Liver Steatosis progression with Integrase Inhibitors in HIV Adults in Low-/Middle-Income Countries

0765

Marie K. Plaisy[1], Thierry Tiendrebeogo[1], Carlotta Riebensahm[2,9], Mark H. Kuniholm[3], Albert Minga[4], Gilles Wandeler[2,9], Rodrigo de Carvalho Moreira[5], Ephrem Mensah[6], Gad Murenzi[7], Ardele Mandiriri[8], Sandra W Cardoso[5], Jean Paul Mivumbi[7], Hugo Perazzo[5], Antoine Jaquet[1], on behalf of the International Epidemiology Databases to Evaluate AIDS (IeDEA)

[1]University of Bordeaux, National Institute for Health and Medical Research (INSERM) UMR 1219, Research Institute for Sustainable Development (IRD) EMR 271, Bordeaux Population Health Centre, Bordeaux, France, [2]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, [3]Department of Epidemiology and Biostatistics, University at Albany, State University of New York, Rensselaer, NY, USA, [4]Blood Bank Medical Center, the HIV care clinic of the National Blood Transfusion Center, Abidjan, Côte d'Ivoire, [5] Evandro Chagas National Institute of Infectious Diseases -Oswaldo Cruz Foundation (INI/FIOCRUZ), Rio de Janeiro, Brazil , [6]NGO Espoir-Vie Togo, Lomé, Togo, [7]Rwanda Military Referral and Teaching Hospital (RMRTH), Kigali, Rwanda , [8] Newlands Clinic, Harare, Zimbabwe, [9]Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

BACKGROUND

- Integrase strand transfer inhibitor (INSTI)-based antiretroviral therapy (ART) regimens are widely used and linked to weight gain, potentially leading to liver steatosis in people with HIV (PWH)
- We assessed predictors of liver steatosis progression over 24 months in PWH from Low-and Middle-Income Countries (LMICs)

METHODS

- We enrolled ART experienced (≥6 months) PWH ≥40 years at five HIV clinics in Brazil, Côte d'Ivoire, Rwanda, Togo and Zimbabwe as part of a prospective observational cohort "The International Epidemiology Database to Evaluate AIDS Sentinel Research Network" (IeDEA-SRN) from October 2020 to October 2023
- Vibration-controlled transient elastography (VCTE) was performed to measure Controlled Attenuation Parameter (CAP)
- The present analysis included participants with valid measurements at both baseline and month 24, excluding those with viral hepatitis co-infection, hazardous alcohol intake, or severe liver steatosis at baseline were excluded from the analysis
- Liver steatosis progression was defined as development of steatosis (CAP ≥248 dB/m) or transition to a higher grade (moderate, CAP ≥268 dB/m; severe, ≥280 dB/m) for those with a lower stage at baseline
- We performed mixed-effects logistic regression, with a random effect for sites to assess predictors of liver steatosis progression, including INSTI exposure
- The model was adjusted for baseline variables (age, sex, BMI, and Type 2 diabetes) based on the Directed Acyclic Graph (DAG) for optimal adjustment.

RESULTS

- A total of 790 participants (62.7% female, median age 50 years, IQR: 45–56) were included
- At recruitment, 391 (49.5%) participants had been exposed to INSTI, with 41.8% for less than 2 years (table)

- **Liver steatosis progression was high among PWH (10.2 per 100 person-years), driven primarily by metabolic disorders such as Type 2 diabetes and overweight/obesity**
- **No association was observed with INSTI exposure**

- At baseline, liver steatosis was present in 16% of participants, with prevalence ranging from 7% in Togo to 30% in Brazil
- Over 24 months, the incidence of liver steatosis progression was 10.2 (95% CI, 8.6–11.7) per 100 person-years
- Factors associated with liver steatosis progression over 24 months of follow-up are presented in figure

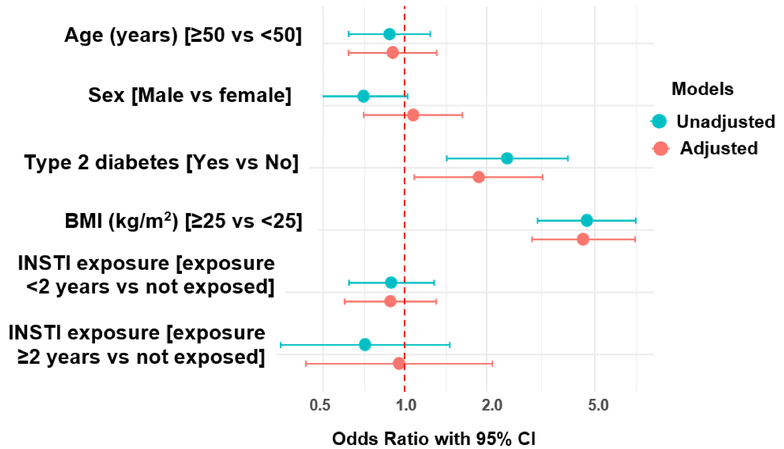
Table: Baseline characteristics of participants included in the study (n=790)

Characteristics	N=790
Median age, years (IQR)	50 (45-56)
Female sex (%)	495 (62.7)
Participating countries	
Brazil	47 (5.90)
Cote d'Ivoire	203 (25.8)
Rwanda	302 (38.2)
Togo	146 (18.5)
Zimbabwe	92 (11.6)
Body mass index (BMI) ≥25 kg/m² (%)	420 (53.2)
Diabetes (%)	73 (9.24)
Median CD4+ count, cells/µl (IQR)	540 (391-718)
ART duration, years (IQR)	12 (7-15)
Unsuppressed HIV RNA viral load (%)	52 (6.58)
InSTI cumulative exposure (years) (%)	
Unexposed	399 (50.5)
<2	330 (41.8)
≥2	61 (7.72)

Abbreviations: IQR, interquartile range; InSTI, integrase strand transfer inhibitor

RESULTS (2)

Figure: Univariable and multivariable analysis of factors associated with the progression of liver steatosis (n=790)



CONCLUSION

- Each year, 10.2 out of 100 PWH experienced a progression of liver steatosis
- No association was found between baseline INSTI exposure and liver steatosis progression over 24 months
- Preexisting metabolic disorders, including Type 2 diabetes and overweight/obesity, were prevalent and predicted liver steatosis progression, highlighting the need for targeted prevention and long-term monitoring, especially in at-risk individuals

ADDITIONAL KEY INFORMATION

Author Contact: Marie Kerbie Plaisy, MD, mariekerbie.plaisy@u-Bordeaux.fr

Acknowledgements

We wish to thank the staff of the HIV clinics participating in the IeDEA SRN collaboration. We are grateful to all participants in the SRN of IeDEA.

IeDEA is supported by the U.S. National Institutes of Health's National Institute of Allergy and Infectious Diseases, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Cancer Institute, the National Institute of Mental Health, the National Institute on Drug Abuse, the National Heart, Lung, and Blood Institute, the National Institute on Alcohol Abuse and Alcoholism, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Fogarty International Center: CCASAnet, **U01AI069923**; Central Africa, **U01AI096299**; Southern Africa, **U01AI069924**; West Africa, **U01AI069919**. Informatics resources are supported by the Harmonist project, **R24AI24872**. This work is solely the responsibility of the authors and does not necessarily represent the official views of any of the institutions mentioned above