NON-OBESE NAFLD IS ASSOCIATED WITH HIGHER SCD14 CONCENTRATIONS IN ADULTS WITH HIV

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CROI Conference on Retroviruses and Opportunistic Infections

#J01

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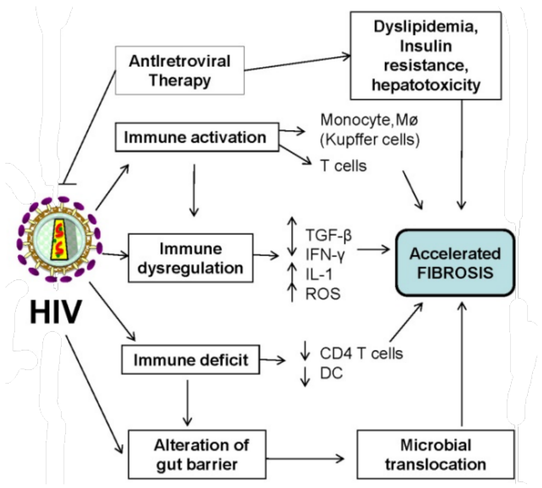
Background



Adapted from Int. J. Mol. Sci. 2014, 15(6), 9184-9208.

- Hepatic steatosis is common among people living with HIV (PLWH).
- Non-obese (BMI <30 kg/m^2), non-alcoholic fatty liver disease (NAFLD) may be more frequent in PLWH than in the general population, but etiology and risk factors are incompletely understood.
- Soluble CD14 (sCD14) is a marker of monocyte/Kupffer cell activation that is associated with (obese) NAFLD severity.
- We sought to understand factors associated with hepatic steatosis and non-obese NAFLD in a multi-ethnic cohort of PLWH.

Methods

Study Design:
- Cross-sectional, observational, single center study in Houston, TX (2017-2020)

Population:
- PLWH ≥18 years of age approached at random

Procedures:
- Screening for hepatic steatosis by FibroScan® controlled attenuation parameter (CAP) measurement
- Biomarkers associated with NAFLD physiology in the general population were measured centrally by ELISA at end of study

Analysis:
- Multivariable regression modeling explored factors associated with hepatic steatosis (all participants) and the subset of PLWH with NAFLD (no heavy alcohol or viral hepatitis).

FibroScan® Interpretation

FibroScan® Fat Results

CAP Score (dB/m)	Steatosis Grade	Amount of Liver showing Fatty Change (%)
150-248	S0	0-10
248-260	S1	11-33
260-280	S2	34-66
> 280	S3	> 67

FibroScan® Stiffness Results

Condition	Kpa Suggested values for Fibrosis staging			
	F0-F1	F2	F3	F4
NAFLD or NASH	2-8.5	8.5-9.5	9.5-13-5	> 13.5

Modified from Tawazun Health Ltd

Results

Table 1: Baseline Characteristics (N=194)

Age (years)	49 (41, 58)
Black race	54%
Hispanic ethnicity	41%
Cisgender female	22%
Transgender female	34%
BMI (kg/m^2)	28 (25, 32)
Time with HIV (years)	15 (10, 22)
Time on ART (years)	11 (8, 15)
Current CD4+ T cell count (cells/µl)	604 (437, 802)
HIV-1 RNA <50 copies/ml	81%
CAP (dB/min)	257 (225, 295)
Stiffness (kPa)	5 (4, 6)
Current HBV	2%
Current HCV	10%
Current heavy alcohol use	5%

*Median and interquartile range or frequency presented

Table 2: Steatosis Prevalence

CAP score cutoff (dB/min)	Steatosis Prevalence
>248	**58%**
>260	**46%**

41% of PLWH with steatosis had BMI <30 kg/m^2

Table 3: Factors associated with moderate-to-severe hepatic steatosis (CAP >260 dB/m)

	Beta estimate	Std Error	P value
Age (per year)	0.01	0.02	0.81
Gender			
Cis woman	-0.20	0.36	0.58
Trans woman	0.37	0.33	0.26
Hispanic ethnicity	**1.10**	**0.43**	**0.01**
BMI (per kg/m^2)	**0.2**	**0.04**	**<0.0001**
sCD14 (per µg/ml)	**0.92**	**0.44**	**0.04**

