HIV NASH CRN

HIV NASH Clinical Research Network (HIV NASH CRN) is sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Elevated Triglyceride and Ceramide Metabolites in MASLD among PWH

0606

Kara Wegermann[1], Xiaoyue Yan[2], Joseph Lucas[2], Laura Wilson[3], Holly Crandall[4], Jennifer Price[5], Richard K. Sterling[6], Sonya Heath[7], Mark Sulkowski[8], Jordan E. Lake[9], Rohit Loomba[10], Naga Chalasani[4], Cynthia Moylan[1], Susanna Naggie[1]

1. Duke University, 2. Vital Statistics, LLC, 3. Johns Hopkins Bloomberg School of Public Health, 4. Indiana University, 5. University of California San Francisco, 6. Virginia Commonwealth University, 7. University of Alabama Birmingham, 8. Johns Hopkins University, 9. UTHealth Houston, 10. University of California San Diego

BACKGROUND

- Metabolic dysfunction-associated steatotic liver disease (MASLD) affects 40% of people with HIV (PWH), yet underlying mechanisms and metabolic signatures remain poorly defined.
- Statins are beneficial for MASLD in the general population → role of lipid metabolism?
- Our preliminary data: PWH and individuals with MASLD have elevated triglycerides and other lipid metabolites
- **Aim: identify unique plasma lipid metabolite patterns in PWH with MASLD.**

MASLD in PWH is characterized by **elevated triglyceride** metabolites → lipid metabolism important and potentially intervenable

METHODS

Figure 1: HIV NASH CRN HNC-01 Cohort

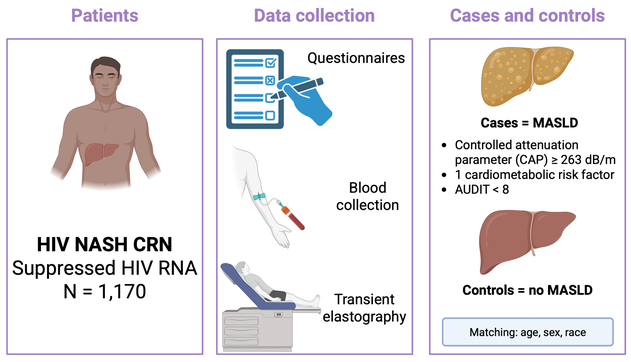
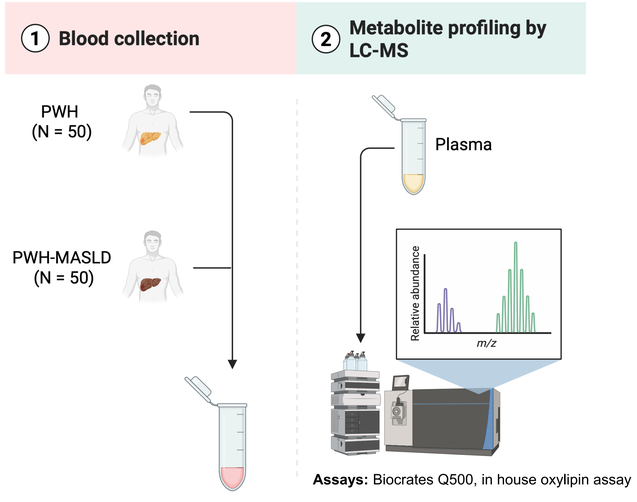


Figure 2: Metabolomics methods



RESULTS

Table 1: Participant demographics

Characteristic	Controls: No MASLD (N=50)	Cases: MASLD (N=50)	p-value
Female sex	14 (28%)	14 (28%)	1.00
Age (median, IQR)	54 [44, 61]	53 [43, 60]	0.76
BMI (median, IQR)	27 [24, 31]	34 [29, 37]	<0.001
Hispanic ethnicity	10 (20%)	10 (20%)	1.00
Race			1.00
Black	25 (50%)	25 (50%)	
Other	3 (6%)	3 (6%)	
White	22 (44%)	22 (44%)	
Hyperlipidemia	15 (30%)	23 (46%)	0.15
Hypertension	25 (50%)	27 (54%)	0.84
Statin within 3 months of enrollment	18 (36%)	20 (40%)	0.84
Diabetes	9 (18%)	15 (30%)	0.24
Years since HIV diagnosis (median, IQR)	17 [9, 24]	18 [9, 27]	0.79
Prior AIDS defining illness	7 (14%)	10 (20%)	0.59
ART regimen			
Entry Inhibitor	1 (2%)	1 (2%)	1.00
INSTI	45 (90%)	43 (86%)	0.76
NNRTI	13 (26%)	9 (18%)	0.47
NTRI	43 (86%)	47 (94%)	0.32
Protease inhibitor	2 (4%)	8 (16%)	0.10
Triglycerides (median, IQR)	94 [71, 166]	138 [94, 179]	0.02
FIB4 (median, IQR)	1.0 [0.8, 1.4]	1.3 [0.9, 2.1]	0.006
CAP (db/m) (median, IQR)	225 [203, 244]	316 [282, 348]	<0.001
Median LSM (kPa) (median, IQR)	4.8 [3.6,5.6]	6.3 [4.5,8.4]	<0.001
LSM >= 8 kPa, n (%)	3 (6.0)	15 (30.0)	0.004

