Revista da Sociedade Brasileira de Medicina Tropical 47(2):149-157, Mar-Apr, 2014
http://dx.doi.org/10.1590/0037-8682-0270-2013

Major Article

Depressive symptoms and harmful alcohol use in hepatitis C patients: prevalence and correlates

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ABSTRACT

Introduction: It is important to understand the characteristics and vulnerabilities of people who have hepatitis C because this disease is currently an important public health problem. The objective of this study was to estimate the prevalence of depressive symptoms and harmful alcohol use in patients with hepatitis C and to study the association between these outcomes and demographic, psychosocial and clinical variables. **Methods:** This cross-sectional, descriptive and analytical study involved 82 hepatitis C patients who were being treated with pegylated interferon and ribavirin at a public university hospital. The primary assessments used in the study were the Alcohol Use Disorders Identification Test and the Beck Depression Inventory. Bivariate analyses were followed by logistic regression. **Results:** The prevalence of depressive symptoms was 30.5% (n=25), and that of harmful alcohol use was 34.2% (n=28). Logistic regression analysis showed that individuals who were dissatisfied with their social support (OR=4.41; CI=1.00-19.33) and were unemployed (OR=6.31; CI=1.44-27.70) were at a higher risk for depressive symptoms, whereas harmful alcohol use was associated with the male sex (OR=6.78; CI=1.38-33.19) and the use of illicit substances (OR=7.42; CI=1.12-49.00). **Conclusions:** High prevalence rates of depressive symptoms and harmful alcohol use were verified, indicating vulnerabilities that must be properly monitored and treated to reduce emotional suffering in this population.

Keywords: Hepatitis C. Depressive symptoms. Depression. Alcohol abuse. Alcohol harmful use.

INTRODUCTION

Hepatitis C is transmitted by parenteral contact and has an estimated prevalence of 2 to 3%, with approximately 170 million people infected worldwide[1]. In Brazil, the prevalence ranges between 1.0 and 1.9%[1]. Chronic hepatitis C (CHC) is associated with the development of cirrhosis, hepatic failure and hepatocellular carcinoma[1]. Studies predict increased morbidity, mortality and economic overload resulting from hepatitis C virus (HCV) infection worldwide[1], thus indicating that it is an important public health problem. The impact of HCV is even greater when it is associated with psychiatric disorders, such as depression and alcohol and/or drug abuse[2].

The prevalence of depressive symptoms and depressive disorder in individuals with HCV ranges from 21% to 58.6% and from 5.7% to 45%, respectively[3]. Several factors are associated with depressive symptoms in this population, including the emotional burden resulting from lifestyle modifications[4], the stigma associated with the diagnosis[5], belonging to groups with greater vulnerability to psychiatric disorders[2] and biological mechanisms of viral action[6]. Hence, a complex interaction between the biological and psychosocial factors is involved in the incidence of depressive manifestations (e.g., depressed mood, loss of interest and enjoyment in usual activities, reduced energy and decreased activity, reduced self-esteem and confidence, ideas of guilt and unworthiness, pessimistic thoughts, disturbed sleep and appetite, ideas of self-harm) among individuals with HCV. The literature shows a continuum of severity in depressive manifestations, ranging from subclinical depressive symptoms in the early stages to the full-blown disorder, which includes both minor and chronic depression (dysthymia) and more severe and recurrent depressive episodes (major depression)[7].

The use of injectable psychoactive substances is an important risk factor for most incidences of HCV transmission[2]. In Brazil, 63.9% of injectable drug users are infected with HCV[8], and the prevalence of HCV ranges from 5.8% to 36.2% among all users of psychoactive substances[9].

Alcoholism is associated with a higher prevalence of anti-HCV[2] and with increased illicit substance use[2] and impulsive behaviors[10] that may enhance the risk of HCV[2] acquisition. Moreover, alcohol use can worsen hepatic problems and can have a negative impact on treatment adherence and the response to antiviral therapy[2].

The impact of CHC is increased in individuals who present comorbidities[11], have no social support[12] and are in stigmatized groups[5]. Therefore, the identification of these aspects is important.

