



Association Between High Serum Alanine Aminotransferase to High Density Lipoprotein Cholesterol Ratio and Metabolic Syndrome among People Living with HIV on Dolutegravir-Based ART in South-Western Uganda

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Abstract

Background: Serum Alanine aminotransferase to High density lipoprotein cholesterol ratio (ALT-to-HDL-C ratio) has been identified as a significant predictor of non-alcoholic fatty liver disease, a hepatic manifestation of metabolic syndrome. This study investigated the association between serum aminotransferases to high-density lipoprotein cholesterol ratios and metabolic syndrome (MetS) among people living with HIV (PLWH) on Dolutegravir (DTG)-based antiretroviral therapy (ART) in South Western Uganda.

Methods: We conducted a secondary analysis study from June 15, 2025 to August 20, 2025 using a dataset generated from hospital-based cross-sectional study that investigated an association between aspartate aminotransferase to alanine aminotransferase ratio and MetS among 377 PLWH who were on DTG-based ART at Ruhoko Health Centre IV, South Western Uganda.

Results: The prevalence of MetS was 44.6% (168/377); 95% CI: 39.6 - 49.6 and significantly increased from the lowest to the highest ALT-to-HDL-C ratio tertiles (30.2% vs 47.7% vs 56.1%, $p < 0.001$). In the adjusted model, higher ALT-to-HDL-C ratio was significantly associated with MetS. Individuals in the second tertile had 2.35-fold higher odds (aOR 2.35, 95% CI: 1.26–4.41, $p = 0.008$), and those in the third tertile had over fourfold higher odds (aOR 4.65, 95% CI: 2.25–9.61, $p < 0.001$) of MetS compared to the lowest tertile. ALT-to-HDL-C ratio at an optimal cutoff of 0.33 had a significant ability (AUC=0.820, 95%CI: 0.782 - 0.861) to differentiate between participants with MetS from those without MetS at a sensitivity of 92% and specificity of 54%.

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Conclusion: Higher ALT-to-HDL-C ratio is potentially associated with MetS. Since both ALT and HDL-C are routine measurements in HIV Care, this warrants further studies on the potential of ALT-to-HDL-C ratio as a biomarker for MetS.

Plain Language Summary

Simple Blood Test Ratio May Help Detect Metabolic Problems in People Living with HIV

Plain Language Summary: - Metabolic syndrome is a group of health problems that increase the risk of heart disease, diabetes, and stroke. These include high blood pressure, high blood sugar, abnormal cholesterol levels, and excess body fat around the waist. People living with HIV (PLWH), especially those taking dolutegravir-based HIV treatment, may have a higher chance of developing these problems. This study examined the link between a simple blood test ratio; alanine aminotransferase (ALT) to high-density lipoprotein cholesterol (HDL-C) and metabolic syndrome among adults living with HIV in South-Western Uganda. ALT is a liver enzyme, and HDL-C is often called the “good cholesterol.” Researchers analyzed health data of 377 people who had been on dolutegravir-based treatment for at least one year. The findings showed that people with higher ALT-to-HDL-C ratios were more likely to have metabolic syndrome. Those with the highest ratios had over four times greater odds of developing metabolic syndrome compared to those with the lowest ratios. This means that the ALT-to-HDL-C ratio could serve as a simple and low-cost indicator for identifying individuals at higher risk of developing metabolic complications, especially in places with limited testing resources. Early identification of people at risk allows healthcare providers to recommend lifestyle changes or treatments that can help prevent serious health complications. Since both ALT and HDL-C tests are commonly done in HIV clinics, using this ratio could help improve care for people living with HIV.

Keywords

ALT-to-HDL-C ratio, metabolic syndrome, insulin resistance, dolutegravir-based ART

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Introduction

Metabolic syndrome (MetS) is a cluster of interrelated cardiometabolic abnormalities typically including central obesity, elevated blood pressure, raised fasting glucose, high triglycerides, and low high-density lipoprotein cholesterol,^{1,2} that together confer greatly increased risk of cardiovascular disease, stroke and type 2 diabetes.^{3–5} In people living with HIV (PLWH), chronic immune activation and some antiretroviral drugs further amplify these risks.⁶

Globally the burden of MetS in PLWH is high with estimates ranging broadly (11–48%) depending on the population and criteria.⁷ Meta-analyses in sub-Saharan Africa (SSA) suggest roughly one in five PLWH are affected.^{3,7} In East Africa, recent studies show MetS prevalence ranging between 20% and 40%.^{8,9} These findings underscore that MetS is a prevalent problem among PLWH in Uganda and the region.

Early detection and management of MetS is critical among PLWH. Dolutegravir (DTG)-based ART regimens are increasingly reported to be associated with excessive weight gain and a higher incidence and prevalence of obesity, hypertension, dyslipidemia, hyperglycemia and MetS.^{6,8,10–18} As an INSTI, DTG induces rapid viral load suppression and a pronounced return-to-health effect that may exaggerate weight gain by reducing resting

energy expenditure.^{8,19} DTG use has also been linked to decreased adiponectin levels, impairing glucose and lipid metabolism and promoting insulin resistance. Furthermore, DTG exhibits pro-adipogenic and pro-lipogenic effects, induces oxidative stress and mitochondrial dysfunction, and may disrupt melanocortin-4 receptor signaling, thereby increasing appetite.^{8,19} Its off-target chelation of magnesium and manganese may further alter metabolic pathways, collectively contributing to insulin resistance, weight gain, and MetS.^{8,19}

Given this elevated metabolic risk profile, individuals receiving DTG-based therapy represent a clinically important subgroup in which early detection of MetS is particularly critical. MetS is conventionally diagnosed by measuring multiple parameters; waist circumference, blood pressure, fasting glucose, triglycerides and HDL cholesterol typically requiring dedicated clinic visits, fasting blood draws and equipment for anthropometry and blood pressure. In many settings, especially high-volume HIV clinics and resource-constrained areas like southwestern Uganda, this comprehensive approach can be logistically burdensome and costly. Consequently, a simpler biomarker for MetS could facilitate screening and early intervention. Serum biomarkers are attractive in this context because they can be obtained from routine blood tests. In particular, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are readily

available biomarkers often used to assess hepatocellular damage. They are strongly linked to non-alcoholic fatty liver disease (NAFLD) and insulin resistance, both of which are hepatic manifestations of metabolic syndrome.^{20–22} Likewise, high-density lipoprotein cholesterol (HDL-C) is a key lipid marker reflecting impaired lipid metabolism and reduced HDL-C levels constitute one of the core diagnostic criteria for MetS.^{20,21,23} The ALT-to-HDL-C and AST-to-HDL-C ratios therefore integrate two pathophysiological dimensions of MetS; hepatic metabolic dysfunction and atherogenic dyslipidemia into a single index.

Emerging evidence in general populations supports the ALT-to-HDL-C and AST-to-HDL-C ratios as metabolic risk indicators.²⁴ Using these ratios could reduce screening burdens. Both ALT, AST, and HDL-C are routinely measured in HIV clinics; serum transaminases as part of liver function tests and HDL-C as part of lipid panels, so the ratios require no additional specialized tests. Compared to standard MetS screening, computing ALT-to-HDL-C and AST-to-HDL-C ratios from an existing blood draw could be faster, cost effective and less inconvenient for patients. However, evidence supporting the association between ALT-to-HDL-C and AST-to-HDL-C ratios with MetS among PLWH on DTG-based ART remains limited. Establishing a clear relationship between these ratios and MetS would provide foundational data to inform future, larger and more robust studies aimed at evaluating the diagnostic utility of these ratio biomarkers for MetS and its individual components.

