

CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN A LARGE COHORT OF HIV-INFECTED SPANISH CHILDREN

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BACKGROUND

HIV infection has become a chronic illness with a good outcome since HAART is used. Morbidity and mortality has decreased dramatically in this population. New problems such as drug toxicity and other chronic infections, which are not controlled by HAART like chronic B or C virus hepatitis.

The presence of hepatitis C virus (HCV) in a co-infected HIV patient is one of the factors that need to be considered before electing a HAART regimen, provided that some antiretroviral drugs should not be used in these patients. Besides, the co-infection causes a worse tolerance to HAART and helps to increase the toxicity of these drugs.

The outcome of HIV infection is worse in co-infected HCV patients, with a more accelerated liver damage progression and worse response to HCV therapies currently available.

Few data exist concerning co-infected paediatric population. Immune tolerance to HCV infection has been observed during the first decade of life in mono-infected patients, but this fact has not been demonstrated in HIV co-infected children.

Characteristics of HCV co-infected children

	mean ± SD	median (range)
Age (years)	15.1 ± 5.15	13.95 (9.0 - 29.3)
Duration ART (months)	113 ± 55.15	113 (0 - 207)
Duration HAART (months)	66.3 ± 41.5	82.36 (0 - 116)
Current CD4 (cells/mm ³)	708.6 ± 373.4	699 (218 - 1462)
Current CD4 %	28.5 ± 8.3	28.5 (13 - 42)
Nadir CD4 %	16.7 ± 10.3	17 (1 - 34)
Current viral load (HIV-1 RNA (log ₁₀))	2.17 ± 1.17	2.48 (1.7 - 5.5)
Timing of infection:		
Vertical transmission (n: 17)	14.3 ± 3.9	13.9 (9 - 21.5)
Transfusion transmission (n:1)	18.1	
	n	(%)
Gender (female):	9	(50%)
Vertical transmission:	18	(95%)
CDC class A/B/C	10/6/3	(53%) (31%) (16%)
Current immune stage 1/2/3	15/3/1	(79%) (16%) (5%)
	n	(%)
Viral load undetectable (<50% of samples below 400 copies/ml)	1	(6%)
(50% - 90 % of samples below 400 copies/ml)	3	(17%)
(>50% of samples below 400 copies/ml)	13	(72%)
Regimen of HAART:	Current treatment:	
1st: 3 (19%)	No therapy:* 2 (10.5%)	
2nd: 8 (50%)	Dual therapy: 1 (5.5%)	
> 3rd: 5 (31%)	HAART: 16 (84%)	

(* 1 child naïve)

OBJECTIVES

The aim of this study has been to assess the prevalence and natural history of HCV in a large cohort of HIV-infected children.

Determinate the HCV genotype. Describe liver stiffness by transient elastography (Fibroscan) of each child and liver biopsy in some of them.

The evolution of 2 children treated with anti-HCV therapy is also described.

RESULTS

Prevalence of HCV in HIV-infected children

	Number	%	CI 95%
Prevalence of HCV:	19	7.2%	3.6% -10-0%
Total HIV-infected children in the cohort:	265		

Four children had repeated negative HCV antibodies and positive PCR despite high CD4 count with HAART.

Clinical characteristics, liver function tests, HCV viral load and Genotype

Clinical characteristics	n	%	Upper level of transaminases: 16/19(89%) children.			
Hepatomegaly:	3/19	16%	Mean ± SD	Median (range)		
Splenomegaly:	2/19	11%	AST (IU/L)	193 ± 197	124 (43-740)	
Coagulation alteration:	1/19	5%	ALT (IU/L)	184 ± 99	167 (56-394)	
Portal hypertension:	0		GGT (IU/L)	89 ± 104	48 (16-357)	
HCV viral load (IU/ml)			HCV Genotype:			
Median (range)			1	1a	1b	3a
7700000 (3490 - 9260000)			4	4c/4d		
	n:		6	1	5	3
			2	2		

Fibroscan and histological characteristics

Fibroscan	n	Stiffness median (range)	Histologic characteristics (2 children with HCV treatment)				
			Metavir index	Portal inflammation	Piecemeal necrosis	Lobular hepatitis	Steatosis
F0-F1	8	5.6 (3.8-6.6)	Patient a*: A1/F1	Moderate	Mild	Moderate	Absent
F2	1	7.8	Patient b*: A3/F3	Marked	Moderate	Marked	Mild
F4	3*	19.5	* Patient a: Liver biopsy after HCV treatment. No Fibroscan.				
			* Patient b: Liver biopsy before HCV treatment. Fibroscan (F4) before and after HCV treatment.				