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Received 12 January 2014
Accepted 11 April 2014

Social support is defined as how much one's psychological needs are attended to by other people[13] or, in other words, the extent to which interpersonal relationships provide relief in stressful situations. Satisfaction with one's social support is a subjective and qualitative evaluation and is related to the feeling that he/she has someone to depend upon in case of necessity. These psychosocial variables may have an important influence on the individual's physical and mental health[12,14]. Specifically, social support has been associated with the absence of depressive symptoms[14].

Chronic hepatitis C is a relevant public health problem given its high prevalence, consequences and socioeconomic impact. A better understanding of the population that seeks antiviral treatment is required to effectively reduce psychological distress and improve disease control.

Brazilian studies on this subject remain scarce[9,10,15-18] and have focused on the prevalence of impulsive behaviors[10] and psychiatric disorders[9,15,17] in CHC sufferers and the impact of the disease on their quality of life[16,18]. The aim of this investigation was to estimate the prevalence of depressive symptoms and harmful alcohol use in patients with CHC at the onset of antiviral treatment and to evaluate the possible demographic, clinical and psychosocial correlates.

METHODS

Participants

This cross-sectional analytical study evaluated 82 adult patients, a non-probabilistic sample composed of all patients who fulfilled the inclusion criteria (described below) from March 2007 to December 2008. All patients were treated at the outpatient clinic for Viral Hepatitis of the University Hospital of Botucatu Medical School (*Universidade Estadual Paulista* - UNESP), Brazil. Most of the participants (80.5%) were receiving their first course of treatment, and 19.5% were undergoing re-treatment.

The following inclusion criteria were used in this study: 1) monoinfection with HCV, diagnosed by ELISA II or III, with confirmation by the qualitative determination of HCV RNA and 2) first week of antiviral treatment (either first treatment or re-treatment) for hepatitis C with pegylated interferon (PEGIFN) and ribavirin (RBV). The following exclusion criteria were also used: 1) coinfection with HBV or HIV; 2) presence of hepatic comorbidity (e.g., autoimmune hepatitis, cholestatic diseases); 3) individuals under 18 years old; and 4) refusal to participate.

Instruments

A standardized sociodemographic and clinical form (available on request) was used to collect information concerning the patients' age; education; occupation; income; marital status; social support; diagnostic confirmation; form of HCV infection; comorbidity; and use of medications, tobacco and psychoactive substances. Social support was directly investigated with open-format questions asking whether his/her objective and subjective needs were attended to and whether he/she was satisfied with this support. Data were obtained by an interpersonal interview conducted by the first author (D.A.M., clinical psychologist)at the university outpatient service, where all assessment instruments were applied.

The Alcohol Use Disorders Identification Test (AUDIT) was developed by Barbor et al.[19] and validated for Brazilian samples by Lima et al.[20]. It assesses harmful alcohol use and dependence in the previous year. Eight points or more were used as a case cutoff point (harmful use); scores between eight and 15 points were considered mild cases; and scores of 16 points or higher were considered severe cases (high risk consumption)[19].

The Beck Depression Inventory (BDI) was developed by Beck et al.[21] and translated and validated for Brazilians by Cunha[22]. The cutoff points suggested by Kendall et al.[23] for undiagnosed samples were selected, and scores above 15 and 20 points indicated depressive symptoms and depression, respectively. Of note, the BDI can be used for screening depressive symptoms in the HCV population due to its good discriminative properties[24].

Data analysis

The data were analyzed using Stata 10.0 software[25]. Descriptive and univariate analyses (Chi square and the Fisher exact tests, when appropriate) were performed. The following two outcomes were considered: the presence of depressive symptoms (BDI score >15) and harmful alcohol use (AUDIT score >7). Two models of logistic regression were used, one for depressive symptoms and one for harmful alcohol use, including clinically relevant variables and variables that showed a p-value ≤0.20 in the bivariate analysis. Additionally, both models were adjusted by sex and age. The standard statistical level of significance of 5% was adopted.

Ethical considerations

This study was approved by the local Research Ethics Committee. After being informed about the study objectives, all individuals who agreed to participate signed an informed consent form.

RESULTS

Clinical, demographic and psychosocial characteristics

The patients were 22 to 69 years old (mean age 45.1; standard deviation (SD)±10.3), and males predominated (63.4%). The mean education level was 11 years of schooling (SD±5.4). The remaining demographic and psychosocial characteristics of the sample are presented in **Table 1**.

