

PREVALENCE AND SEVERITY OF STEATOTIC LIVER DISEASE IN WOMEN WITH AND WITHOUT HIV

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ABSTRACT

Introduction: Steatotic liver disease (SLD) is highly prevalent in people with HIV (PWH) and is a major cause of morbidity and mortality in this population. However, it remains unclear whether SLD is influenced by HIV infection and whether the clinical management of PWH who have SLD should differ from non-HIV populations.

Methods: Liver steatosis and fibrosis were assessed using vibration-controlled transient elastography (VCTE) among 1,580 women (1,117 with HIV; 463 without) enrolled in the Women's Interagency HIV Study between 2013 and 2018. Steatosis was defined by a controlled attenuation parameter (CAP) ≥ 248 dB/m, and clinically significant fibrosis by liver stiffness ≥ 7.1 kPa. Participants were classified according to the AASLD diagnostic algorithm for SLD. Differences in fibrosis prevalence by HIV status were evaluated, and multivariable logistic regression was performed to identify factors associated with SLD and fibrosis, adjusting for age, ethnicity, BMI, alcohol use, diabetes, and smoking.

Results: Prevalence of SLD was 740 of 1580 (47%) and did not differ by HIV serostatus. Most SLD was metabolic dysfunction-associated steatotic liver disease (MASLD; 629 of 740 [82%]). HIV infection was associated with higher odds of clinically significant fibrosis only among women with SLD (adjusted OR 1.48, 95% CI 1.01–2.16, $p=0.04$; HIV*SLD interaction among entire cohort $p=0.03$).

Discussion: In this study, most SLD in women living with HIV is classified as MASLD. HIV infection is associated with higher odds of hepatic fibrosis only among those with SLD. Further work is needed to understand how HIV may potentiate fibrosis in the setting of SLD.

Key words: MASLD, HIV, Fibrosis, VCTE

INTRODUCTION

In 2023, multiple societies released guidance changing the nomenclature and classification of steatotic liver disease (SLD, formerly “fatty liver disease”).¹ Non-alcoholic fatty liver disease (NAFLD) was replaced by metabolic dysfunction-associated steatotic liver disease (MASLD), and a new entity, Met-ALD (combined MASLD and moderate alcohol use) was created. SLD is highly prevalent in people with HIV (PWH) and is a major cause of morbidity and mortality in this population.^{2–4} However, it remains unclear whether SLD is influenced by the presence of HIV in individuals, separate from or overlapping with MASLD and Met-ALD.

To date, few studies have examined how steatosis is classified among PWH using the new diagnostic criteria, and none have included persons without HIV as a comparison. This has important implications as the management and prognosis of SLD in PWH may differ from those without HIV.⁵ In addition, studies of SLD in PWH are overwhelmingly in men, but women with HIV may have unique risk factors for liver disease development and progression.

Here, we aimed to characterize the prevalence of SLD and severity of fibrosis among women with and without HIV in the US enrolled in the Women’s Interagency HIV Study (WIHS), the largest cohort of women representative of the HIV epidemic in the US. We also aimed to explore which factors were associated with prevalent SLD and clinically significant hepatic fibrosis in this group. We hypothesized that the prevalence and severity of SLD subtypes would differ in those with HIV versus those without, and that women with HIV would have higher odds of hepatic fibrosis.

