Research Article

A Survey on the Prevalence of Depression in Blood Donors with Hepatitis C in Shiraz

Leila Kasraian,[1,*] Neda Negarestani,[2] Mohammad Hossein Karimi,[3] and Sahar Dehbidi[4]

[1]Associate Professor, Community Medicine Specialist, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Shiraz, IR Iran
[2]Assistant Professor, Psychiatrist, Manager of Consultation Center, Iranian Blood Transfusion Research Center, Shiraz, IR Iran
[3]PhD of Immunology, Director, President, Iranian Blood Transfusion Research Center, Shiraz Blood Transfusion Organization, Shiraz, IR Iran
[4]Master of Cellular and Molecular Science, Shiraz, IR Iran

[*]*Corresponding author*: Leila Kasraian, No 164 lane 37 Besat Boulevard, 7174715357 Shiraz, IR Iran. Tel: +98-9177157413, Fax: +98-7116264006, E-mail: LKasraian@yahoo.com

Abstract

Background: Depression is the most common psychiatric disorder associated with hepatitis C.

Objectives: This study aimed to survey the prevalence rate of depression in patients with Hepatitis C Virus (HCV) before they were aware of their HCV test result.

Methods: This cross-sectional study was conducted on all blood donors with confirmed positive HCV test results who donated blood between March 21, 2012 to March 21, 2013 at Fars blood transfusion center in Iran as case group and age- and sex-matched blood donors with negative screening test results as control group. A semi-structured interview based on DSM IV-TR depressive disorder criteria and Beck depression inventory (BDI) was conducted. BDI contained 21 items, each scored from 0 to 3 and total score of 0 to 63 for the whole scale computed by summing up all the items. A cut-off score of $\geq$ 19 indicated clinically significant depressive symptoms. The prevalence rate and risk factors of depression were determined.

Results: The most frequent risk factors for HCV infection were intravenous drug abuse (59.3%), unsafe sexual contact (30.5%), and history of being imprisoned (25.4%). The prevalence rate of depression in the HCV group was 55.9 % (95% CI: 42.99 - 68.87%) that was significantly higher than the corresponding rate of the control group as 17.7 % (95% CI: 8.49% - 28.79%) (P < 0.001). The severity of depression was also more in the HCV group (P < 0.001). Besides, the prevalence rate of depression was higher among HCV patients with lower education level, previous history of drug abuse, unsafe sexual contact, and previous history of psychiatric diseases. The prevalence rate of depression was higher in the case group even after adjusting for other variables.

Conclusions: Our study underlined the remarkable prevalence of depression among HCV patients. Therefore, designing depression screening tests is suggested to help such patients before starting the treatment.

Keywords: Hepatitis C, Depression, Blood Donor, Risk Factor, Intravenous Drug Abuse

1. Background

Hepatitis C Virus (HCV) is a common blood borne disease and one of the major health problems in the world (1). Chronic hepatitis C is the leading cause of cirrhosis, hepatocellular carcinoma (HCC), and end-stage liver disease requiring liver transplantation. It is estimated that 50% - 80% of acute HCV infection will progress to chronic carrier status and, 20% will result in cirrhosis development and its complications after 20 to 30 years (2). In addition, about 3% of the world population (more than 170 million individuals) is chronically infected by hepatitis C, which is responsible for approximately 475,000 deaths around the world annually (2).

It is estimated that depression is affecting 350 million individuals around the world every year (3). Similar to other chronic diseases, mood disorders and psychiatric problems are more prevalent in hepatitis C patients. Besides, depression is common among the HCV patients, which could be due to direct effect of the virus, the secondary effects of the inflammatory process on the brain , fear of long-term outcome of the disease, coexisting problems, and life style factors, such as past or present substance abuse, comorbid psychiatric diseases, and comorbid personality disorders (4, 5). Furthermore, treatment of HCV by Peginterferon or Ribavirin was also accompanied by physical, behavioral, and psychiatric side effects, including flu-like symptoms, fatigue, insomnia, depression, and irritability (6). All these could decline psychosocial functioning, worsen physical symptoms , decrease patients' quality of life, cause poor treatment adherence and efficacy, and increase the burden of disease in terms of medical costs, morbidity, and mortality (3, 7). Thus, depression

could be a main barrier to start the treatment in the HCV patients ([6]). It seems that screening and management of depression in HCV patients before and during HCV treatment may lead to increase their adherence to therapy, enhance their cooperation with physician, improve response to treatment, and decrease the end-stage complications, mainly cirrhosis and hepatocellular carcinoma ([8]).

