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Prevalence and risk factors of metabolic dysfunction-associated steatotic liver disease in south Central Uganda: A cross-sectional survey

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Summary

Background: Despite numerous risk factors and serious consequences, little is known about metabolic dysfunction-associated steatotic liver disease (MASLD) at population level in Africa.

Aim: The aim of the study was to estimate the prevalence and risk factors of MASLD in people living with and without HIV in Uganda.

Methods: We collected data from 37 communities in South Central Uganda between May 2016 and May 2018. We estimated MASLD prevalence using the fatty liver index and advanced liver fibrosis using the dynamic aspartate-to-alanine aminotransferase ratio. We collected additional data on sociodemographics, HIV and cardiovascular disease (CVD) risk factors. We used multivariable logistic regression to determine the association between HIV, CVD risk factors and MASLD.

Results: We included 759 people with HIV and 704 HIV-negative participants aged 35–49. MASLD prevalence was 14% in women and 8% in men; advanced liver

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fibrosis prevalence was estimated to be <1%. MASLD prevalence was more common in women (15% vs. 13%) and men (9% vs. 6%) with HIV. Being female (odds ratio [OR] = 2.1; 95% confidence interval [CI] = 1.4–3.3) was associated with a higher odds of MASLD after adjustment for confounders; HIV infection was borderline associated with MASLD (OR = 1.4; 95% CI: 1.0–2.0).

Conclusions: In a relatively young cohort in Uganda, 14% of women and 8% of men had MASLD. There was an indication of an association between HIV and MASLD in multivariable analysis. These data are the first to describe the population-level burden of MASLD in sub-Saharan Africa using data from a population-based cohort.

1 | INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as Non-Fatty Liver disease (NAFLD), is the most common chronic liver disease with an estimated global prevalence of 32%.[1] However, estimates from Africa, feeding into the global prevalence estimate, are based on very few, non-population-based studies.

MASLD encompasses a spectrum of conditions which are characterised by hepatic steatosis, the deposit of fat in the liver, and in addition presence of a cardiometabolic risk factor.[2] While the majority of previous studies have used the NAFLD definition, it has been estimated that 99% of NAFLD patients meet the MASLD criteria.[3] MASLD is recognised as the hepatic manifestation of metabolic syndrome while additionally being an independent risk factor for cardiovascular disease (CVD), diabetes and all-cause mortality.[4,5]

For people living with HIV, antiretroviral therapy (ART) has had a substantial impact on life expectancy such that CVD, non-AIDS-related malignancies and liver disease are now the leading causes of mortality for this population.[6] MASLD is increasingly recognised as a major contributor to liver diseases among people living with HIV in high-income settings and likely to become the leading cause of liver cirrhosis in the future, overtaking viral hepatitis.[7,8] A meta-analysis conducted in people living with HIV from high-income settings found a high prevalence of MASLD (32%) with non-alcoholic steatohepatitis and liver fibrosis a common finding among those selected for liver biopsy.[9] The increased risk for MASLD among people living with HIV is thought to be multifactorial, including the disproportional prevalence of traditional CVD risk factors, HIV infection itself and the use of ART.[10]

In sub-Saharan Africa (SSA), home to two thirds of all people living with HIV, there are few available studies on the prevalence of MASLD in the general population as well as in the people living with HIV population.[11,12] This is likely a result of limited access or unavailability of tools for MASLD diagnosis.[13] However, for the study of steatosis at the population level, the use of serum biomarkers is an alternative that has been recommended with the fatty liver index (FLI) being the best validated while additionally being found accurate for use in in people living with HIV populations.[14–16] The FLI is an algorithm that utilises serum and anthropometric measurements and has been found to be associated with liver-related and all-cause mortality.[17,18]

Given the scarcity of MASLD burden data available in SSA and particularly data drawn from population-based studies, this study aims to further gain insight into the prevalence of MASLD measured using FLI, by HIV status and investigate the association between HIV, socio-economic and CVD risk factors drawn from a large population-based cohort in South Central Uganda.

2 | METHODS

2.1 | Study design and sample selection

The data source for this study has been described in detail elsewhere.[19,20] In brief, the Rakai Community Cohort Study (RCCS) is an open population-based cohort established in 1994 by the Rakai Health Sciences Programme in South Central Uganda. For the current study, 37 communities were included. For possible inclusion into the RCCS, participants must be between the ages of 15–49 and be resident for at least 6 months. Approximately 18,000 individuals participate in each survey round, with a response rate among age eligible persons of about 78% with losses due primarily to out-migration, absentia due to work or school.