To the best of our knowledge, no prior studies have investigated the association between serum aminotransferases to high-density lipoprotein cholesterol ratios and MetS among PLWH on DTG-based ART in Uganda. Therefore, this study sought to assess the association between ALT-to-HDL-C and AST-to-HDL-C ratios with MetS among PLWH on DTG-based ART, and to evaluate the predictive performance of these ratios, including identifying optimal cut-off values for distinguishing individuals with and without MetS in Southwestern Uganda.

Material and Methods

The reporting of this study conforms to the STROBE guidelines for observational studies.²⁵

Study Design, Population, and Variables

We conducted a secondary data analysis study from June 15, 2025 to August 20, 2025 using a dataset generated from a hospital-based cross-sectional study by Nzaramba et al,¹⁸ which investigated the association between a low aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio and metabolic syndrome (MetS) among 377 PLWH receiving DTG-based ART at Ruhoko

Health Centre IV in Ibanda Municipality, Southwestern Uganda. This primary study was conducted from July 1, 2024 to August 15, 2024. Ruhoko Health Centre IV is located approximately 74 kilometers from Mbarara City accessible via Ibanda Road. The facility also serves as a referral point for surrounding lower-level health centers, including Nyamirima, Nyakatokye, and Kyikuchu. The ART clinic of this facility operates four days a week (Tuesday to Friday) from 8:00 AM to 5:00 PM and reviews more than 150 patients each day. All the PLWH receiving care at this facility is on DRG-based ART regimens. The source population in the primary study comprised all PLWH in South-Western Uganda. The study population consisted of PLWH on dolutegravir-based ART who were receiving HIV care and follow-up at Ruhoko Health Centre IV in South-Western Uganda during the study period and who met the eligibility criteria.

In the primary study,¹⁸ adult patients aged 18 years and above who had been on DTG-based ART for at least 12 months and had provided informed consent were systematically enrolled where by every third eligible participant was consecutively selected until the desired sample size of 377 was obtained. Exclusion criteria included missing clinical records, pregnancy, interrupted ART, or attendance for acute illnesses such as hepatitis. Participants receiving treatment for diabetes, lipid-lowering therapy, corticosteroids, or oral contraceptive pills were also excluded.

The primary study used a structured questionnaire that consisted of standard measurement tool to collect a wide range of variables which included socio-demographics (sex, age, education level, residence, religion, and employment status), household factors (presence of a ventilated kitchen), and lifestyle behaviors (smoking status, alcohol consumption, and intake of fruits and vegetables), reported family history of Diabetes Mellitus and hypertension. This questionnaire was administered by well-trained research assistants. Anthropometric measurements (weight, height, waist circumference, hip circumference, neck circumference, mid-upper arm circumference (MUAC)), systolic and diastolic blood pressure were performed by a clinician. A digital sphygmomanometer was used to measure blood pressure. Two readings were taken five minutes apart, and their average was recorded as the participant's blood pressure. Weight and height were measured using a portable weight and height scale. Waist and hip circumferences were measured using a non-stretchable SECA 201 ergonomic tape. Two measurements were taken, and when the difference between them exceeded 3 cm, a third measurement was obtained. The final waist and hip circumference values were recorded as the mean of the two or three measurements.

About 4 mL of venous blood was collected from each participant after an overnight fast using fluoride-oxalate (grey-top) and plain (red-top) vacutainer tubes. Plasma and serum were separated within one hour of collection.

Biochemical analyses, including plasma glucose, serum total cholesterol, LDL-C, HDL-C, triglycerides, AST, ALT, ALP, GGT, and electrolytes, were performed using the HumaStar 100 clinical chemistry analyzer (Human Diagnostics, Germany) by a qualified Laboratory Technologist at Ruhoko Health Centre IV Clinical Chemistry Laboratory, Ibanda Municipality. This spectrophotometric instrument determines analyte concentrations at predefined wavelengths and has a throughput of approximately 100 tests per hour. The analyzer performs automated sample and reagent pipetting, photometric reading, incubation, and result calculations. Calibration was carried out using AutoCal (EFILive, Auckland, New Zealand), and both normal (HumaTrol N) and pathological (HumaTrol P) quality control materials were analyzed daily prior to processing study samples. All procedures adhered strictly to the manufacturer's instructions for both the instrument and the reagents.

Ruhoko Health Centre IV Laboratory, where the analyses were performed, is nationally accredited at a 2-star level by the National Health Laboratory Services/Central Public Health Laboratories (NHLS/CPHL), Ministry of Health, Uganda. To further ensure analytical accuracy, 10% of all collected samples were retested at the Mbarara Regional Referral Hospital clinical chemistry laboratory as an external quality assurance measure.

Dependent and Independent Variables in the Secondary Analysis

The primary outcome of interest was metabolic syndrome (MetS), defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria.²⁶ Based on this criteria, participants are classified as having MetS if they meet at least three of the following criteria: waist circumference >102 cm for men or >88 cm for women; triglycerides ≥ 150 mg/dL; HDL-C <40 mg/dL for men or <50 mg/dL for women; blood pressure >130/85 mm Hg or use of antihypertensive medication; and fasting plasma glucose ≥ 110 mg/dL or use of diabetes treatment. However for classification of waist circumference, we used International Diabetes Federation (IDF) recommended African-specific cut-offs (≥ 94 cm for male and ≥ 80 cm for female for Sub-Saharan Africans)^{27,28} instead of NCEP ATP III waist circumference cut-offs (>102/88 cm).

The main independent variables were the alanine aminotransferase to high-density lipoprotein cholesterol ratio (ALT-to-HDL-C ratio) and the aspartate aminotransferase to high-density lipoprotein cholesterol ratio (AST-to-HDL-C ratio). The ALT-to-HDL-C ratio was calculated by dividing serum ALT levels (IU/L) by HDL-C levels (mg/dL), while the AST-to-HDL-C ratio was calculated by dividing serum AST levels (IU/L) by HDL-C levels (mg/dL). We did not find established clinical or

epidemiological cut-off points in the literature to define "high" or "low" values for these enzyme-to-lipid ratios in relation to prediction of a likelihood of MetS. In the absence of validated thresholds, data-driven categorization is commonly applied, and tertiles provide a balanced approach that maintains adequate sample size within each group. Tertiles also enhance interpretability by allowing comparison across low, medium, and high groups without over-stratifying the data. Therefore both ALT-to-HDL-C and AST-to-HDL-C ratios were categorized into tertiles for analysis.

Additional independent variables included sex, age, education level, residence, religion, and employment status, presence of a ventilated kitchen, smoking status, alcohol consumption, and intake of fruits and vegetables, family history of chronic conditions Diabetes Mellitus and hypertension, total cholesterol, low-density lipoprotein, ALP, GGT, serum electrolytes sodium, potassium, and chloride, sleep quality, risk of obstructive sleep apnea (OSA), sleep duration, body mass index, duration on DTG-based ART. OSA was assessed using the STOP-Bang scoring tool.²⁹ Sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI). Poor sleep quality was defined as a global PSQI score ≥ 6 .³⁰ Sleep duration was categorized as <5, 5–6, 6–7, and >7 hours.³¹ Body Mass Index was categorized as <25 Kg/m², 25–29.9 Kg/m², ≥ 30 Kg/m.³² Low fruit and vegetable intake was defined as consuming less than five servings of fruit and vegetables per day.³³ All standardized tools used to collect data have been previously validated and widely applied in similar populations.

