

Factors associated with severe liver disease in newly referred hepatitis C virus-infected French drug users: a multicenter study of 4 373 patients, 2001-2004

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Background

A national program was implemented in France in 1999 to reduce HCV transmission, increase screening of at risk populations, and improve access to treatment for HCV infected patients.

To contribute to the evaluation of this program, a national surveillance system was set up in 2000 to describe changes in epidemiological and clinical characteristics of HCV-infected patients at first referral in 26 reference centers. The reference centers are hepatology wards located in university hospitals throughout France.

Objectives

To analyze factors associated with severe liver disease in drug users (DUs) infected with hepatitis C virus (HCV) at first referral clinical evaluation to a hepatology reference center in France, between 2001 and 2004.

Methods

- Patients included in this analysis are those recorded in the surveillance system from 2001 to 2004 with past or current injecting or nasal drug use.
- Data on risk factors, suspected year of infection, past or current alcohol consumption, HCV RNA status, ALT level, HBV and HIV status are routinely collected. The estimated duration of HCV infection was assessed by the time between suspected year of infection and year of first referral in the reference center.
- History of past excessive alcohol intake is defined as consumption of > 21 glasses a week for women and > 28 glasses a week for men.
- Severe liver disease (SLD) was defined by cirrhosis or primary liver cancer and was assessed either:
 - by "clinical" evaluation based on biochemical tests and morphological examination (mainly ultrasonography),
 - or by histological evaluation (Metavir scores F4 at liver biopsy).
- The outcome of interest was defined as cirrhosis (with or without complication) or primary liver cancer at first referral, based on the "clinical" evaluation data.
- For the multivariate analysis, to avoid the reduction of the total number of included DUs due to missing data (0 to 29%), we estimated missing values from observed values using multiple imputation (ICE procedure, STATA®.9). Several complete data sets were created. Each data set was, then, analysed separately, and the results were combined to obtain statistical inference of the Odds Ratios (OR).

Results

Between 2001 and 2004,

- 4 373 DUs, mainly (75%) male, were newly referred for HCV infection.
- Median age was 39 years [min: 18; max: 82].
- Median duration of HCV infection, estimated for 3 605 (82%) DUs, was 18 years [min: 0; max: 51].
- Past excessive alcohol consumption was reported by 38% (unknown: 19%).
- HCV RNA was positive for 78% (missing: 13%).
- Among the 3 400 DUs with positive HCV RNA, SLD was assessed:
 - by liver biopsy in 1 627 (no biopsy: 46%; missing: 6%) and was found in 10%,
 - by "clinical" evaluation in 3 153 (missing: 7%) and was present in 7%.

TABLEAU 1		FACTORS ASSOCIATED WITH SEVERE LIVER DISEASE (SLD) AT 1 ST "CLINICAL" EVALUATION IN DRUG USERS NEWLY REFERRED IN HEPATOLOGY REFERENCE CENTERS WITH A POSITIVE HCV RNA, 2001-2004, FRANCE (UNIVARIATE ANALYSIS)					
N = 3 153		% of SLD	Total	OR*	CI# 95%	p	
Sex	female	3	729	1			
	male	8	2 424	2.4	1.6-3.7	< 10 ⁻³	
Age	≤ 40 years	4	1 879				
	> 40 years	12	1 274	3.3	2.5-4.5	< 10 ⁻³	
Duration of HCV infection at referral							
	< 18 years	3	1 326	1			
	≥ 8 years	11	1 433	4.0	2.8-5.7	< 10 ⁻³	
	unknown/missing	7	394				
Time between HCV diagnosis and referral							
	< 1 year	6	1 245	1			
	≥ 1 year	8	1 544	1.4	1.1-2.0	0.02	
	unknown/missing	7	364				
Past excessive alcohol consumption							
	no	4	1 403	1			
	yes	11	1 289	3.1	2.2-4.3	< 10 ⁻³	
	unknown/missing	5	461				
HBs Ag							
	negative	7	2 556	1			
	positive	14	66	2.0	1.0-4.2	0.06	
	unknown/missing	5	531				
HIV Ab							
	negative	7	2 402	1			
	positive	11	209	1.7	1.1-2.7	0.03	
	unknown/missing	6	542				
HCV genotype 3							
	no	6	1 449	1			
	yes	9	775	1.4	1.0-1.9	0.06	
	unknown/missing	7	929				

*Odds Ratio - #confidence interval

TABLEAU 2		FACTORS ASSOCIATED WITH SEVERE LIVER DISEASE AT 1 ST "CLINICAL" EVALUATION IN DRUG USERS NEWLY REFERRED IN HEPATOLOGY REFERENCE CENTERS WITH A POSITIVE HCV RNA, 2001-2004, FRANCE (MULTIPLE IMPUTATION, MULTIVARIATE ANALYSIS)			
N = 3 153		aOR*	CI# 95%	p	
Sex	female	1			
	male	2.1	1.3-3.4	10 ⁻³	
Age	≤ 40 years	1			
	≥ 40 years	2.0	1.4-2.9	<10 ⁻³	
Duration of HCV infection at referral					
	< 18 years	1			
	≥ 18 years	2.5	1.7-3.8	<10 ⁻³	
Past excessive alcohol consumption					
	no	1			
	yes	2.6	1.8-3.6	<10 ⁻³	
HIV Ab					
	negative	1			
	positive	1.6	1.0-2.5	0.06	
HCV genotype 3					
	no	1			
	yes	1.6	1.2-2.2	0.03	

*adjusted Odds Ratio - #confidence interval

Conclusion

- We underscore the role played by excessive alcohol consumption in the severity of the liver disease linked to HCV infection in patients who reported drug use.
- Our results underline the need of an integrated treatment of HCV and HIV infections associated to a management of alcohol excessive consumption.
- Interestingly, we showed the association of HCV genotype 3 and SLD in patients at first referral, naive of any antiviral therapy, independently of the role of age, sex, duration of HCV infection, HIV infection and alcohol consumption.
- Steatosis is frequent and more severe in patients infected with HCV genotype 3, and, thus, it could play a role in the severity of the liver disease observed in these patients. The role of genotype 3 needs to be further characterized.