The current study was nested into the 18th survey round of the RCCS, which took place from May 2016 to May 2018. The following data were collected from all participants aged 35–49 that provided consent: sociodemographic and CVD risk factors data from questionnaires; anthropometric (weight, height, hip and waist circumference) and blood pressure measurements; HIV status based on a three rapid test algorithm with a confirmatory laboratory test for incident cases[21]; and non-fasting venous blood samples for laboratory

measurements. The study sample included the oldest age category in the study population, those aged 35–49.

In total, 4865 participants aged 35–49 participated in the 18th survey round, 1018 participants living with HIV and 3847 HIV-negative participants. Among these, 1013 participants living with HIV provided venous blood samples that were then matched 1:1 by sex to HIV-negative participants using simple random sampling for a total initial sample of 2026 participants. Then 563 participants were excluded, either due to pregnancy ($n=57$), being under the age of 35 ($n=1$) or being a frequent alcohol drinker ($n=505$). Pregnant women were excluded from the analysis as pregnancy would have an impact on measurements of body mass index, waist circumference and possibly biochemical profile. Participants that reported frequent alcohol consumption (defined as reporting to consume any alcohol in the last 7 days) were excluded. In total, the final sample consisted of 1463 participants (759 HIV+ and 704 HIV−). Figure 1 details the sample selection in full.

2.2 | Variable definitions

MASLD was defined using the FLI, which is an algorithm that utilises four measures: (i) serum levels of triglycerides (in milligrams per decilitre), (ii) gamma-glutamyl transferase (GGT) (in units per litre) (iii) waist circumference (in cm) and (iv) body mass index (BMI) to determine the risk of MASLD.[22] BMI was calculated according to the equation BMI = weight(kg)/height(m^2). The FLI score varies from 0 to 100 with participants that score ≥60 considered to have MASLD.[22]

Liver fibrosis was defined using the dynamic aspartate-to-alanine aminotransferase ratio (dAAR), a model that utilises age (in years), alanine aminotransferase (ALT) (in units per litre) and the aspartate aminotransferase (AST)/ALT ratio to predict 10-year incidence of severe liver disease, a composite of diagnoses attributed to cirrhosis, but also to predict presence of advanced fibrosis (stage 3–4 on liver biopsy) at baseline. The presence of advanced liver fibrosis was considered among participants that scored ≥2.63.[23] We did not use other more established scores such as the FIB-4 since data on platelet count were not available.

Metabolic syndrome was defined according to a modified version of the 2004 National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) definition[24] and considered present with any three of the following conditions: raised blood sugar defined as a non-fasting plasma glucose ≥7.8 mmol/L; increased waist circumference as >102 cm for males and >88 cm for females; high triglycerides ≥1.7 mmol/L or low high-density lipoprotein (HDL) cholesterol <1.03 mmol/L for men and <1.29 mmol/L for women; and raised blood pressure ≥130/85 mm Hg. As fasting blood samples could not be obtained due to the data collection procedures of the RCCS in which participants may be seen over several hours throughout the day, the definition of raised blood sugar was modified using a cut-off 7.8, the definition for hyperglycaemia, as opposed to 5.5 in the standard NCEP-ATP III definition. In addition, BMI was defined as <18.5 kg/m^2 for underweight, ≥18.5 to <25 kg/m^2 for normal, ≥25 to <30 kg/m^2 for overweight and ≥30 kg/m^2 for obese.[25] Finally, GGT, ALT, and AST reference values were defined according to local upper reference cut-off points used by the Rakai Health Science Programme laboratories. Abnormal GGT ranges were defined as ≥70.7 U/L in males and ≥41.3 U/L in females while abnormal ALT ranges were defined as ≥43.4 U/L in males and ≥39.9 U/L in females. Finally abnormal AST ranges were defined as ≥35.9 in males and ≥28.8 U/L in females.

Socio-demographic variables included sex, age, residence location (categorised as rural or semi-urban), education attainment (none, <5, or ≥5 years), occupation (agricultural or non-agricultural