Sample Size Determination

For the secondary analysis, a sample size calculation was based on the prevalence (35.3%) of MetS¹⁸ among PLHIV on DTG-based ART in a study conducted in South-western Uganda. We used the Kish Leslie formula (1965) with a 5% margin of error and a 95% confidence interval.

$$n = 1.96^2 \times 0.353(1 - 0.353) / 0.05^2 = 351.$$

Since the primary study enrolled 377 participants, this sample size was adequate for the secondary data analysis study.

Statistical Analysis

Data was analyzed using STATA Software version 17. Categorical variables were summarized using frequencies and proportions. The distribution of categorical variables between the different ALT-to-HDL-C tertiles was compared using Chi-square test or Fishers exact test. Continuous variables were tested for normality using

Shapiro-wilk normality test and all were not normally distributed (p -value <0.05). Therefore, they were all summarized using Median (IQR) and their distribution between the ALT-to-HDL-C tertiles compared using the Kruskal-Wallis rank test. A p -value <0.05 was considered statistically significant.

Logistic regression was used to assess the association between ALT-to-HDL-C ratio and AST-to-HDL-C ratios with MetS. MetS was the binary dependent variable (1 = present, 0 = absent) while ALT-to-HDL-C and ALT to-HDL C ratios were the primary independent variables. At the bivariate level, crude associations between MetS and each independent variable, including ALT-to-HDL-C and ALT-to-HDL-C ratios, were evaluated. Associations were quantified using crude odds ratios (ORs) with corresponding 95% confidence intervals (CIs), and statistical significance was determined at a p -value <0.2 . The primary exposure variables and other variables that demonstrated statistical significance at the bivariate level, along with those that were not statistically significant but were considered biologically plausible confounders such as serum ALP, GGT, and potassium were included in the multivariable model to ensure adequate adjustment for potential confounding. Adjusted odds ratios (aORs) with 95% CIs were reported and p -values were reported. In the multivariable model, variables such as residence, ventilated kitchen, and fruit and vegetable intake were excluded because they did not contribute meaningfully to the model and their removal improved model precision without compromising its validity. The model's goodness of fit was then assessed using the Hosmer-Lemeshow test, with a p -value >0.05 indicating a good fit ($p=0.8632$) in our final model). The final model was also tested for the absence of severe multi-collinearity with a mean VIF of 1.54 being below the acceptable value of 5. In the final multivariable model, associations were considered significant at a p -value <0.05 .

To evaluate the predictive ability of the ALT-to-HDL-C ratio for identifying participants with MetS, we conducted a Receiver Operating Characteristic (ROC) curve analysis. ROC analysis was selected because it is an established method for evaluating the diagnostic or discriminative performance of a continuous biomarker in classifying a binary outcome. The area under the curve (AUC) was computed to quantify the overall discriminative performance of the ALT-to-HDL-C ratio. An AUC value closer to 1.0 indicates better predictive power, whereas an AUC of 0.5 suggests no better classification than chance. Predictive performance was considered statistically significant if the 95% CI for the AUC did not include the null value of 0.5. Additionally, the interpretation of AUC values is summarized as: AUC 0.90–1.00 = Excellent; 0.80–0.89 = Good; 0.70–0.79 = Fair; 0.60–0.69 = Poor; 0.50–0.59 = Failure.³⁴

Results

All the 377 PLWH on DTG-based ART in the primary study met eligibility and were analyzed in the secondary analysis study. Participants were divided into tertiles of ALT/HDL-C ratio: first tertile ($n=126$), second tertile ($n=128$), and third tertile ($n=123$). MetS prevalence was 30.2%, 47.7%, and 56.1% across the tertiles from lowest to highest, respectively, totaling 168 cases (44.6%) (Figure 1).

Socio-Demographic and Clinical Characteristics of the Study Participants

Our study enrolled 377 participants with a median age of 44 years (IQR: 30–59), of whom 56.2% were female. Most had attained tertiary (40.1%) or secondary (19.9%) education, while 22.0% had no formal education. Over half (57.3%) resided in urban areas, and 36.6% were Protestant, followed by Catholics (29.7%). The majority were employed (84.1%) and lived in homes with ventilated kitchens (85.4%). Regarding lifestyle factors, 11.9% reported ever smoking, and 62.1% reported alcohol consumption. Most participants had a BMI <25 kg/m² (69.0%), with 23.3% overweight and 7.7% obese. A high proportion (70.3%) had been on dolutegravir-based ART for more than two years. We did not observe statistically significant differences in the distribution of sociodemographic and clinical characteristics across the ALT-to-HDL-C tertiles ($p>0.05$) in this study as indicated in Table 1.

Metabolic Syndrome, its Components and Biochemical Parameters by ALT/HDL-C Status

The prevalence of MetS was 44.6%(168/377); 95% CI: 39.6 - 49.6 and significantly increased from the lowest to the highest ALT-to-HDL-C ratio tertiles (30.2% vs 47.7% vs 56.1%, $p<0.001$). Elevated fasting plasma glucose was also more common in the upper tertile (22.8%) than in the lowest (8.7%, $p=0.005$). Low HDL-C levels showed a strong gradient across tertiles, rising from 15.1% in the lowest tertile to 78.0% in the highest ($p<0.001$). Elevated LDL-C (≥ 130 mg/dL) was also more frequent in the higher tertiles, affecting 19.5% of participants in the third tertile compared to only 6.3% in the first ($p=0.008$). However, elevated triglycerides were significantly more frequent in the lower tertiles, observed in 78.6% of participants in the first tertile compared to 64.1% and 68.3% in the second and third tertiles, respectively ($p=0.034$). Regarding total cholesterol, high levels (≥ 200 mg/dL) were also most common in the lowest tertile (42.9%), decreasing progressively to 17.9% in the highest tertile ($p<0.001$) as indicated in Table 2.

