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ORIGINAL ARTICLE

Evaluation of the severity of depression and anxiety in hepatitis B and hepatitis C patients: a case control study

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ABSTRACT

Background: Although several studies have reported the poor mental health of patients with chronic viral hepatitis, few reports exists over the correlation of mental health and virus type. Current study was conducted to compare the severity of anxiety and depression in chronic hepatitis C, B and healthy subjects.

Materials and methods: This case control study was conducted in Tehran Hepatitis Center (THC) in 2006. Group I (chronic hepatitis C, n=14), group II (chronic hepatitis B, n=65) and group III (healthy subjects, n=65) were matched for age, sex and educational level and were compared by means of the severity of anxiety and depression measured by Hospital Anxiety Depression Scale (HADS). The correlation between clinical or para-clinical findings of the patients with viral hepatitis and severity of anxiety and depression was also assessed.

Results: Group I in comparison to other groups reported a higher anxiety (9.57±3.86 vs. 7.45±4.52 vs. 4.81±4.80, p=0.001) and depression (6.43±3.76 vs. 5.23±3.74 vs. 4.76±4.40, p=0.05). Anxiety and depression score were also both correlated with total serum bilirubin level, but were not correlated with other para-clinical findings. However the patients who had received interferon reported higher depressive symptoms but the difference did not reach statistically significant level.

Conclusion: According to the higher severity of anxiety and depression in the case of chronic HCV infection in comparison to HBV infection or healthy subjects and the importance of mental health issues in viral hepatitis, we recommend a more close mental health observation in patients affected with HCV infection. Psychiatrist and psychologist visits and consultations can help in this approach.

Keywords: *Anxiety, Depression, Hepatitis C, Hepatitis B, Viral hepatitis*.
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INTRODUCTION

Viral hepatitis is one of the critical national health problems and a leading cause of liver diseases worldwide (1). There is a huge number of patients suffering from asymptomatic chronic hepatitis who will show the progressive clinical manifestations of hepatitis in upcoming 10 to 20 years (2). Chronic viral hepatitis is the leading cause of cirrhosis, hepatocellular carcinoma and

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liver transplantation in the United States and results in significant mortality (3-5).

There are about 170 million hepatitis C chronic carriers (about 3% of the global population) worldwide (7). This virus has infected 3.9 million individuals in the United States (8), 2.3 million individuals in Japan (9), 1.2% of the population of France (10) and 1% of Iran population (11). Hepatitis B virus is estimated to infect 350 million individuals (5% of the global population) worldwide (12) considering the prevalence range of 0.01% to 20% in various countries (4).

Mental health of patients with chronic viral hepatitis is an imperative theme in hepatitis disease research (2,13,14). Depression has been focused more than other psychiatric disorders in these patients (15-17). Psychiatric disorders are important in patients with hepatitis virus infection for their influence on daily function of hepatitis positive patients by increasing their extra hepatic manifestations (18). They also can decrease quality of life (19,20), increase risk of cancer, mortality (21) and suicide attack probability (2,22) in these patients. Patients with psychiatric disorders have the least compliance to drug therapy which increases the risk of treatment failure in the affected patients (23,24).

Nevertheless, definite coincidence of chronic hepatitis virus infection and psychiatric disorders (25) and its reason (26,27) have not been illuminated well. This is also a matter of debate that which type of hepatitis virus infection has the most coincidence with psychiatric disorders. This study was performed to compare depression and anxiety symptoms in patients with hepatitis B, hepatitis C and healthy controls.

PATIENTS and METHODS

For this case control study, 185 hepatitis patients and healthy controls were requested to participate from which 144 individuals accepted our invitation. We used simple non-accidental method for registering patients suffering from hepatitis infection from clients of Tehran Hepatitis Center. Healthy controls were registered from volunteer blood donors referred to Tehran Blood Transfusion Institute. The study population included: group I (chronic hepatitis C, n=14), group II (chronic hepatitis B, n=65) and group III (healthy subjects, n=65). All three groups were matched for age, sex and educational level. Chronic viral hepatitis was diagnosed by the presence of positive serologic markers for at least 6 months. These serologic markers were HBsAg (along with normal or abnormal liver enzymes and histopathology) for hepatitis B virus and anti-HCV antibody for hepatitis C virus. Written consent was obtained from all patients and ethical committee of Baqiyatallah University approved the study.