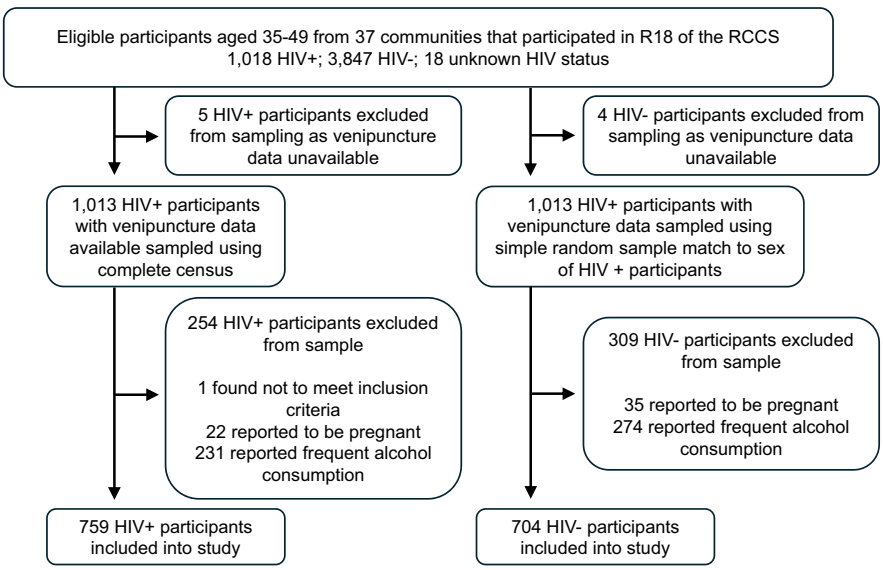

FIGURE 1 Participant selection for MASLD study in Uganda.

TABLE 1 MASLD study participant characteristics by sex and HIV status.

	Females		Males		Total		
Characteristic	**HIV+ *n* (%)**	**HIV− *n* (%)**	**HIV+ *n* (%)**	**HIV− *n* (%)**	**HIV+ *n* (%)**	**HIV− *n* (%)**	**Total *n* (%)**
Age	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Age, mean (SD in years)	41 (4.0)	41 (4.0)	41 (4.0)	41 (4.2)	41 (4.0)	41 (4.0)	41 (4.0)
35–39	220 (41%)	231 (45%)	82 (38%)	73 (39%)	302 (40%)	304 (43%)	606 (41%)
40–44	200 (37%)	186 (36%)	85 (39%)	63 (34%)	285 (38%)	249 (35%)	534 (37%)
45–49	123 (23%)	102 (20%)	49 (23%)	49 (26%)	172 (23%)	151 (21%)	323 (22%)
Residence location	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Rural	272 (50%)	292 (56%)	119 (55%)	93 (50%)	391 (52%)	385 (55%)	776 (53%)
Semi-urban	271 (50%)	227 (44%)	97 (45%)	92 (50%)	368 (48%)	319 (45%)	687 (47%)
Education	*n* = 543	*n* = 518	*n* = 216	*n* = 185	*n* = 759	*n* = 703	*n* = 1462
<5 years of study	170 (31%)	130 (25%)	66 (31%)	50 (27%)	236 (31%)	180 (26%)	416 (28%)
≥5 years of study	373 (69%)	388 (75%)	150 (69%)	135 (73%)	523 (69%)	523 (74%)	1046 (72%)
Occupation[a]	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Agricultural focused	330 (61%)	332 (64%)	95 (44%)	78 (42%)	425 (56%)	410 (58%)	835 (57%)
Non-agricultural focused	213 (39%)	187 (36%)	119 (55%)	107 (58%)	332 (44%)	294 (42%)	626 (43%)
Marital status	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Single	303 (56%)	161 (31%)	51 (24%)	35 (19%)	354 (47%)	196 (28%)	550 (38%)
Married	240 (44%)	358 (69%)	165 (76%)	150 (81%)	405 (53%)	508 (72%)	913 (63%)
Alcohol consumption	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
None	400 (74%)	363 (70%)	130 (60%)	118 (64%)	530 (70%)	481 (68%)	1011 (69%)
Infrequent (last drink >1-month)	143 (26%)	156 (30%)	86 (40%)	67 (36%)	229 (30%)	223 (32%)	452 (31%)
Smoking status	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Non-smoker	532 (98%)	497 (96%)	185 (86%)	167 (90%)	717 (94%)	664 (94%)	1381 (94%)
Smoker	11 (2%)	22 (4%)	31 (14%)	18 (10%)	42 (6%)	40 (6%)	82 (6%)
Physical activity	*n* = 542	*n* = 518	*n* = 215	*n* = 184	*n* = 757	*n* = 702	*n* = 1461
Physically active (>30 min)	523 (96%)	508 (98%)	200 (93%)	179 (97%)	723 (96%)	687 (98%)	1410 (97%)
Physically inactive (≤30 min)	19 (4%)	10 (2%)	15 (7%)	5 (3%)	34 (4%)	15 (2%)	49 (3%)
Daily fruit and vegetable consumption	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	*n* = 1463
Consumption, median servings	1.7	1.4	1.3	1.1	1.6	1.3	1.5
Below average (<1.14 servings)	176 (32%)	221 (43%)	123 (57%)	111 (60%)	299 (39%)	332 (47%)	631 (43%)
Above average (≥1.14 servings)	367 (68%)	298 (57%)	93 (43%)	74 (40%)	460 (61%)	372 (53%)	832 (57%)

Abbreviation: SD, standard deviation.