METHODS

Study population and data collection

Participants were drawn from the Liver Disease and Reproductive Aging (LIVRA) study, an ancillary study nested within the MACS/WIHS Combined Cohort Study (MWCCS), a multicenter prospective cohort with standardized recruitment and longitudinal follow-up of women with and without HIV.⁶ Women with and without HIV were enrolled contemporaneously from the same clinical sites and underwent Vibration Controlled Transient Elastography (VCTE) scan, which were performed between 2013 and 2018, as previously described.^{7,8} The study population included 1580 women (1117 women with HIV [WWH] and 463 women without HIV [WWOH]). Data collected included at the VCTE study visit included: demographic covariates (age; ethnicity), behavioral covariates (self-reported alcohol drinks per week, with 1 drink equivalent to 14 grams of alcohol; self-reported tobacco use), clinical (self-reported menopausal state; body mass index (BMI); diabetes (defined by elevated fasting glucose, elevated hemoglobin A1c, prior diagnosis of diabetes, or being on diabetes therapy); waist circumference; total, HDL, and LDL cholesterol; serum triglyceride levels; Hepatitis C (HCV) antibody and RNA level, and current medications), and HIV-related covariates (viral load (detectable/undetectable and continuous); CD4 count (current CD4 count and CD4 nadir); history of AIDS; and current ART use (yes/no and by medication)). These covariates were selected based on either definition for SLD category or potential association with VCTE-measured liver steatosis and fibrosis. All measures were taken from the study visit closest to the VCTE. We compared the demographic, behavioral and clinical characteristics of WWH and WWOH and using chi 2 and t-tests.

Definitions of SLD and fibrosis

We first determined whether participants met criteria for SLD and hepatic fibrosis. Steatosis was defined as a CAP score ≥ 248 dB/m, a threshold validated against magnetic resonance spectroscopy in our cohort and used in prior published analyses.^{9,10} Clinically significant fibrosis was defined as LS ≥ 7.1 kPa (F2 or greater), a threshold previously validated against liver biopsy in people with HIV and

used in prior MWCCS and LIVRA analyses.^{10,11}

Those with SLD were then assessed for the following cardiometabolic criteria: 1) BMI ≥ 25 kg/m² OR waist circumference > 80 cm, 2) fasting serum glucose ≥ 100 mg/dL OR hemoglobin A1c (HbA1c) $\geq 5.7\%$ OR an existing diagnosis or treatment for type 2 diabetes, 3) blood pressure $\geq 130/85$ OR treatment for hypertension (HTN), 4) triglyceride level ≥ 150 mg/dL OR on lipid-lowering treatment, 5) HDL-cholesterol ≤ 50 OR on lipid-lowering treatment. Participants with at least one of the five cardiometabolic criteria and no other potential reasons for SLD were classified as having MASLD.

If participants reported alcohol use, then they were categorized as having Met-ALD (if alcohol use was 20- 50 g/day and they met cardiometabolic criteria for MASLD), or alcohol-related liver disease (ALD; if alcohol use exceeded 50 g/day). If participants met criteria for MASLD and there was another reason for hepatic steatosis, including chronic Hepatitis C (HCV) infection (defined as HCV seropositivity with a detectable RNA) or exposure to drugs that cause steatosis (methotrexate, corticosteroids, amiodarone, 5-fluorouracil and irinotecan, per AASLD guidance),¹² then they were labeled as having combination etiology SLD. Notably, antiretroviral medications were not included in this definition. If participants did not meet any of the cardiometabolic criteria and had no other reasons for hepatic steatosis, they were categorized as having cryptogenic SLD.

After sorting participants into each SLD category, we Fisher's exact tests to measure whether the proportion of women in each SLD category differed by HIV status, and whether the proportion with clinically significant fibrosis (defined as F2 or greater fibrosis, or VCTE-measured LS ≥ 7.1 kPa) and advanced fibrosis (defined as F3 or greater fibrosis, or VCTE-measured LS ≥ 9.5 kPa) within each category differed by HIV status. Finally, we tested whether participants who were previously classified as having NAFLD (defined as the presence of steatosis in the absence of alcohol use or other liver conditions, without the specific cardiometabolic conditions required for a diagnosis of MASLD)¹² were

classified any differently using the new criteria, and whether the cardiometabolic criteria for MASLD differed with HIV status

