Incidence of Hepatitis E virus in HIV infected patients: a longitudinal prospective study

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Background & Aims

Hepatitis E virus (HEV) incidence in HIV infected patients has not been well established. Studies reporting HEV seroprevalence and incidence in this populations present several methodological limitations such as retrospective analysis and small population samples. As a result, the current magnitude of this emerging disease in this population cannot be established. Therefore, we designed a study to evaluate the incidence of HEV and its clinical implications in HIV infected patients.

Methods

Design: Prospective study set up in Southern Spain including.

Patients: HIV-infected patients who were followed up between September 2012 and July 2014 in the Infectious Diseases Unit of the Hospital Universitario Reina Sofía de Córdoba. All patients included were tested for anti-HEV IgG/IgM using EIA (Wantai HEV-IgG ELISA), and only those bearing negative were included in the study.

Follow-up: In all patients an EIA anti-HEV IgG/IgM was performed each 6 during the follow-up (4 EIA determination). In each visit demographic, clinical and analytical variables were collected. Visit matched with routinely clinical visit. In those patients showing anti-HEV IgG/IgM positive, a RT-PCR was performed.

HEV-screening: The serological evaluation was performed using:

- ELISA IgG/IgM: Wantai Diagnostic
- RT-PCR: Amplicube (Mikrogen). Detection limit set at 1.000 copies/mL

Definition of case: Case was defined as anti-HEV IgG and/or IgM seroconversion during the study follow-up.

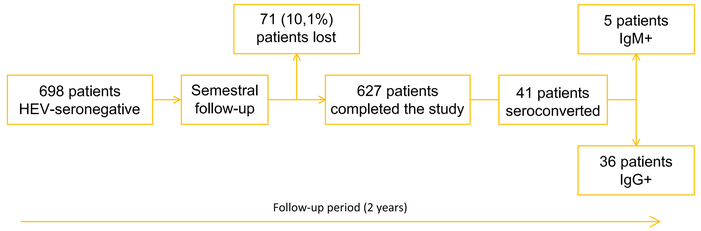
Statistical analysis: Incidence rate was calculated. A bivariate analysis was performedin sense to identify potential factors associated with HEV-seroconversion.

Ethical aspect: The Local Ethical Committee approved the protocol of the study.

Results

Eight-hundred and eighty-six patients were included at baseline. Of them, 188 (21.07%) showed positive for anti-HEV IgG, consequently, 698 patients were included in the study (Figure 1). Six-hundred and twenty-seven (89.9%) complete the study period (Figure 1). The median follow-up (interquartile range) was 11.96 months (8.52-14.52).

Figure 1. Patients flow diagram.



Fourty-one (cumulative incidence = 6.5%) patients seroconverted for anti-HEV IgG during the follow-up. This represent an incidence rate of **7.2 seroconversion /100 patients-year** (95% CI: 5.04-9.16 cases).

When was analyzed the clinical and demographic potential risk factors associated with HEV-seroconversion, only **rural habitat** was associated. The incidence rate of those patients living in rural habitat was significantly higher than the observed in those living in urban area (Table 1).

Table 1. Clinical and demographic associated risk factor for HEV seroconversion.

Factor	Condition	Non Seroconversion	Seroconversion	p	Incidence rate	Log Rank
Sex, n (%)	Male	425 (92.8)	33 (7.2)	0.362		
	Female	161 (95.3)	8 (4.7)			
Age (year), mean (SD)		44.9 (8.8)	45.3 (10)	0.784		
AIDS-defining criteria in the past, n (%)	Yes	153 (91.1)	15 (8.9)	0.148		
	No	433 (94.3)	26 (5.7)			
On-HAART, n (%)	Yes	572 (91.1)	15 (8.9)	0.282		
	No	14 (87.5)	2 (12.5)			
Baseline CD4+ total count (cell/mL), mean (SD)		525 (286)	468 (239)	0.153		
Baseline CD4+ count < 200 cells/mL, n (%)	Yes	63 (96.9)	2 (3.1)	0.298		
	No	523 (93.1)	39 (6.9)			
HCV and/or HBV co-infection, n (%)	Yes	208 (92.4)	17 (7.6)	0.501		
	No	378 (94)	24 (6)			
Habitat, n (%)	Urban	514 (94.7)	29 (5.3)	**0.006**	5.8 cases per 100 patients/year	**< 0.001**
	Rural	70 (85.4)	12 (14.6)		17.4 cases per 100 patients/year	

Twenty-four patients (58.3%) presented clinical manifestation and/or changes in liver function test at the time of seroconversion. Main clinical manifestations and analytical alteration are show in Table 2. The main identified syndrome was **fever with hepatic citolisis** (31.7%) (Table 2).

Table 2. Main clinical manifestation and analytical alteration during HEV seroconversion.

Clinical manifestation	N	%
Asthenia	21	46.8
Fever	16	39
Digestive manifestation	12	29.3
Diffuse abdominal pain	10	24.4
Myalgia	6	14.6
Analytical alteration	**N**	**%**
Altered liver function test	19	46.3
CD4 count decline	18	43.9
HIV blips	14	34.1
Syndrome	**N**	**%**
Febrile syndrome with hepatic citolisis	13	31.7
Febrile syndrome without hepatic citolisis	3	7.3
Hepatic Citolisis without febrile syndrome	6	14.6
Liver cirrhosis decompensation	2	4.8
Asymptomatic	17	41.4

HIV blips (Figure 2) and **liver cirrhosis decompensation** (Figure 3) were associated with HEV-seroconversion.

Of a total of 50 HIV-blips identified during the follow-up, 14 (28%) coincided with the HEV-seroconersion (Figure 2).

During the study follow-up, 4 (5.7%) cirrhotic patients suffered liver decompensation. Two live cirrhosis decompensations were observed among the 6 cirrhotic patients that seroconverted for HEV. Both patients experience hydropic decompensation. The liver cirrhosis aethiology of these patients was HBV and HCV co-infection, respectively (Figure 3).

Figure 2. Association of HIV-blips with HEV seroconversion

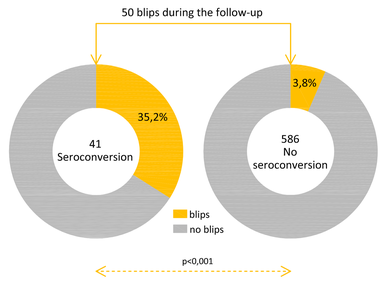
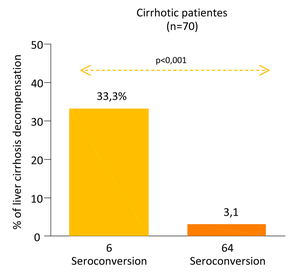


Figure 3. Association of liver cirrhosis decompensation with HEV seroconversion



Conclusions

The HEV-incidence in our study was 7.1 cases per 100 HIV infected patients /year. The only factor associated with HEV-seroconversion was to live in rural habitat. The majority of patients resulted symptomatic when HEV-seroconversion occurred, being febrile syndrome with liver Citolisis the most frequent. HIV-blips and liver cirrhosis decompensation were associated with HEV-seroconversion.

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