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ORIGINAL RESEARCH

Spectrum and Correlates of Dyslipidemia in People Living with HIV on Dolutegravir-Based Regimen Attending Kabutare Hospital, Southern Rwanda: A Cross-Sectional Study

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Background: Dyslipidemia, a risk factor for cardiovascular disease (CVD), is common among people living with the human immunodeficiency virus (HIV). The interaction between HIV, dolutegravir (DTG)- based antiretroviral therapy (ART), and lifestyle factors contribute to dyslipidemia, increasing CVD risk. Rwanda has made significant progress in expanding access to ART, achieving high coverage and viral suppression rates. However, comprehensive data on dyslipidemia among people living with HIV (PLWH) in Rwanda is lacking. Therefore, this study aimed to fill this gap by examining the prevalence, types, and correlates of dyslipidemia among PLWH.

Methods: This cross-sectional study with 264 participants analyzed serum lipid profiles to estimate the prevalence of dyslipidemia and specific lipid abnormalities. Demographic and lifestyle factors were collected using a questionnaire. Differences in categorical variables between HIV-positive and HIV-negative groups were assessed using chi-square or Fisher's exact tests. Continuous variables were compared using the Wilcoxon rank-sum test. Multivariable logistic regression models, stratified by HIV status, identified factors independently associated with dyslipidemia, reported as adjusted odds ratios (aOR) and 95% confidence intervals (CI). Statistical significance was defined as p-value < 0.05.

Results: Dyslipidemia (NCEP ATP III criteria) was present in 74.2% of participants, significantly higher among PLWH (82.7%) than HIV-negative group (59.4%). Hypoalphalipoproteinemia and hyperbetalipoproteinemia were more common in PLWH (72.6% and 53.0%) vs HIV-negative (57.3% and 3.1%). Male gender reduced odds of dyslipidemia in both groups; smoking significantly increased risk among PLWH (aOR 8.8; 95% CI 1.73–44.59), while alcohol consumption was protective (aOR 0.2; 95% CI 0.07–0.55). DTG-based ART duration > 6–12 months increased odds of dyslipidemia vs ≤ 6 months (aOR 4.8; 95% CI 1.11–20.93).

Conclusion: The study found a high prevalence of dyslipidemia among PLWH on ART, linked to ART duration, age, smoking and sex, highlighting the need for regular screening, lifestyle interventions, and tailored HIV care.

Keywords: dyslipidemia, HIV, dolutegravir, antiretroviral therapy, lipid profiles, cardiovascular diseases risk

Introduction

Dyslipidemia, characterized by abnormal lipid profiles, is a significant risk factor for cardiovascular disease (CVD) and is commonly observed in people living with human immunodeficiency virus (PLWH).[1,2] The interaction between human immunodeficiency virus (HIV) infection, antiretroviral therapy (ART), and various lifestyle factors significantly contributes to the development of dyslipidemia, thereby increasing the risk of CVD.[3,4] The pathophysiology of dyslipidemia in PLWH is complex, involving HIV-related inflammation, immune activation, and ART-induced metabolic changes.[5]

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Protease inhibitors (PI's) such as lopinavir and certain nucleoside reverse transcriptase inhibitors (NRTIs) such as stavudine disrupt lipid metabolism, resulting in increased serum triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) levels, and decreased high-density lipoprotein cholesterol (HDL-C) levels.[6] Additionally, HIV-related infections can lead to increased lipolysis, impaired reverse cholesterol transport, and altered lipid receptor expression.[7,8]

Recent studies suggest that dolutegravir (DTG)-based regimens may be associated with increased lipid levels and weight gain among people living with HIV. These effects may reflect the broader metabolic impact of Integrase Strand Transfer Inhibitor (INSTI)-based therapies, as observed in resource-limited settings and summarized in recent studies.[3,9] In a cross-sectional study conducted at Mengo Hospital in Uganda, Chikanza et al reported a dyslipidemia prevalence of 78.0% among adults living with HIV receiving DTG-based ART, with low HDL-C (72.1%) as the most common abnormality.[10] Older NRTIs such as stavudine (d4T) and zidovudine (AZT) have been associated with dyslipidemia, particularly during early months of therapy. These drugs have shown adverse effects on lipid profiles, as highlighted in comparative trials.[5]

