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ORIGINAL RESEARCH

Psychiatric and substance use disorders in HIV/hepatitis C virus (HCV)-coinfected patients: does HCV clearance matter? [Agence Nationale de Recherche sur le SIDA et les Hépatites Virales (ANRS) HEPAVIH CO13 cohort]

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Objectives

The objective of this nested study was to assess the prevalence of psychiatric disorders in a sample of HIV/hepatitis C virus (HCV)-coinfected patients according to their HCV status.

Methods

The nested cross-sectional study, untitled HEPAVIH-Psy survey, was performed in a subset of HIV/HCV-coinfected patients enrolled in the French Agence Nationale de Recherche sur le SIDA et les Hépatites Virales (ANRS) CO13 HEPAVIH cohort. Psychiatric disorders were screened for using the Mini International Neuropsychiatric Interview (MINI 5.0.0).

Results

Among the 286 patients enrolled in the study, 68 (24%) had never received HCV treatment, 87 (30%) were treatment nonresponders, 44 (15%) were currently being treated and 87 (30%) had a sustained virological response (SVR). Of the 286 patients enrolled, 121 patients (42%) screened positive for a psychiatric disorder other than suicidality and alcohol/drug abuse/dependence, 40 (14%) screened positive for alcohol abuse/dependence, 50 (18%) screened positive for drug abuse/dependence, 50 (17.5%) were receiving an antidepressant treatment and 69 (24%) were receiving an anxiolytic. Patients with an SVR did not significantly differ from the other groups in terms of psychiatric disorders. Patients receiving HCV treatment screened positive less often for an anxiety disorder. The highest rate of drug dependence/abuse was among HCV treatment-naïve patients.

Conclusions

Psychiatric disorders were frequent in HIV/HCV-coinfected patients and their rates were comparable between groups, even for patients achieving an SVR. Our results emphasize the need for continuous assessment and care of coinfected patients, even after HCV clearance. Drug addiction remains an obstacle to access to HCV treatment. Despite the recent advent and continued development of directly acting antiviral agents (DAAs), it is still crucial to offer screening and comprehensive care for psychiatric and addictive disorders.

Keywords: coinfection, drug/alcohol abuse, hepatitis C virus, HIV, psychiatric disorders

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Introduction

Psychiatric disorders are frequent among HIV/hepatitis C virus (HCV)-coinfected patients [1–3]. The most common of these include major depressive disorders, dysthymia, substance use disorders, post-traumatic stress disorders (PTSDs), childhood conduct disorders, and cognitive and generalized anxiety disorders [1]. Among coinfected patients, psychiatric (in particular depression-linked) and substance use disorders are a critical issue, as they are not only risk factors for HIV and HCV transmission [4–6] but are also factors associated with reduced antiretroviral therapy adherence [7–10], clinical progression [11], reduced virological response [12] and mortality [13]. Moreover, they can significantly impair quality of life [14,15]. Exposure to HCV treatment regimens based on pegylated interferon (Peg-IFN) plus ribavirin has been associated with psychiatric side effects, mainly depressive and anxiety disorders, as well as incapacitating symptoms such as irritability [16], hostility, insomnia and fatigue [17–19]. To date, few data are available on the burden of psychiatric disorders and their prevalence in coinfected patients, particularly in patients who clear HCV following anti-HCV treatment (hereafter "HCV clearers") as a result of achieving a sustained virological response (SVR).

The primary aims of this cross-sectional study nested within the ANRS HEPAVIH CO13 cohort study were to estimate the overall prevalence of diagnosed psychiatric and substance use disorders among a sample of HIV/HCV-coinfected patients, and their prevalence according to specific HCV statuses (HCV naïve, ongoing HCV treatment, treatment nonresponder and HCV clearer). Secondary aims were to determine whether psychiatric disorders persisted in HCV clearers after adjustment for known confounders, and to draft recommendations for future strategies to be implemented with new directly acting antiviral agents (DAAs).

Methods

The ANRS CO13 HEPAVIH cohort

The ANRS CO13 HEPAVIH cohort is a hospital-based cohort established to investigate clinical and public health issues surrounding HIV/HCV coinfection [20]. Recruitment of 1175 patients followed up in 17 hospital wards throughout France took place between January 2006 and December 2008. The cohort was designed and implemented in accordance with the Declaration of Helsinki, and was approved by the ethics committee of Cochin University Hospital in Paris. Patients provided written informed consent to participate.

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*See Appendix.