A previous study in Iran showed that the prevalence rate of anxiety and mood disorders was 8.35% and 4.29% among the normal population in 2005 ([9]). Up to now, no studies have been conducted on the prevalence rate of depression in the HCV patients in Iran. Since the awareness of the disease condition and the stress caused by its uncertain prognosis may contribute to depression, in this study we examined the patients before they were aware of their HCV status.

2. Objectives

The present study aimed at determining the prevalence rate of depression and factors associated with its occurrence in HCV patients before they were aware of their HCV results by conducting structured interviews based on defined depression criteria.

3. Methods

3.1. Setting

This cross-sectional study was conducted at Fars blood transfusion centre, one of the main transfusion centers in southwest of Iran. The study was approved by the blood transfusion organization review committee (No: P.IBTO. 08.24 January 2011). The research was carried out regarding every precaution to respect the privacy of the participants and the confidentiality of the patient's information.

3.2. Subjects

In the study period, 152 292 individuals (5656 women and 146636 men) aged 18 - 65 donated blood at Fars blood transfusion center. Among them, 146 636 (96.3%) were male. All blood donors with positive results in HCV screening test (anti-HCV antibody, Hepanostika HCV Ultra, Beijing United Biomedical) followed by positive confirmatory test (HCV Blot3.0, MP Diagnostics, Ingbert, Germany) between March 21, 2012 to March 21, 2013 were eligible for this study (69 out of 152 292). The exclusion criteria were being aware of HCV results, family history of any psychiatric disorder, history of consuming any drug affecting their mood during the past three years, and history of any chronic general medical problem. All blood donors with confirmed positive HCV were invited to participate in this

study (69 individuals). One person (1.4%) could not be contacted on phone after ten attempts during both daytime and evening hours. Three of them (4.3%) refused participation. Six of them (8.6%) were excluded because of meeting the exclusion criteria. In total, 59 individuals included in the study. The control group was selected among blood donors who had negative screening test results and were age- and sex-matched with the case group in the study period.

3.3. Procedure

Every participant was adequately informed of the aim of the study, methods, and anticipated benefits and potential risks of the study. Written informed consent was obtained from subjects prior to interviews. The interview was performed on both groups by a psychiatrist. The psychiatrist was blinded to the status of HCV at the time of interview. Participants were asked about the demographic characteristics, the risk factors probably related to hepatitis infection, the risk factors probably related to depression, history of any psychiatric or medical problems, and use of any medication. The psychiatrist interviewed subjects using the NIMH Diagnostic interview schedule (DIS) ([3]). The Beck depression inventory (BDI) (Persian one) as a reliable, validated, standardized questionnaire, which assesses presence and severity of depressive symptoms, is a self-report measure that rates severity of depressive symptoms ([3]). This instrument has a good reliability (r = 0.72) and high internal consistency (Cronbach's α = 0.94). ([10]).

The BDI is thought to be an adequate tool to evaluate depression in HCV individuals ([7]). It contains 21 items each scored from 0 to 3. The zero score represents no symptoms (e.g., for the response "I do not feel sad") and 1 - 3 scores represent different levels of the symptoms (e.g., for "I feel sad," "I am sad all of the time, and I can't snap out of it," and "I am so sad or unhappy that I can't stand it"). Total score of this scale is computed by summing up the scores of all items scores, and ranges from 0 to 63, with scores of 0 - 9 indicating no likelihood of depression, 10 - 18 indicating the likelihood of mild to moderate depression, 19 - 29 indicating the likelihood of moderate to severe depression, and 30 - 63 indicating the likelihood of severe depression ([3]). In other words, higher scores represent more severe depressive symptoms. A cut-off score of $\geq$ 19 indicates clinically significant depressive symptoms. The prevalence of depression was determined in both groups.

3.4. Analysis

Data were analyzed using statistical package for the social sciences (SPSS) (Chicago, Illinois, United States v. 22). Chi square test was used to compare qualitative variables

between the groups. Binary logistic regression analysis was employed to assess the association between depression and risk factors. To ensure about reliability of our results due to the low sample size, we used the bootstrap analysis with 1000 replications.