In sub-Saharan Africa (SSA), where HIV rates are highest, dyslipidemia is a major concern. Studies show that ART can alter lipid levels, raise total cholesterol (TC) and TG, and LDL-C.[11] These changes heighten the risk of CVD. Thus, regular lipid monitoring and risk-reduction strategies are essential for those on ART.[11] For example, research conducted in South Africa revealed that over 80% of PLWH on ART had dyslipidemia, while a study in Zimbabwe observed significant changes in lipid levels in patients on a DTG-based ART regimen.[9,12] A study in Ethiopia reported a dyslipidemia prevalence of 82.3% among PLWH, while Eritrea and Cameroon showed rates of 64.3% and 47% respectively, influenced by ART duration and regimen.[13–15]

Rwanda has made remarkable progress in combating HIV, with significant declines in mortality rates and improvements in life expectancy among PLWH.[16] However, this success may have also contributed to the reported rising burden of non-communicable diseases (NCDs), including CVD, among others.[17] Given the reports from other parts of Africa, it is plausible that a similar high prevalence of dyslipidemia exists among PLWH on ART in Rwanda, highlighting the need for further research and potential intervention. Despite the growing public health concern, there is a surprising lack of data on the prevalence, types, and risk factors of dyslipidemia among PLWH in Rwanda. The limited studies available present conflicting results, emphasizing the need for further research. For instance, Anastos et al found that women living with HIV in Rwanda had lower HDL-C levels and elevated TG levels, regardless of the cluster of differentiation 4 (CD4) T-cell counts.[18] In contrast, Bushaku et al reported no significant differences in HDL-C, TC, and LDL-C levels between PLWH and uninfected individuals, but observed significant differences in serum TG levels.[19] This study improves upon previous designs by including an HIV-negative control group, stratifying participants by ART duration, and excluding individuals with major dyslipidemia confounders. It also uses standard National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) definitions and analyzes specific lipid fractions to inform future prevention strategies. Therefore, this study aims to fill the knowledge gap on dyslipidemia in PLWH in Rwanda by investigating its prevalence, types, and risk factors among individuals receiving routine HIV-related care at Kabutare District Hospital in the Southern Province.

Materials and Methods

Study Design and Setting

This quantitative cross-sectional study was conducted from December 4, 2023, to April 1, 2024, at Kabutare District Hospital, a leading healthcare institution specializing in the care of PLWH, located in the Ngoma sector of Huye district in southern Rwanda. The hospital has established facilities, diverse patient populations, and comprehensive patient records that made it an ideal setting for this research.

Study Population and Eligibility Criteria

The study population included PLWH and an HIV-negative control group. The inclusion criteria were restricted to adults aged 18 years and above with documented HIV-infection status. To elucidate the impact of HIV infection and ART on lipid metabolism, participants with self-reported conditions associated with secondary dyslipidemia, such as diabetes

mellitus, hypothyroidism, liver disease, or those taking lipid-altering medications, were excluded. Additionally, pregnant women were excluded to avoid the confounding effects of pregnancy on lipid metabolism.

Sample Size Determination

The sample size was estimated using the formula for comparing two independent proportions:[20] $n = [\left(Z_{1-}\alpha/2 + Z_{1-}\beta\right)^2 X(P_1(1-P_1) + P_2(1-P_2))\Big]/(P_1 - P_2)^2$, assuming a 20% absolute difference in dyslipidemia prevalence between PLWH (80%) and HIV-negative controls (60%), with 95% confidence ($Z_{1-}\alpha/2 = 1.96$) and 80% power ($Z_{1-}\beta = 0.84$), the minimum required sample size was 158 participants (79 per group). To allow for stratified analysis by ART duration among PLWH and account for an anticipated 10% non-response rate, the final sample size was adjusted to 264 participants, comprising 96 HIV-negative controls and 168 PLWH across three ART-duration strata.

