ETIOLOGY OF LIVER DISEASE IN ADULTS WITH HIV IN LOW AND MIDDLE-INCOME COUNTRIES

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BACKGROUND

- In high-income countries, liver disease represents a growing cause of morbidity and mortality among people living with HIV (PLHIV), and is linked to an increased burden of non-communicable diseases, including metabolic disorders, in this population
- While chronic viral hepatitis accounts for the majority of liver disease in low and middle-income countries (LMIC), there is limited information about the relative contribution of non-infectious causes of liver disease in PLHIV
- Our aim was to estimate the prevalence of liver disease among PLHIV in LMIC and assess the contributing role of infectious and non-infectious conditions

METHOD

Population and Design

- PLHIV aged ≥40 years, on ART for ≥6 months in six HIV clinics
- Cross-sectional analysis of PLHIV at enrollment in two prospective cohorts: the Sentinel Research Network (SRN) of IeDEA (Côte d'Ivoire, India, Kenya, Rwanda and Zambia) and the PROSPEC-HIV study (Brazil)

Procedure

1. Administered standardized questionnaire
- Age, Sex, Country of residence
- Alcohol use during the past 12 months (AUDIT questionnaire)
  - Hazardous alcohol use (score ≥8 for men/ ≥7 for women)

2. Screening for Metabolic Diseases
- Obesity (BMI≥30 Kg/m^2)
- Dyslipidemia (LDL cholesterol >4.13 mmol/l , total cholesterol ≥6.2 mmol/l, triglycerides >2.25 mmol/l; HDL cholesterol <1.03 for men and <1.29 for women)
- Hypertension (Systolic BP ≥140 mmHg or Diastolic BP≥ 90 mmHg
- Type 2 Diabetes (plasma glucose ≥7.0 mmol/l (126 mg/dl) or HbA1c ≥6.5%)

3. Screening for viral hepatitis infections
- HBs antigen (SD Bioline® or Abon® or Determine®)
- anti-HCV antibodies (SD Bioline®)

If positive for HBV/HCV infection, blood sample were collected for viral load quantification by PCR

4. Screening for Liver disease
Transient Elastography device (Fibroscan E401®, Echosens, Paris)
- Liver fibrosis (LSM ≥7.1 KPA)
- Liver steatosis (CAP ≥248 dB/m)

5. HIV-related data
Antiretroviral regimen, CD4 count, extracted from medical chart review

Statistical analysis
- Factors associated with liver fibrosis (METAVIR score>=2) and steatosis (≥S1) were assessed using multivariable logistic regression models
- Population Attributable Fraction (PAF) for liver fibrosis was estimated using Levin's formula

RESULTS

- In total, 1,632 PLHIV (58.9% female, median age 50 years (IQR 45-52)) were included in the analysis with a median CD4 count of 545 cells/mm^3 (IQR 373-751)
- The overall prevalence of liver fibrosis and steatosis was 11.7% (95% confidence interval (CI) 10.0-13.9) and 31.3% (CI 28.7-33.8), respectively. The highest prevalence was found in Brazil and India (figure 1)

MAIN FINDINGS

Metabolic disorders, including **obesity** and **type 2 diabetes,** are emerging as main factors associated with **liver fibrosis** and **steatosis** among **PLHIV** in **LMIC**

RESULTS

- Participants were reported to have obesity (19.5%), Type 2 diabetes (11.3%), hypertension (24.9%), dyslipidemia (53.9%), hepatitis B (4.5%) and hepatitis C (3.4%)
- Among PLHIV co-infected with hepatitis B, 67.6% were currently on tenofovir
- Hazardous alcohol use (AUDIT score ≥8) was found in 246 (15.1%) participants
- Factors independently associated with liver fibrosis and liver steatosis are presented in Table 1 and Table 2, respectively

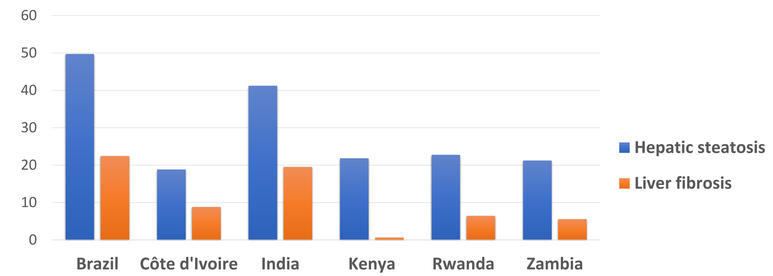

Figure 1. Prevalence of hepatic steatosis (n=1279) and liver fibrosis (n=1492) according to participating sites