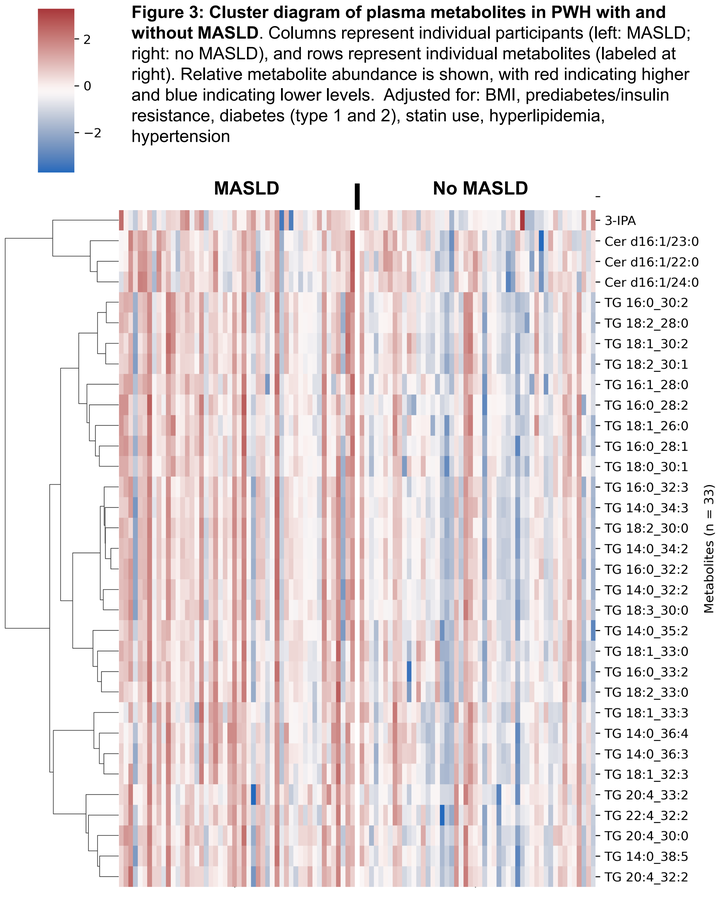


Figure 3: Cluster diagram of plasma metabolites in PWH with and without MASLD. Columns represent individual participants (left: MASLD; right: no MASLD), and rows represent individual metabolites (labeled at right). Relative metabolite abundance is shown, with red indicating higher and blue indicating lower levels. Adjusted for: BMI, prediabetes/insulin resistance, diabetes (type 1 and 2), statin use, hyperlipidemia, hypertension

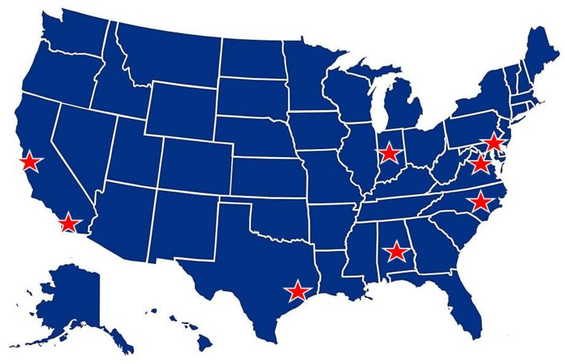
CONCLUSIONS

- MASLD in PWH is associated with **distinct** alterations in plasma **lipid and gut microbiota**–derived metabolites.
- We found elevated triglyceride and ceramide metabolites even after adjustment for metabolic comorbidities.
- These findings:
  - Implicate dysregulated lipid metabolism in MASLD
  - Support further investigation of targeted metabolic interventions (including lipid-lowering strategies) to prevent or treat MASLD in PWH.

ADDITIONAL KEY INFORMATION

- Study contact information:
  - Holly Crandall, Project Manager (hrking1@iu.edu)
  - Kara Wegermann (kara.Wegermann@duke.edu)

Figure 4: HIV NASH CRN sites



PLAIN LANGUAGE SUMMARY

Steatotic liver disease in people with HIV is linked to higher levels of blood fats, suggesting that fat processing in the body may be an important and treatable pathway.