Participant Enrolment and Data Collection Methods

A total of 264 participants comprising 96 HIV-negative participants and 168 PLWH of whom 41 had been on ART for ≤ 6 months, 42 for > 6–12 months, and 85 for > 12 months were enrolled. A stratified sampling strategy was employed to recruit consenting PLWH attending Kabutare Hospital for routine HIV care, categorizing them based on duration on ART. HIV-negative participants were recruited from outpatient departments and voluntary counseling and testing (VCT) services at the same hospital. Only individuals with documented HIV-negative test results within the previous three months were included after retesting to confirm the HIV status. Before enrolment and obtaining written informed consent, the study objectives, procedures, and measures to ensure participant privacy were explained to potential participants. Additionally, participants were assured of their right to withdraw from the study at any point without any impact on the quality of care they were entitled to receive. Once consent was obtained, researchers accessed the participants' medical records to extract HIV-related clinical information such as treatment duration, latest CD4 count and viral load, and ART regimen details. The CD4 count and viral load results were limited to within the past six months. A questionnaire was administered to each participant to gather additional information, including lifestyle habits (eg, diet, physical activity, smoking status) and history of CVD.

The BMI index was calculated as previously reported.[21] Briefly, height was measured in meters (m) using a stadiometer (Seca, Hamburg, Germany) with participants standing upright without shoes. Weight was measured in kilograms (kg) using a weight scale (Seca, Hamburg, Germany) with participants wearing minimal clothing. BMI was calculated by dividing each participant's weight by their height (in meters) squared. BMI categories were defined as follows: Underweight < 18.5; Normal weight 18.5–24.9; Overweight 25.0 −29.9; and Obesity ≥ 30 kg/m².[22]

Blood Sample Collection and Laboratory Procedures

A total of 5 mL of venous blood was collected by venipuncture from each participant into a plain blood collection tube. The samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 5 minutes to extract serum, which was stored at −80°C until laboratory analysis. Serum levels of TC, LDL-C, HDL-C, and TG were measured using Humalyser 4000 semi-automated chemistry analyzer (Human Diagnostics, Wiesbaden, Germany).[21] Kits from Fortress Diagnostics (Antrim, United Kingdom) were used to measure serum TG, HDL-C, and TC, while LDL-C kits were obtained from Coral Clinical Systems (Goa, India). The principles of good clinical laboratory practice were strictly adhered to during all laboratory analyses.

Dyslipidemia was defined as the presence of at least one or more serum lipid profile abnormalities according to the NCEP ATP-III guidelines.[23] Briefly, TC levels < 5.2 mmol/L were considered desirable, while TC concentrations of 5.2 mmol/L or higher were classified as hypercholesterolemic. TG levels < 1.7 mmol/L were deemed desirable, whereas levels of 1.7 mmol/L or higher were classified as hypertriglyceridemia. LDL-C levels < 2.58 mmol/L were considered optimal, while levels of 2.58 mmol/L or higher were classified as hyperbetalipoproteinemia. HDL-C levels < 1.03 mmol/L for males and < 1.29 mmol/L for females were classified as hypoalphalipoproteinemia, while levels equal to or above these cut-off points were considered desirable.[23]

Statistical Analysis

All statistical analyses were performed using Stata version 15 (Stata Corp, College Station, TX, USA). Categorical variables were summarized as frequencies and percentages, while continuous variables were presented as medians and interquartile ranges (IQR) due to non-normal distribution assessed by visual inspection and the Shapiro–Wilk test. Group comparisons between PLWH and HIV-negative participants were compared using the chi-square test or Fisher's exact test when expected cell counts were less than five; continuous variables were compared using the Wilcoxon rank-sum test (Mann–Whitney *U*-test). To identify factors independently associated with dyslipidemia, multivariable logistic regression models were constructed separately for PLWH and HIV-negative groups. Variables with p-values <0.05 in bivariate analyses or those considered clinically relevant based on existing literature were considered for inclusion in multivariable models. aORs and 95% CIs were reported to quantify associations. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and multicollinearity was assessed via variance inflation factors (VIF). Statistical significance was defined as a two-sided p-value < 0.05.

Results

Characteristics of Participants

A total of 264 participants were enrolled in the study, including 168 PLWH on ART and 96 HIV-negative individuals. Key differences were observed between PLWH and HIV-negative participants. The median age was significantly higher among HIV-positive individuals (37 years) compared to HIV-negative participants (21 years) ($p < 0.001$). Females constituted a larger proportion of the PLWH group (60.7%) than the HIV-negative group (42.7%) ($p = 0.005$). Cigarette smoking was reported exclusively among PLWH participants (22.0%) and absent in HIV-negative participants ($p = 0.001$). Alcohol consumption was more common among PLWH (42.9%) than HIV-negative participants (13.5%) ($p < 0.001$). Underweight BMI status was more prevalent in PLWH (27.4%) versus the HIV-negative group (4.2%) ($p = 0.001$). Among PLWH, half had been on ART for 12 months or longer, with the majority on a TLD regimen. The sociodemographic and clinical characteristics of the study population are presented in Table 1.