The HEPAVIH-Psy survey

HEPAVIH-Psy is a cross-sectional nested survey performed in a subset of volunteer HIV/HCV-coinfected patients enrolled in 10 care centres participating in the ANRS HEPAVIH cohort. As part of the HEPAVIH-Psy study, psychiatric screening was proposed to all patients during regular scheduled HEPAVIH follow-up visits. In order to increase recruitment, the survey was also proposed in these centres to HIV/HCV-coinfected patients not participating in the HEPAVIH cohort, but meeting the same inclusion criteria (aged $\geq$ 18 years and chronically coinfected with HIV-1/HCV, as confirmed by a positive HIV antibody test and an HCV RNA assay). This nested study was approved by the ethical committee of the Cochin University Hospital in Paris and all patients provided written consent to participate.

Data on sociodemographic characteristics and information about psychiatric follow-up, drug and alcohol use, and current antidepressant, anxiolytic and other psychotropic treatment prescription were collected using a standardized medical questionnaire. Clinical data were extracted for each HEPAVIH patient from the cohort database. For non-HEPAHIV patients, additional information was collected through the medical questionnaire, including HIV viral load, CD4 count, cirrhosis status and HCV status. Patients' individual HCV status was classified as follows: HCV treatment naïve (never treated), HCV treatment nonresponder, HCV clearer (i.e. having an SVR, defined as negative HCV RNA 6 months after the end of anti-HCV treatment) or currently on treatment (receiving anti-HCV treatment or treatment ended less than 6 months previously).

Current psychiatric and substance use disorders were screened for by trained psychologists using the Mini International Neuropsychiatric Interview (MINI 5.0.0 – Diagnostic and statistical manual of mental disorders DSM IV), which is a structured diagnostic psychiatric interview based on the DSM-IV criteria [21] and records major depressive episodes, suicidality, (hypo)manic episodes, panic disorder, social phobia, post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), psychotic disorder, and substance use disorders (i.e. alcohol and drug abuse/dependence). Patients who screened positive for major depressive disorder, (hypo)-manic episodes, medium or high suicide risk and/or psychotic disorder were reported to the medical staff.

Statistical analysis

The prevalences of psychiatric and substance use disorders were computed for the whole study group and a 95% confidence interval (CI) was computed for each prevalence. All anxiety and mood disorders, except major depressive episodes, were aggregated in the statistical analyses.

The prevalences of psychiatric and substance use disorders were also computed according to individual HCV status. Where appropriate, a χ^2 or Fisher exact test was implemented to determine whether a significant association existed between HCV status and any of the disorders investigated. Finally, using a fixed logistic regression model, we identified disorders whose prevalence remained significantly higher in HCV clearers, and determined whether this result was confirmed after adjustment for known/possible confounders (age, sex, living in a couple and current drug use) whose inclusion in the model was justified by the international literature. Adjusted odds ratios (ORs) and their 95% CIs enabled us to estimate the strength of the association between HCV status and each specific psychiatric disorder.

Results

In the 10 participating centres in Bordeaux, Nice, Marseille, Toulouse and Paris, 289 HIV/HCV-coinfected patients were screened for psychiatric disorders using the MINI questionnaire between February 2012 and July 2013. Of these, 198 were in the HEPAVIH cohort. The remaining 91 were followed up in centres participating in HEPAVIH (31%). Among the 289 patients, three spontaneously cleared HCV and were removed from the study group which then comprised 286 individuals, of whom 68 (24%) had never received any HCV treatment, 87 (30%) were nonresponders, 44 (15%) were currently on a classic bi-therapy or protease inhibitor (PI)-containing HCV therapy, and 87 (30%) were HCV clearers. Among the 44 patients being treated at the time of the survey, only two were receiving an interferon-free HCV treatment. All nonresponder patients and HCV clearers had received Peg-IFN-containing regimes.

The main sociodemographic and clinical characteristics of the study population (n = 286) as well as the prevalence of psychiatric disorders are presented in Tables 1 and 2.