Statistical Analysis

We compared the demographic, behavioral and clinical characteristics of WWH and WWOH and using χ^2 and t-tests. Covariates were selected based on definition for SLD category or potential association with VCTE-measured liver steatosis and fibrosis. All measures were taken from the study visit closest to the VCTE. Fisher's exact tests were used to measure whether the proportion of women in each SLD category differed by HIV status, and whether the proportion with clinically significant fibrosis (defined as F2 or greater fibrosis, or VCTE-measured LS ≥ 7.1 kPa) and advanced fibrosis (defined as F3 or greater fibrosis, or VCTE-measured LS ≥ 9.5 kPa) within each category differed by HIV status. Fisher's exact test were also used to evaluate whether participants who were previously classified as having NAFLD (defined as the presence of steatosis in the absence of alcohol use or other liver conditions, without the specific cardiometabolic conditions required for a diagnosis of MASLD)¹² were classified any differently using the new criteria, and whether the cardiometabolic criteria for MASLD differed with HIV status.

Next, univariable and multivariable logistic regression models were constructed, controlling for covariates previously associated with SLD and fibrosis in the cohort: age, HIV serostatus, BMI, Hispanic ethnicity, menopause state, alcohol use (abstinent/mild (0-7 drinks per week), moderate (7-14 drinks per week) and heavy (14+ drinks per week)), diabetes and smoking (yes/no).^{7,8} For multivariable regressions, we excluded women with chronic viral hepatitis, defined as detectable HCV or HBV viral load, as well as those with resolved HCV (defined as positive antibody with negative HCV RNA), to better evaluate associations independent of viral hepatitis. The unadjusted and

adjusted associations of HIV serostatus with the following outcomes were evaluated: 1) SLD; 2) fibrosis in those with steatosis (SLD-fibrosis); 3) fibrosis in those without steatosis (non-SLD fibrosis). An additional model evaluating MASLD in WWH was also created; covariates for that model were the same as the fibrosis models but did not include BMI, alcohol and diabetes to avoid collinearity as they are part of the MASLD diagnostic criteria. Models were also stratified by HIV serostatus. HIV-related factors (viral load, CD4 count, CD nadir, history of AIDS and current antiretroviral use) were added to the models for WWH. We performed additional analyses excluding women with HIV who did not have suppressed viral load (n=313) evaluating the same outcomes as the primary analysis. A sensitivity analysis investigating the association of various antiretroviral medications with MASLD was also performed. Additional sensitivity analyses evaluated the effect of race and a CAP threshold of 275 dB/m which has been recommended in non-HIV populations.^{13,14}

To further explore potential effect modification in the relationship between HIV infection and hepatic fibrosis across different SLD categories, a formal interaction analysis between HIV and SLD in the entire cohort (main logistic regression model) was conducted.

Stata software (version 17) was used to conduct the analysis.

RESULTS

Prevalence and distribution of steatotic liver disease

Among the 1,580 women in our cohort (1117 WWH and 463 WWOH), the overall prevalence of SLD was 47% (n=740), with no significant difference between WWH and WWOH (47% each; p=0.95). MASLD was most common SLD classification, accounting for 82% of all SLD cases (629/740, Figure 1). Among WWH with SLD, 83% were classified as MASLD, compared to 80% of WWOH with SLD (p=0.27, Figure 1). The specific cardiometabolic criteria for MASLD (e.g., BMI, insulin resistance,

HTN, hyperlipidemia) met did not differ by HIV serostatus (data not shown). Among women without SLD, current or resolved hepatitis C was present in almost half of fibrosis cases (n=72/162).

SLD classifications did show differences by HIV serostatus: WWH were less likely to have ALD than WWOH (2% versus 7%, $p=0.005$) and more likely to have cryptogenic SLD (3% versus 0.4%, $p=0.03$, Table 1, Figure 1). Rates of Met-ALD (5% vs. 8%) and combination etiologies (7% vs. 6%) were similar. Among women with SLD, proportions of clinically significant fibrosis were higher in WWH than in WWOH (Figure 1). Furthermore, 82% of women with SLD met criteria for NAFLD using the prior definition (607/740),¹² and all of them also were classified as MASLD using the new definition.

