Current and Lifetime Alcohol Drinking Associations with Liver Disease Markers in People Living with HIV (PLWH) and the Role of Hepatitis C

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Background

- Increased life expectancy in PLWH has increased non HIV-related comorbidities.
- Coinfection with Hepatitis C Virus (HCV) promotes fat accumulation in the liver (steatosis) and liver scarring (fibrosis), hallmarks of liver disease.
- Liver disease is the 2nd most common non HIV-related cause of death due in PLWH
- PLWH and HCV-infected individuals have higher rates of hazardous drinking and alcohol use disorders (AUDs).
- The impact of past and current alcohol use on liver injury in PLWH has not been well examined.

Objectives

- To assess whether current and lifetime alcohol use is differentially associated with noninvasive markers of liver disease in PLWH, and determine if HCV coinfection acts as an effect modifier.

Methods

- 365 PLWH (≥18) under care were enrolled in the **N**ew **O**rleans **A**lcohol use in **H**IV [NOAH] study.
- Alcohol use was measured by Lifetime Drinking History (LDH) 30-day Timeline-Followback (TLFB), Alcohol Use Disorder Identification Test (AUDIT), and the biological marker phosphatidylethanol (PEth).
- Aspartate aminotransferase (AST) to platelet ratio index (APRI) and FIB-4 index scores were used to assess liver disease.

Definitions of Fibrosis Markers	
Abnormal APRI	> 0.4
Advanced APRI	> 1.5
Abnormal FIB-4	> 1.45
Advanced FIB-4	> 3.25

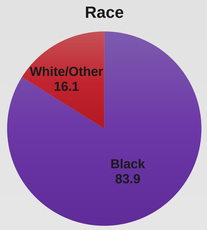
APRI: $\frac{(AST\ level(IU/L))}{\frac{\text{Upper Limit of Normal AST}}{\text{platelet count}\ (109/L)}}$ x 100

FIB-4: $\frac{age\ (years) * AST\ level\ (U/L)}{platelet\ count(109/L) * \sqrt{ALT}}$

- Descriptive statistics and multivariable logistic regression analyses were performed to assess the association between alcohol consumption and noninvasive markers of fibrosis. All analyses were conducted using SAS version 9.4.

Results

	LDH < 100 kg (n=155)	LDH 100-600 kg (n=142)	LDH > 600 kg (n=56)	p-value
Mean Age (SD)	44.7 (11.0)	50.4 (9.4)	52.7 (7.2)	**< 0.0001**
	% (n)			
Sex				**0.001**
Female	40.6 (63)	23.2 (33)	21.4 (12)	
Male	59.4 (92)	76.8 (109)	78.6 (44)	
Race				0.448
Black	85.8 (133)	81.7 (116)	83.9 (47)	
White	12.3 (19)	18.3 (26)	16.1 (9)	
Other	1.9 (3)	-	-	
BMI Category				0.099
Underweight	3.9 (6)	3.6 (5)	7.3 (4)	
Normal weight	34.2 (53)	45.0 (63)	32.7 (18)	
Overweight	30.3 (47)	25.0 (35)	34.6 (19)	
Obese	16.8 (26)	16.4 (23)	23.6 (13)	
Extremely Obese (>35)	14.8 (23)	10.0 (14)	1.8 (1)	
Smoking Status				**0.002**
Never	33.6 (52)	16.9 (24)	12.5 (7)	
Former	14.2 (22)	19.7 (28)	16.1 (9)	
Current	52.3 (81)	63.4 (90)	71.4 (40)	
Viral Load				0.112
≤ 50	71.0 (110)	78.9 (112)	80.4 (45)	
51-200	7.7 (12)	7.8 (11)	10.7 (6)	
201-1000	4.5 (7)	6.3 (9)	1.8 (1)	
> 1000	16.8 (26)	7.0 (10)	7.1 (4)	
Hepatitis B	5.2 (8)	7.0 (10)	-	0.128