Regarding social support, 86.6% reported feeling supported, and 78.1% showed satisfaction with the support received **(Table 1)**. The predominant source of support was the patient's family (65.8%; data not shown).

Previous smoking was reported by 61% of the patients (data not shown), and current smoking was reported by 32.9%; 43.9% had used some type of illicit substance in their lifetime, and 14.6% reported current use. Tobacco use and illicit substance use were

TABLE 1 – Sociodemographic characteristics and lifestyle of the sample, according to sex (n = 82).

	Male (n=52)		Female (n=30)		Total (n=82)	
	n	%	n	%	n	%
Age ≥ 40 years-old	37	71.1	20	66.7	57	69.5
Educational level ≥ 8thgrade	37	71.1	16	53.3	53	64.6
Qualified occupation	47	90.4	20	66.7	67	81.7
Employed	35	67.3	17	56.7	52	63.4
Per capita income < 1 minimum wage	18	34.6	9	30.0	55	67.1
Marital status (with partner)	34	65.4	19	63.3	53	64.6
Householder	38	73.1	10	33.3	48	58.5
Social support (yes)	45	86.5	26	86.7	71	86.6
Satisfaction with support (yes)	42	80.8	22	73.3	64	78.1
Current tobacco use	22	42.3	5	16.7	27	32.9
Previous illicit-drug use	34	65.4	2	6.7	36	43.9
Current illicit-drug use	12	23.1	0	0.0	12	14.6

more frequently reported by males than by females **(Table 1)**. The previous and current most frequently used drugs were cocaine (52.8%) and cannabis (66.7%), respectively (data not shown).

Almost half (46.3%) of the patients had been diagnosed by routine exams an average of 3.5 years before the interview was conducted (less than five years previously for 76.8% of them). Twenty-eight percent suspected that they had hepatitis C and chose to be screened **(Table 2)**. Reports that HCV had been acquired during transfusions/medical-dental procedures predominated (53.7%), while 24.4% reported transmission through the use of illicit psychoactive substances. Patients reported acquiring the virus an average of 22.8 years previously (SD±6.3), and 13.4% of them reported infection through the shared use of syringes while administrating *Gluconergan*® (a vitamin complex frequently used as a stimulant from the 1960s to the 1980s, particularly in the context of sports practice)[26] **(Table 2)**. Infection resulting from sharing syringes for illicit substances (95%) and *Gluconergan*® (100%) use was more frequent among males than among females (data not shown).

Clinical comorbidity was reported by 42.7% of the patients and primarily consisted of diabetes (14.3%) and hypertension (14.3%). Antiviral therapy was initiated for the first time by 80.5% of the patients, while among those resuming treatment (19.5%), 50% did not respond to previous therapy (data not shown).

Prevalence of depressive symptoms and harmful alcohol use

Almost one-third (30.5%) of the patients presented depressive symptoms, and 76% of those patients presented clinically severe symptoms (BDI >20) **(Table 3)**. Harmful alcohol use was identified in 34.2% of individuals and occurred more frequently in males than in females. A high-risk consumption pattern was observed in 39.3% of those who reported harmful alcohol use **(Table 3)**.

In the logistic regression of depressive symptoms, the following variables were integrated into the model: sex, age, having a paid job, being the head of the family, income, comorbidity, harmful alcohol use, current smoking, current substance use and satisfaction with the social support received. Not having a paid job (OR=6.31; CI=1.44-27.70) and dissatisfaction with social support (OR=4.41; CI=1.00-19.33) remained independently associated with this outcome **(Table 4)**.

The variables sex, age, education, mode of transmission, number of treatments, current use of tobacco or psychoactive substances and satisfaction with social support comprised the regression logistic model used to study which factors were independently associated with harmful alcohol use. The male sex (OR=6.78; CI=1.38-33.19) and current use of illicit substances (OR=7.42; CI=1.12-49.00) remained in the model **(Table 5)**.

