- [16] Ministry of Health. Guidelines on use of antiretroviral drugs for treating and preventing HIV in Kenya 2018. 2018. Cited 19 June 2020. Available from: https://www.nascop.or.ke/?page_id=2431
- [17] Ministry of Health. Guidelines on use of antiretroviral drugs for treating and prevention of HIV infection in Kenya. 2016 Edition. Cited 19 June 2020. Available from: https://www.prepwatch.org/wp-content/uploads/ 2016/08/Guidelines-on-ARV-for-Treating-Preventing-HIV-Infectionsin-Kenya.pdf
- [18] National Cholesterol Education Program (NCEP) Expert Panel on Detection Ea, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel iii) final report. Circulation 2002;106:3143–421.
- [19] Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; american heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation 2009;120:1640–5.
- [20] World Health Organization. Healthy Diet. 2018. Cited 19 June 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/ healthy-diet2018
- [21] World Health Organization. Global Recommendations on Physical Activity for Health. 2010. Cited 19 June 2020. Available from: https:// www.who.int/dietphysicalactivity/publications/9789241599979/en/
- [22] Osoti A, Temu TM, Kirui N, et al. Metabolic syndrome among antiretroviral therapy-naive versus experienced hiv-infected patients without preexisting cardiometabolic disorders in western kenya. AIDS Patient Care STDS 2018;32:215–22.
- [23] Katoto P, Thienemann F, Bulabula ANH, et al. Prevalence and risk factors of metabolic syndrome in HIV-infected adults at three urban clinics in a post-conflict setting, eastern democratic republic of the Congo. Trop Med Int Health 2018;23:795–805.
- [24] Kiama CN, Wamicwe JN, Oyugi EO, et al. Prevalence and factors associated with metabolic syndrome in an urban population of adults living with HIV in Nairobi, Kenya. Pan Afr Med J 2018;29:90.
- [25] Muronya W, Sanga E, Talama G, et al. Cardiovascular risk factors in adult Malawians on long-term antiretroviral therapy. Trans R Soc Trop Med Hyg 2011;105:644–9.
- [26] Njoroge A, Guthrie BL, Bosire R, et al. Low HDL-cholesterol among HIV-1 infected and HIV-1 uninfected individuals in Nairobi, Kenya. Lipids Health Dis 2017;16:110.
- [27] Woudberg NJ, Mendham AE, Katz AA, et al. Exercise intervention alters HDL subclass distribution and function in obese women. Lipids Health Dis 2018;17:232.
- [28] Asuako B, Moses MO, Eghan BA, et al. Fasting plasma glucose and lipid profiles of diabetic patients improve with aerobic exercise training. Ghana Med J 2017;51:120–7.
- [29] Calza L, Manfredi R, Chiodo F. Hyperlipidaemia in patients with HIV-1 infection receiving highly active antiretroviral therapy: epidemiology, pathogenesis, clinical course and management. Int J Antimicrob Agents 2003;22:89–99.