Chronic Hepatitis E virus infection is uncommon in HIV-infected patients

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Background & Aims

The seroprevalence of the Hepatitis E virus (HEV) and its chronicity rate in the HIV-infected population has not been well established. Consequently, the magnitude of this emerging disease in this population cannot be established. The objective of our study was to evaluate the serological/virological HEV situation and factors associated with it in HIV-infected patients.

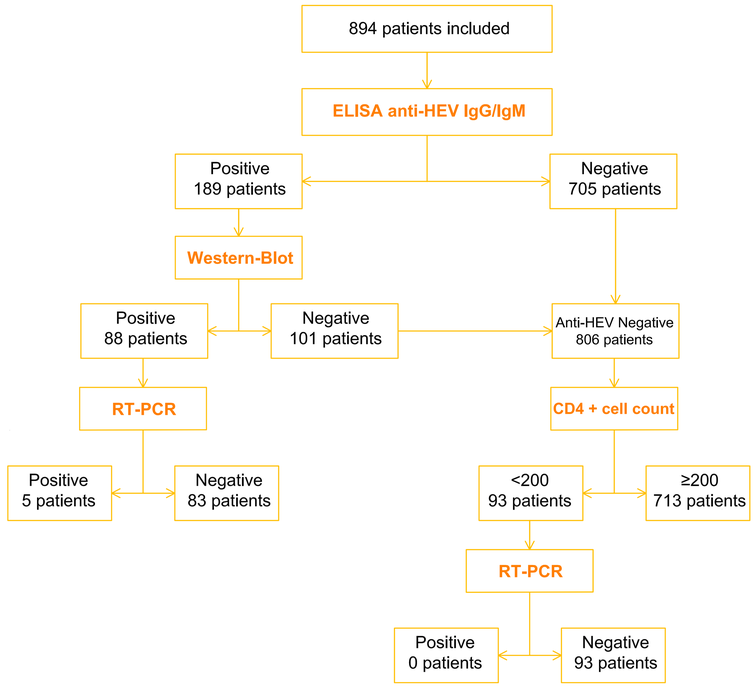
Methods

Prospective study in Southern Spain that included HIV-infected patients who were followed up between September 2012 and May 2013. All patients included were tested for anti-HEV IgG/IgM (Wantai HEV-IgG/IgM ELISA®; Beijing Wantai Biological Pharmacy Interprise© LTD, Beijing, China). In those patients with confirmed anti-HEV IgG/IgM positivity by Western-blot (recomBlot HEV IgG/IgM®; Mikrogen Diagnsotik GmbH, Neuried, Germany), a RT-PCR was performed (amplicube HEV®; Mikrogen Diagnsotik GmbH, Neuried, Germany). In patients where HEV-RNA was amplified, a second RT-PCR was performed 6 months later to identify transient or chronic HEV infections. Additionally, we performed a RT-PCR in all patients with CD4+ cell counts that were lower than 200 cells/mL regardless of the anti-HEV IgG/IgM status. HEV seroprevalence and its associated factors were evaluated.

Results

Eight-hundred and ninety-four HIV infected patients were enrolled in the study. Of these patients, 399 (44.6%) were monoinfected with HIV; 462 (51.6%) were co-infected with HIV/HCV; 12 (1.3%) were co-infected with HIV/HBV; and 21 (2.3%) were coo-infected with HIV/HCV/HBV. In 88 patients, anti-HEV IgG/IgM (86 IgG+/IgM- and 2 IgG+/IgM+) were detected, and consequently, the overall HEV seroprevalence in our population was 9.8% (95% CI: 8.02%-11.9%) (Figure 1)

Figure 1. Flow diagram



The anti-HEV IgG/IgM positive patients were older than those with serum that was anti-HEV IgG negative ($p < 0.001$) (Table 1). In the logistic multivariate analysis model, only age was associated with a positive anti-HEV IgG/IgM status (OR = 1.053; 95% CI: 1.017-1.091) (Table 1).