Demographic characteristics (age, gender, marital status and educational level), clinical figures (receiving treatment, type and duration of therapy) and laboratory examinations including liver enzymes (Hitachi biochemical analysis device 7170, Japan), blood glucose level, direct and total bilirubin and histopathologic findings in hepatitis positive patients were all documented.

Anxiety and depression were assessed by Hospital Anxiety Depression Scale (HADS) questionnaire. This questionnaire includes 14 questions and two subscales of anxiety and depression. Each question has 4 choices (0-3). Maximum score of anxiety and depression in this questionnaire is 21. Scores higher than 11 in each subscale indicate presence of psychological disorder (28). Validated Iranian version of HADS questionnaire developed by Montazeri A. et al. (29) was used in our study. HADS is a routine questionnaire for assessment of anxiety and depression in outpatient settings and its usage in published articles has been quadrupled from year 1996 to 2002 (30).

Ifudu scale was used to evaluate clinical comorbidities. This scale was first introduced for the assessment of comorbidities in patients receiving hemodialysis and includes 14 fractions for evaluating the function of 14 major body systems. Following diseases are being assessed in this scale: 1) stable angina or myocardial infarction (ischemic heart disease), 2) other cardiovascular disorders (hypertension, congestive heart failure, cardiomyopathy and other non-ischemic heart diseases), 3) respiratory diseases, 4) autonomic neuropathies (gastroparesis, diarrhea, cystopathy, abstipation and orthostatic hypotension), 5) other neurologic disorders including cerebrovascular accident, 6) musculoskeletal diseases, 7) infections including acquired immunodeficiency syndrome, 8) disorders of liver, pancreas and biliary system (hepatitis, hepatic disorders and pancreas enzyme disorder), 9) hematologic disorders except anemia, 10) spinal disorders, low back pain and arthritis, 11) visual impairment (decline of visual acuity to blindness), 12) limb amputation (amputation of fingers to amputation of lower limbs), 13) mental or emotional illnesses (neurosis, depression and psychosis) and 14) genitourinary diseases. Each fraction has a score of 0 (no comorbidity) to 3 (presence of comorbidity in its severe form). Total comorbidity score is the sum of scores from the above 14 mentioned fractions. In this study, these evaluations were performed by an experienced internist. Consultation was achieved, when appropriate. Comorbidity score ranges from 0 to 42 with higher scores indicate more comorbidities (31). This scale has been used previously in many investigations for the assessment of comorbidities in Iran (32-33).

For statistical analysis, mean anxiety and depression scores in three groups were analyzed using Kruskal-Wallis and Chi-square tests, when appropriate. For all tests, significance was defined as $p<0.05$.

RESULTS

Mean (±SD) duration of suffering from hepatitis in group I and II was 6.1±7.6 and 8.3±6.4 years, respectively (NS). Alanine aminotransferase (ALT) was abnormal in 24 (30%) patients suffering from viral hepatitis, aspartate aminotransferase (AST) in 13 (16%), total bilirubin in 12 (15%), direct bilirubin in 7 (9%) and glucose in 6 (8%) of them. Forty-six (58%) viral hepatitis patients had histopathologic liver samples. Mean of stage, grade and score in these patients was 2.1±1.1, 4.2±2.8 and 5.5±4.0, respectively.

Demographic characteristics and Ifudu comorbidity score of the three groups have been demonstrated in table 1. Mean age of the participants had no statistical difference between three groups (NS), but mean comorbidity scores showed to be statistically different ($p<0.001$).

