High prevalence of Hepatic Steatosis in a cohort of People Living With HIV: exploring the role of metabolic and HIV-related factors

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BACKGROUND

- Liver fat accumulation is increasingly being recognised in PLWH, potentially due to a combination of metabolic and lifestyle risk factors and HIV- or antiretroviral therapy-related variables[1]
- Therefore, the prevalence and correlates of Hepatic Steatosis (HS) need to be adequately investigated in PLWH

METHODS

- Prospective single-center cross-sectional study, consecutively enrolling PLWH during routine visits at the University Hospital of Siena
- Exclusion criteria: age <18 years, active viral hepatitis, pregnancy, hazardous alcohol intake
- Patients underwent transient elastography (FibroScan) to measure HS by controlled attenuation parameter CAP (dB/m) and liver fibrosis by liver stiffness (kPa)
- Lifestyle habits were investigated by a structured questionnaire
- Clinical and laboratory variables were retrieved through medical record review
- Variables associated with significant HS or liver fibrosis were investigated by logistic regression, while those associated with CAP were studied by linear regression analysis. Correlation among variables was investigated by Spearman test

RESULTS

POPULATION MAIN CHARACTERISTICS (N=210)

Table 1: Population main characteristics	
Variables	**N (%) or median (IQR)**
Age (years)	54.2 (47.2-60.8)
Female gender	56 (26.7)
Risk factor: IDU	13 (6.2)
Comorbidities:	
- Diabetes	18 (8.6)
- Hypertension	67 (31.9)
- Ischemic heart disease	7 (3.3)
- Cerebrovascular disease	4 (1.9)
- Peripheral vascular disease	21 (10.0)
- Chronic renal diseases	42 (20.0)
- Cancer	7 (3.3)
- Liver cirrhosis	3 (1.4)
Coinfections:	
- HBV	5 (2.4)
- Previous HCV	25 (11.7)
Concomitant therapies:	
- Statin	25 (11.9)
- Other lipid lowering drugs	26 (12.4)
- Anti-hypertensive drugs	60 (28.6)

METABOLIC AND LIFESTYLE FINDINGS

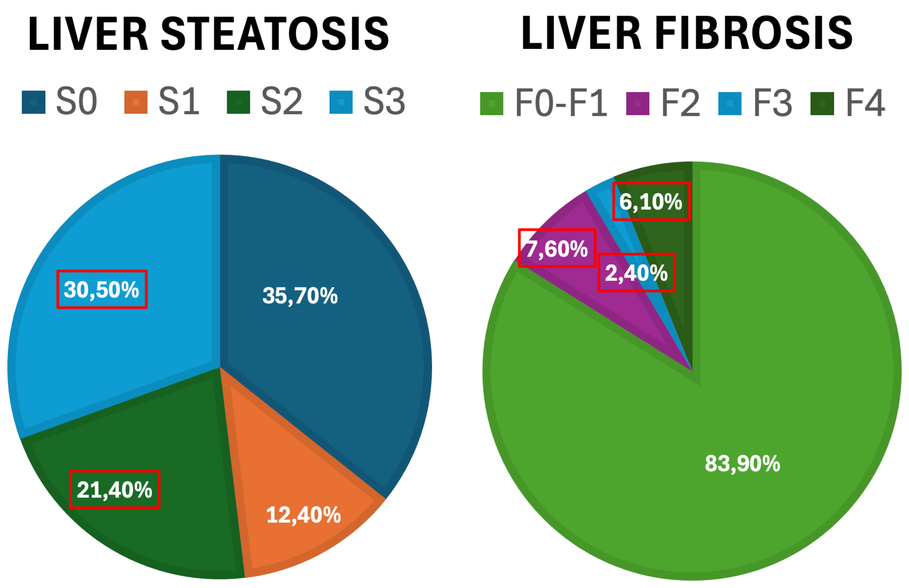
Table 2: Metabolic and lifestyle parameters	
Variables	**N (%) or median (IQR)**
Cigarette smoking	79 (37.6)
Regular alcohol intake	127 (60.5)
Regular physical activity	87 (41.4)
Sedentary work	97 (46.2)
Body mass index (BMI kg/m²)	25.5 (22.7-27.4)
Pathologic waist circumference (>102 cm in men and >88 cm in women)	87 (41.4)
Pathologic waist/hip ratio (>0.9 in men and >0.85 in women)	184 (87.6)
Pathologic blood pressure (>130/85 mmHg)	74 (35.2)
Metabolic syndrome	40 (19.0)
10-year ASCVD risk (%)	5.0 (2.3-11.9)
ASCVD categories:	
- Low (<5%)	103 (49)
- Borderline (5-7.4%)	29 (13.8)
- Intermediate (7.5-19.9%)	59 (28.1)
- High (>=20%)	16 (7.6)
- Unknown	3 (1.4)
HOMA score	2.07 (1.19 – 4.20)
Insulin resistance	99 (47.1)