Using a higher threshold for steatosis of CAP score 275 dB/m, 474 of 1,580 participants met criteria for steatosis. Among these, 342 were women with HIV and 132 were women without HIV.

Factors associated with steatotic liver disease and hepatic fibrosis

In multivariable logistic regression analysis of the entire cohort controlling for age, BMI, menopause status, alcohol use, diabetes and tobacco use, increasing age (OR 1.09 per 5 years, 95% CI 1.00–1.20, $p=0.05$), higher BMI (OR 1.84 per 5 kg/m², 95% CI 1.69–2.00, $p<0.01$), and diabetes (OR 1.96, 95% CI 1.47–2.61, $p<0.01$) were associated with higher odds of SLD (Table 2). Women with HIV did not have higher odds of SLD (OR 1.19, 95% CI 0.93–1.53, $p=0.16$, Table 2)..

Though HIV was not associated with SLD, there was an association between HIV and fibrosis that existed only in the presence of steatosis. In models stratified by steatosis, HIV was significantly associated with higher odds of SLD-fibrosis (OR 1.48, 95% CI 1.01–2.16, $p=0.04$), along with increasing age (OR 1.17 per 5 years, 95% CI 1.02–1.35, $p=0.02$) and BMI (OR 1.26 per 5 kg/m², 95% CI 1.14–1.40, $p<0.01$; Table 2). In contrast, HIV was *not* associated with non-SLD fibrosis (OR 0.72, 95% CI 0.49–1.06, $p=0.10$). Older age (OR 1.16 per 5 years, 95% CI 1.00–1.34, $p=0.05$) and current

tobacco use (OR 2.10, 95% CI 1.46–3.02, $p<0.01$) were associated with non-SLD fibrosis (Table 2).

There was no association of race with any of the outcomes (data not shown).

The effect modification by HIV and SLD on fibrosis was formally explored via a multivariable model of the entire cohort that included an interaction term between HIV and SLD. In this model, the joint presence of HIV and steatosis was associated with significantly higher odds of fibrosis (OR 1.51, 95% CI 1.11–2.05, $p<0.01$), and the HIV*SLD interaction was statistically significant ($p=0.03$, Table 2).

Factors associated with steatotic liver disease and hepatic fibrosis in women with HIV

Factors independently associated with higher odds of SLD specifically among WWH were similar to those identified in the entire cohort: increased BMI (OR 1.85 per 5 kg/m², 95% CI 1.67–2.06, $p<0.01$) and diabetes (OR 2.00, 95% CI 1.40–2.84, $p<0.01$, Table 3), with no observed associations of CD4 count or antiretroviral use with SLD.

Odds of SLD-fibrosis in WWH increased with age (OR 1.28 per 5 years, 95% CI 1.08–1.51, $p<0.01$), BMI (1.21 per 5 kg/m², 95% CI 1.07–1.36, $p<0.01$), and having a detectable viral load (OR 2.41, 1.50–3.88, $p<0.01$, Table 3). Non-SLD fibrosis in WWH was associated with tobacco use (OR 2.34, 1.48–3.70, $p<0.01$), as in the entire cohort. Increasing CD4 count was associated with lower odds of non-SLD fibrosis (OR 0.85 per 100 cells/mm³, 0.77–0.94, $p<0.01$, Table 3).

In an additional model evaluating MASLD as the outcome, higher CD4 count was associated with higher odds of MASLD (OR 1.06 per 100 cells/mm³, 95% CI 1.01–1.10, $p=0.02$), as was current antiretroviral use (OR 2.34, 95% CI 1.39–3.93, $p<0.01$; Supplemental Table 1).

In analyses excluding WWH with unsuppressed viremia, HIV serostatus remained unassociated with SLD prevalence (OR 1.25, 95% CI 0.96–1.62, Supplemental Table 2), MASLD, and with non-SLD fibrosis (OR 0.60, 95% CI 0.36–1.07) both consistent with the primary analysis. As in the primary analysis, the interaction between HIV and steatosis was statistically significant. Unlike the primary

analysis however, in those with steatosis HIV was no longer associated with higher odds of fibrosis, though the direction of the odds ratio was similar to the primary analysis (OR 1.26 95% CI 0.84-1.88, Supplemental Table 2).