Table 1 Sociodemographic and Clinical Characteristics of the Study Population

Variable[a]	Category	Total (n = 264)	HIV Positive (n=168)	HIV Negative (n=96)	p - value
Age (years)[b]	n/a	31.5 (22–40)	37(32–47)	21 (21–23)	< 0.001
Gender	Female	143 (54.2)	102 (60.7%)	41 (42.7%)	0.005
	Male	121 (45.8)	66 (39.3%)	55 (57.3%)	
Cigarette smoking	No	227 (86.0)	131 (78.0%)	96 (100.0%)	0.001
	Yes	37 (14.0)	37 (22.0%)	0 (0.0%)	
Alcohol consumption	No	179 (67.8)	96 (57.1%)	83 (86.5%)	< 0.001
	Yes	85 (32.2)	72 (42.9%)	13 (13.5%)	
BMI	Underweight	50 (18.9)	46 (27.4%)	4 (4.2%)	0.001
	Normal	208 (78.8)	117 (69.6%)	91 (94.8%)	
	Overweight	5 (1.9)	4 (2.4%)	1 (1.0%)	
	Obese	1 (0.4)	1 (0.6%)	0 (0.0%)	
ART Duration	≤ 6 months	41 (24.4)	41 (24.4)	n/a	n/a
	>6-12 months	42 (25.0)	42 (25.0)	n/a	
	≥ 12 months	85 (50.6)	85 (50.6)	n/a	

(*Continued*)

Table 1 (Continued).

Variable[a]	Category	Total (n = 264)	HIV Positive (n=168)	HIV Negative (n=96)	p - value
CD4 cell count	≥ 500 cells/μL)	47 (28.0)	47 (28.0)	n/a	n/a
	<500 cells/μL)	121 (72.0)	121 (72.0)	n/a	
CD4 counts[b] (cells/μL)	n/a	360.5 (337–520.5)	360.5 (337–520.5)	n/a	n/a
ART Regimen	TLD	161 (95.8)	161 (95.8)	n/a	n/a
	ABC/3TC/DTG	7 (4.2)	7 (4.2)	n/a	
Viral Load	<20 copies/mL	49 (29.2)	49 (29.2)	n/a	n/a
	TND	119 (70.8)	119 (70.8)	n/a	

Notes: [a]All n (%), [b]Median (IQR) unless otherwise stated.
Abbreviations: HIV, human immunodeficiency virus; BMI, body mass index; ART, antiretroviral therapy; CD4, cluster of differentiation 4; TLD, tenofovir/ dolutegravir/ lamivudine; ABC/3TC/DTG, abacavir/ lamivudine/ dolutegravir; TND, target not detected; n/a, not applicable; IQR, interquartile range.

Dyslipidemia Prevalence

Table 2 shows the prevalence of dyslipidemia and lipid abnormalities stratified by HIV status. Overall, 74.2% (n = 196) of participants had dyslipidemia, with a significantly higher prevalence among PLWH (82.7%; n = 139) compared to HIV-negative participants (59.4%; n = 57) ($p < 0.001$). Hypertriglyceridemia and hypercholesterolemia were rare or absent across groups. However, hypoalphalipoproteinemia (low HDL-C) was present in 67.0% (n = 177) of all participants, with a higher prevalence in the PLWH (72.6%) than in HIV-negative individuals (57.3%) ($p = 0.011$). For LDL-C, 34.8% of participants had hyperbetalipoproteinemia, predominantly among PLWH (53.0%) compared to only 3.1% in the HIV-negative group ($p < 0.001$).

Table 3 presents a comprehensive overview of lipid profiles, dyslipidemia patterns, and nutritional status among PLWH, stratified by duration on DTG based ART. A comparative analysis of lipid parameters revealed subtle but significant variations associated with the duration of ART. Median TG levels remained within the desirable range across all groups, with no cases of hypertriglyceridemia observed. However, a modest but statistically significant difference in TG concentrations was detected between groups ($p = 0.038$), with the highest levels occurring between 6 and 12 months on ART. Total cholesterol levels were relatively elevated in ART-exposed participants compared to reported HIV-negative reference values, though all remained within desirable thresholds. The TC concentrations peaked slightly between 6 and 12 months of therapy, but overall differences across groups were significant ($p = 0.024$).