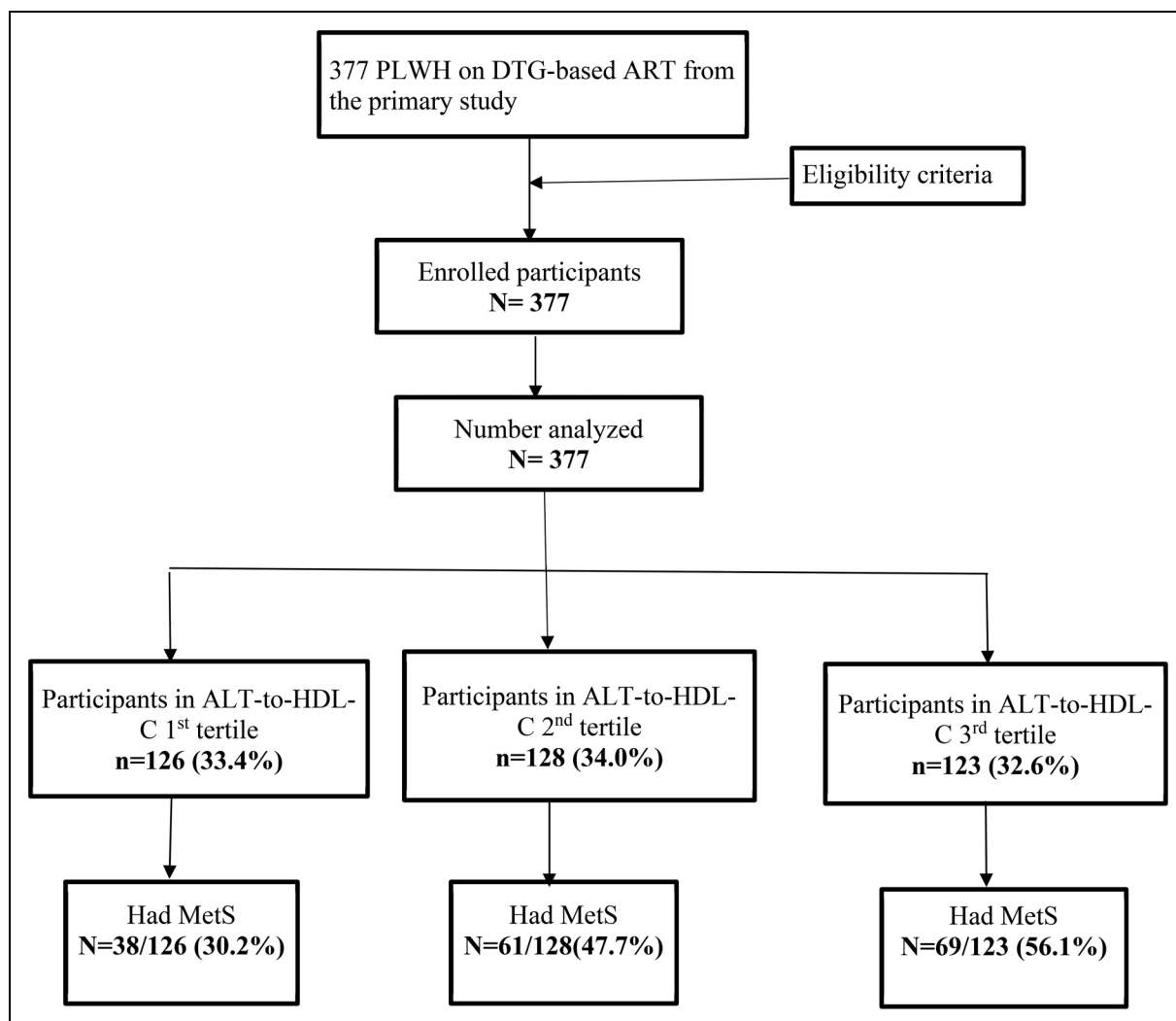


Figure 1. Narrative of the study flow chart.

Association Between High ALT-to-HDL-C Ratio and Metabolic Syndrome

At bivariate analysis (Table 3), higher ALT-to-HDL-C and AST-to-HDL-C ratios were significantly associated with increased odds of MetS. Participants in the second tertile of ALT-to-HDL-C ratio had more than double the odds (cOR 2.11, 95% CI: 1.26–3.53, $p=0.005$), and those in the third tertile also had over twofold higher odds of MetS (cOR 2.95, 95% CI: 1.75–4.98, $p<0.001$) compared to the participants in the first tertile. However, for AST-to-HDL-C ratio, only participants in the third tertile had significantly higher odds of MetS in comparison to those in first tertile (cOR 1.89, 95% CI: 1.14–3.13, $p=0.014$). After adjusting for potential confounders including age, sex, education level, smoking, alcohol consumption, body mass index, sleep quality, sleep duration, obstructive sleep apnea, family history of hypertension, DTG-based ART duration, ALP, GGT, and serum electrolytes

(sodium, potassium, and chloride)) in multivariate analysis (Table 3), only the association between higher ALT-to-HDL-C and MetS remained statistically significant and even stronger. Individuals in the second tertile had 2.35-fold higher odds (aOR 2.35, 95% CI: 1.26–4.41, $p=0.008$), and those in the third tertile had over fourfold higher odds (aOR 4.65, 95% CI: 2.25–9.61, $p<0.001$) of MetS compared to those in the lowest tertile. ALT-to-HDL-C ratio at an optimal cutoff of 0.33 had a significant ability (AUC=0.820, 95%CI: 0.782 - 0.861) to differentiate between participants with MetS from those without MetS at a sensitivity of 92% and specificity of 54% as indicated in Figure 2.

Discussion

Our study found a significant and graded association between serum ALT-to-HDL-C ratio and MetS among

Table I. Socio-Demographic and Clinical Characteristics by ALT-to-HDL-C Tertiles.

Variable	Total N = 377	ALT-to-HDL-C tertiles			p-value
		First N = 126	Second N = 128	Third N = 123	
Age in years: Median(IQR)	44 (30–59)	41 (29–58)	44 (30.5–58)	46 (32–60)	0.74
Sex					0.24
Male	165 (43.8%)	54 (42.9%)	50 (39.1%)	61 (49.6%)	
Female	212 (56.2%)	72 (57.1%)	78 (60.9%)	62 (50.4%)	
Education level					0.11
No education	83 (22.0%)	26 (20.6%)	23 (18.0%)	34 (27.6%)	
Primary	68 (18.0%)	16 (12.7%)	26 (20.3%)	26 (21.1%)	
Secondary	75 (19.9%)	32 (25.4%)	26 (20.3%)	17 (13.8%)	
Tertiary	151 (40.1%)	52 (41.3%)	53 (41.4%)	46 (37.4%)	
Residence					0.73
Urban	216 (57.3%)	75 (59.5%)	70 (54.7%)	71 (57.7%)	
Rural	161 (42.7%)	51 (40.5%)	58 (45.3%)	52 (42.3%)	
Religion					0.97
Catholic	112 (29.7%)	39 (31.0%)	37 (28.9%)	36 (29.3%)	
Protestant	138 (36.6%)	42 (33.3%)	49 (38.3%)	47 (38.2%)	
Moslem	32 (8.5%)	10 (7.9%)	11 (8.6%)	11 (8.9%)	
Others	95 (25.2%)	35 (27.8%)	31 (24.2%)	29 (23.6%)	
Employment status					0.55
Unemployed	60 (15.9%)	23 (18.3%)	17 (13.3%)	20 (16.3%)	
Employed	317 (84.1%)	103 (81.7%)	111 (86.7%)	103 (83.7%)	
Ventilated Kitchen					0.79
No	55 (14.6%)	18 (14.3%)	17 (13.3%)	20 (16.3%)	
Yes	322 (85.4%)	108 (85.7%)	111 (86.7%)	103 (83.7%)	
Smoking					0.95
Non smoker	332 (88.1%)	110 (87.3%)	113 (88.3%)	109 (88.6%)	
Ever smoked	45 (11.9%)	16 (12.7%)	15 (11.7%)	14 (11.4%)	
Alcohol Consumption status					0.69
Never consumed	143 (37.9%)	44 (34.9%)	51 (39.8%)	48 (39.0%)	
Ever consumed	234 (62.1%)	82 (65.1%)	77 (60.2%)	75 (61.0%)	
Body mass index					0.43
< 25 kg/m ²	260 (69.0%)	85 (67.5%)	83 (64.8%)	92 (74.8%)	
25–29 kg/m ²	88 (23.3%)	32 (25.4%)	32 (25.0%)	24 (19.5%)	
≥ 30 kg/m ²	29 (7.7%)	9 (7.1%)	13 (10.2%)	7 (5.7%)	
Vegetable and fruit intake					0.92
< 5 servings per day	367 (97.3%)	123 (97.6%)	124 (96.9%)	120 (97.6%)	
≥ 5 servings per day	10 (2.7%)	3 (2.4%)	4 (3.1%)	3 (2.4%)	
Number of days per week of fruit and vegetable intake					0.86
≤ 4 days	24 (6.4%)	9 (7.1%)	7 (5.5%)	8 (6.5%)	
> 4 days	353 (93.6%)	117 (92.9%)	121 (94.5%)	115 (93.5%)	
Sleep duration in hours					0.61
> 7	72 (19.1%)	22 (17.5%)	21 (16.4%)	29 (23.6%)	
6–7	251 (66.6%)	88 (69.8%)	87 (68.0%)	76 (61.8%)	
5–6	38 (10.1%)	10 (7.9%)	16 (12.5%)	12 (9.8%)	
< 5	16 (4.2%)	6 (4.8%)	4 (3.1%)	6 (4.9%)	
Obstructive Sleep Apnea					0.57
Low risk of OSA	302 (80.1%)	104 (82.5%)	103 (80.5%)	95 (77.2%)	
High risk of OSA	75 (19.9%)	22 (17.5%)	25 (19.5%)	28 (22.8%)	
Family of Hypertension					0.56
No	314 (83.3%)	104 (82.5%)	104 (81.3%)	106 (86.2%)	
Yes	63 (16.7%)	22 (17.5%)	24 (18.8%)	17 (13.8%)	
Family of Diabetes Mellitus					0.88
No	285 (75.6%)	96 (76.2%)	98 (76.6%)	91 (74.0%)	
Yes	92 (24.4%)	30 (23.8%)	30 (23.4%)	32 (26.0%)	
DTG-ART duration					0.36
≤ 2years	112 (29.7%)	43 (34.1%)	37 (28.9%)	32 (26.0%)	
> 2years	265 (70.3%)	83 (65.9%)	91 (71.1%)	91 (74.0%)	