*Patient 1: has received HCV treatment. Genotype 4. Age: 14.5 years. CD4% nadir: 13%. TARGA duration: 82.2 months.
*Patient 2: Not HCV treatment because low platelet count and coagulation alteration. Genotype 1. Age: 12.5 years. CD4% nadir: 24.7%. TARGA duration: 82.6 months. Currently, psychological disorder.
*Patient 3: Not HCV treatment Currently, psychological disorder. Genotype: 3a. Age: 13.2 years. CD4% nadir: >25%. TARGA duration: >80 months.

CONCLUSIONS

- While HCV prevalence is low in HIV-coinfected Spanish patients, it seems to be much higher than in non-HIV infected children.
- Although most vertically HCV-coinfected children are entering in adolescence with apparent low hepatic fibrosis by elastometry, some patients (15.7% in our series) may have histologic progression.
- Despite high CD4 cell count, children vertically coinfecting may have false negative HCV antibodies.
- Liver disease in HCV and HIV-coinfected children is of great concern and warrants studies on treatment outcomes.

PATIENTS AND METHODS

A multicenter retrospective study was performed reviewing clinical records of a large cohort of HIV infected children in order to analyze the HCV co-infection incidence. Patients were being followed up in nine tertiary care hospitals from Madrid, Spain, which include most of the infected children of Madrid.

Data regarding clinical situation, HIV immunological and virological stage, antiretroviral regimens prescribed, transmission mode and demographic features of patients were recorded. CD4+ and CD8+ T-lymphocyte subpopulations were analyzed by means of flow cytometry (Becton-Dickinson Immunocytometry Systems, San José, CA, USA), and HIV-1 RNA was measured in plasma through a quantitative method of reverse transcriptase-polymerase chain reaction (RT-PCR) (Amplicor monitor, Roche Diagnostic Systems, Braderburg, NJ, USA). The antiretroviral therapy received was also analyzed.

Data concerning HCV infection like genotype and viral load (HCV-RNA), specific treatments and response to therapy were also recorded. Transient elastography (Fibro scan, Echoscans, Paris, France) for assessment of liver fibrosis was made in all patients by measuring liver stiffness in kilopascal units (kpa). METAVIR fibrosis stage was used for analyzing these results (F0F1:<7 kpa, F2: 7-9.4 kpa, F3: 9.4-12 kpa, F4:>12 kpa). Liver biopsy was performed in two patients, assessing fibrosis and necro-inflammatory activity accordingly to METAVIR score, which graduates fibrosis according to F0: no fibrosis, F1: portal fibrosis without septa, F2: portal fibrosis and few septa, F3: many septa without cirrhosis; and activity according to A0: none, A1: slight, A2: mild, A3: severe.

HCV treatment and evolution

	Patient x	Patient y
Age of initiation HCV treatment	14 years	13 years
Clinical Symptoms	Acute hepatitis with ascites, asthenia and fever during one month after starting HAART.	Acute hepatitis after withdrawing HAART with CD4 count of 285 cell/mm ³
Liver function test	Increases of bilirubin and transaminases over 10 times over normal values.	Increases of transaminases and bilirubin.
HCV serology	Negative	Negative
Genotype	1b	4
Fibroscan	No done	F4
Biopsy	No done before treatment	A3/F3 (before treatment)
Antiretroviral treatment	D4T + 3TC + Efavirenz	Abacavir + Lopinavir + Tenofovir
HCV treatment	Alfa-interferon subcutaneous (3000000 IU) 3 times at week + Rivabirin (1000 mg qd) 12 months	Peginterferon (Pegasys) (180 µg/1.73 m ²) sc once a week + Ribavirin (400 mg bid) 12 months
Duration		
Side effects	No	Fever, headache, anorexia and asthenia. ↓ Platelet count
Evolution	Clinical symptoms and liver function improved ↓ Viral load (Not undetectable, reduced 2 log. A1/F1 (3 years after HCV treatment)	No changes in viral load No changes in Fibroscan Next treatment: Liver Transplant at 5 th month.