Incidence and Impact of Hepatic Steatosis in People with HIV: Insights from the NA-ACCORD Cohort

761

Jennifer C. Price[1], Nina Kim[2], Marina B. Klein[3], Vincent Lo Re[4], John Gill[5], Michael A. Horberg[6], Jennifer O. Lam[7], Catherine Lesko[8], Angel Mayor[9], Richard Moore[10], George Yendewa[11], Giada Sebastiani[3], for the NA-ACCORD Cohort
[1]University of California San Francisco, San Francisco, CA, United States, [2]University of Washington, Seattle, WA, United States, [3]McGill University, Montreal, QC, Canada, CA, [4]University of Pennsylvania, Philadelphia, PA, United States, [5]Southern Alberta HIV Clinic, Calgary, Canada, [6]Mid-Atlantic Permanente Research Institute, Washington, DC, United States, [7]Division of Research, Kaiser Permanente Northern California, Pleasanton, CA, United States, [8]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [9]Universidad Central del Caribe, Bayamón, Puerto Rico, United States, [10]Johns Hopkins School of Medicine, Baltimore, MD, United States, [11]Case Western Reserve University, Cleveland, OH, United States

BACKGROUND

- Hepatic steatosis is an increasingly important comorbidity in aging people with HIV (PWH).
- Population-representative estimates of incidence, risk factors and association with liver-related events are not well understood.
- We evaluated the incidence of hepatic steatosis and its association with liver-related events and overall mortality within the NA-ACCORD.

METHODS

Study population and definitions

- Adult PWH without viral hepatitis coinfection from 11 cohorts
- Hepatic steatosis was defined using the hepatic steatosis index (HSI): 8 x ALT/AST + BMI(+ 2 if type 2 diabetes, + 2 if female) *(Lee JH, et al Dig Liver Dis, 2020)*
- Steatosis was defined as an HSI >36.

Statistical analysis

- Participants were followed from first HSI measurement after 1/1/2000 until first occurrence of a liver-related event (ascites, encephalopathy, variceal bleeding, or hepatorenal syndrome confirmed by adjudication), death, one year after last CD4 or HIV RNA, or 12/31/2015.
- We reported the incidence of and risk factors for hepatic steatosis and its association with liver-related events and overall mortality.

RESULTS

- 20,903 PWH without viral hepatitis (mean age 39 years, 81% males) were included.
- The incidence rate (IR) of hepatic steatosis was 180 per 1000 person-years (PY) (95% CI 173-185).
- The IR by calendar year was (Figure 1):
  - 2000-2004: 188/1000 PY (95% CI 177-201)
  - 2005-2008: 206/1000 PY (95% CI 196-217)
  - 2009-2015: 168/1000 PY (95% CI 162-174)
- ART use and hypertension were associated with higher risk of hepatic steatosis, and increasing CD4 count was associated with lower risk (Table 1).

Hepatic steatosis incidence among PWH in a large North American cohort was relatively high. Elevated hepatic steatosis index was associated with increased overall mortality.