[a]Information on those that reported to be unemployed (2 HIV+ males, 1 treatment naïve and 1 on treatment) not included in the table but included in the denominator shown.

focused) and marital status (single or currently married). Lifestyle-related CVD variables included alcohol consumption (none or infrequent, defined as last drink more than a week ago), smoking status (smoker or non-smoker), physical activity (exercising or engaging in physical labour above or below 30 min per day) and fruit and vegetable consumption consuming either above or below the daily median consumption of fruit and vegetables among surveyed participants. The variables on physical activity and fruit and vegetable consumption are based on the FINDRISC questionnaire, assessing 10-year risk of developing diabetes.[26]

2.3 | Statistical analyses

Baseline characteristics were tabulated by sex and HIV status. Prevalence rates of MASLD, advanced liver fibrosis and CVD risk

TABLE 2 MASLD and advanced liver fibrosis estimated by fatty liver index and dynamic aspartate-to-alanine aminotransferase ratio, variables and score by sex and HIV status.

	Females		Males		Total			
	HIV+ *n* (%)	HIV− *n* (%)	HIV+ *n* (%)	HIV− *n* (%)	HIV+ *n* (%)	HIV− *n* (%)	*p*-value[a]	Total *n* (%)
FLI	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704		*n* = 1463
Triglycerides (mmol, mean)	1.3	1.3	1.5	1.5	1.3	1.3	0.65	1.3
GGT (U/L, mean)	65.6	20.7	102.0	30.7	76.0	23.3	<0.001	50.6
	n = 542	*n* = 515	*n* = 216	*n* = 185	*n* = 758	*n* = 700		*n* = 1458
Waist circumference (cm, mean)	79.3	82.2	77.4	78.6	78.8	81.2	<0.001	80.0
	n = 542	*n* = 519	*n* = 214	*n* = 184	*n* = 756	*n* = 703		*n* = 1459
BMI, (kg/m^2, mean)	23.4	25.0	21.2	22.3	22.8	24.3	<0.001	23.5
FLI score	*n* = 542	*n* = 515	*n* = 214	*n* = 184	*n* = 756	*n* = 699		*n* = 1455
Low (<30)	356 (66%)	361 (70%)	145 (68%)	144 (78%)	501 (66%)	505 (72%)	0.05	1006 (69%)
Indeterminate (30 to <60)	104 (19%)	88 (17%)	50 (23%)	29 (16%)	154 (20%)	117 (17%)		271 (19%)
High (≥60)[b]	82 (15%)	66 (13%)	19 (9%)	11 (6%)	101 (13%)	77 (11%)	0.17	178 (12%)
dAAR	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704		*n* = 1463
Age (years, mean)	41	41	41	41	41	41	0.38	41
ALT (U/L, mean)	13.9	12.4	17.4	15.3	14.9	13.1	0.01	14.0
AST/ALT ratio	2.5	1.9	2.4	1.8	2.5	1.9	<0.001	2.2
Advanced liver fibrosis (≥2.63)	5 (<1%)	0 (0%)	2 (<1%)	0 (0%)	7 (<1%)	0 (0%)	0.02	7 (<1%)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index, dAAR, dynamic aspartate-to-alanine aminotransferase ratio; FLI, fatty liver index; GGT, gamma-glutamyl transferase.

[a]*p*-values presented in table are either calculated using chi-squared test, *t* test or fisher's exact test and only calculated to assess the difference by HIV status.

[b]Metabolic dysfunction-associated steatotic liver disease (MASLD) is defined as scoring ≥60 on the FLI.

factors (high BMI, metabolic syndrome, including individual CVD risk factor sub-components), were tabulated by sex and HIV status with differences assessed by either chi-squared test, two-tailed *t* test or Fisher's exact test. Bivariate and multivariable logistic regression models were then used to identify variables associated with MASLD. Variables explored in bivariate analysis included socio-demographic factors (age, sex, residence location, occupation and education), HIV risk factors (HIV status), CVD-related risk factors (alcohol consumption, smoking, daily fruit and vegetable consumption, hyperglycaemia, low HDL and raised blood pressure). Physical activity was not included into the analysis given the high prevalence of overall physical activity in our population, 96% among people living with HIV and 98% among HIV negative participants. The CVD risk factors of triglycerides and increased waist circumference were specifically not included in bivariate and multivariable analysis as these variables are used to determine the presence of MASLD using the FLI. Variables that had a $p \leq 0.20$ in bivariate analysis were included in the multivariable model with variables that had a $p \leq 0.05$ considered to be statistically significant. Stata 15 (Stata Corporation, College Station, USA) was used for all analyses.

3 | RESULTS

In our study population, a greater percentage of females were enrolled as compared to the initial sample (73% vs. 63%). The difference is due to a larger percentage of males subsequently excluded from the study due to reporting frequent alcohol consumption as compared to females (44% vs. 15%). The mean age was 41 years, and ART use was reported among 89% of participants living with HIV. Minimal differences were found for CVD behaviour risk factors by HIV status. Table 1 presents complete baseline sociodemographic characteristics of study participants by sex and HIV status.

