Prevalence and correlates of dyslipidemia in HIV positive and negative adults in Western Kenya

A cross-sectional study

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Abstract

There is increasing morbidity and mortality from cardiovascular diseases (CVD) in sub-Saharan Africa (SSA). Dyslipidemia is a well-known CVD risk factor which has been associated with human immunodeficiency virus (HIV) infection and its treatment in high-income 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

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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. Cardiovascular diseases (CVD) are the leading cause of mortality from non-communicable diseases and are projected to increase over the next decade. Dyslipidemia is a well-known risk factor for CVD globally and in developing regions such as sub-Saharan Africa. 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. 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%. 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.

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. 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. 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. 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. 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. Protease-inhibitor based therapy was reserved for second and third line therapy.

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 cholesterol <40 mg/dl (1.03 mmol/L) OR men or high-density lipoprotein cholesterol <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) according to the National Cholesterol Education Program Adult Treatment Panel III. 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. 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. 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. Current alcohol was defined as alcohol consumption in the last 30 days. A viral
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

3.1. 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 1

| General characteristics of study participants by HIV status (N = 564)*. | Total (N = 564) | HIV + (N = 287) | HIV - (N = 277) | $P$ 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** | | | | .20 |
| Current | 27 (5) | 11 (4) | 16 (6) | |
| Previous | 43 (7) | 27 (9) | 16 (6) | |
| Never | 494 (88) | 240 (87) | 254 (90) | |
| **Alcohol** | | | | .30 |
| Current | 71 (12) | 30 (10) | 41 (14) | |
| Ever | 116 (21) | 62 (22) | 54 (20) | |
| Never | 377 (67) | 195 (68) | 182 (66) | |
| **Body Mass Index** | | | | .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) | |
| **Abdominal Obesity** | | | | .01 |
| Yes | 136 (24) | 55 (19) | 81 (29) | |
| No | 428 (76) | 232 (81) | 196 (71) | |
| **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.
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 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 2.2-fold 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

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**Table 2**

| HIV-specific baseline variables^a^ | HIV positive (N = 287)^b^ | N (%)
|------------------------------------|--------------------------|-------
| HIV duration since diagnosis, years | 9 (5, 11) | 8 (4, 10)
| ART duration, years | 512 (364, 666) | 365 (213, 571)
| Current CD4, cells/mm³ | 275 (96) | 36 (13)
| Nadir CD4, cells/mm³ | 281 (102) | 61 (24)
| Suppressed Viral Load, <1000 copies/ml | 48 (9) | 39 (14)
| ART Regimen | 97 (17) | 52 (18)

^a^ Excludes 13 participants not included in dyslipidemia analysis since no blood sample available.

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**Table 3**

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

^a^ Excludes 34 participants without blood samples who were not included in the dyslipidemia analysis.
history, salt intake and sugar intake were not associated with increased risk of dyslipidemia.

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

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
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 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. Since the diet and exercise data was self-reported 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. 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 anthropometric variables among HIV positive and negative individuals have not been consistent. When ART naive HIV positive participants in South Africa and Kenya were compared with HIV negative participants, there was no significant difference in waist circumference or BMI. 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. 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.

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