HDL-C demonstrated a marked and statistically significant decline with increasing ART exposure ($p = 0.002$). Median values decreased from 1.18 mmol/L in the ≤ 6-month group to 0.93 mmol/L at 6–12 months, with only a marginal

Table 2 Prevalence and Spectrum of Dyslipidemia in the Study Population by HIV Status

Variables	Lipid Abnormality	Overall (n=264)	HIV Positive n (%)	HIV Negative n (%)	p - value
Dyslipidemia	Absent	68 (25.8%)	29 (17.3%)	39 (40.6%)	< 0.001
	Present	196 (74.2%)	139 (82.7%)	57 (59.4%)	
TG	Hypertriglyceridemia	1 (0.4%)	0 (0.0%)	1 (1.0%)	0.185
TC	Hypercholesterolemia	0(0.00)	0(0.00)	0(0.00)	n/a
HDL-C	Hypoalphalipoproteinemia	177 (67.0%)	122 (72.6%)	55 (57.3%)	0.011
LDL-C	Hyperbetalipoproteinemia	92 (34.8%)	89 (53.0%)	3 (3.1%)	< 0.001

Abbreviations: HIV, human immunodeficiency virus; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; n/a, not applicable.

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Table 3 Lipid Levels, Spectrum of Dyslipidemia and BMI Categories According to the Duration on Treatment

		Duration on ART			
Variable[a]	**Category**	**≤ 6 Months n=41**	**> 6–12 Months n=42**	**>12 Months n=85**	**p-value**
TG[b]		0.50(0.42–0.59)	0.60(0.52–0.70)	0.54(0.45–0.69)	0.038
TC[b]		4.00(3.41–4.34)	4.05(3.70–4.32)	3.77(3.19–4.27)	0.024
HDLC[b]		1.18(0.89–1.41)	0.93(0.84–1.11)	0.95(0.85–1.17)	0.002
LDLC[b]		2.55(1.91–2.97)	2.82(2.42–3.11)	2.54(1.92–2.95)	0.039
TG n (%)	Desirable	41(100.0.0)	42(100)	85(100.0)	n/a
	Hypertriglyceridemia	0	0	0	
TC n (%)	Desirable	41(100.0)	42(100.0)	85(100.0)	n/a
	Hypercholesterolemia	0	0	0	
HDL-C n (%)	Desirable	21(51.2)	7(16.7	18(21.2)	< 0.001
	Hypoalphalipoproteinemia	20(48.8	35(83.3)	67(78.8)	
LDL-C n (%)	Desirable	24(58.5)	12(28.6)	45(52.9)	0.011
	Hyperbetalipoproteinemia	17(41.5)	30(71.40	40(47.1)	
Lipid Status n (%)	Non-dyslipidemia	14(34.1)	3(7.1)	13(15.3)	0.004
	Dyslipidemia	27(65.9)	39(92.9)	72(84.7	
BMI n (%)	Underweight	1(2.4)	15(35.7)	30(35.3)	0.004
	Normal	39(95.1)	27(64.3)	52(61.2)	
	Overweight	1(2.4)	0	2(2.4)	
	Obese	0	0	1(1.2)	

Notes: [a]All in mmol/L, [b]Median (IQR) unless otherwise stated.
Abbreviations: ART, antiretroviral therapy; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; n/a, not applicable; IQR, interquartile range.

recovery thereafter. This was reflected in the sharp rise in hypoalphalipoproteinemia prevalence, increasing from 48.8% to 83.3%, then modestly decreasing to 78.8% in participants on DTG based ART for more than 12 months. LDL-C exhibited a peak trend at 6–12 months of ART (median 2.82 mmol/L), followed by a slight reduction in the >12-month group (2.54 mmol/L), yielding a statistically significant difference across groups (p = 0.039). The proportion of participants with hyperbetalipoproteinemia followed a similar trajectory, rising from 41.5% at ≤ 6 months to 71.4% at 6–12 months, then declining to 47.1% beyond 12 months (p = 0.011).