A total of 178 participants in our study population were classified as having MASLD (defined by a FLI score ≥60), resulting in a prevalence estimate of 14% in women and 8% in men. The MASLD prevalence was slightly higher among participants living with HIV as compared to HIV-negative participants (15% vs. 13% in women, and 9% vs. 6% in men). Evidence of advanced liver fibrosis as defined by a dAAR score ≥2.63, was present in seven participants with an estimated prevalence of <1%. All seven cases with advanced liver fibrosis were found in participants living with HIV (Table 2).

TABLE 3 Prevalence of cardiovascular risk factors by sex and HIV status in MASLD study participants.

	Females		Males		Total			
Variable	**HIV+ *n* (%)**	**HIV− *n* (%)**	**HIV+ *n* (%)**	**HIV− *n* (%)**	**HIV+ *n* (%)**	**HIV− *n* (%)**	***p*-value[a]**	**Total *n* (%)**
BMI	*n* = 542	*n* = 519	*n* = 214	*n* = 184	*n* = 756	*n* = 703	<0.001	*n* = 1459
Underweight (<18.5 kg/m^2)	43 (8%)	24 (5%)	23 (11%)	9 (5%)	66 (9%)	33 (5%)		99 (7%)
Normal (≥18.5 to <25 kg/m^2)	334 (62%)	267 (51%)	174 (81%)	139 (76%)	508 (67%)	406 (58%)		914 (63%)
Overweight & obese (≥25 kg/m^2)	165 (30%)	228 (44%)	17 (8%)	36 (20%)	182 (24%)	264 (38%)		446 (31%)
Waist circumference	*n* = 542	*n* = 515	*n* = 216	*n* = 185	*n* = 758	*n* = 700	<0.001	*n* = 1458
Normal (males: ≤102 cm & females: ≤88 cm)	444 (82%)	382 (74%)	214 (99%)	182 (98%)	658 (87%)	564 (81%)		1222 (84%)
Increased (males: >102 cm & females: >88 cm)	98 (18%)	133 (26%)	2 (1%)	3 (2%)	100 (13%)	136 (19%)		236 (16%)
Blood pressure	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	0.06	*n* = 1463
Normal (<130/85 mm Hg)	387 (71%)	354 (68%)	166 (77%)	127 (69%)	553 (73%)	481 (68%)		1034 (71%)
Raised blood pressure (≥130/85 mm Hg)	156 (29%)	165 (32%)	50 (23%)	58 (31%)	206 (27%)	223 (32%)		429 (29%)
Random plasma glucose	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	0.26	*n* = 1463
Normal (<7.8 mmol/L)	529 (97%)	507 (98%)	214 (99%)	183 (99%)	743 (98%)	690 (98%)		1433 (98%)
Hyperglycaemia (≥7.8 mmol/L)	14 (3%)	12 (2%)	2 (1%)	2 (1%)	16 (2%)	14 (2%)		30 (2%)
HDL	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	<0.001	*n* = 1463
Normal (males: ≥1.03 mmol/L & females: ≥1.29 mmol/L)	180 (33%)	94 (18%)	125 (58%)	51 (28%)	305 (40%)	145 (21%)		450 (31%)
Low (males: <1.03 mmol/L & females: <1.29 mmol/L)	363 (67%)	425 (82%)	91 (42%)	134 (72%)	454 (60%)	559 (79%)		1013 (69%)
Triglycerides	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	0.69	*n* = 1463
Normal (<1.7 mmol/L)	435 (80%)	419 (81%)	158 (73%)	137 (74%)	593 (78%)	556 (79%)		1149 (79%)
High (≥1.7 mmol/L)	108 (20%)	100 (19%)	58 (27%)	48 (26%)	166 (22%)	148 (21%)		314 (21%)
GGT	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	<0.001	*n* = 1463
Normal (males: <70.7 U/L & females: <41.3 U/L)	266 (49%)	481 (93%)	136 (63%)	170 (92%)	402 (53%)	651 (92%)		1053 (72%)
Abnormal (males: ≥70.7 U/L & females: ≥41.3 U/L)	277 (51%)	38 (7%)	80 (37%)	15 (8%)	357 (47%)	53 (8%)		410 (28%)
ALT	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	<0.001	*n* = 1463
Normal (males: <43.4 U/L & females: <39.9 U/L)	528 (97%)	516 (99%)	206 (95%)	183 (99%)	734 (97%)	699 (99%)		1433 (98%)
Abnormal (males: ≥43.4 U/L & females: ≥39.9 U/L)	15 (3%)	3 (1%)	10 (5%)	2 (1%)	25 (3%)	5 (1%)		30 (2%)
AST	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	<0.001	*n* = 1463
Normal (males: <35.9 U/L & females: <28.8 U/L)	399 (73%)	483 (93%)	170 (79%)	178 (96%)	569 (75%)	661 (94%)		1230 (84%)
Abnormal (males: ≥35.9 U/L & females: ≥28.8 U/L)	144 (27%)	36 (7%)	46 (21%)	7 (4%)	190 (25%)	43 (6%)		233 (16%)
Modified metabolic syndrome[b]	*n* = 543	*n* = 519	*n* = 216	*n* = 185	*n* = 759	*n* = 704	0.10	*n* = 1463
Not present	467 (86%)	433 (83%)	203 (94%)	168 (91%)	670 (88%)	601 (85%)		1271 (87%)
Present	76 (14%)	86 (17%)	13 (6%)	17 (9%)	89 (12%)	103 (15%)		192 (13%)