Table 2. Distribution of Metabolic Syndrome, its Components and Biochemical Parameters by ALT-to-HDL-C Status.

Variable: n(%), Median(IQR)	Total N = 377	ALT-to-HDL-C tertiles			p-value
		First N = 126	Second N = 128	Third N = 123	
Metabolic syndrome					
Absent	209 (55.4%)	88 (69.8%)	67 (52.3%)	54 (43.9%)	<0.001
Present	168 (44.6%)	38 (30.2%)	61 (47.7%)	69 (56.1%)	
High fasting plasma glucose					
Absent	322 (85.4%)	115 (91.3%)	112 (87.5%)	95 (77.2%)	0.005
Present	55 (14.6%)	11 (8.7%)	16 (12.5%)	28 (22.8%)	
Central obesity					0.32
Absent	202 (53.6%)	69 (54.8%)	62 (48.4%)	71 (57.7%)	<0.001
Present	175 (46.4%)	57 (45.2%)	66 (51.6%)	52 (42.3%)	
Low high-density lipoprotein levels					
Absent	196 (52.0%)	107 (84.9%)	62 (48.4%)	27 (22.0%)	0.48
Present	181 (48.0%)	19 (15.1%)	66 (51.6%)	96 (78.0%)	
High blood pressure					
Absent	145 (38.5%)	50 (39.7%)	44 (34.4%)	51 (41.5%)	0.034
Present	232 (61.5%)	76 (60.3%)	84 (65.6%)	72 (58.5%)	
Elevated triglycerides					
Absent	112 (29.7%)	27 (21.4%)	46 (35.9%)	39 (31.7%)	<0.001
Present	265 (70.3%)	99 (78.6%)	82 (64.1%)	84 (68.3%)	
Total cholesterol					
< 200 mg/dL	266 (70.6%)	72 (57.1%)	93 (72.7%)	101 (82.1%)	<0.001
≥ 200 mg/dL	111 (29.4%)	54 (42.9%)	35 (27.3%)	22 (17.9%)	
LDL-cholesterol					
< 130 mg/dL	328 (87.0%)	118 (93.7%)	111 (86.7%)	99 (80.5%)	0.008
≥ 130 mg/dL	49 (13.0%)	8 (6.3%)	17 (13.3%)	24 (19.5%)	
ALP(IU/L)	101 (82–119)	104.9 (93–119)	99 (83–120.5)	98 (74–116)	0.058
GGT(IU/L)	19 (13–29)	20.1 (13–29.1)	19 (14–27)	19 (14–28)	0.99
Na ⁺ (mmol/L)	137.8 (135.4–141)	138.95 (135.5–141.8)	137.9 (135.95–140.1)	137.1 (134.3–141.1)	0.26
K ⁺ (mmol/L)	4.0 (3.8–4.4)	4.0 (3.8–4.3)	4.1 (3.8–4.5)	4.0 (3.8–4.5)	0.79
Cl [−] (mmol/L)	99.4 (97.3–102.7)	100.4 (97.4–103.1)	99.3 (97.7–102.7)	98.8 (97–101.6)	0.063

Table 3. Association Between High ALT-to-HDL-C Ratio and Metabolic Syndrome.

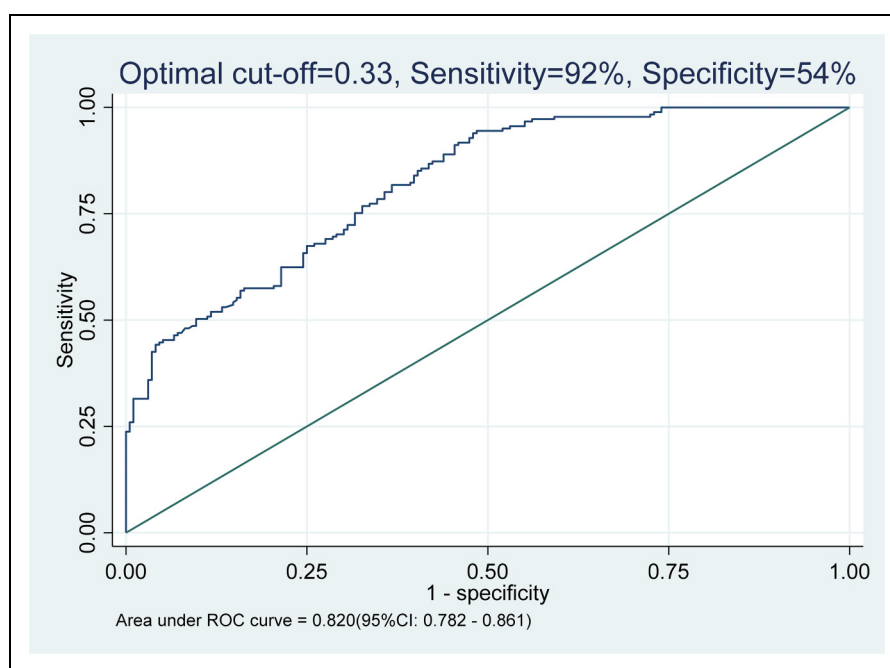
Variable	Bivariate analysis		Multivariate analysis	
	cOR(95%CI)	P-value	aOR(95%CI)	P-value
ALT/HDL-C ratio				
First tertile	1.00		1.00	
Second tertile	2.11(1.26–3.53)	0.005	2.35(1.26–4.41)	0.008
Third tertile	2.95(1.75–4.98)	<0.001	4.65(2.25–9.61)	<0.001
AST/HDL-C ratio				
First tertile	1.00		1.00	
Second tertile	1.59(0.96–2.63)	0.074	1.16(0.61–2.21)	0.640
Third tertile	1.89(1.14–3.13)	0.014	0.99(0.49–2.01)	0.977
Age	1.03(1.01–1.04)	<0.001	1.01(0.99–1.04)	0.346
Sex				
Male	1.00		1.00	
Female	3.51(2.27–5.42)	<0.001	4.97(2.84–8.72)	<0.001
Education level				
No education	1.00		1.00	
Primary	0.82(0.43–1.56)	0.548	0.88(0.38–2.01)	0.755
Secondary	0.75(0.40–1.40)	0.367	1.19(0.49–2.87)	0.698
Tertiary	0.32(0.18–0.56)	<0.001	0.54(0.21–1.36)	0.193
Residence				
Urban	1.00			
Rural	1.32(0.87–1.98)	0.190		
Religion				
Catholic	1.00			
Protestant	1.09(0.66–1.80)	0.743		
Moslem	1.95(0.88–4.33)	0.102		
Others	0.93(0.53–1.62)	0.793		
Employment status				
Unemployed	1.00			
Employed	0.77(0.44–1.34)	0.356		
Ventilated kitchen				
No	0.67(0.37–1.21)	0.187		
Yes	1.00			
Smoking				
Non smoker	1.00		1.00	
Ever smoked	1.65(0.88–3.09)	0.116	2.33(1.05–5.18)	0.038
Alcohol consumption status				
Never consumed	1.00		1.00	
Ever consumed	0.63(0.41–0.95)	0.029	0.61(0.36–1.00)	0.054
Body mass index				
< 25 kg/m ²	1.00		1.00	
25–29 kg/m ²	2.32(1.42–3.79)	0.001	1.90(1.06–3.39)	0.031
≥ 30 kg/m ²	3.73(1.64–8.53)	0.001	2.24(0.84–5.98)	0.106
Vegetable and fruit intake				
< 5 servings per day	1.21(0.33–4.37)	0.769		
≥ 5 servings per day	1.00			
Fruit and vegetable intake in a week				
≤ 4 days	0.49(0.20–1.21)	0.123		
> 4 days	1.00			
Sleep quality				
Good	1.00		1.00	
Poor	1.15(0.73–1.81)	0.553	0.66(0.35–1.22)	0.183
Sleep duration (Hours)				
> 7	1.00		1.00	
≤ 7	0.66(0.40–1.11)	0.120	0.77(0.41–1.46)	0.425
Obstructive Sleep Apnea(OSA)				
Low risk of OSA	1.00		1.00	
High risk of OSA	1.78(1.07–2.96)	0.027	1.75(0.78–3.92)	0.177