Table 1 Sociodemographic and clinical characteristics of the sample population (n = 286) and prevalence of psychiatric disorders

	HEPAVIH-Psy % (95% CI)
Sex	
Male	71.0 (65.7–76.2)
Female	28.7 (23.5–33.9)
Transgender	0.43
Age	
≤40 years	4.2 (1.9–6.5)
>40 years	95.8 (93.5–98.1)
High school certificate	
No	63.6 (57.7–68.9)
Yes	36.7 (31.1–42.3)
Employment	
No	51.9 (46.1–57.7)
Yes	47.4 (41.6–53.2)
Student	0.7
Tobacco consumption	
Nonsmoker	40.6 (34.9–46.3)
0–10 cigarettes per day	30.4 (25.0–35.8)
>10 cigarettes per day	29.0 (23.7–34.3)
History of injecting drug use	
No	34.0 (28.5–39.5)
Yes	66.0 (60.5–71.5)
CD4 count	
<200 cells/μL	5.6 (2.9–8.3)
200–500 cells/μL	37.5 (31.9–43.1)
>500 cells/μL	56.8 (51.0–62.6)
HIV viral load	
Undetectable	90.2 (86.7–93.7)
Detectable	9.8 (6.3–13.3)
Receiving ART	
No	2.1 (0.4–3.8)
Yes	97.9 (96.2–99.6)
Receiving opioid substitution treatment	
No	86.1 (82.1–90.1)
Yes	13.9 (9.9–17.9)
Major depressive episode (current) (n = 285)	26.0 (20.9–31.1)
(Hypo)manic episode (current) (n = 285)	4.6 (2.2–7.0)
Social phobia (n = 286)	4.9 (2.4–7.4)
Post-traumatic stress disorder (n = 286)	3.5 (1.4–5.6)
Panic disorder (current) (n = 281)	3.6 (1.4–5.8)
Psychotic disorder (current) (n = 283)	1.4 (0.0–2.8)
Generalised anxiety disorder (n = 286)	19.9 (15.3–24.5)
Suicide risk (n = 286)	35.7 (30.1–41.3)
Drug dependence (n = 280)	9.3 (5.9–12.7)
Drug abuse/dependence (n = 280)	17.9 (13.4–22.4)
Alcohol dependence (n = 286)	7.7 (4.6–10.8)
Alcohol abuse/dependence (n = 286)	14 (10.0–18.0)

ART, antiretroviral therapy; CI, confidence interval.

Prevalence of psychiatric disorders

In the study group (Tables 1 and 2), 180 (63%) patients had at least one psychiatric disorder (including alcohol and/or drug abuse/dependence and suicide risk). More specifically, 71 (25%) had one psychiatric disorder, 50 (17%) two, 37 (13%) three, 19 (7%) four, two (1%) five and one (0.4%) six. When we excluded suicide risk (which was reported for 36% of the study group, and by definition was present even when only a past history of suicide attempt was reported), 55% of the patients still had at least one psychiatric disorder.

The most common psychiatric disorder (excluding suicide risk) was major depressive disorder (26%) followed by generalized anxiety disorder (20%), drug abuse/dependence (previous 12 months) (18%) and alcohol abuse/

Table 2 Prevalence of diagnosed psychiatric and substance use disorders according to hepatitis C virus (HCV) infection status (HEPAVIH-Psy)

Diagnosed psychiatric and substance use disorders according to HCV infection status	Total (n = 286) [% (95% CI)]	Naïve (n = 68) (%)	Nonresponders (n = 87) (%)	Ongoing Treatment (n = 44) (%)	Responders (HCV clearers) (n = 87) (%)	P
Any psychiatric disorder (excluding suicide risk and substance dependence/abuse) (n = 286)	42.3 (36.6–48.0)	41.2	41.4	40.9	44.8	0.95
Any anxiety disorder* (n = 286)	28.3 (23.1–33.5)	29.4	29.9	11.4	34.5	0.05
Any mood disorder† (n = 286)	28.3 (23.1–33.5)	23.5	29.9	36.4	26.4	0.49
Major depressive episode (current) (n = 285)	26.0 (20.9–31.1)	23.9	26.4	34.1	23.0	0.56
Psychotic disorder (current) (n = 283)	1.4 (0.0–2.8)	1.5	1.2	2.3	1.2	1.0
Suicide risk (n = 286)	35.7 (30.1–41.3)	41.2	42.5	22.7	31.0	0.08
Drug consumption (n = 286)	40.2 (34.5–45.9)	47.1	41.4	29.5	39.1	0.32
Drug abuse/dependence (n = 280)	17.9 (13.4–22.4)	27.3	20.0	9.3	12.8	0.05
Alcohol abuse/dependence (n = 286)	14 (10.0–18.0)	13.2	21.8	6.8	10.3	0.08