Abbreviations: BMI, body mass index; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein.

[a]*p*-values presented in table were calculated using chi-squared test and only to assess the difference by HIV status.

[b]Modified Metabolic Syndrome was defined according to the 2004 National Cholesterol Education Program's Adult Treatment Panel III as a combination of any three of the following five conditions: increased waist circumference, raised blood pressure, raised blood sugar, low HDL and triglycerides. The threshold for raised blood sugar was modified from 5.5 to 7.8 mmol/L to account for the fact that non-fasting blood samples were used for laboratory measurements.

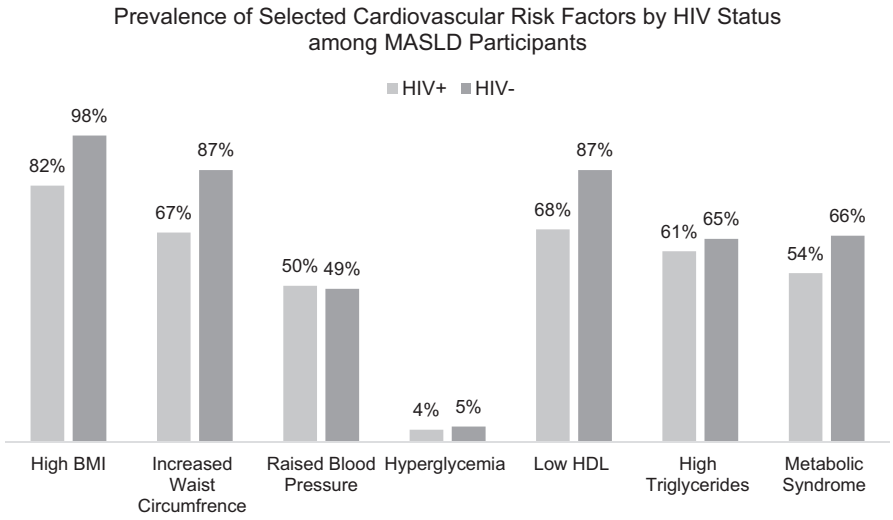

FIGURE 2 Prevalence of cardiovascular risk factors by HIV status among MASLD participants.

Table 3 presents BMI, metabolic syndrome, including individual sub-components and liver enzyme profiles by sex and HIV status. No significant difference was found in the prevalence of metabolic syndrome by HIV status (12% in participants living with HIV vs. 15% in HIV-negative participants, $p=0.10$). Notable differences by HIV status included overweight and obesity as determined by a BMI ≥ 25 kg/m^2 (24% for participants living with HIV vs. 38% for HIV-negative participants, $p<0.001$) and low LDL as determined by a cutoff of <1.03 mmol/L in males and <1.29 mmol/L in females resulting in 60% for participants living with HIV vs. 79% for HIV-negative participants, $p<0.001$. Among participants with MASLD, those living with HIV were found to have both lower individual CVD risk factors and overall metabolic syndrome as compared to HIV-negative participants apart from raised blood pressure defined as ≥130/85 mm Hg (Figure 2).

Bivariate and multivariable logistic regression analyses of socio-economic, HIV and CVD-related risk factors associated with MASLD are presented in Table 4. In multivariable analysis, being female (OR = 2.11, 95% CI = 1.36–3.27, $p=0.001$), having a high blood pressure (OR = 2.64, 95% CI = 1.90–3.68, $p<0.001$) and low HDL (OR = 1.55, 95% CI = 1.05–2.29, $p=0.03$) were associated with a higher odds of MASLD. Having less than 5 years of education (OR = 0.67, 95% CI = 0.45–0.99, $p=0.05$) and working in an agriculture-focused occupation (OR = 0.49, 95% CI = 0.34–0.69, $p<0.001$) was associated with a lower odds of MASLD.

