DIABETES MELLITUS AND LIVER DISEASE PROGRESSION IN PWH WITH METABOLIC-DYSFUNCTION ASSOCIATED SLD

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BACKGROUND

- Type-2 Diabetes mellitus (T2DM) and liver disease are significant comorbidities that complicate the clinical management of people with HIV (PWH).
- Data are limited regarding the progression liver stiffness measurements that are evaluated using vibration-controlled transient elastography (VCTE) in this population.
- We investigated the risk of liver stiffness progression and advanced liver fibrosis by diabetes mellitus (DM) status among people with HIV with metabolic-dysfunction associated stetotic liver disease (MASLD).

METHODS

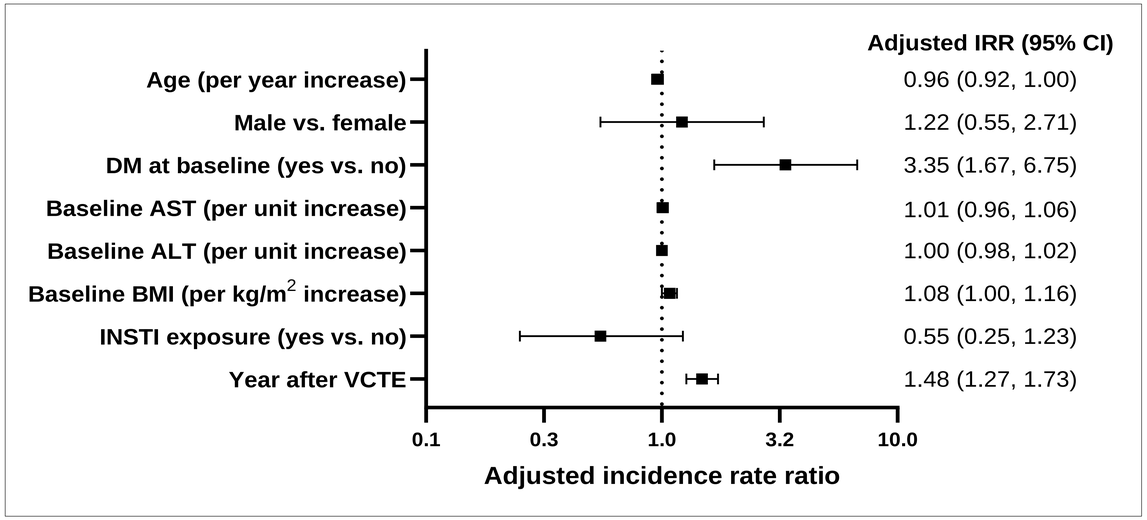
- PWH who had MASLD at their first Vibration-controlled Transient Elastography or VCTE with both liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) available (defined as baseline) and had >1 LSM over follow-up were included.
- **MASLD** was defined as having liver steatosis (CAP ≥248 dB/m) plus one of the cardiometabolic conditions:
  - ❑ body mass index (BMI) ≥23 kg/m^2;
  - ❑ fasting serum glucose level ≥100 mg/dL or T2DM diagnosis or treatment for T2DM;
  - ❑ blood pressure ≥130/85 mmHg or use of antihypertensive treatment;
  - ❑ plasma triglyceride level ≥150 mg/dL; and
  - ❑ plasma high-density lipoprotein cholesterol level ≤40 mg/dL for men and ≤50 mg/dL for women
- **Change in LSM from baseline (ΔLSM)** was evaluated using a linear mixed-effects model, adjusting for age, sex, duration since DM diagnosis, BMI, ALT and AST all fixed at baseline and time-updated exposure to INSTI.
- An interaction term between time and baseline DM was included to assess the effect of DM on ΔLSM.
- Multivariable Poisson regression was used to evaluate **the association between baseline T2DM and the incidence of advanced liver fibrosis** (defined as LSM ≥8kPa) among PWH without LF at baseline.

Type-2 diabetes mellitus was strongly associated with an increased risk of advanced liver fibrosis among PWH with VCTE-diagnosed MASLD. Increased baseline BMI was a key factor for advanced fibrosis while INSTI use was not associated with LSM changes or advanced liver fibrosis.

RESULTS

- Among 345 PWH with MASLD included (35% female), the median age was 48 (IQR, 43-54) years, median BMI was 25 (23-28) kg/m^2 and median CD4 was 662 (500-826) cells/µL. At baseline, 94% had HIV RNA <50 copies/mL and median duration of antiretroviral therapy (ART) was 15 (7-18) years.
- The median baseline LSM was 5.9 (4.8-7.4) kPa, 9.9% had LSM 7.9-9.6 kPa and 10.7% had >9.6 kPa.
- Ninety-seven (28%) had T2DM at baseline. PWH with T2DM at baseline had higher FIB-4 (0.76 [0.59-1.01] vs. 0.92 [0.69-1.26]) and LSM (6.6 [5.4-8.2] vs. 5.5 [4.6-7.2] kPa).
- The median duration between the first and the last VCTE measurements was 47 (42-61) months.

Figure. Forest plot showing the factors associated with the risk of advanced liver fibrosis using multivariable Poisson regression



Advanced liver fibrosis was defined as liver stiffness measurement (LSM) ≥8 kPa. Participants who were free of liver fibrosis (i.e., those with baseline LSM <8 kPa) were included in the analysis. Multivariable model included age, sex, body mass index (BMI), alanine transaminase (ALT), aspartate aminotransferase (AST) – all fixed at baseline and time since first VCTE assessment and time-updated INSTI exposure. There was no significant interaction between baseline DM and integrase strand transfer inhibitors (INSTI) exposure for liver fibrosis risk (P-interaction=0.54). Sensitivity analyses additionally adjusted for smoking, alcohol consumption, HBV and HCV co-infection were consistent with the results from the primary analysis.

RESULTS (Cont.)

- In adjusted analysis, **small LSM decline over time with an average of -0.15 kPa per year** was observed (95%CI, -0.28, -0.01, p=0.03).
- The ΔLSM over time was not associated with baseline T2DM (P-interaction=0.40).
- However, **among PWH without LF at baseline (n=260), the risk of LF** (incidence rate 3.7 [2.6-5.2]/100 PYS) **was more than three times higher in PWH with baseline DM** (adjusted risk ratio [aIRR]: 3.35, 95%CI 1.67-6.75).
- There was no strong evidence suggesting the association between baseline T2DM and advanced LF risk differed by INSTI exposure (P-interaction=0.54).
- In a separate multivariable model using time-updated BMI, every kg/m^2 increase was also associated with a heightened risk of developing advanced fibrosis among PWH with MASLD (aIRR, 1.10, 95% CI 1.03-1.18).

CONCLUSIONS

- Despite stable LSM during follow-up, baseline T2DM was strongly associated with a higher risk of advanced liver fibrosis among PWH with VCTE-diagnosed MASLD, even after adjusting for multiple confounders.
- Prioritizing this population for more intensive monitoring and treatment strategies may help mitigate liver disease progression.

ACKNOWLEDEGMENTS

The authors acknowledge the participation of the HIV-NAT 006 participants.

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