To explore the potential association between certain antiretroviral medications (ART) and MASLD, an additional sensitivity analysis investigating different types of antiretroviral regimens was performed. This found that NRTI use—specifically tenofovir disoproxil fumarate and emtricitabine—was associated with MASLD in univariable analysis, but this association was attenuated in multivariable models controlling for age, ethnicity, and HIV-specific covariates (data available upon request). Other antiretroviral medications were not associated with MASLD.

DISCUSSION

Overall, we found a high prevalence of VCTE-measured SLD in our cohort, which was similar in women with and without HIV. Consistent with other recent studies, most SLD in our cohort (86%) was due to MASLD.¹⁵ While the MWCCS is not a population-based sample, it is well suited for internal comparisons by HIV serostatus, which was the primary analytic objective of this study. In this context, we found that women with HIV had higher odds of clinically significant fibrosis if they had concomitant steatotic liver disease, and that factors associated with fibrosis varied by SLD status.

In this study, established risk factors for SLD, such as increasing BMI and diabetes demonstrated the expected associations. Notably, all participants in our cohort who would have previously been diagnosed with NAFLD met the current criteria for MASLD.¹⁵ Interestingly, the prevalence of certain categories of non-MASLD SLD differed by HIV serostatus. For instance, ALD was more prevalent in WWOH than WWH, and cryptogenic SLD was more prevalent in WWH than WWOH. These findings raise the possibility that HIV-specific factors may contribute to steatosis in individuals classified as having cryptogenic SLD, though the current study was not designed to address this question.

Though the proportions of MASLD among WWH and WWOH did not differ, we did find that current antiretroviral use and higher CD4 count were associated with an increased odds of MASLD in women with HIV. This may represent a “return to health” phenomenon, which has been described previously in the literature,¹⁶ in which suppression of HIV viremia during the first 1-2 years after starting ART leads to weight gain and increased cardiometabolic risk. Emerging data suggest that specific antiretroviral agents may differentially influence metabolic risk and steatosis.¹⁷ Although we did not observe a consistent association between antiretroviral class and fibrosis outcomes, our sub-cohort and analysis was not designed to evaluate drug-specific effects and further studies are needed to better define the impact of individual antiretroviral agents on steatosis and fibrosis risk. Moreover, widespread use of tenofovir alafenamide (TAF) did not occur until more than midway through the collection of data for this study, which further limits our ability to comment on this drug. Another important limitation is that since the majority of women with HIV were receiving ARV, we were unable to distinguish the effects of untreated HIV infection from those of treated, chronic HIV. To address this, we performed sensitivity analyses excluding women with HIV who did not have suppressed viral load, evaluating the same outcomes as in the primary analysis. These results were similar to the primary analysis except that the presence of HIV infection did not confer statistically higher odds of fibrosis among those with steatosis. These findings suggest that incomplete viral suppression may contribute to the observed association between HIV and fibrosis in the presence of steatosis.

An additional limitation of this study is the absence of liver biopsy. While VCTE offers a non-invasive and scalable approach suitable for large cohort studies and clinical practice,¹³ steatosis and fibrosis are assessed indirectly and are subject to measurement error, particularly in milder disease stages. Histopathologic features such as inflammatory activity and architectural remodeling cannot be assessed, and misclassification may have biased results toward the null. In addition, the VCTE thresholds used in this study differ from some contemporary MASLD risk-stratification algorithms,