4 | DISCUSSION

This is the first population-based study to our knowledge from sub-Saharan Africa that examines the prevalence of MASLD in persons with and without HIV. As determined by the FLI, we found an overall MASLD prevalence estimate of 14% in women and 8% in men, reflecting a higher BMI in women. There was a tendency, that people living with HIV had a higher odds of MASLD. The prevalence of advanced fibrosis was rare, <1%, but all 7 cases found were in people living with HIV. In multivariable logistic regression, being female, raised blood pressure and low HDL were associated with a higher odds of MASLD.

Our overall MASLD prevalence estimate is broadly consistent with a regional-level MASLD estimate in a global meta-analysis that places the MASLD prevalence lowest in Africa as compared to other regions of the world (14% in women and 8% in men, as compared to 32% globally).[1] However, of 8,500,000 individuals included in the meta-analysis, only 250 were from Africa, and of these 33 participants had MASLD, resulting in a prevalence of 13%.[27,28] Outside of the meta-analysis, there are three studies available for comparison, two conducted in diabetic populations and one in overweight or obese population with MASLD estimates ranging from 17% to 47%.[29–31] Of these studies, only one included a general population comparison group in which MASLD was estimated to be 1.2%.[29] Given the variation in the limited set of published estimates, further research is warranted to better characterise MASLD across SSA given the heterogeneous nature of populations within the region.

In relation to estimates conducted in participants living with HIV, there are two studies available for comparison, and none that used the FLI: A South African study that reported an estimate of 28% using liver biopsies and a Nigerian study that reported an estimate of 13% using ultrasound.[32,33] The South African prevalence estimate is likely to be an overestimation given that the study was a retrospective review of biopsies conducted in a hospital setting with biopsies likely collected among those suspected of having severe liver disease. Regardless, the South African study did include a small comparison population of HIV-negative participants and found that participants living with HIV were more likely to present with steatosis as compared to HIV-negative participants. In our study, MASLD was more common in people living with HIV, albeit not reaching statistical significance. All seven cases of advanced fibrosis were found in people living with HIV. Given the limited body of research available for comparison in SSA, further research to better understand if people living with HIV are at increased risk for MASLD and the role, if any, that HIV infection or ART play is needed.

Regardless of HIV status, female participants presented with higher prevalence rates of both MASLD and metabolic syndrome as

TABLE 4 Influence of HIV status, socio-economic status and CVD-related risk factors on MASLD.

	Bivariate[a] OR (95% CI)	*p*-value[a]	Multivariable OR (95% CI)	*p*-value
HIV status				
HIV−	Ref.	0.17	Ref.	
HIV+	1.25 (0.91–1.71)		1.39 (1.00–1.95)	0.06
Sex				
Female	2.00 (1.32–3.01)	<0.001	2.11 (1.36–3.27)	0.001
Male	Ref.		Ref.	
Age				
35–39	Ref.	0.43	–	
40–44	1.01 (0.70–1-45)		–	
45–49	1.28 (0.86–1.91)		–	
Residence location				
Rural	Ref.	<0.001	Ref.	
Semi-urban	1.83 (1.33–2.52)		1.38 (0.98–1.95)	0.07
Education				
<5 years of study	0.62 (0.42–0.91)	0.01	0.67 (0.45–0.99)	0.05
≥5 years of study	Ref.		Ref.	
Alcohol consumption				
None	Ref.	0.99	–	
Infrequent (last drink >1-month)	1.00 (0.71–1.41)		–	
Occupation				
Agricultural focused	0.51 (0.37–0.70)	<0.001	0.49 (0.34–0.69)	<0.001
Non-agricultural focused	Ref.		Ref.	
Smoking status				
Non-smoker	Ref.	0.14	Ref.	
Current smoker	0.55 (0.24–1.29)		0.83 (0.34–2.01)	0.74
Daily fruit and vegetable consumption				
Below average (<1.14 servings)	0.98 (0.71–1.34)	0.88	–	
Above average (≥1.14 servings)	Ref.		–	
Blood pressure				
Normal (<130/85 mm Hg)	Ref.	<0.001	Ref.	
Raised blood pressure (≥130/85 mm Hg)	2.76 (2.00–3.79)		2.64 (1.90–3.68)	<0.001
Random plasma glucose				
Normal (<7.8 mmol/L)	Ref.	0.03	Ref.	
Hyperglycaemia (≥7.8 mmol/L)	2.68 (1.18–6.13)		2.22 (0.92–5.37)	0.08
HDL				
Normal (males: ≥1.03 mmol/L & females: ≥1.29 mmol/L)	Ref.	0.02	Ref.	
Low (males: <1.03 mmol/L & females: <1.29 mmol/L)	1.52 (1.05–2.19)		1.55 (1.05–2.29)	0.03

[a]Variables that had a *p*-value of 0.20 in bivariable analysis were included in the multivariable model.