DISCUSSION

This study describes the demographic, clinical and psychosocial characteristics of individuals with hepatitis C who were undergoing the first week of antiviral therapy with pegylated interferon (PEG-IFN) and ribavirin (RBV) at a reference university hospital in Brazil. The prevalence of depressive symptoms and harmful alcohol use and their associated factors were estimated. To our knowledge, very few Brazilian studies have systematically investigated the sociodemographic and lifestyle characteristics (e.g., tobacco and illicit drug use, social support) of CHC patients at the

TABLE 2 - Clinical characteristics and HCV related factors of the sample, according to sex (n = 82).

	Male (n=52)		Female (n=30)		Total (n=82)	
	n	%	n	%	n	%
Diagnostic confirmation						
blood donor	11	73.3	4	26.7	15	18.3
active search for confirmation	18	78.3	5	21.8	23	28.1
check up	19	50.0	19	50.0	38	46.3
Specific symptoms	4	66.7	2	33.3	6	7.3
Time since diagnostic confirmation(years)						
≤ 5	37	58.7	26	41.3	63	76.8
6 to 10	7	63.6	4	36.4	11	13.4
≥ 11	8	100.0	0	0.0	8	9.8
Acquisition of HCV						
transfusions/medical-odontological procedures	19	43.2	25	56.8	44	53.7
injected and/or inhaled Illicit psychoactive substances	19	95.0	1	5.0	20	24.4
Gluconergan®	11	100.0	0	0.0	11	13.4
unknown/others	3	42.9	4	57.1	7	8.5
Estimated period of infection (years)*						
≤ 10	2	66.7	1	33.3	3	3.8
11 to 20	16	66.7	8	33.3	24	30.4
21 to 30	32	64.0	18	36.0	50	63.3
≥ 30	1	50.0	1	50.0	2	2.5
Clinical comorbidity	23	65.7	12	34.3	35	42.7
Medication use for comorbidity	19	63.3	11	36.7	30	36.6

HCV: hepatitis C virus; *three cases missing.

TABLE 3 - Prevalence of depressive symptoms and harmful alcohol use, according to sex (n = 82).

	Male (n=52)		Female (n=30)		Total (n=82)		
	n	%	n	%	n	%	p-value
Depressive symptoms*	14	26.9	11	36.7	25	30.5	0.36
Severe depressive symptoms**	11	78.6	8	72.7	19	76.0	0.55
Harmful alcohol use**	25	48.1	3	10.0	28	34.2	0.001
Severe harmful alcohol use**	11	100.0	0	0.0	11	39.3	0.21

* $\chi 2$ test. ** Fisher exact test.

TABLE 4 - Logistic regression: sociodemographic and clinical risk factors for depressive symptoms (n = 82).

	Depressive symptoms			
	crude OR	95%CI	adjusted OR	95% CI
Sex				
female (n = 11)	1			
male (n = 14)	0.63	0.24-1.67	0.40	0.08-2.04
Age				
< 40 years-old (n = 6)	1			
> 40 years-old (n = 19)	1.58	0.54-4.61	0.94	0.20-4.45
Employed				
yes (n = 8)	1			
no (n = 17)	7.19	2.53-20.42	6.31	1.44-27.70
Householder				
yes(n = 10)	1			
no (n = 15)	3.00	1.13-7.92	1.65	0.33-8.15
Income				
per capita income < 1 minimum wage(n = 11)	1			
per capita income > 1 minimum wage (n = 14)	2.01	0.76-5.36	3.21	0.80-12.80
Clinical comorbidity				
no (n = 10)	1			
yes (n = 15)	2.78	1.05-7.30	2.45	0.62-9.65
Current tobacco use				
no (n = 13)	1			
yes (n = 12)	2.58	0.97-6.90	3.21	0.83-12.44
Current illicit-substance use				
no (n = 21)	1			
yes (n = 4)	1.17	0.32-4.30	0.90	0.11-7.28
Harmful alcohol use				
no (n = 14)	1			
yes(n = 11)	1.84	0.70-4.89	3.53	0.68-18.23
Satisfaction with social support				
yes (n = 14)	1			
no (n = 11)	5.61	1.83-17.16	4.41	1.00-19.33

OR: odds ratio; 95%CI: 95% confidence interval.

beginning of antiviral treatment or examined the association of these characteristic with psychiatric conditions[10,15-17]. Moreover, in the present study depressive symptoms and harmful alcohol use were evaluated using standardized instruments.