(continued)

Table 3. Continued.

Variable	Bivariate analysis		Multivariate analysis	
	cOR(95%CI)	P-value	aOR(95%CI)	P-value
Family History of Hypertension				
No	1.00		1.00	
Yes	1.99(1.15–3.44)	0.014	1.55(0.73–3.31)	0.253
Family History of DM				
No	1.00			
Yes	1.19(0.74–1.91)	0.469		
DTG-based ART duration				
≤ 2years	1.00		1.00	
> 2years	2.22(1.39–3.53)	0.001	1.21(0.65–2.28)	0.544
Total cholesterol	0.99(0.99–1.00)	0.049		
LDL-Cholesterol	1.00(1.00–1.01)	0.716		
ALP	1.00(1.00–1.01)	0.788	1.00(1.00–1.01)	0.477
GGT	0.99(0.98–1.01)	0.482	0.99(0.97–1.01)	0.385
Na+	0.97(0.93–1.00)	0.064	0.97(0.93–1.01)	0.138
K+	0.81(0.57–1.14)	0.223	0.75(0.49–1.15)	0.190
Cl-	0.98(0.95–1.01)	0.179	0.99(0.95–1.03)	0.556

cOR: Crude Odds ratio, aOR: adjusted Odds ratio, CI: 95% Confidence interval.

**Figure 2.** Receiver operating characteristic curve showing predictive performance of ALT-to-HDL-C ratio for MetS.

PLWH on DTG-based ART. Participants in the second tertile of ALT-to-HDL-C ratio had 2.35-fold higher odds of MetS and those in the third tertile had 4.65-fold higher odds of MetS compared to those in the first tertile. This indicates that an elevated ALT-to-HDL-C ratio reflecting both increased liver injury and lower protective HDL is a potential marker of metabolic dysregulation in this population. In terms of diagnostic performance, the ALT-to-HDL-C ratio showed good discriminative ability with AUC of 0.820. At

the optimal cutoff of 0.33, sensitivity was very high (92%) while specificity was modest (54%), meaning that nearly all subjects with MetS would be identified, but about half of those without MetS would be false positives. Clinically, this suggests ALT-to-HDL-C ratio has potential as a screening indicator for MetS due to high sensitivity but would require confirmatory tests because of moderate specificity. The ease of obtaining ALT and HDL-C levels makes the ratio a practical noninvasive marker. Indeed, similar metabolic risk

indices have been proposed in other contexts: for example, Zhou et al recently found that a higher ALT-to-HDL-C ratio strongly correlated with insulin resistance and could serve as a screening indicator in American adults.²⁰ Likewise, Xuan et al showed that ALT-to-HDL-C was a useful noninvasive diagnostic tool for identifying NAFLD; a hepatic manifestation of MetS.²¹ These and our results together suggest that ALT-to-HDL-C ratio captures key elements of MetS and has substantial predictive power as a biomarker.

To the best of our knowledge, no published study to date has directly examined the ALT-to-HDL-C ratio in relation to MetS either in the general population or among PLWH on DTG-based ART. Rather, the ALT-to-HDL-C ratio has been studied mainly for related metabolic conditions such as type 2 Diabetes Mellitus, insulin resistance, and NAFLD. In these contexts, findings broadly support our results. For example, Xuan et al (US population) found that higher ALT-to-HDL-C ratio was independently associated with NAFLD and liver fibrosis,²¹ concluding that the ratio is a useful noninvasive diagnostic tool to identify individuals at high metabolic risk. Similarly, Zhou et al analyzed NHANES data and reported that ALT-to-HDL-C ratio was significantly correlated with insulin resistance and yielded higher AUC for IR (0.725 in men, 0.696 in women) than ALT or HDL alone.²⁰ Although their AUC values are lower than our 0.820, the pattern is consistent: elevated ALT-to-HDL-C ratio flags metabolic disturbance. Studies linking ALT-to-HDL-C to diabetes also mirror our findings. Cao et al (Japanese cohort) showed a positive association between higher baseline ALT-to-HDL-C ratio and incident type 2 diabetes mellitus.³⁵ In another community survey, an ALT-to-HDL-C ratio higher than 14.9 (HDL-C in mmol/L) was associated with 44% higher odds of diabetes mellitus,³⁶ leading authors to suggest ALT-to-HDL-C ratio as a combined marker for DM risk. These observations agree that ALT-to-HDL-C ratio rises with worsening metabolic syndrome elements and hence it's strong linkage to MetS. Independently, several studies have shown ALT alone predicts MetS and diabetes. For instance, Goessling et al found that each standard-deviation increase in log(ALT) raised 20-year odds of MetS by about 21%.³⁷ In effect, combining ALT (liver injury) with HDL-C into one ratio enhances sensitivity to metabolic derangements consistent with the superior performance of ALT-to-HDL-C ratio over single markers seen elsewhere.^{21,37}

Not all previous findings align perfectly with our study results. Cao et al cautioned that in their population the ALT-to-HDL-C ratio was only a moderate predictor of Diabetes Mellitus (AUC 0.75) and recommended it as a secondary marker rather than a primary screening tool.³⁵ By contrast, our AUC of 0.820 suggests stronger overall discrimination power of ALT-to-HDL-C ratio for MetS. This discrepancy may reflect differences in outcome (a composite syndrome vs diabetes alone), ethnicity, or study design. Xuan et al²¹ observed a higher cut-off point

(ALT-to-HDL-C = 0.53) for NAFLD risk, much above our 0.33 cutoff; such variation also comes from different outcome variables (NAFLD vs MetS) though the two share common metabolic derangements. Furthermore, in Zhou's US cohort, ALT-to-HDL-C ratio was more predictive in older or obese participants,²⁰ implying that demographic factors can influence its utility. Our high sensitivity (94%) and modest specificity (52%) likewise suggest the ratio is especially good for ruling out MetS but less specific, a feature also seen in some diabetes studies.