*At least one disorder from among the following: social phobia, post-traumatic stress disorder, current panic disorder and generalized anxiety disorder.
†At least one disorder from among the following: current major depression episode, current manic episode and current hypomanic episode.
CI, confidence interval.

dependence (previous 12 months) (14%). Considering anxiety and mood disorders in general (Table 2), 28% of patients had at least one anxiety disorder (one current disorder from among the following: social phobia, PTSD, panic disorder and generalized anxiety disorder), while 28% had at least one mood disorder (one current disorder from among the following: major depressive disorder, hypomanic episodes and manic episodes). Among our patient sample, 17.5% were receiving an antidepressant treatment and 24% an anxiolytic. Of the 74 and 81 patients who, respectively, reported a major depressive episode and an anxiety disorder, 70.3% and 70.4%, respectively, were untreated, and only 21.6% and 30.9%, respectively, had seen a psychiatrist in the previous 12 months.

Rates for alcohol and drug dependence (previous 12 months) were, respectively, 7.7% and 9.3%. The most commonly used drugs were cannabis (39%), cocaine/crack (7.3%), diverted buprenorphine (2.7%), other opioids such as heroin, codeine or morphine sulphate (2.4%), and diverted methadone (2%).

Frequencies of psychiatric disorders are presented in Table 2 according to HCV status. The only significant difference among the four status groups was found for the variable "patients with at least one anxiety disorder", the lowest proportion being observed in patients treated at the time of the survey (11%), and the highest in HCV clearers (34%). No significant difference among groups was observed at the specific anxiety disorder level. With respect to alcohol and drug abuse/dependence, treatment-naïve patients had the highest rate of drug abuse/dependence (P = 0.05) while nonresponders had the highest rate of alcohol abuse/dependence (P = 0.08).

Factors associated with having at least one anxiety disorder (univariate model) are presented Table 3. In the multivariate model (Table 4), the association between HCV status and having an anxiety disorder remained significant even after adjustment for possible/known confounders including cirrhosis, gender and living in a couple. Comparing the four different HCV status groups using the HCV clearer group as a reference, a significantly lower risk of having an anxiety disorder was observed in patients receiving treatment. This result was confirmed even after introducing current drug use into the model (which was neither a significant confounder nor a correlate). No difference was observed between HCV treatment-naïve patients or HCV treatment nonresponders and HCV treatment responders.

Discussion

The main result of this survey is that individuals who cleared HCV following treatment did not have significantly lower rates of psychiatric disorders than people in other HCV status groups and, more specifically, their rates were very close to those of treatment-naïve patients. This was also true for drug consumption. The high prevalence of anxiety disorders among HCV clearers is also intriguing. These patients more frequently reported at least one anxiety disorder than patients still on treatment. This suggests that HCV clearance and treatment cessation are not systematically associated with a recovery from psychiatric disorders related or not to the nervous system tropism of HCV [22], or to long-term Peg-IFN + ribavirin treatment side effects [23]. This raises questions about the pathophys-

Table 3 Factors associated with having at least one anxiety disorder;* univariate logistic regression analysis (HEPAVIH-Psy study; $n = 286$)