The demographic and clinical characteristics of the sample were similar to those in other Brazilian studies[15-16,27-28]; this similarity increases the external validity of our findings.

Most participants reported that their diagnosis had been confirmed by routine exams less than five years previously, although they had been infected for an average of 22.8 years (range 1-40). The large time interval between infection and diagnosis is most likely due to the asymptomatic nature of the disease. This finding reinforces the fact that the disease is frequently under-diagnosed and highlights the need for public policies directed toward early detection and treatment[1].

TABLE 5 - Logistic regression: sociodemographic and clinical risk factors for harmful alcohol use (n = 82).

	Harmful alcohol use			
	crude OR	95%CI	adjusted OR	95% CI
Sex				
female (n = 3)	1			
male (n = 25)	8.33	2.24-30.91	6.78	1.38-33.19
Age				
< 40 years-old (n = 8)	1			
> 40 years-old (n = 20)	1.15	0.42-3.13	1.21	0.33-4.46
Educational level				
< 7th grade (n = 7)	1			
> 8th grade (n = 21)	0.48	0.17-1.33	0.48	0.13-1.75
Acquisition of HCV				
transfusions/medical-odontological procedures (n=9)	1			
others (n = 19)	3.89	1.47-10.26	0.99	0.26-3.73
Number of antiviral treatments				
re-treatment (n = 3)	1			
Naïve (n = 25)	0.37	0.09-1.46	0.27	0.05-1.31
Current tobacco use				
no (n = 14)	1			
yes (n = 14)	3.15	1.19-8.30	1.60	0.47-5.46
Current illicit-substance use				
no (n = 18)	1			
yes (n = 10)	14.44	2.89-72.26	7.42	1.12-49.00
Satisfaction with social support				
yes (n = 20)	1			
no (n = 8)	1.76	0.60-5.13	2.83	0.67-11.84

OR: odds ratio; 95%CI: 95% confidence interval; HCV: hepatitis C virus.

In the present study, a higher percentage of individuals attributed infection with HCV to the use of illicit drugs (24.4%) compared with the rates reported by other Brazilian researchers (8.9%[16]and 11.5%[29]). This finding may be due to the inclusion of inhaled substances among the drugs investigated because non-injectable illicit substances are also a risk factor for HCV acquisition[30]. However, the percentage obtained herein is similar to that reported by blood donor candidates at the same institution[31].

The overall prevalence of harmful alcohol use was 34.2%, with 48.1% among men and 10.1% among women, whereas high-risk intake (AUDIT ≥16) occurred in 39.3% of the study patients, all of whom were men. A population inquiry[32] conducted in the State of São Paulo (Brazil) determined prevalences of 52.9% and 26.8% for harmful alcohol use among males and females, respectively; however, harmful use was defined only by self-report. In the same study[32], 10.4% of men and 2.6% of women were alcohol dependent, according to the CAGE instrument. Another study using the AUDIT obtained a rate of 21% for risky alcohol use in patients with HCV[33]. As previously indicated, alcohol use is related to higher exposure to substance use[2] and impulsive behaviors[10], both of which are associated with HCV acquisition[2]. Moreover, identifying and treating alcohol abuse in this population are very important because alcohol abuse can contribute to the worsening of hepatic disease and can increase treatment non-adherence[2].

Among the participants, 43.9% reported lifetime use of illicit substances, which is one of the possible causes of HCV infection. Compared with the results obtained by Carlini et al.[34] regarding the use of illicit substances by the Brazilian general population (22.8%), the percentage determined herein is considered rather high, thus confirming this population's

vulnerability to HCV exposure. Nevertheless, the percentage of those patients who continued to use illicit substances at the beginning of treatment remained quite high (14.6%), showing that special care must be directed toward these individuals.