4. Results

The demographic characteristics in case and control groups are summarized in Table 1. As can be seen, the education level was significantly lower in the case group than the control group (P < 0.001). Additionally, the case group had lower proportion of professional jobs compared to the control group (P < 0.001). The study results revealed no significant differences between the two groups regarding marital status (P = 0.189). The risk factors of HCV are shown in Table 2. As the table depicts, the most frequent risk factors for HCV infection were intravenous drug abuse (59.3%), unsafe sexual contact (30.5%) and history of being imprisoned (25.4%). However, 18.9% of the HCV patients did not mention any risk factors. The prevalence rate of depression in HCV group was 55.9% (95% CI: 42.99 - 68.87%) that was significantly higher than the corresponding rate of the control group as 17.7% (95% CI: 8.49 - 28.79%) (P < 0.001).

In the case group, 26 ones (44.1%) suffered from minimal depression, 12 (20.3%) had mild depression, 10 (16.9%) had moderate depression, and 11 (18.7%) suffered from severe depression. In the control group, on the other hand, 48 ones (81.3%) suffered from minimal depression, 4 (6.7%) had mild depression, 5 (8.6%) had moderate depression, and 2 (3.4%) suffered from severe depression. the analysis showed that the severity of depression was higher in the HCV group (P < 0.001). In addition, the prevalence rate of depression was higher among the individuals with lower education level. Nonetheless, the prevalence rate of depression was not related to the subjects' marital status. Furthermore, the prevalence rate of depression was higher among the HCV patients who had a previous history of drug abuse, unsafe sexual contact, and psychiatric diseases (Table 3). The prevalence rate of depression was higher in the case group even after adjusting for other variables (Table 4).

5. Discussion

Similar to other chronic diseases, psychological symptoms and mood disorders are prevalent among HCV patients. Depression is the most common psychiatric disorder associated with hepatitis C (11). In our study, the prevalence rate of depression was higher in HCV patients (55.9%). This finding was independent of side effect of treatment

with Interferon or fear of uncertain outcome of disease. In fact, these confounding factors were ruled out by the inclusion criteria of the study (i.e. patients unaware of their HCV status). Thus, HCV may have direct effect on brain function. However, further studies must be conducted to confirm this hypothesis. In previous studies, the prevalence rate of depression in HCV patients were 10% - 50%, in spite of differences in the study methods, ranging from self-report and chart review by self-completion to formal psychiatric interview (12-14). Biological factors (e.g. neurotoxicity of HCV, changes in the metabolism of brain, etc.), psychosocial factors (e.g. reactive depression related to excessive fatigue, fear of unfavorable long-term outcomes, lack of information about the course of the disease, stigmatization, etc.), and additional risk factors for depression such as concurrent substance abuse may be the reason for high prevalence rate of depression in HCV individuals (15-17).

Differences in prevalence rate of depression may also be related to different social and cultural patterns of patients, population subgroup in which HCV more occurs ,and their high risk behavior which involve them in HCV. Iran is a unique country, culturally, religiously, and politically. Urban living has dramatically increased in Iran in recent years, so that large cities have been facing big problems such as overpopulation and unemployment. The stresses of urban life may induce more mental illness in this group. Besides, many crises like a decade of long war with Iraq and sanction occurred in Iran .These events which may put people under social and economic pressures which may explain higher prevalence rate of depression (9).

In the present study, the most common risk factor for HCV infection was intravenous drug abuse (IDU) (ODDs ratio: 88.95, CI: 11.53 - 146.26). The big confidence interval may be related to high prevalence of IDU in the case group compare to the control group or the small sample size. Previous studies also reported that 74% to 100% of IDU are infected with HCV (15, 18, 19). Furthermore, the prevalence of depression was more in IDU itself without assuming their HCV status because of both lower socio demographic characteristics, and higher prevalence of antisocial personality in this Group (14). In addition, depressed patients may be more likely to engage in behaviors such as IV drug abuse. Moreover, previous studies have also indicated the higher prevalence rate of depression among the IV drug abusers that may be assumed as a barrier to treat these patients (19, 20). In our study, the prevalence rate of depression was higher in the case group even after adjusting for IDU. This result is in agreement with those of previous studies reporting mild cognitive dysfunction in HCV patients even after exclusion of the patients with the history of IDU or substance abuse (21)