	Anxiety disorder				
	No	Yes	Total	OR (95% CI)	*P*
Cirrhosis					
No	168 (82.35)	61 (75.31)	229 (80.35)		
Yes	36 (17.65)	20 (24.69)	56 (19.65)	1.53 (0.82–2.85)	0.18
ART					
No	6 (2.93)	0 (0.00)	6 (2.10)		
Yes	199 (97.07)	81 (100.00)	280 (97.90)	–	
Anaemia					
No	123 (80.39)	34 (79.07)	157 (80.10)	1	
Yes	30 (19.61)	9 (20.93)	39 (19.90)	1.09 (0.47–2.50)	0.85
Living in a couple					
No	105 (51.22)	50 (61.73)	155 (54.20)	1	
Yes	100 (48.78)	31 (38.27)	131 (45.80)	0.65 (0.39–1.10)	0.11
Sex					
Male	151 (73.66)	53 (65.43)	204 (71.33)	1	
Female	54 (26.34)	28 (34.57)	82 (28.67)	1.48 (0.85–2.57)	0.17
Age	50 (48–53)	52 (49–54)	51 (48–54)	1.04 (0.99–1.09)	0.10
High school certificate					
No	36 (69.23)	23 (62.16)	59 (66.29)	1	
Yes	16 (30.77)	14 (37.84)	14 (37.84)	1.37 (0.56–3.33)	0.49
Employment					
No	100 (49.02)	48 (59.26)	148 (51.93)	1	
Yes	104 (50.98)	33 (40.74)	137 (48.07)	0.66 (0.39–1.11)	0.12
Number of cigarettes/day					
Nonsmoker	82 (40.39)	33 (41.25)	115 (40.64)	1	
0–10 cigarettes	63 (31.03)	23 (28.75)	86 (30.39)	0.91 (0.49–1.70)	0.93
>10 cigarettes	58 (28.57)	24 (30.00)	82 (28.98)	1.03 (0.55–1.92)	
Alcohol dependence					
No	192 (93.66)	72 (88.89)	264 (92.31)	1	
Yes	13 (6.34)	9 (11.11)	22 (7.69)	1.85 (0.76–4.51)	0.18
Drug dependence					
No	183 (91.04)	71 (89.87)	254 (90.71)	1	
Yes	18 (8.96)	8 (10.13)	26 (9.29)	1.15 (0.48–2.75)	0.76
History of injecting drug use					
No	70 (34.48)	26 (32.91)	96 (34.04)	1	
Yes	133 (65.52)	53 (67.09)	186 (65.96)	1.07 (0.62–1.86)	0.80
CD4 count					
<200 cells/μL	14 (6.86)	2 (2.47)	16 (5.61)	1	
200–500 cells/μL	74 (36.27)	33 (40.74)	107 (37.54)	3.12 (0.67–14.52)	0.35
>500 cells/μL	116 (56.86)	46 (56.79)	162 (56.84)	2.78 (0.61–12.70)	
HIV load					
Undetectable	184 (90.20)	73 (89.12)	257 (90.18)	1	
Detectable	20 (9.80)	8 (9.88)	28 (9.82)	1.01 (0.43–2.39)	0.99
Receiving opioid substitution treatment					
No	176 (87.56)	66 (82.50)	242 (86.12)	1	
Yes	25 (12.44)	11 (17.50)	39 (13.88)	1.49 (0.73–3.05)	0.27
HCV status					
Never treated or treated without success	109 (53.17)	46 (56.79)	155 (54.20)	0.80 (0.46–1.40)	0.44
Ongoing treatment	39 (19.02)	5 (6.17)	44 (15.38)	0.24 (0.09–0.68)	0.01
Treated with success	57 (27.80)	30 (37.04)	87 (30.42)	1	

*At least one disorder from among the following: social phobia, post-traumatic stress disorder, current panic disorder and generalized anxiety disorder.
ART, antiretroviral therapy; CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio.

iology of psychiatric disorders during HCV infection, anti-HCV treatment and recovery. Among untreated patients, risk factors associated with drug use, stigmatization and the burden of a chronic infectious disorder, as well as direct or indirect biological changes induced in the central nervous system by chronic hepatitis C, have all been identified as possibly responsible for the psychiatric symptoms observed [22]. Psychiatric disorders observed during Peg-IFN + ribavirin treatment may be associated with pre-existing risk factors (a high depression score at treatment initiation and personality traits such as increased anger, low agreeableness or a high neuroticism score) or with 5-hydroxytryptamine (5-HT) dysregulation and/or involvement of cytokines [23]. Late onset of anxiety/depressive symptoms after IFN-based treatment discontinuation has already been described in HCV-treated patients [24–29],

Table 4 Association between hepatitis C virus (HCV) infection status and having at least one anxiety disorder* after adjustment for known/possible confounders (HEPAVIH-Psy study; $n = 286$)

	OR (95% CI)	*P*
Cirrhosis		
No	1	
Yes	1.86 (0.96–3.58)	0.06
Living in a couple		
No	1	
Yes	0.58 (0.34–1.01)	0.05
Gender		
Male	1	
Female	1.64 (0.92–2.92)	0.09
HCV infection status		
Treatment naïve or HCV treatment Nonresponder	0.85 (0.48–1.51)	0.58
Ongoing HCV treatment	0.23 (0.08–0.64)	0.005
HCV treatment responder	1	

*At least one disorder from among the following: social phobia, post-traumatic stress disorder, current panic disorder and generalized anxiety disorder.
CI, confidence interval; OR, odds ratio.