Nutritional status, as measured by BMI categories, shifted considerably with DTG-based ART duration. The prevalence of underweight individuals rose markedly from 2.4% in the early treatment group to 35.7% and 35.3% in the 6–12 and >12-month groups, respectively (p = 0.004). Conversely, the proportion with normal weight declined across these intervals. Overweight and obesity remained infrequent and did not differ significantly among the cohorts.

Correlates of Dyslipidemia

Table 4 shows correlates independently associated with dyslipidemia stratified by HIV status. Among PLWH, male gender was significantly associated with lower odds of dyslipidemia (aOR 0.2, 95% CI 0.08–0.56). Cigarette smoking increased the odds of dyslipidemia more than eightfold (aOR 8.8, 95% CI 1.73–44.59). Alcohol consumption was protective, associated with 80% reduction in odds (aOR 0.2, 95% CI 0.07–0.55). Additionally, ART duration of > 6–12 months was associated with higher odds of dyslipidemia (aOR 4.8, 95% CI 1.11–20.93) compared to ≤ 6 months. Among

Table 4 Correlates of Dyslipidemia Stratified by HIV Status

Variable	Category	HIV Positive		HIV Negative	
		cOR (95% CI)	aOR (95% CI)	cOR (95% CI)	aOR (95% CI)
Age (years)[a]	n/a	1.0 (0.96, 1.04)	1.0 (0.94, 1.04)	1.1 (0.82, 1.47)	1.2 (0.82, 1.67)
Gender	Female	Referent	Referent	Referent	Referent
	Male	0.3 (0.14, 0.74) **	0.2 (0.08, 0.56) **	0.1 (0.03, 0.25) ***	0.1 (0.03, 0.25) ***
Alcohol consumption	No	Referent	Referent	Referent	Referent
	Yes	0.2 (0.09, 0.53) ***	0.2 (0.07, 0.55) **	0.8 (0.24, 2.50)	0.71 (0.18, 2.85)
Cigarette smoking	No	Referent	Referent		
	Yes	4.5 (1.03, 20.09) *	8.8 (1.73, 44.59) **		
ART Duration	≤ 6 months	Referent	Referent	n/a	n/a
	7-12 months	6.0 (1.57, 23.19) **	4.8 (1.11, 20.93) *	n/a	n/a
	≥ 12 months	2.6 (1.06, 6.22) *	2.8 (0.82, 9.64)	n/a	n/a

Notes: [a]Median (IQR); *p-value < 0.05; **p-value < 0.01; ***p-value < 0.001.
Abbreviations: cOR, Crude odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ART, antiretroviral therapy; n/a, not applicable; IQR, interquartile range.

HIV-negative participants, male gender was also independently associated with reduced odds of dyslipidemia (aOR 0.1, 95% CI 0.03–0.25). BMI, CD4 count and ART regimen, though identified in previous literature as potential risk factors for dyslipidemia, were excluded from this multivariable analysis as they did not demonstrate significant associations in bivariate analyses.

Discussion

The study revealed a high prevalence of dyslipidemia among PLWH on ART, affecting 82.14% of PLWH. Dyslipidemia was more common in PLWH compared to the control group (59.4%), with low HDL-C and high LDL-C being the most prevalent phenotypes in both groups. These results are consistent with findings from studies in Ethiopia (82.3%), South Africa (85%), and Eritrea (86.6%), but higher than the reported prevalence in Cameroon (64.3%) and Kenya (47%).[12–15,24]

Our findings align with a recent study in Uganda, where 78% of PLWH on DTG-based therapy developed at least one form of dyslipidemia, most commonly low HDL-C (72.1%).[10] Similarly, in Zimbabwe, Chakanetsa et al reported notable increases in LDL-C and TGs among patients initiated on a DTG-based regimen.[9] These findings support the emerging evidence that DTG, while effective, may contribute to adverse lipid changes and reinforce the need for routine lipid monitoring in PLWH on this regimen.