Table 1. Univariate and mulitvariate analysis for HEV positive serostatus

Characteristics	Anti-HEV status		Univariate *P*	Adjusted OR (95% CI)	Multivariate *P*
	Pos	Neg			
N	88	806			
Sex male. N (%)	70 (79.5)	604 (74.9)	0.365	0.897 (0.442-1.821)	0.764
Age (years). Median (IQR)	50.7 (44.8-59.4)	46.7 (41.9-51.1)	<0.001	1.053 (1.017-1.091)	0.004
Sexual risk. N (%)	33 (37.5)	322 (39.5)	0.389		
AIDS-defining criteria in the past. N (%)*	24 (27.3)	186 (23.1)	0.349	1.311 (0.714-2.409)	0.38
HIV undetectable viral load. N (%)†	78 (88.6)	668 (82.9)	0.226		
On HAART. N (%)	87 (98.8)	785 (97.4)	0.715		
CD4+ cell count (cell/mL). Median (IQR)	486 (303-670)	469 (310-643)	0.594	1.001 (1-1.002)	0.109
ALT (IU/mL). Median (IQR)	26 (19-40)	28 (18-46)	0.908		
AST (IU/mL). Median (IQR)	24 (19-34)	26 (19-41)	0.545		
Triglycerides (mg/dL). Median (IQR)	153 (108-222)	141 (104-190)	0.157	1.001 (0.997-1.005)	0.555
Total cholesterol (mg/dL). Median (IQR)	183 (155-211)	182 (154-214)	0.854		
LDL cholesterol (mg/dL). Median (IQR)	110 (87-131)	111 (87-138)	0.702		
HDL cholesterol (mg/dL). Median (IQR)	40 (32-49)	40 (32-49)	0.665		
Bilirubin (mg/dL). Median (IQR)	0.6 (0.4-1.1)	0.6 (0.4-1)	0.801		

In five patients (0.5%; 95% CI: 0.2%-1.2%), RNA-HEV was detected, which indicated 5.7% (95% CI: 2.1%-12.1%) anti-HEV IgG/IgM-positive patients; however, none of those patients had detectable HEV-RNA six months later (Table 2). None of the 98 anti-HEV IgG/IgM negative patients with a CD4+ cell count lower than 200 cells/mL had detectable HEV-RNA (Figure 1).

Table 2. Clinical and virological characteristics of pacients with detectable HEV-RNA

Case	Sex	Age	AIDS*	Coinfection	HAART	Visit	HEV	IgM	HIV viral load	CD4	ALT
1	M	44.7	C	No	LPV/rtv+RAL+3TC	**Baseline**	+	-	U	205	16
						6	-	-	U	205	31
2	M	51.1	A	HCV	DRV+ABC+3TC	**Baseline**	+	+	U	90	19
						6	-	-	U	146	24
3	F	38.3	B	No	DRV/rtv+TDF+FTC	**Baseline**	+	+	U	734	27
						6	-	-	U	675	14
4	M	46.1	C	No	ATV/rtv+TDF+FTC	**Baseline**	+	-	U	675	28
						6	-	-	U	802	10
5	M	36.4	A	HBV	ETV+ABC+3TC	**Baseline**	+	-	61	241	24
						6	-	-	U	366	32

When patients were sorted according to hepatitis virus co-infection, serum anti-HEV IgG/IgM was detected in 40 HIV monoinfected patients (10.03%; 95% CI: 7.3%-13.3%) and in 48 HIV/hepatotropic virus co-infected patients (9.7%; 95% CI: 7.3%-12.5%). However, no difference in the seroprevalence was found between the groups (p=0.866).

Conclusions

Our study found that despite HEV infection is frequent in HIV-infected patients, the detection of HEV-RNA in our study was low, and no development of chronic infection was found. Furthermore, in immunosuppressed patients with the absence of HEV-serum-marker positivity, HEV-RNA was not detected.

Funding

The study was funded by the Fundación Progreso y Salud, Consejería de Salud de la Junta de Andalucía (grants for health research projects: refs. PI: 0036/2010; PI-157/2011; 430/2012). A.R-J is the recipient of a Post-Doctoral Research Extension Grant from the Fundación Progreso y Salud (Consejería de Salud, Innovación y Ciencia de la Junta de Andalucia).