including the AASLD 2025 guidance on non-invasive assessment of hepatic fibrosis, which is primarily intended for clinical decision-making and does not address HIV monoinfection. That guidance nevertheless cites optimal liver stiffness measurement thresholds in the 7–8 kPa range for individuals with HIV/HCV and HIV/HBV coinfection. The fibrosis thresholds applied here were selected to support epidemiologic comparisons and have been validated against gold-standard measurements in people with HIV, including within this cohort.^{9,11} In this analysis, we also utilized a CAP threshold of 248 dB/m to define mild or greater steatosis. This is consistent with prior literature in PWH and has been validated as accurately measuring 5% or greater hepatic steatosis (against MRI-spectroscopy) in our cohort. However, recent guidelines suggest higher cutoffs may be used to define steatosis in those without HIV.^{13,14} When we evaluated the commonly used cutoff of 275 dB/m, the prevalence of steatosis in WWH decreased from 47% to 29%. As expected, use of the lower CAP threshold results in higher estimated prevalence compared with studies using ≥ 275 dB/m.

The most notable findings in this study center on the relationship between HIV, SLD, and fibrosis. While prior studies have established an association between HIV and liver fibrosis,^{18,19} the extent to which HIV modifies the natural history of SLD remains unclear. Prior studies have demonstrated a higher prevalence of at-risk steatohepatitis and fibrosis in people with HIV and SLD, suggesting that in PWH, SLD may progress to steatohepatitis and fibrosis at faster rates than the general population.^{2,3,20,21} We found that amongst women with SLD, those with HIV had a higher proportion of clinically significant fibrosis than those without HIV. Notably, significant rates of non-SLD fibrosis were present in both WWH and WWHO, and about half of these cases were associated with current or chronic HCV infection. When we performed multivariate regression excluding current or resolved viral hepatitis, we found that HIV infection remained significantly associated with an increased odds of fibrosis only in women with steatosis..

This study is limited by its cross-sectional design, which precludes assessment of causality. In addition, other potential contributors to fibrosis that are not fully captured by our current measures

may include prior alcohol exposure, possible “burned-out” steatohepatitis, and other unmeasured confounders. We also considered potential differences in body fat distribution by race. Prior studies have shown that Black women tend to have lower visceral adiposity at a given BMI compared with other groups,²² which may influence metabolic risk and the development of steatosis and fibrosis. In our analyses, adjustment for race did not materially change the results, and race was not independently associated with fibrosis or MASLD. However, our use of BMI does not capture differences in fat distribution. Further longitudinal studies incorporating direct measures of visceral adiposity are needed to better elucidate the pathogenesis of SLD and to refine risk-stratification criteria in populations with HIV, including men. Longitudinal follow-up of this cohort is ongoing, with repeat imaging and clinical assessments at approximately three-year intervals, which will enable future analyses of steatosis and fibrosis progression and regression in women with and without HIV. Overall, the early identification of liver fibrosis in people with HIV remains clinically critical, and targeting modifiable risk factors such as alcohol use and metabolic syndrome may be essential for improving outcomes in this population.

In summary, we found that most SLD observed in WWH is due to MASLD, and HIV is associated with higher odds of fibrosis in women with SLD. Future studies are needed to clarify underlying mechanisms and to characterize SLD patterns in other populations with HIV, including in men and those with viral hepatitis co-infection.

Supplemental Tables -- <https://links.lww.com/QAI/C760>

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Table 1: Cohort Characteristics by HIV Serostatus