Figure 1. Incidence rates of hepatic steatosis by year 2000-2015

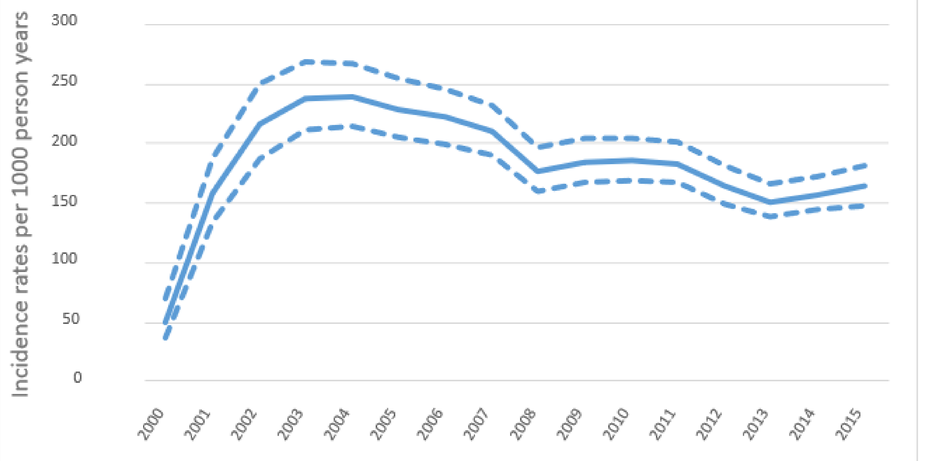


Table 1. Factors associated with hepatic steatosis*

Characteristic	Hazard Ratio	95% CI
ART	1.90	1.02-1.16
Dyslipidemia	1.14	0.99-1.31
Hypertension	1.41	1.22-1.62
CD4 cell count		
0-203 cells/mm^3	1.0	
204-386 cells/mm^3	0.85	0.79-0.93
387-585 cells/mm^3	0.80	0.73-0.87
>585 cells/mm^3	0.75	0.68-0.82

*Adjusted for covariates listed and age, ethnicity, smoking, alcohol use, HIV viral load

Table 2. Factors associated with overall mortality*

Characteristic	Hazard Ratio	95% CI
Hepatic steatosis index	1.02	1.01-1.04
Dyslipidemia	1.44	1.16-1.78
Hypertension	1.34	1.08-1.65
CD4 cell count		
0-203 cells/mm^3	1.0	
204-386 cells/mm^3	0.50	0.43-0.57
387-585 cells/mm^3	0.33	0.28-0.39
>585 cells/mm^3	0.32	0.27-0.38

*Adjusted for covariates listed and age, ethnicity, smoking, alcohol use

RESULTS

- Among PWH with hepatic steatosis, the IR of liver-related events was 1.7/1000 PY (95% CI 1.5-2.0) and the IR of death was 15.2/1000 PY (95% CI 14.4-15.9).
- Elevated hepatic steatosis index was **not** associated with liver-related events but **was** associated with overall mortality (adjHR 1.02, 95% 1.01-1.04), after adjusting for age, ethnicity, smoking, alcohol use, CD4 cell count, dyslipidemia, and hypertension (Table 2)

CONCLUSIONS

- Hepatic steatosis was prevalent among PWH in this large cohort but did not increase the risk of liver-related events.
- However, the association of HSI with overall mortality underscores the need for further research into the long-term health implications of hepatic steatosis in PWH.

ACKNOWLEDGEMENTS

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This work was supported by National Institutes of Health grants U01AI069918, F31AI124794, F31DA037788, G12MD007583, K01AI093197, K01AI131895, K23EY013707, K24AI065298, K24AI118591, K24DA000432, KL2TR000421, N01CP01004, N02CP055504, N02CP91027, P30AI027757, P30AI027763, P30AI027767, P30AI036219, P30AI050409, P30AI050410, P30AI094189, P30AI110527, P30MH62246, R01AA016893, R01AG053100, R01AI177010, R01DA011602, R01DA012568, R24AI067039, R34DA045592, U01AA013566, U01AA020790, U01AI038855, U01AI038858, U01AI068634, U01AI068636, U01AI069432, U01AI069434, U01DA036297, U01DA036935, U10EY008057, U10EY008052, U10EY008067, U01HL146192, U01HL146193, U01HL146194, U01HL146201, U01HL146202, U01HL146203, U01HL146204, U01HL146205, U01HL146208, U01HL146240, U01HL146241, U01HL146242, U01HL146245, U01HL146333, U24AA020794, U54GM133807, UL1RR024131, UL1TR000004, UL1TR000083, UL1TR002378, Z01CP010214 and Z01CP010176; contracts CDC-200-2006-18797 and CDC-200-2015-63931 from the Centers for Disease Control and Prevention, USA; contract 90047713 from the Agency for Healthcare Research and Quality, USA; contract 90051652 from the Health Resources and Services Administration, USA; the Grady Health System; grants CBR-86906, CBR-94036, HCP-97105 and TGF-96118 from the Canadian Institutes of Health Research, Canada; Ontario Ministry of Health and Long Term Care, and the Government of Alberta, Canada. Additional support was provided by the National Institute Of Allergy And Infectious Diseases (NIAID), National Cancer Institute (NCI), National Heart, Lung, and Blood Institute (NHLBI), Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), National Human Genome Research Institute (NHGRI), National Institute for Mental Health (NIMH) and National Institute on Drug Abuse (NIDA), National Institute On Aging (NIA), National Institute Of Dental & Craniofacial Research (NIDCR), National Institute Of Neurological Disorders And Stroke (NINDS), National Institute Of Nursing Research (NINR), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).