Table 1. The Demographic Characteristics of the Participants

Variables	Controls	Patients	95% CI	P Value
Education level			4.013 (1.857 - 8.673)	< 0.0001
Diploma or below	33.9	67.3		
Above Diploma	66.1	32.7		
Marital Status			2.241 (0.769 - 6.532)	0.189
Single	9.8	19.6		
Married	90.2	80.4		
Donation Status			7.257 (3.147 - 16.736)	< 0.0001
First-time donor	17.7	61		
Repeat donor	82.3	39		
Occupation			0.117 (0.032 - 0.419)	< 0.0001
Non-professional job	67.7	94.7		
Professional job	32.3	5.3		

Abbreviation: CI, confidence interval.

Table 2. The Risk Factors of HCV

Risk Factors	HCV Patients, %	OR (%95 CI for OR)[a]	P Value
Intravenous drug abuse	59.3	88.95 (11.53 - 146.26)	< 0.0001
Unsafe sexual contact	30.5	0.695 (0.587 - 0.823)	< 0.0001
Scarification	22	0.780 (0.681 - 0.893)	< 0.0001
History of being imprisoned	25.4	0.746 (0.643 - 0.866)	< 0.0001
Previous history of surgery	22	0.780 (0.681 - 0.893)	< 0.0001
Going to a dentist	20.8	0.492 (0.379 - 0.637)	< 0.0001
Stab wound	20.3	0.797 (0.700 - 0.906)	< 0.0001
Tattoo	15.3	0.847 (0.761 - 0.944)	< 0.001
History of living with HCV patients	8.5	0.915 (0.847 - 0.989)	0.02
History of blood transfusion	8.5	0.915 (0.847 - 0.989)	0.02

Abbreviation: OR, odds ratio.
[a] Confidence interval for OR.

Table 3. The Risk Factors of Depression

Variables	Prevalence Rate, %	95% CI[a]	P Value
Intravenous drug abuse	47.7	0.265 (0.117 - 0.600)	< 0.001
Unsafe sexual contact	29.5	0.165 (0.054 - 0.505)	< 0.001
Tattoo	13.6	0.257 (0.061 - 1.084)	0.07
Scarification	15.9	0.447 (0.140 - 1.426)	0.1
History of being imprisoned	15.9	0.613 (0.206 - 1.823)	0.2
Previous history of surgery	13.6	0.633 (0.199 - 2.02)	0.5
Positive result in confirmatory HCV test	75	0.17 (0.074 - 0.390)	< 0.001
Low education level	66.7	0.333 (0.151 - 0.735)	0.003
Being single	17.5	0.704 (0.246 - 2.015)	0.4
Previous history of psychiatric problems	27.3	0.353 (0.135 - 0.923)	0.028
Unprofessional job	25	0.164 (0.049 - 0.555)	< 0.001

Abbreviation: OR, odds ratio.
[a] 95% confidence interval for prevalence rate.

The detection of depression in HCV patient is essential because undetected depression may decrease adherence to therapy, decline drug efficacy, jeopardize treatment continuity, decrease quality of life, and reduce the chances of eradicating the virus (14, 22). In addition, another previous study showed patients who suffer from both depression and comorbid medical illness had approximately twice impairments in social functioning compare to medical illness or depression alone (13). In addition, HCV patients with depression have poor prognosis, more mortality rate, more requirement to medical services, greater number of

Table 4. Results of the Logistic Regression

Variable	β	S.E.	OR	CI95	Bootstrap CI	P Value
IV drug abuse					0.24 - 3.8	0.928
-			1			
+	0.053	0.58	1.05	0.33 - 3.28		
Unsafe sexual					0.57 - 12.56	0.228
-			1			
+	0.82	0.68	2.27	0.59 - 8.67		
Previous history of psychiatric problems					0.61 - 8.8	0.222
-			1			
+	0.71	0.58	2.05	0.64 - 6.5		
Positive result in confirmatory HCV test					1.3 - 18.2	0.014
-			1			
+	1.47	0.59	4.36	1.35 - 14.07		
Education level					0.72 - 7.87	0.136
-			1			
+	0.79	0.53	2.20	0.78 - 6.24		
Occupation					0.05 - 1.28	0.070
-			1			
+	1.21	0.67	0.29	0.079 - 1.10		

Abbreviations: CI95, 95% confidance interval for the reference level OR 1 is reported; β, regression coefficient; OR, odds ratio; SE, standard error of β.

pain sites, higher pain intensity, longer duration of pain, lower levels of treatment response, more fatigue, more functional disability, and more decline in quality of life even after adjusting for other variables, including MELD score (23, 24).