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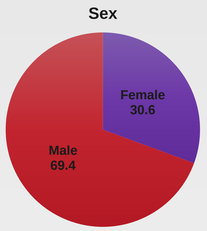
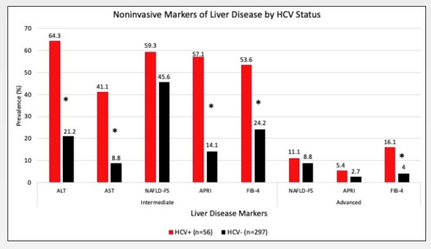
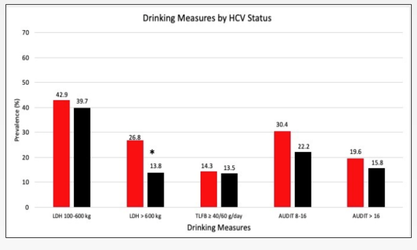


- PLWH with higher LDH were more likely to be older, male, and current smokers than those with lower LDH.



*** P-value (<0.05)**



- HIV/HCV coinfected individuals still showed evidence of being active drinkers.

Table 2. Adjusted odds ratios (ORs) of fibrosis markers among LDH categories**

	Abnormal APRI	Advanced APRI	Abnormal FIB-4	Advanced FIB-4
LDH				
< 100 kg	Ref.	Ref.	Ref.	Ref.
100-600 kg				
HCV+	2.28 (0.54, 9.67)	-	4.65 (0.57, 38.13)	**21.89 (1.19, 402.36)**
HCV-	0.81 (0.35, 1.89)	1.41 (0.24, 8.22)	0.94 (0.45, 1.97)	1.41 (0.28, 7.11)
> 600 kg				
HCV+	1.17 (0.25, 5.38)	-	0.31 (0.06, 1.75)	0.19 (0.01, 5.72)
HCV-	0.84 (0.28, 2.52)	-	0.48 (0.17, 1.33)	0.31 (0.02, 3.90)

** Adjusted for age, sex, BMI, smoking status, HIV viral load, and Hepatitis B

- LDH was only significantly associated with advanced FIB-4 markers among HIV/HCV coinfected individuals.

Table 3. Adjusted ORs of fibrosis markers among current drinking measures**

	Abnormal APRI	Advanced APRI	Abnormal FIB-4	Advanced FIB-4
TLFB ≥ 40/60				
HCV+	1.06 (0.14, 8.11)	**67.55 (1.09, -)**	1.52 (0.17, 13.93)	3.68 (0.23, 60.33)
HCV-	**2.90 (1.18, 7.16)**	**11.79 (2.17, 64.16)**	1.81 (0.71, 4.62)	**7.68 (1.90, 31.08)**
AUDIT > 16				
HCV+	2.78 (0.51, 14.93)	4.43 (0.13, 147.70)	0.49 (0.08, 2.90)	2.46 (0.19, 31.60)
HCV-	1.49 (0.55, 4.05)	**8.91 (1.56, 50.90)**	0.82 (0.31, 2.17)	**7.08 (1.60, 31.25)**
PEth > 400				
HCV+	**1.40 (1.33, 1.48)**	**0.41 (0.35, 0.49)**	**16.57 (1.12, 244.18)**	-
HCV-	**3.18 (3.12, 3.24)**	**26.20 (25.71, 26.70)**	**3.16 (1.17, 8.51)**	**46.95 (6.15, 358.70)**

- TLFB and PEth were significantly associated with most liver disease markers among PLWH.
- HCV was not a statistically significant effect modifier.

Conclusions

- Hepatic injury is prevalent in this cohort of PLWH, despite being a relatively virally controlled patient population under care.
- Alcohol-related biological markers may be more reliable in predicting liver injury than self-reported measures of drinking.
- Clinicians should consider multiple drinking measures in PLWH when classifying disease risk and recommending treatment options.
- HCV+ PLWH had higher rates of liver disease than HCV-
- HCV infection did not significantly change the magnitude of association between any of the drinking measures and liver disease markers.

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