In summary, this study demonstrates a strong association between the ALT-to-HDL-C ratio and MetS among PLWH receiving DTG-based ART, with a ratio ≥ 0.33 showing good discriminatory performance. While our findings align with prior evidence linking ALT-to-HDL-C ratio to insulin resistance, diabetes, and NAFLD, they should be interpreted with caution. Some methodological limitations including the cross-sectional study design, reliance on some self-reported variables, and the possibility of residual confounding limit the strength of causal inference. Moreover, the paradoxical patterns observed for elevated triglycerides and total cholesterol across ALT-to-HDL-C tertiles highlight internal inconsistencies that warrant further investigation rather than assumptions of biological coherence. To avoid overstating the clinical applicability of this biomarker, we emphasize that prospective studies with longitudinal follow-up, comprehensive metabolic and inflammatory assessments, and more rigorous control of potential confounders are needed to validate these findings and determine whether the ALT-to-HDL-C ratio has practical utility for identifying MetS in this population.

Conclusion

This study found a strong and graded association between higher ALT-to-HDL-C ratio and MetS among PLWH on DTG-based ART in Southwestern Uganda. The ALT-to-HDL-C ratio also demonstrated good discriminatory performance, with an optimal cutoff of 0.33 yielding high sensitivity for identifying individuals with MetS. These findings suggest that this ratio, derived from routinely available clinical tests, may serve as a practical adjunct marker for early identification of metabolic risk in HIV care settings. However, prospective studies are needed to validate this association, assess temporal relationships, and determine whether integrating the ALT-to-HDL-C ratio into metabolic risk screening improves detection of MetS.

Limitations and Recommendations

We acknowledge that some confounders related to liver function, metabolic status, and HIV virological suppression were not captured in the primary study. Information on presence or stage of other chronic liver diseases, the

dose and frequency of alcohol use, and concomitant hepatotoxic medications (including non-ART drugs), HIV viral load, and CD4 count was not available in the dataset and therefore could not be controlled for in our analysis. Consequently, despite adjusting for all relevant confounders available in our data, the possibility of residual confounding remains, and the observed associations should be interpreted with caution. Additionally, some variables including family history of hypertension and diabetes mellitus, alcohol use and smoking were self-reported and therefore there is a likelihood of provision of incorrect information. The generalizability of our results is restricted to PLWH on DTG-based ART, and the findings might not be relevant to other populations or to individuals on other ART regimens. Our results showed that high triglycerides and total cholesterol were most common in the lowest ALT-to-HDL-C ratio tertile may challenge the ratio's comprehensiveness as a metabolic marker. Finally, our discussion referenced evidence on NAFLD, insulin resistance, and diabetes mellitus to provide biological context, although these conditions were not directly assessed in our dataset.

In light of the limitations identified in this study, several areas warrant further investigation to strengthen understanding of the relationship between the ALT-to-HDL-C ratio and MetS among PLWH receiving DTG-based ART. Longitudinal studies are needed to establish temporal and causal pathways linking elevated ALT-to-HDL-C ratio to the development of MetS, overcoming the limitations of cross-sectional data. Future research should also incorporate objective clinical and biochemical measures rather than self-reported information for variables such as family history, smoking, and alcohol use to minimize misclassification. A more comprehensive assessment of potential confounders, including detailed alcohol intake, liver disease evaluation, HIV viral load, CD4 count, and concomitant medications, is essential. Interventional studies could further examine whether lifestyle modification or lipid-lowering therapy in individuals with elevated ALT-to-HDL-C ratio reduces MetS risk. Finally, studies involving more diverse HIV-positive populations across different ART regimens and geographic settings are needed to enhance the generalizability of these findings.

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Ethical Approval and Informed Consent

Ethical approval for the primary study¹ was obtained from the Research Ethics Committee (REC) of Mbarara University of Science and Technology (REC number: MUST-2024-1575) on June 10, 2024. All participants provided written informed consent prior to enrollment. To ensure comprehension, the consent forms were translated into the local language, Runyankore. Participants with formal education provided consent by signing the forms, whereas for those without formal education, the consent form was read aloud in Runyankore, followed by administration of a comprehension screening tool approved by the REC. Only participants who demonstrated understanding were allowed to provide consent via thumbprint. Participants were also explicitly asked for consent to allow their data to be used for secondary analysis, which they approved. This study was conducted in accordance with the Declaration of Helsinki (1975), as revised in 2024. Participant confidentiality was maintained by assigning study codes that were not traceable to individuals, and all personal identifiers were removed to protect privacy. Permission to conduct the secondary analysis was obtained from the principal investigator of the primary study.

Consent for Publication

All authors have consented to the publication of this work.

Authors' Contributions

CNB and CN participated in conceptualization of the study. CNB did data analysis and results interpretation. CNB, CN, MJM, B.A, A.O, DN, J.T, C.L, BM, LOO, B.S and R.O.O contributed to writing the first draft of the manuscript with C.L, BM, LOO, B.S and R.O.O providing critical revisions. All authors read and approved the first draft of the manuscript.

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Availability of Data and Materials

The data set for this study is available upon reasonable request from the corresponding author.