In spite of high prevalence of depression in the case group, all of the participants never took part any psychiatric evaluation before. The reason for failure to detect depression in the patient group may be due to not paying attention to depressive symptoms as complications that need medical evaluation such as low quality of life, low socioeconomic status, having no information regarding depression importance, fear of stigma because of assuming psychiatric disorder as stigmatization thing, which prohibit them to refer to psychiatrist service.

One of the primary treatments of HCV is Interferon which has been associated with development of major depression as a result of a decrease in the amount of serotonin at the neurosynaptic junction (25-27). Therefore, identification of the risk factors for the subsequent development of depression in HCV patients is necessary (28). Yet, physicians must consider the risk of depression particularly in the patients with a current or past history of depression, other psychiatric diseases, hospitalization for

any psychiatric diseases, and suicide attempts before stating the treatment. Some physicians start antidepressant therapy prior to starting HCV treatment, while some others start HCV treatment first and then monitor the patients for the emergence of depression and begin antidepressant medication if necessary (29). Prophylactic treatment may reduce the incidence of depression and decrease the level of depressive symptoms, and improve the patients' quality of life while they are receiving HCV treatment (26, 29). Overall, assessment of the potential risk factors that affect the development of depression could help physicians decide regarding antidepressant therapy and psychological support during treatment.

In our study, the prevalence rate of depression was not related to the subjects' marital status. However, we expected that married ones due to better family support show lower prevalence of depression. In addition, a previous study revealed no significant relationship between development of depression and some demographic factors, including age, gender, ethnicity, and education level. In that study, lower social support was the only social risk factor related to depression (30). In the current study, the researchers could not assess the relationship between gender and depression due to the adjustment of the case and

control groups. However, a previous study showed that being female was a risk factor for development of depression only in the early phase of PEG-IFN-α treatment (31). Another study also showed that females had more psychiatric side effects at PEG-IFN-α (32). However, some previous studies did not find any significant relationship between gender and depression in PEG-IFN-α therapy (33).

In the present study, the prevalence rate of depression was higher in the patients who had a previous history of psychiatric diseases or other medical disorders. In another study also it was shown that lifetime depression, previous suicidal attempt, and suffering from other psychiatric diseases were mostly associated with the risk of development of depressive symptoms in the HCV patients who received PEG-IFN-α (34). In other studies, development of depression was related to disease-related risk factors (duration of the disease) and consumption of psychoactive substances as a way of transmission (35). Thus, it is necessary to ask about the history of any psychiatric disease, lifetime depression, previous suicidal attempt, and suffering from other psychiatric diseases before stating HCV treatment.

There are several limitations that should be considered in the interpretation of study results. The cross-sectional design of this study prevents causal inference. Prospective research is needed to confirm these findings. Furthermore, given the characteristics of our sample, generalizability of our results is limited. Specifically, all participants were blood donors with HCV, predominantly consisted of males. In addition, a relatively small sample of HCV patients was studied, limiting the ability to generalize findings to all HCV patients. Also the current study did not evaluate the relationship between the disease severity or progression and development of depression. One of the strong points of the study was surveying the prevalence of depression before informing the participants regarding the disease and starting antiviral therapy for HCV .Thus, the effects of diseases-related stigma, acceptance of the disease, work and social adjustment, symptoms of disease, fear of disease outcomes, and side effects of the therapy were not assessed in this study.

Our study highlights the significant relationship between depression and hepatitis C. Depression seems to be an important problem in HCV patients, which may increase morbidity and mortality and also interfere with effective treatment of the disease. Depression can also reduce the risk of elimination of the virus with treatment due to non-compliance of the patients and premature discontinuation of the therapy. Moreover, failure in management of depression has a significant impact on the well-being of this population. Thus, designing simple and practical depression screening tests, focusing on diagnosis and treatment of depression in HCV patients is highly recommended before starting the treatment. More research must be conducted to demonstrate the efficacy of antidepressants in preventing depression during Interferon therapy.

Acknowledgments

Footnote

Conflict of Interests: None.

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