NAFLD AND ITS COMBINATION WITH NASH PREDICT DIABETES DEVELOPMENT IN PEOPLE WITH HIV

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BACKGROUND

- NAFLD prevalence ranges from 25-33% in adults[1,2]
- It is strongly associated with obesity, DM, metabolic complications (which are more prevalent in PWH), hence increase the risk of NAFLD and/or NASH.
- However, little is known regarding the risk factors and complications of NAFLD in PWH.
- We investigated the association of non-alcoholic fatty liver disease (NAFLD) plus or minus a concurrent diagnosis of non-alcoholic steatohepatitis (NASH) with incident diabetes mellitus (DM) among Thai people living with HIV (PWH).

METHODS

- This prospective study analysed PWH aged ≥18 years, on stable antiretroviral therapy (ART), in a long-term cohort in Bangkok, Thailand. Liver stiffness (LS) and controlled attenuated parameter (CAP) values were collected from FibroScan.
- **NAFLD** was defined as CAP >248 dB/m, whereas **NASH with significant activity and liver fibrosis** was defined as FibroScan-AST (FAST) score ≥0.67. Baseline was defined as the first FibroScan date. PWH with hepatitis B or C virus infection, those with excessive alcohol consumption or with DM diagnosed prior to baseline were excluded.
- Cox proportional hazard models were used to investigate the association of NAFLD and NASH with incident DM.
- We also investigated the association of NAFLD with DM at baseline with incident NASH.

In a Thai cohort, people living with HIV who had non-alcoholic fatty liver disease (NAFLD) are more likely to develop diabetes mellitus (DM) than those without NAFLD. Combined NAFLD and NASH with fibrosis further increased the risk of incident DM.

Study design

- A prospective cohort study
- Location – Bangkok, Thailand
- **NAFLD** – defined as CAP >248 dB/m (Karlas T, J Hepatol 2017)
- **NASH with significant activity and liver fibrosis** – defined as FibroScan-AST (FAST) score* ≥0.67

Study population

- PWH aged ≥18 years without hepatitis B or C virus infection and without excessive alcohol consumption AND without DM diagnosis prior to baseline
- Baseline was defined as the first FibroScan date

Endpoints

- **New-onset DM**

(defined as fasting plasma glucose at least 126 mg/dL on two consecutive study visits, or reported onset of diabetes and initiation of antidiabetic therapy)

Statistical analysis

- Hazard ratios (HR) were estimated using Cox proportional regression model
- Models adjusted for age*, sex, family history of DM, duration of ART, and didanosine exposure*, and BMI*, hypertension* and dyslipidemia*

(*time-varying variables)*

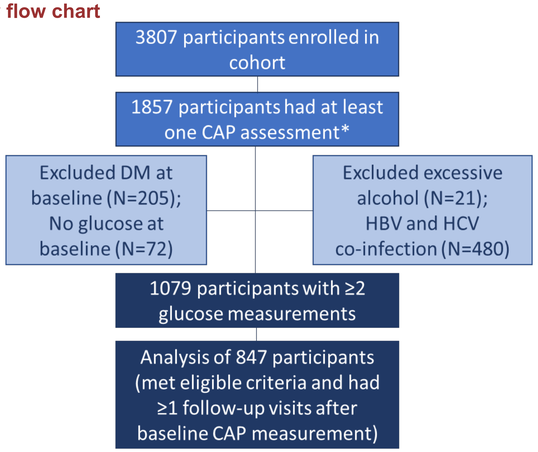
RESULTS

- Among **847 eligible PLWH (Figure 1)**, the median age at baseline was 46 (IQR 39-52) years (43% female). Median baseline CD4 was 588 (IQR 443-759) cells/mm3 and 90% had HIV-1 RNA <50 copies/mL.
- Median CAP value and FAST score was 215 (IQR 184-254) dB/m and 0.22 (IQR 0.12-0.43) respectively. 28% (235/847) and 15% (116/781) had NAFLD and NASH at baseline, respectively.
- During a median follow-up time of 3.3 (IQR 2.7-3.6) years, 28 developed DM (incidence rate=11.0 [95%CI 7.6-15.9] per 1000 person-years).
- **Baseline NAFLD was associated with an increased risk of incident DM** (hazard ratio[HR]: 2.8, 95%CI 1.3-6.4) after adjusting for age, sex, family history of DM, duration of ART, and didanosine exposure, and time-updated BMI, hypertension and dyslipidemia.
- **Combined NAFLD and NASH with significant activity and liver fibrosis at baseline increased the risk of incident DM** (HR: 3.1, 95%CI 1.1-9.3).
- **Figure 2A and 2B** show that the probability of incident DM was higher in PWH with NAFLD or NAFLD/NASH at baseline.
- Baseline NASH alone showed a non-significant but elevated risk of incident DM (HR:1.8, 0.7-4.4).
- In a separate adjusted analysis including DM at baseline (but excluding NASH with fibrosis at baseline), **NAFLD with DM at baseline** (HR: 2.82, 95%CI 1.17-6.78) and **TAF use** (HR: 2.59, 95% CI: 1.12-6.02) was associated with incident NASH with significant activity and liver fibrosis .

CONCLUSIONS

- NAFLD alone or combined with NASH strongly was associated with DM development in PLWH, highlighting the need for DM risk assessment and management in PLWH with NAFLD.
- Further mechanistic studies investigating the underlying metabolic associations of NAFLD or NASH and DM development in PLWH are warranted.

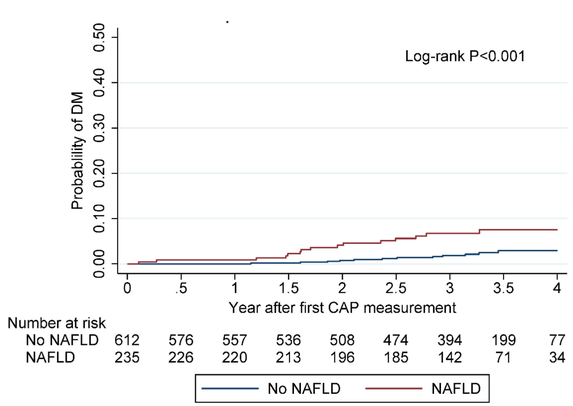
Figure 1. Study flow chart

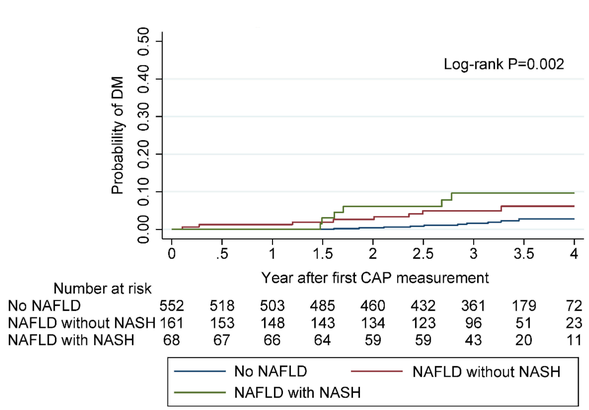


*Baseline was defined as first CAP measurement in primary analysis

*FAST score was calculated as exp(model prediction equation)/[1 + exp(model prediction equation)], where model prediction equation = -1.65 + 1.07*ln(LSM) + 2.66*10−8*(CAP^3)− 63.3*(1/AST), where LSM in kPa, CAP in dB/m, and AST in U/L

Figure 2. Probability of DM development by NAFLD status (A) and by NAFLD with or without NASH with fibrosis (B)





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References 1. Chalasani N, et. al. Hepatology 2017; 2. Paik JM, et. al. Hepatology 2022