	Women without HIV N=463	Women with HIV N=1,117	Total N=1,580	p-value
Age, years	49 (9)	50 (8)	50 (8)	<0.01
Race/Ethnicity				
African-American (Hispanic)	3%	1%	2%	0.06
African-American (Non-Hispanic)	74%	74%	74%	
Asian/Pacific Islander	1%	0.6%	0.8%	
NTV Amer/Alaskan	2%	1%	1%	
Other	3%	2%	2%	
Other (Hispanic)	5%	6%	6%	
White (Hispanic)	5%	5%	5%	
White (Non-Hispanic)	7%	10%	9%	
Post-menopausal	48%	60%	57%	<0.01
Drink any alcohol	15%	8%	10%	<0.01
Heavy alcohol use	6%	2%	3%	<0.01
Use any tobacco	47%	40%	42%	<0.01
BMI	32 (8)	31 (8.)	31 (8)	0.01
Waist circumference (cm)	101 (17)	100 (17)	100 (17)	0.2
HOMA-IR	3 (8)	4 (7)	4 (7)	0.2
Diabetes	22%	20%	20%	0.4
Liver-Related				
AST (IU/L)	21 (15)	24 (17)	23 (17)	<0.01
ALT (IU/L)	18 (12)	20 (16)	20 (15)	<0.01
Chronic HCV infection	10%	10%	10%	0.95
Any steatosis	47%	47%	47%	0.9
CAP over 275	29%	31%	30%	0.2
Any fibrosis	23%	23%	23%	0.7
F2 or greater fibrosis	24%	24%	24%	0.85
F3 or greater fibrosis	9.5%	11%	11%	0.4
MASLD diagnosis ⁺	80%	83%	82%	0.3
BMI criteria met	92%	91%	91%	0.4
Insulin criteria met	78%	76%	77%	0.6
BP criteria met	60%	60%	60%	0.9
Lipid criteria met	38%	43%	41%	0.1
Met-ALD diagnosis ⁺	8%	5%	3%	0.2
ALD diagnosis ⁺	7%	2%	2%	<0.01
Combination SLD ⁺	4%	6%	3%	0.3
Cryptogenic SLD ⁺	0.4%	3%	1%	0.03
HIV-specific factors				
History of AIDS	-	32%	-	-
Current CD4 Count (cells/mm ³)	-	682 (147)	-	-
CD4 Nadir (cells/mm ³)	-	250 (198)	-	-
Undetectable viral load	-	72%	-	-

Current viral load (copies/mL)	-	3.8k (2.5k)	-	-	Table 1: Cohort Characteristics, by HIV serost
Current antiretroviral use	-	90%	-	-	
NNRTI	-	27%	-	-	
NRTI	-	84%	-	-	
INSTI	-	24%	-	-	
PI	-	24%	-	-	

atus. Values are reported to one significant figure. Continuous variables displayed as mean (SD). Abbreviations: BMI (body mass index), HOMA-IR (homeostatic model for insulin resistance), ALD (alcohol associated liver disease), SLD (steatotic liver disease), NRTI (nucleoside reverse transcriptase inhibitor), NNRTI (non-nucleoside reverse transcriptase inhibitor), PI (protease inhibitor), INSTI (integrase strand transfer inhibitor). Heavy alcohol use was defined as 14 or more drinks per week. P values were calculated by chi-2 (for categorical variables), Fisher's exact test (for SLD categories) and students t-test (for continuous variables). Current viral load was calculated among those with positive viral load. Chronic HCV infection included all participants with RNA+ HCV at the time of the study visit. *Among women with steatosis.

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Table 2: Multivariable Association of Risk Factors for SLD and Fibrosis in the Entire Cohort

	Steatotic Liver Disease (N=1580)	Clinically Significant Fibrosis	
		With SLD (N=740)	Without SLD (N=840)
Covariate	SLD aOR (95% CI)	SLD-Fibrosis aOR (95% CI)	Non-SLD-Fibrosis aOR (95% CI)
Living with HIV	1.19 (0.93–1.53)	1.48 (01.01–2.16)* ⁺	0.72 (0.49–1.06)
Age (per 5 years)	1.09 (1.00–1.20)*	1.17 (1.02–1.35)*	1.16 (1.00–1.34)*
Hispanic ethnicity	1.24 (0.89–1.72)	0.98 (0.59–1.62)	1.40 (0.84–2.34)
Postmenopausal	0.95 (0.71–1.28)	1.02 (0.66–1.57)	1.14 (0.70–1.85)
Alcohol use			
Mild (1-7 drinks/week)	0.98 (0.77–1.24)	0.87 (0.61–1.24)	0.76 (0.52–1.13)
Moderate (8-14 drinks/week)	1.58 (0.86–2.88)	0.41 (0.12–1.43)	1.63 (0.68–3.94)
Heavy (> 14 drinks per week)	1.51 (0.99–2.30)	1.20 (0.64–2.23)	0.79 (0.41–1.55)
BMI (per 5 kg/m ²)	1.84 (1.69–2.00)*	1.26 (1.14–1.40)*	1.10 (0.96–1.26)
Diabetes	1.96 (1.47–2.61)*	1.22 (0.85–1.75)	1.54 (0.95–2.50)
Tobacco	1.02 (0.81–1.29)	1.25 (0.88–1.77)	2.10 (1.46–3.02)*
HIV*Steatosis	-	1.51 (1.11–2.05)*	