This study also sheds light on the differential correlates of dyslipidemia in PLWH compared to HIV-negative individuals, emphasizing both lifestyle factors and ART exposure. Notably, the regression analyses revealed distinct gender-based and behavioral disparities in lipid disturbances across both populations. Among PLWH, male sex was independently associated with a significantly lower risk of dyslipidemia, with an aOR of 0.2 (95% CI: 0.08–0.56, $p < 0.01$). This aligns with findings from Irira et al who reported sex-based differences in lipid profiles among Tanzanian adolescents receiving ART.[25] Similar patterns have been observed in adult populations by Malindisa et al, with hormonal and behavioral factors likely contributing to these disparities.[26]

Alcohol consumption also emerged as protective against dyslipidemia in PLWH (aOR = 0.2, 95% CI: 0.07–0.55, $p < 0.01$), a somewhat paradoxical finding. While moderate alcohol use has been shown to raise HDL-C levels, the significant protective effect observed here warrants cautious interpretation, possibly reflecting residual confounding or reverse causality.[27] Further qualitative exploration of alcohol patterns in this cohort may help disentangle these

associations. Conversely, cigarette smoking demonstrated a strong, independent association with dyslipidemia in PLWH (aOR = 8.8, 95% CI: 1.73–44.59, $p < 0.01$). This aligns with established literature showing that smoking promotes atherogenic lipid profiles (namely elevated LDL-C and reduced HDL-C), thereby compounding cardiovascular risk in HIV.[28] Given the additive cardiometabolic burden of HIV and ART, targeted smoking cessation interventions remain a critical public health priority.

Duration on ART also emerged as a significant contributor to lipid alterations. Compared to ART-naïve or recently initiated individuals, those on ART for 6–12 months had nearly five-fold higher odds of dyslipidemia (aOR = 4.8, 95% CI: 1.11–20.93, $p < 0.05$). This suggests a temporal pattern of metabolic disruption, likely reflecting early-onset ART-induced lipid perturbations. Previous longitudinal studies, including our own findings in a resource-limited setting, have reported similar biphasic lipid changes, with most adverse effects manifesting within the first year of therapy.[9,29] Interestingly, this risk plateaued beyond 12 months, hinting at possible lipid homeostasis or adaptation with prolonged therapy. In contrast, among HIV-negative participants, male sex remained protective (aOR = 0.1, 95% CI: 0.03–0.25, $p < 0.001$), while neither alcohol nor smoking demonstrated significant associations. This divergence underscores the unique metabolic and behavioral landscape in PLWH, likely modulated by ART, chronic inflammation, and syndemic factors. Collectively, these findings support the need for tailored cardiovascular risk assessments in HIV care, integrating sex-specific considerations, behavioral risk profiling, and early monitoring post-ART initiation. Future studies should investigate whether specific ART regimens or immune reconstitution markers mediate these associations and whether interventions targeting modifiable risk factors can attenuate the burden of dyslipidemia and its sequelae.

Several mechanisms have been proposed to explain the pathogenesis of dyslipidemia in PLWH, including the direct effects of HIV on lipid metabolism, immune activation and inflammation, genetic factors, and adverse effects of ART.[3] Among ART drugs, PIs and NRTIs have the most deleterious effects on lipid profiles, while INSTIs and NNRTIs have fewer adverse effects on lipid metabolism.[30,31] Although INSTIs have been reported to have fewer adverse effects, they have only recently been incorporated into the preferred first-line ART regimen in Rwanda.[16] Evidence of potential long-term effects is still accumulating, with a prospective study in Zimbabwe also showing deleterious effects of INSTIs on lipid profiles.[9] However, the impact of different ART regimens on dyslipidemia may also vary depending on individual patient characteristics, the duration of treatment, and the specific drug combinations used.

The observed patterns of dyslipidemia prevalence, peaking at > 6–12 months and slightly declining afterward, are not widely reported. This may suggest that ART initiation may in the interim induce cardiometabolic changes in plasma lipid composition, potentially exacerbated by inflammatory biomarkers, which increase CVD risk.[32] This phenomenon could also reflect the natural progression of dyslipidemia in HIV patients, which may vary depending on the stage of infection, immune status, and viral load. Alternatively, it might indicate the effects of switching or discontinuing ART drugs due to toxicity, intolerance, or resistance, which can impact lipid profiles.[33] Therefore, further research is needed to clarify the temporal relationship between dyslipidemia and ART duration in PLWH.