but also among patients treated for renal cancer [28]. If IFN treatment is indeed responsible for serious long-term and incapacitating psychiatric side effects, then the argument for using DAAs instead of IFN is a strong one, particularly for the most vulnerable populations, such as drug users or patients who already have psychiatric disorders. Nevertheless, the psychiatric-related innocuousness of DAAs has not yet been fully demonstrated. Another explanation for the high prevalence of anxiety disorders observed among HCV clearers could be the premature cessation of care after the end of anti-HCV treatment, despite persisting long-term side effects of Peg-IFN and IFN [27]. Furthermore, dynamic factors may also be involved: being "in treatment" means being in an active positive recovery process, and benefitting from the full attention of the medical staff. Treatment end and recovery mean that the individual no longer has "patient" status and new challenges emerge related to work, family and social rehabilitation. In most studies on the topic, psychiatric assessment is limited to the treatment period and to mood disorders, and rarely includes anxiety disorders. Further studies with long-term psychiatric follow-up including anxiety disorder assessment after treatment discontinuation should be conducted to assess the reproducibility of these results and to determine the influences of HCV, IFN treatment [for example comparing DAAs and IFN-based treatment in patients with HCV and hepatitis B virus (HBV) infection] and HIV coinfection on anxiety disorders.

Individuals with ongoing HCV treatment tended to present lower rates of specific psychiatric disorders and a significantly lower risk of having an anxiety disorder. The fact that patients on anti-HCV treatment did not have a higher rate of psychiatric disorders, despite the well-established psychiatric impact of anti-HCV treatments with IFN + ribavirine [30], suggests recruitment bias. Indeed, in general, physicians probably prescribe HCV treatment to those patients who wish to start treatment and whom they clinically consider to have a greater capacity to cope with the burden of treatment side effects while remaining adherent. The fact that the rate of patients with drug abuse/dependence in our study was higher among treatment-naïve patients supports this hypothesis. Access to treatment for drug users is a crucial question, as they represent the most at risk group for HCV transmission. Several studies have already shown that active drug users can be successfully treated for HCV infection if the conditions for adherence are met [31–33]. Another possible explanation for why patients on anti-HCV treatment in our study did not have a higher rate of psychiatric disorders is that, when anti-HCV treatment is started, medical staff provide patients with a comprehensive care package, including social support and antidepressants, which could limit the onset of anxiety disorders.

Half of the sample population of HIV/HCV-coinfected patients had at least one psychiatric and one substance use disorder (i.e. alcohol or substance abuse/dependence). Psychiatric disorder prevalences are usually high among HIV/HCV-coinfected patients, partly because of the sociodemographic characteristics of this population, who are usually infected via injecting drug use [1], but perhaps also as a consequence of the burden of their double diagnosis. This suggests the need for at least a basic routine psychiatric assessment of this population. The burden of psychiatric disorders is substantial and their impact on quality of life considerable [34,35]. Despite this, they remain underdiagnosed and undertreated.

Limitations

Our survey cannot be considered a prevalence study of psychiatric disorders among HCV/HIV-coinfected patients, as recruitment was on a voluntary basis and took place during specialized consultations for HIV-infected patients either already being followed up and included in a cohort or recruited using the same selection criteria as those from the cohort. It is therefore possible that we underestimated the prevalence in the overall HIV/HCV-infected population, as the most severely affected patients may have been more reluctant to be interviewed (because of fatigue, severe disorders, etc.). Another limitation is related to the cross-sectional design of the survey. The influences of HCV itself, of anti-HCV treatment and of other factors in the differences observed between HCV-cleared patients, those being currently treated, those never treated and treatment nonresponders would have been easier to clarify in a long-term, prospective follow-up survey. Our cross-sectional design

only enabled us to build hypotheses which need to be confirmed with complementary studies, for example by comparing DAA- with IFN-based treatments, or HCV infection with other chronic diseases, such as chronic hepatitis B.

The importance of the results of this study should not be undermined by the advent of DAAs, as individuals who achieve HCV clearance are not fully cured. They still have liver disease and a pattern of psychiatric and substance use disorders similar to those of patients requiring treatment. Access to treatment for active drug users should be facilitated and included in a comprehensive care approach [31]. However, considering the impact of psychiatric and substance use disorders on morbidity/mortality, on reduced adherence, on quality of life, on access to care and on risk behaviours, access to novel DAAs should provide stakeholders with the opportunity to screen for psychiatric and substance use disorders, help caregivers provide adequate and tailored care to coinfected patients, and assist in monitoring patient evolution before, during and after treatment.

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Disclosure statement

The authors declare no conflict of interest that may be relevant to the submitted work.

Appendix : HEPAVIH study group

Scientific committee of the ANRS CO13 HEPAVIH study group

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