Tryptophan catabolism is altered among persons with HIV who have steatosis.

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BACKGROUND

Persons with HIV (PWH) have increased inflammation which may influence tryptophan metabolism.

We aimed to explore if steatosis was associated with

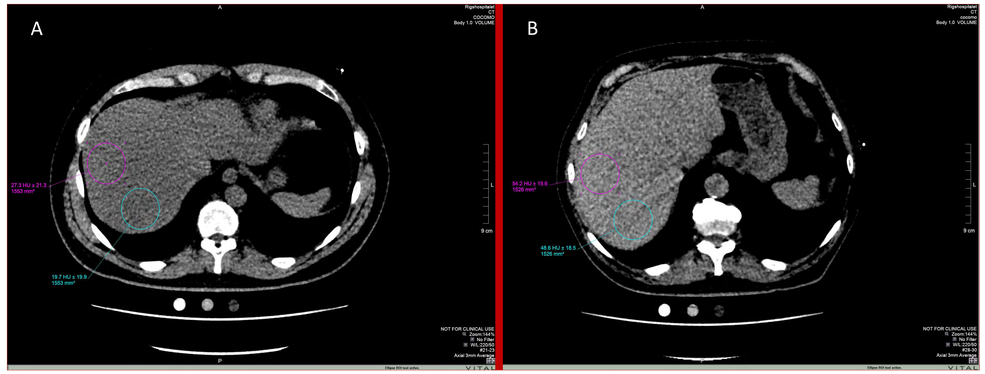
- Kynurenine-to-tryptophan ratio (KTR)
- Quinolinic acid

METHODS

- PWH were recruited from the Copenhagen comorbidity in HIV infection (COCOMO) study.
- Steatosis was defined as liver attenuation ≤ 48 Hounsfield Units.
- Hypotheses were tested using linear regression of log-transformed serum biomarker - adjusted for age, sex, smoking status, waist-to-hip ratio and physical activity.

Variable	Steatosis + N=61	Steatosis - N=738
Age years (SD)	54 (10)	51 (11)
Male sex, n (%)	55 (90)	632 (49)
Smoking status, n (%)		
• Current	11 (18)	217 (29)
• Former	28 (46)	259 (35)
• Never	21 (34)	248 (34)
Physical activity, n (%)		
• Sedentary	14 (23)	55 (7.5)
• Moderately Active	39 (64)	544 (74)
• Very Active	4 (7)	103 (14)
Waist-hip-ratio (SD)	1.0 (0.1)	0.9 (0.1)
CD4⁺ count, cells/nL		
• <200	1 (1.6)	12 (1.6)
• 200-349	7 (11)	35 (4.7)
• 350-500	8 (13)	104 (14)
• >500	45 (74)	580 (79)
CD4⁺ nadir <200 cells/nL, n (%)	31 (61)	278 (38)

Steatosis defined using non-contrast computed tomography scan of the liver



Steatosis was defined as an average liver attenuation below or equal to 48 Houndsfield Units in two selected regions of interest located in Coinaud liver segments 5 and 6, with a median area size of 1500mm² (+/- 100mm²).
A: Study participant with CT-defined steatosis. **B:** Study participant without CT-defined steatosis

Steatosis was associated with higher concentration of quinolinic acid and this was *not* mediated by IFN-γ.

RESULTS

- Steatosis was present in 61 (8 %) of 799 included PWH.
- KTR was 27.2 [95%CI 25.1; 29.4] nmol/µmol among those with steatosis and 25.3 [95%CI: 24.8; 25.8] in those without steatosis, p=.046.
- Quinolinic acid concentrations were 466nM [95%CI: 425; 512] among those with steatosis compared to 384nM [95%CI: 375; 394] in those without steatosis, p<.001.
- A doubling in IFN-γ was associated with 7 % [95%CI: 5; 9] higher KTR (p<.001) and 12 % [95%CI: 9; 15] higher quinolinic acid (p<.001).
- After adjustment for potential confounders, steatosis was associated with 14 % [95%CI: 4; 25] higher levels of quinolinic acid and further adjusting for IFN-γ did not attenuate this.
- KTR was not associated with steatosis after adjustment for potential confounders.

CONCLUSIONS

- Serum levels of quinolinic acid were significantly higher among PWH with steatosis
- Kynurenine-to-tryptophan ratio was not associated with steatosis.
- This effect was not mediated by IFN-γ

Our results indicate that pro-inflammatory changes in the kynurenine pathway accompany steatosis in PWH irrespective of IFN-γ.

ADDITIONAL KEY INFORMATION

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