References

- Wei H, Qiu Z, Gao Z, Wei Y, Xiao J, Huang W. Metabolic syndrome and the risk of incident heart failure: a prospective cohort study. *American Journal of Preventive Cardiology*. 2025;101279.
- Bosho DD, Dube L, Mega TA, Adare DA, Tesfaye MG, Eshetie TC. Prevalence and predictors of metabolic syndrome among people living with human immunodeficiency virus (PLWHIV). *Diabetol Metab Syndr*. 2018;10(1):10. doi:10.1186/s13098-018-0312-y
- Kiyimba T, Kigozi F, Yiga P, et al. The cardiometabolic profile and related dietary intake of Ugandans living with HIV and AIDS. *Front Nutr*. 2022;9:976744. doi:10.3389/fnut.2022.976744
- Rochlani Y, Pothineni NV, Kovelamudi S, Mehta JL. Metabolic syndrome: Pathophysiology, management, and modulation by natural compounds. *Ther Adv Cardiovasc Dis*. 2017;11(8):215-225. doi:10.1177/1753944717711379
- Chopra AK. Metabolic syndrome or insulin resistance: Evolution, controversies and association with cardiovascular disease risk. *Indian Journal of Clinical Cardiology*. 2020;1(2):77-85. doi:10.1177/2632463620935030
- Jemal M. A review of dolutegravir-associated weight gain and secondary metabolic comorbidities. *SAGE Open Med*. 2024;12:20503121241260613. doi:10.1177/20503121241260613
- Tang J, Chen L, Pan W, et al. Prevalence of metabolic syndrome in people living with HIV and its multi-organ damage: A prospective cohort study. *BMC Infect Dis*. 2025;25(1):351. doi:10.1186/s12879-025-10735-7
- Mirai TE, Kilonzo KG, Sadiq AM, et al. Metabolic syndrome and associated factors among people living with HIV on dolutegravir-based antiretroviral therapy in northern Tanzania. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2024;23:23259582241306492. doi:10.1177/23259582241306492
- Muyanja D, Muzoora C, Muyingo A, Muyindike W, Siedner MJ. High prevalence of metabolic syndrome and cardiovascular disease risk among people with HIV on stable ART in southwestern Uganda. *AIDS Patient Care STDS*. 2016;30(1):4-10. doi:10.1089/apc.2015.0213
- Timbigamba F, Bagenda CN, Sembogga H, et al. Dyslipidemia and associated factors among people living with HIV on dolutegravir-based antiretroviral therapy in central Uganda. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2025;24:23259582251395549. doi:10.1177/23259582251395549
- Byereta LH, Olum R, Mutebi EI, et al. Prevalence and factors associated with hyperglycemia among persons living with HIV/AIDS on dolutegravir-based antiretroviral therapy in Uganda. *Ther Adv Infect Dis*. 2024;11:20499361241272630. doi:10.1177/20499361241272630
- Kigongo VJ, Nankabirwa JI, Kitutu FE, et al. Dyslipidemia among adult people living with HIV on dolutegravir-based antiretroviral therapy at a private tertiary hospital in Kampala, Uganda: Burden and determinants. *BMC Infect Dis*. 2024;24(1):53. doi:10.1186/s12879-023-08892-8
- Kasoma Mutebi R, Weil Semulimi A, Mukisa J, et al. Prevalence of and factors associated with hypertension among adults on dolutegravir-based antiretroviral therapy in Uganda: A cross sectional study. *Integr Blood Press Control*. 2023;16:11-21. doi:10.2147/IBPC.S403023
- Nsengumuremyi H, Nsanzimana V, Mapira HT, Gori E, Musarurwa C. Spectrum and correlates of dyslipidemia in people living with HIV on dolutegravir-based regimen attending Kabutare hospital, southern Rwanda: A cross-sectional study. *HIV/AIDS-Research and Palliative Care*. 2025;17:203-213. doi:10.2147/HIV.S529826
- Hirigo AT, Abera A, Yilma D, Astatkie A, Debebe Z. The association between dolutegravir based first-line antiretroviral regimens and dyslipidemia among adults living with HIV on follow-up at health facilities in Hawassa city administration, Sidama region: A cross-sectional study. *Atherosclerosis Plus*. Sep 2025;61:48-57. doi:10.1016/j.athplu.2025.08.001
- Nakatudde I, Katana E, Agnes Odongpiny EL, et al. Prevalence of overweight and obesity among adolescents living with HIV after dolutegravir-based antiretroviral therapy start in Kampala, Uganda. *AIDS Res Ther*. 2024;21(1):23. doi:10.1186/s12981-024-00615-6
- Kasibante NM, Tokema N, Kilama AD, et al. Prevalence of weight gain and associated factors among people living with HIV 6-and 12-months post dolutegravir-based antiretroviral regimen initiation in Gulu, Uganda; A hospital-based retrospective cohort study. *HIV/AIDS-Research and Palliative Care*. 2025;17:361-372. doi:10.2147/HIV.S548947
- Nzaramba D, Bagenda CN, Mudondo H, et al. Low Aspartate Aminotransferase/Alanine Aminotransferase Ratio as an Indicator of Metabolic Syndrome Among HIV Patients on Dolutegravir Therapy in Southwestern Uganda. *Cureus*. 2025;17(1).
- Wood BR, Huhn GD. Excess weight gain with integrase inhibitors and tenofovir alafenamide: what is the mechanism and does it matter? Paper presented at: Open forum infectious diseases 2021.
- Zhou X, Xu J, Dai H. The ratio of alanine aminotransferase to high-density lipoprotein cholesterol is positively correlated with the insulin resistance in American adults: A population-based cohort study. *Front Med (Lausanne)*. 2024;11:1418364. doi:10.3389/fmed.2024.1418364
- Xuan Y, Wu D, Jin Y, Yu X, Yu J, Zhang Y. Utility of the serum alanine aminotransferase to high density lipoprotein cholesterol ratio in evaluating nonalcoholic fatty liver disease and liver fibrosis. *Sci Rep*. 2025/07/01 2025;15(1):21292. doi:10.1038/s41598-025-06171-x
- Xuan Y, Wu D, Zhang Q, Yu Z, Yu J, Zhou D. Elevated ALT/AST ratio as a marker for NAFLD risk and severity: Insights from a cross-sectional analysis in the United

- States. *Front Endocrinol (Lausanne)*. 2024;15:1457598. doi:10.3389/fendo.2024.1457598
23. Wang Z, Barinas-Mitchell E, Brooks MM, et al. HDL-C criterion of the metabolic syndrome and future diabetes and atherosclerosis in midlife women: The SWAN study. *American Journal of Preventive Cardiology*. 2024;19:100687. doi:10.1016/j.ajpc.2024.100687
 24. Zhou X, Xu J, Dai H. The ratio of alanine aminotransferase to high-density lipoprotein cholesterol is positively correlated with the insulin resistance in American adults: A population-based cohort study. *Front Med (Lausanne)*. 2024;11:1418364. doi:10.3389/fmed.2024.1418364
 25. Elm V, Altman E, Egger DG, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453-1457. doi:10.1016/S0140-6736(07)61602-X
 26. Grundy SM, Cleeman JJ, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/national heart, lung, and blood institute scientific statement. *Circulation*. 2005;112(17):2735-2752. doi:10.1161/CIRCULATIONAHA.105.169404
 27. Federation ID. The IDF consensus worldwide definition of the metabolic syndrome. *IDF Communications*. 2006;23(5):1-24.
 28. 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(16):1640-1645.
 29. Nagappa M, Liao P, Wong J, et al. Validation of the STOP-bang questionnaire as a screening tool for obstructive sleep apnea among different populations: A systematic review and meta-analysis. *PloS One*. 2015;10(12):e0143697.
 30. Avelino DC, Ad S, Chaves LO, Carraro JCC, FdC V, Bressan J. Triglyceride-glucose index is associated with poor sleep quality in apparently healthy subjects: A cross-sectional study. *Arch Endocrinol Metab*. 2022;67(1):73-91.
 31. Bertolazi AN, Fagundes SC, Hoff LS, et al. Validation of the Brazilian Portuguese version of the Pittsburgh sleep quality index. *Sleep Med*. 2011;12(1):70-75.
 32. Organization WH. Obesity: preventing and managing the global epidemic: report of a WHO consultation. 2000.
 33. Hannon BA, Khan NA, Teran-Garcia M. Nutrigenetic contributions to dyslipidemia: A focus on physiologically relevant pathways of lipid and lipoprotein metabolism. *Nutrients*. 2018;10(10):1404.
 34. Çorbacıoğlu ŞK, Aksel G. Receiver operating characteristic curve analysis in diagnostic accuracy studies: A guide to interpreting the area under the curve value. *Turkish Journal of Emergency Medicine*. 2023;23(4):195-198.
 35. Cao C, Hu H, Han Y, et al. The nonlinear correlation between alanine aminotransferase to high-density lipoprotein cholesterol ratio and the risk of diabetes: A historical Japanese cohort study. *BMC Endocr Disord*. 2023/05/29 2023;23(1):124.
 36. Emamian A, Emamian MH, Hashemi H, Fotouhi A. The association of ALT to HDL-C ratio with type 2 diabetes in 50–74 years old adults: A population-based study. *Sci Rep*. 2024/04/24 2024;14(1):9390.
 37. Goessling W, Massaro JM, Vasan RS, D'Agostino RS, Ellison RC, Fox CS. Aminotransferase levels and 20-year risk of metabolic syndrome, diabetes, and cardiovascular disease. *Gastroenterology*. Dec 2008;135(6):1935-1944. 1944.e1931.