The study also observed that the median levels of TC, TG, and LDL-C increased initially before decreasing with ART duration, peaking in the > 6–12 months group. While similar studies in Eritrea, Kenya, and Ethiopia have reported increased levels of TC, TG, and LDL-C, none have delineated their association with ART duration.[12–14,34] This pattern may be explained by ART-induced initial increases in lipid levels due to immune system reconstitution and reduced inflammation, which are associated with increased cholesterol synthesis and decreased cholesterol clearance.[35] Subsequent decreases in lipid levels may be due to the adaptation of lipid metabolism or switching to regimens with potentially minimal adverse effects, such as TLD, which are associated with decreased cholesterol synthesis and increased cholesterol clearance.[36] The study also noted that median HDL-C levels decreased initially and then increased with ART duration, reaching a trough in the > 6–12 months group. This may be due to ART suppressing the production and secretion of HDL-C, an atheroprotective lipoprotein that removes excess cholesterol from tissues and transports it to the liver for excretion, while also stimulating the expression and activity of HDL-C receptors, enhancing its uptake and clearance from circulation.[37]

The gender difference in dyslipidemia prevalence among PLWH is in concordance with findings from South Africa, Eritrea, Cameroon, and Ethiopia.[9,13–15,34] Such difference may stem from hormonal factors, such as contraceptive use and menopause-related declines in estrogen.[38] Hormonal contraceptives can affect cholesterol levels differently, with

estrogen typically increasing HDL-C and lowering LDL-C, while progestin has the opposite effects.[39,40] These contraceptives may also heighten CVD risk when combined with factors like smoking or obesity.[41] Estrogen declines with age, especially after menopause, further contributes to higher LDL-C and lower HDL-C levels.[41] However, data on contraceptive use were not collected in this study.

Several limitations of this study should be acknowledged. One limitation was the inability to assess the association between dyslipidemia and the ART regimen ABC/3TC/DTG, due to the small number of patients receiving this treatment. It is important to note that various ART regimens have been shown to influence lipid profiles differently.[24,30] ABC/3TC/DTG, a relatively recent and potent regimen, has demonstrated minimal effects on lipid levels and cardiovascular risk in clinical trials.[42] However, real-world evidence on its long-term safety and effectiveness in resource-limited settings remains limited. Further research is required to explore its impact on dyslipidemia and other metabolic complications in HIV patients. Also, the cross-sectional design of the study restricted the ability to infer causality between ART and changes in lipid profiles. Additionally, the sample size, particularly after participant stratification, may have been insufficient to detect significant differences in some lipid parameters. Finally, participant recruitment from a single hospital and self-reporting of excluded conditions may have introduced selection bias, potentially limiting the generalizability of the findings.

Nevertheless, this study also possesses several strengths that enhance its validity and reliability. First, it targeted a well-defined population of PLWH on ART, enabling a comprehensive analysis of ART's effects on lipid profiles. The use of standardized laboratory methods for lipid profile analysis ensured precise and reliable findings. Moreover, the inclusion of an HIV-negative control group allowed for meaningful comparisons between HIV-positive and HIV-negative individuals, offering valuable insights into the impact of HIV infection on lipid metabolism.

Conclusion

This study highlights a notably high prevalence of dyslipidemia among PLWH at Kabutare Hospital, surpassing that of the control group. Low HDL-C and high LDL-C emerged as the most prevalent dyslipidemias, with significant associations identified between dyslipidemia and factors such as ART duration, smoking, age and sex. These findings underscore the importance of regular lipid profile screening particularly for individuals at elevated risk due to age, gender, or prolonged ART exposure. To address this issue, healthcare providers should adopt comprehensive dyslipidemia management protocols as part of routine HIV care, supplemented by accessible pharmacological treatments. Future longitudinal studies are essential to evaluate the long-term effects of ART on lipid metabolism and cardiovascular outcomes, thereby guiding more effective therapeutic approaches for this population.

Data Sharing Statement

All data generated in this study are included in this manuscript.

Ethics Approval and Informed Consent

This study was conducted following the principles of the Declaration of Helsinki. Ethical approval was granted by the University of Rwanda, College of Medicine and Health Sciences (Reference number: CMHS/IRB/352/2023). Additionally, permission to conduct the study was obtained from the Director General of Kabutare District Hospital (Reference number: 329/10/Hop.Kab/2023). All participants provided a written informed consent before they participated in the study. To ensure confidentiality and anonymity, all data were anonymized by assigning unique study identification numbers to each participant.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval for the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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