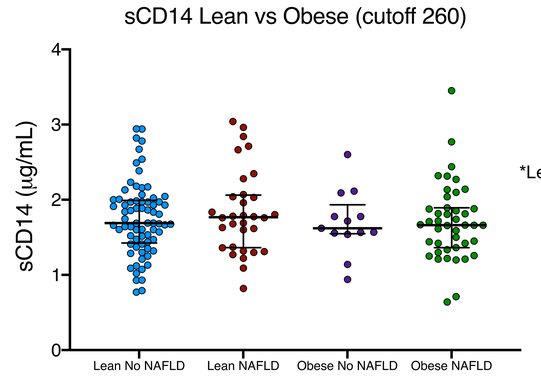
- Model results were similar when CAP cutoff was made more or less restrictive.
- Model for non-obese NAFLD subset similar, though hypertension diagnosis replaced BMI as significant.

Table 4. Biomarkers Concentrations by BMI Groups (CAP ≥260 dB/m)

	Lean Normal N=85	Lean Steatosis N=36	Obese Normal N=19	Obese Steatosis N=51	P-value
Total Adiponectin (ng/mL)	**5089 (2625, 7776)**	**3869 (2077, 6769)**	**4710 (1288, 6209)**	**1786 (771, 4641)**	**0.0003**
sCD14 (ug/mL)	1.7 (1.47, 2.02)	1.78 (1.44, 2.05)	1.72 (1.56, 2.11)	1.71 (1.42, 2.04)	0.88
E-Selectin (ug/mL)	42.6 (33.3, 52.6)	49.7 (35.6, 57.8)	37.8 (33.3, 54.8)	49.7 (39.4, 57.8)	0.19
FABP4 (pg/mL)	**14056 (8114, 20474)**	**14402 (9951, 20959)**	**25629 (15261, 38433)**	**23533 (18519, 32599)**	**<0.0001**
FGF21 (pg/mL)	**142 (75, 249)**	**216 (144, 276)**	**115 (52, 196)**	**166 (127, 313)**	**0.010**
PCSK9 (pg/mL)	**51480 (29746, 72744)**	**46823 (26653, 70903)**	**84095 (54478, 129261)**	**55176 (26643, 82239)**	**0.033**
IL-6 (pg/mL)	2.3 (0.92, 4.33)	2.16 (0.67, 5.31)	2.46 (1.41, 3.96)	2.46 (1.24, 6.07)	0.58
PAI1/SerpinE1 (pg/mL)	135165 (108932, 160578)	129279 (98138, 164709)	137451 (105874, 179613)	134993 (95495, 159666)	0.95
Insulin (pmol/mL)	66.3 (46.2, 95.8)	45.5 (32.6, 87.2)	60.3 (36.1, 99.8)	64.6 (32.8, 177.4)	0.28

*Median and interquartile range presented

Figure 1: sCD14 Levels by BMI* and NAFLD Status



	Lean No NAFLD	Lean NAFLD	Obese No NAFLD	Obese NAFLD
Median (IQR)	1.69 (1.44, 1.98)	1.77 (1.37, 2.05)	1.67 (1.56, 1.98)	1.66 (1.39, 1.97)
Mean (SD)	1.75 (0.48)	1.84 (0.56)	1.71 (0.41)	1.72 (0.51)
N	73	32	14	44

sCD14 remained the only biomarker associated with hepatic steatosis presence regardless of CAP cutoff for the model

Summary & Conclusions

In this cohort of adult PLWH on contemporary ART undergoing random screening for hepatic steatosis:

- **The majority of participants had at least mild hepatic steatosis.**
- **Non-obese steatosis was prevalent in 20% of the cohort, a rate 5x higher than the US general population.**
- **Higher sCD14 concentrations were associated with steatosis/NAFLD in obese and non-obese PLWH.**
- **sCD14 concentrations were the highest among persons with non-obese NAFLD.**
- **The pathophysiology of non-obese NAFLD in PLWH demands further exploration.**

References and Acknowledgements

The investigators thank the study staff and participants for their generous time and support. This work was funded in part by K23 AI110532, P30 AI161943 and R01 DK126042 to JEL.

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