VIRO-IMMUNOLOGICAL VARIABLES

Table 3: Viro – immunological variables	
Variables	**N (%) or median (IQR)**
Years from HIV diagnosis	14.8 (8.9 – 24.7)
CD4 at nadir (cells/mmc)	166 (62 – 321)
HIV-RNA at zenith (log copies/mL)	5.10 (4.49 – 5.62)
Past AIDS defining events	37 (17.6)
Years from first ART	11.5 (7.9 – 20.0)
On ART	207 (98.6)
Years from last ARV regimen	2.5 (1.3 – 4.3)
Types of ART:	
- InSTI based	75 (36.2)
- PI based	12 (5.8)
- NNRTI based	38 (18.4)
- Dual	74 (35.7)
- Other regimens	8 (3.9)
Therapeutic line	5 (3 – 7)
HIV-RNA <50 copies/mL	198 (89.5)
CD4 cell count	753 (536-1047)
CD4%	35 (28-42)
CD4/CD8 ratio	0.91 (0.57-1.28)

TRANSIENT ELASTOGRAPHY FINDINGS

- Overall, advanced S2 and severe S3 steatosis were observed in 45 (21.4%) and 64 (30.5%) PLWH, respectively
- Liver stiffness was correlated with CAP (r = 0.399, p<0.001). Significant liver fibrosis (F2-F4) was observed in 34 (16.2%) PLWH.



Liver steatosis categories[2]:

- S0: < 238 dB/m
- S1: 238-259 dB/m
- S2: 260-291dB/m
- S3: >292 dB/m

Liver stiffness categories[3]:

- F0-F1: < 6.65 kPa
- F2: 6.65-7.9 kPa
- F3: 7.9-9.6 kPa
- F4: >9.6 kPa

- When compared to those with no/mild steatosis, S2-S3 patients had:
  - A significantly higher BMI (26.9 vs 23.2 Kg/m^2, p<0.001)
  - A significantly higher waist (102 vs 86 cm, p<0.001) and hip circumference (102 vs 93 cm, p<0.001)
  - A higher prevalence of hypertension (40.4% vs 22.8%, p=0.006), metabolic syndrome (30.3% vs 6.9%, p<0.001) and intermediate/high cardiovascular risk (45.9% vs 24.8%, p=0.006).
- After adjustment for several confounding factors, a longer time from HIV diagnosis (aOR 2.03 per 10 years increase, p=0.016) and a higher BMI (aOR 1.71 per 1 Kg/m^2 increase, p<0.001) were significantly associated with S2-S3 steatosis.
- Integrase inhibitors use was associated to increased CAP at univariate linear regression analysis (mean change +21 dB/m, p=0.027), but this association was not confirmed at multivariate analysis.
- At multivariate analysis, S3 steatosis (aOR 3.09, p=0.024), a longer time from HIV diagnosis (aOR 1.88 per 1 year increase, p=0.004) and a higher BMI (aOR 1.15 per 1 Kg/m^2 increase, p=0.031) were independently associated with higher risk of significant liver fibrosis (F2-F4), while having HIV-RNA <50 copies/mL was associated with a lower risk (aOR 0.15, p=0.002).

CONCLUSIONS

- A high prevalence of HS was observed in our cohort PLWH
- BMI and a longer time from HIV diagnosis were independently associated with HS, suggesting that also HIV-related variables could play a role in the pathogenesis of liver fat accumulation
- An independent role of antiretroviral therapy was not demonstrated
- Given the association between HS and significant liver fibrosis, this metabolic condition should be adequately approached in PLWH to avoid progression to advanced liver disease.

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