Among the patients in our study, 30.5% showed depressive symptoms, and of these patients, 76% were considered to have severe clinical depression; these numbers are in agreement with other studies that used the same instrument[12,35]. Of note, patients who could have had depressive symptoms previously were also included in the sample due to the study design and objective. Other authors have reported the prevalence of depressive symptoms between 21% and 58.6%[3] among patients with CHC. Using the Hospital Anxiety and Depression Scale, researchers described prevalence rates ranging from 27%[36] to 72.6%[37], most likely due to differences in the assessment instruments and procedures. A meta-analysis[38] concluded that the presence of depressive symptoms at the beginning of anti-viral treatment enhances the incidence of major depression episodes during treatment and may have a negative impact on treatment adherence and outcome.

The high prevalence of depressive symptoms and other psychiatric disorders detected in individuals with hepatitis C prior to therapy with pegylated interferon and ribavirin has been explained by various theories. One theory indicates that individuals with HCV already belong to subgroups that are at high risk of psychiatric disorders[2]. Another theory argues that the psychiatric disorders may be a consequence of the HCV infection diagnosis because it may have caused an emotional burden that led to the development or accentuation of the psychological morbidity[5]. The role played by inflammatory and immunological mechanisms in the neuroendocrine system and the action of neurotransmitters as well as the effect of HCV on the central nervous system have also been proposed as a risk factor for psychiatric morbidity[6]. These studies highlight the complex interaction between psychological, environmental and biological aspects that could be involved in the manifestation of depressive symptoms. The data presented herein reinforce the need to identify the mechanisms underlying the development of these symptoms. Moreover, the treatment recommended for HCV can also be a risk factor for depression[2].

Our findings highlight the relevance of psychosocial factors in association with depressive symptoms in HCV patients. These circumstances can be indicative of the vulnerability of these individuals. For example, not working can indicate greater disease severity or discrimination due to treatment requirements, whereas being dissatisfied about the social support received may result from difficulties in the affective and relational lives of these individuals. In this study, not having a paid job was also independently associated with depressive symptoms. Golden et al.[39] identified an association between depressive symptoms and poor adjustment at work. A recent review[40] reported high absentee rates and reduced productivity at work in this population. Although they did not refer exclusively to HCV patients, Lagerveldet al.[41] reinforced the association between the duration of a depressive episode and the incapacity for work, regardless of the severity of this disorder. These data highlight the need to identify and treat depressive symptoms at an early stage, thus improving the well-being of these individuals and preventing their occupational lives from being compromised.

Dissatisfaction concerning social support increased the chance of presenting depressive symptoms by almost five-fold, in accordance with the literature[12,42]. Ibarra-Rovillard et al.[43] suggested that the mechanism involved in a person's well-being could be explained by the perception of the fulfillment of their psychological needs by significant others or people on whom the individual feels he/she can rely in stressful situations. This finding shows the need for systematic interventions to ensure participation and acceptance by the social and emotional milieus of patients with hepatitis C to reduce their suffering and promote greater treatment adherence.

In the regression logistic, harmful alcohol use was independently associated with the male sex and with illicit substance use[2,44], in agreement with the literature. This scenario is a cause for concern because these behaviors can lead to a cycle of exposure to risky sexual behaviors, including those involved in HCV transmission[2] (e.g., unprotected sexual relationships, multiple sexual partners), and may also have a strong impact on treatment adherence and outcome[2].

This study has certain limitations that must be considered when analyzing the results. Although we included all patients who initiated treatment or re-treatment in a reference service during a time period of almost two years, the sample size is relatively small and may have led to type 2 error. A standardized instrument was not used to investigate social support, and no diagnostic interview was used to evaluate depressive disorders; depressive symptoms were only evaluated according to the BDI. Finally, causal relations cannot be assumed due to the cross-sectional design.

The prevalence of depressive symptoms in individuals with HCV is high at the onset of antiviral treatment. Dissatisfaction with the social support received and not having a paid job were associated with depressive symptoms in these patients. The prevalence of harmful alcohol use was also high, predominantly among males who used illicit substances.

These findings indicate that certain situations of social and health vulnerability must be properly monitored and addressed or treated to help maintain antiviral treatment adherence and reduce the emotional suffering of individuals with HCV.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Jair Lício Ferreira Santos for his assistance with the statistical analysis.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FINANCIAL SUPPORT

This study was funded by the São Paulo Research Foundation – *Fundação de Amparo à Pesquisa do Estado de São Paulo* (FAPESP) (process 2007/52693-9).

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