Table 1. Factors associated with liver fibrosis in PLHIV in care at referral HIV clinics in Brazil, Côte d'Ivoire, India, Kenya, Rwanda, and Zambia (n = 1,492)*

	Univariate analysis		Multivariable analysis		PAF$^{\Phi}$,
	OR (95% CI)	p-value	OR (95% CI)	p-value	%
Age (per 10 years increase)	1.28 (1.04,1.58)	0.02			
Sex (males vs females)	1.94 (1.41-2.67)	<0.001	1.51 (1.06-2.17)	0.02	
Metabolic features					
Obesity (BMI, Kg/m^2)	2.09 (1.41-3.09)	<0.001	2.47 (1.55-3.94)	<0.001	18
Type 2 diabetes	3.76 (2.55-5.54)	<0.001	2.56 (1.67-3.94)	<0.001	12
Dyslipidemia	1.24 (0.89-1.73)	<0.001			
Hypertension	1.21 (0.85,1.72)	0.29			
CD4 count (<200 versus ≥200 cells/mm^3)	1.78 (1.07-2.97)	0.008	2.22 (1.27-4.12)	0.02	
Country		< 0.001		<0.001	
Zambia	1		1		
Brazil	4.93 (2.33-10.46)		3.0 (1.37-6.58)		
Côte d'Ivoire	1.64 (0.72-3.73)		1.34 (0.58-3.09)		
India	4.15 (1.84-9.36)		3.88 (1.67-8.99)		
Kenya	0.10 (0.01-0.81)		0.10 (0.01-0.82)		
Rwanda	1.17 (0.50-2.70)		1.19 (0.51-2.78)		
Chronic viral hepatitis markers					
Positive HBs Ag	1.82 (0.97-3.4)	0.06	1.87 (0.93-3.76)	0.07	3
Positive HCV Ab/RNA	9.17 (5.26-15.98)	<0.001	5.57 (2.97-10.46)	<0.001	8
AUDIT Score ≥8**	0.91 (0.27-3.05)	0.42			

*1,492 PLHIV with reliable LSM measures out of the 1,632 patients. **≥8 for men and ≥7 for women.
$^{\Phi}$ PAF Population Attributable Fraction

RESULTS

Table 2. Factors associated with liver steatosis in PLHIV in care at referral HIV clinics in Brazil, Côte d'Ivoire, India, Kenya, Rwanda, and Zambia (n = 1,279)*

	Univariate analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (per 10 years)	1.15 (0.98-1.36)	0.07		
Sex (males vs females)	1.05 (0.83-1.33)	<0.69		
Metabolic features				
Obesity (BMI ≥30 Kg/m^2)	6.27 (4.53-8.67)	<0.001	5.51 (3.62-8.39)	<0.001
Type 2 diabetes	3.66 (2.55-5.26)	<0.001	3.01 (2.01-4.53)	<0.001
Dyslipidemia	1.91 (1.47-2.48)	<0.001		
Hypertension	1.60 (1.23-2.08)	<0.001		
CD4 count (<200 cells/mm^3)	0.48 (0.28-0.83)	0.008		
Country		< 0.001		<0.001
Zambia	1		1	
Brazil	3.67 (2.23-6.03)		2.79 (1.62-4.8)	
Côte d'Ivoire	0.86 (0.5-1.47)		0.57 (0.32-1.02)	
India	2.61 (1.52-4.49)		3.06 (1.68-5.59)	
Kenya	1.04 (0.57-1.87)		0.97 (0.52-1.84)	
Rwanda	1.44 (0.86-2.4)		1.67 (0.96-2.91)	
AUDIT Score ≥8**	0.35 (0.1-1.18)	0.13		

*1,279 PLHIV with reliable CAP measures out of the 1,632 patients. **≥8 for men and ≥7 for women.

CONCLUSION

- Metabolic disorders contributed to a higher proportion of liver fibrosis than chronic viral hepatitis in this cohort of PLHIV from LMIC
- As access to effective antiviral therapies against chronic viral hepatitis expands, preventive measures against diabetes and obesity for PLHIV are urgently needed

ADDITIONAL KEY INFORMATION

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