compared to male participants and being female was positively associated with MASLD. Research focused on understanding sex differences in MASLD remains insufficient,[7] but a 2019 global review study reported that overall MASLD prevalence was higher in males as compared to females of reproductive age.[34] Females presenting with a higher metabolic syndrome prevalence as compared to males is consistent with previously published research in Uganda and SSA with the difference theorised to be driven by obesity differences found by sex across the region.[35,36] Higher rates of both obesity and increased waist circumference among females in our population may additionally explain the higher MASLD rates we found as the FLI algorithm utilises measurements of body mass index and waist

circumference to determine MASLD prevalence. Further research is needed to understand whether females in the region are indeed at increased risk for MASLD and subsequently validate the FLI for use in this setting. The latter is particularly important as MASLD screening tools such as the FLI are likely to be adopted for use as compared to other MASLD diagnostic tools, such as ultrasound, in resource-constrained settings.[16]

The main strengths of our study are the large sample size and that the initial sample was drawn from a well-established population-based cohort that included almost all participants living with HIV in our age group and with the comparison population of HIV-negative participants drawn randomly from the same study population, reducing the risk of selection bias. However, our study has some limitations that are important to mention. First of all, we used FLI and dAAR to estimate MASLD and advanced fibrosis instead of imaging or biopsies. Nevertheless, in the given context, this is by far the most feasible way, where access to modern diagnostics is very low. Second, to discriminate between MASLD and MetAld (MASLD and alcohol-related liver disease, for people who meet both MASLD and alcohol-related fatty liver disease criteria), those who consume greater amounts of alcohol per week (140 and 210 g/week for females and males respectively) should be excluded.[2] However, data on weekly alcohol consumption was not collected in the present study, and instead everyone who reported drinking any alcohol within the last 7 days (as a proxy for excessive alcohol consumption) were excluded. This may have resulted in an underestimation of the prevalence of MASLD in our population. Another major limitation is the lack of data on HIV characteristics, such as duration of HIV infection, HIV clinical data such as CD4 levels and individual ART regimens. Information on type, duration or previous use of ART use was not collected for our study participants and, therefore, its potential impact on lipid profiles cannot be clarified. However, nucleoside reverse transcriptase inhibitors that have been previously found to be associated with MASLD have been phased out from nearly all national HIV programmes, including in Uganda.[37,38] The use of ART regimens containing protease inhibitors have been known to cause dyslipidaemia, but protease inhibitors have only been used as second line treatment, and in less than 5% of participants. Furthermore, our study did not screen for either hepatitis B virus (HBV) or hepatitis C virus (HCV). However, the impact of either HBV is likely to be minimal to our MASLD estimate.[39] Previous research has estimated the prevalence of HBV to be low, 4% among participants aged 30–50 while additionally for participants living with HIV, the use of ART has been found to be effective against HBV acquisition.[40,41] For HCV, no detectable viremia of HCV has previously been found in a previous study conducted within the RCCS and suggestive of a low prevalence of ongoing chronic HCV infection in our population.[42] Finally, for our liver fibrosis estimate, we did not have access to more refined methods such as transient elastography or platelets which is why we could not use other non-invasive scores.

5 | CONCLUSION

In this population-based, cross-sectional study in rural Uganda, we estimated the prevalence of MASLD to be 14% in women and 8% in men as measured by the FLI, and advanced liver fibrosis to be <1% as measured by the dAAR. A positive HIV status was almost significantly associated with MASLD. Our findings suggest that while MASLD is relatively common in this population, cirrhosis due to MASLD is unlikely to be a major problem in either people living with HIV or in the general population. These findings are relevant for MASLD and HIV researchers and for national health policymakers and programmes for the planning of scarce healthcare resources.

AUTHOR CONTRIBUTIONS

Rocio Enriquez: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; writing – original draft; writing – review and editing. **Mahmoud Homsi:** Conceptualization; formal analysis; methodology; writing – original draft; writing – review and editing. **Robert Ssekubugu:** Conceptualization; methodology; writing – original draft; writing – review and editing. **Dorean Nabukalu:** Conceptualization; writing – original draft; writing – review and editing. **Zangin Zeebari:** Formal analysis; writing – original draft; writing – review and editing. **Gaetano Marrone:** Conceptualization; writing – original draft; writing – review and editing. **Bruna Gigante:** Supervision; writing – original draft; writing – review and editing. **Larry W Chang:** Resources; writing – original draft; writing – review and editing. **Steven J Reynolds:** Resources; writing – original draft; writing – review and editing. **Fred Nalugoda:** Conceptualization; writing – original draft; writing – review and editing. **Anna Mia Ekström:** Conceptualization; writing – original draft; writing – review and editing. **Hannes Hagström:** Formal analysis; methodology; writing – original draft; writing – review and editing. **Helena Nordenstedt:** Conceptualization; formal analysis; funding acquisition; methodology; project administration; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

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