Table 2: Multivariable associations with SLD and fibrosis in the entire cohort. Clinically significant fibrosis was defined as F2 or greater (LSM ≥ 7.1) fibrosis and was assessed in those with steatosis (SLD) and those without steatosis (without SLD). In multivariable analysis, each covariate was included in the adjusted models. *p<0.05. In an additional model including a formal HIV×steatosis interaction term, steatosis was associated with significantly higher odds of fibrosis among women with HIV (aOR 1.51, 95% CI 1.11–2.05, p=0.009).

Table 3: Multivariable Association of Risk Factors with SLD and Fibrosis in Women with HIV

	Steatotic Liver Disease (N=1117)	Clinically Significant Fibrosis	
		With SLD (N=522)	Without SLD (N=595)
Covariate	SLD aOR (95% CI)	SLD-Fibrosis aOR (95% CI)	Non-SLD Fibrosis aOR (95% CI)
Age (per 5 years)	1.07 (0.96–1.20)	1.28 (1.08–1.51)*	1.14 (0.94–1.38)
Hispanic ethnicity	1.41 (0.94–2.12)	0.86 (0.46–1.60)	1.38 (0.72–2.67)
Postmenopausal	1.02 (0.72–1.45)	0.92 (0.55–1.55)	1.47 (0.78–2.78)
Alcohol use			
Mild (1-7 drinks/week)	1.18 (0.89–1.58)	0.83 (0.55–1.27)	0.84 (0.52–1.35)
Moderate (8-14 drinks/week)	1.45 (0.69–3.05)	0.11 (0.01–0.87)*	1.73 (0.57–5.28)
Heavy (>14 drinks per week)	1.62 (0.90–2.89)	0.97 (0.42–2.22)	0.54 (0.19–1.54)
BMI (per 5 kg/m²)	1.85 (1.67–2.06)*	1.21 (1.07–1.36)*	1.23 (1.03–1.46)*
Diabetes	2.00 (1.40–2.84)*	1.18 (0.76–1.83)	1.43 (0.76–2.69)
Tobacco	0.89 (0.67–1.18)	1.37 (0.90–2.10)	2.34 (1.48–3.70)*
CD4 (per 100 cells/uL)	1.03 (0.98–1.08)	1.04 (0.98–1.11)	0.85 (0.77–0.94)*
CD4 nadir (per 100 cells/uL)	1.01 (0.93–1.09)	1.06 (0.94–1.19)	1.05 (0.89–1.23)
Detectable viral load	0.95 (0.68–1.32)	2.41 (1.50–3.88)*	1.48 (0.89–2.47)
History of AIDS	0.74 (0.55–1.00)	1.41 (0.90–2.22)	1.08 (0.67–1.74)
Current antiretroviral use	1.63 (0.98–2.71)	0.99 (0.45–2.19)	1.49 (0.70–3.19)

Table 3: Multivariable associations with SLD, and fibrosis in women with HIV. Clinically significant fibrosis was defined as F2 or greater (LSM ≥ 7.1) fibrosis and was assessed in those with steatosis (SLD) and those without steatosis (without SLD). In multivariable analysis, each covariate was included in the adjusted models. *p<0.05

Figure 1: Prevalence and distribution of steatotic liver disease and fibrosis in women with and without HIV in our cohort