Twenty-nine (37%) hepatitis patients had anxiety and 13 (16%) had depression symptoms. Mean anxiety and depression score was significantly higher in group I when compared with other groups (table 2). In patients suffering from viral hepatitis, mean anxiety score was 6.9±4.0 and 5.5±3.4 in patients with normal and abnormal serum ALT levels, respectively (NS). Mean depression score in viral hepatitis patients with normal and abnormal serum ALT levels was 7.3±4.2 and 5.4±3.9, respectively ($p<0.05$).

Table 1. *Demographic characteristics of patients in different groups*

Variables	Subgroups	Group I (N=14)	Group II (N=65)	Group III (N=64)
Gender	Male	13 (93)*	55 (77)	44 (67)
	Female	1 (7)	15 (23)	20 (33)
Educational level	Diploma and higher	7 (50)	44 (68)	44 (69)
	Lower than diploma	7 (50)	21 (32)	20 (31)
Marital status	Married	1 (7)	0 (0)	10 (18)
	Single	13 (93)	65(100)	54 (82)
Age (year)		44.0±8.3	40.3±10.6	38.4±10.7
Comorbidity score#		9(7-11)	7(6-8)	0(0-2)

* Numbers in parenthesis are percentage

\# The difference was statistically significant ($p<0.001$)

Table 2. *Anxiety and depression scores in different groups*

Variable	Group I (N= 14)	Group II (N= 65)	Group III (N= 64)	P value
Anxiety score	9.5 ± 3.8	7.4 ± 4.5	4.8 ± 2.8	< 0.001
Depression score	6.4 ± 3.7	5.2 ± 3.7	4.7 ± 2.4	< 0.05

Mean anxiety score in patients suffering from viral hepatitis with normal and abnormal serum AST levels was 6.8±3.9 and 4.7±3.1, respectively ($p<0.05$), however, mean depression score in viral hepatitis patients with normal and abnormal serum AST levels was 7.1±4.1 and 4.5±3.6, respectively ($p<0.05$).

Mean anxiety score in viral hepatitis patients with normal and abnormal serum total bilirubin levels was 6.2±3.6 and 8.5±4.4, respectively ($p<0.05$) while mean depression score was 6.2±3.9 and 9.7±4.0, respectively ($p<0.05$).

In patients suffering from viral hepatitis, mean anxiety score was not significantly different in patients receiving interferon in comparison with other patients (5.78±5.09 vs. 7.26±3.92, NS).

Anxiety and depression scores in patients suffering from viral hepatitis were not associated with other related variables including serum direct bilirubin, glucose levels and presence of pathological features of these patients.

DISCUSSION

Results reveal that patients with hepatitis C showed more anxiety and depression comparing with those suffering from hepatitis B and normal controls.

Albeit most investigations have focused on one type of viral hepatitis, especially chronic hepatitis C, an investigation has demonstrated that hepatitis C positive patients have more psychiatric disorders than hepatitis B positive patients (34). In another study, hepatitis C patients showed to have more anxiety, depression and mood disorders in comparison with other liver diseases (17). It has also been demonstrated that more subscales of quality of life decreases in chronic hepatitis C patients in comparison with chronic hepatitis B patients (35).

Various hypotheses have been formed for explanation of the presence of more anxiety and depression manifestations in patients suffering from hepatitis C in comparison with those who have hepatitis B. Some of these associate the higher probability of psychiatric disorders in hepatitis C positive patients to the following: 1)direct effect of different viruses, 2) side effect of different medications, 3) different effects of having insight from being contaminated with hepatitis B or hepatitis C virus, 4) coincidence of psychiatric disorders with some risk factors of these viruses (25) and 5) differences in quantity and types of somatic comorbidities in patients with hepatitis B or hepatitis C virus contamination. This can be in favor of the first hypothesis mentioned that the occurrence of cognitive disorders has been reported after being infected with hepatitis C virus (36) while there are no such reports for hepatitis B virus contamination. Anyway, absence of such reports for hepatitis B virus may be due to the lack of investigations in this field, so further studies for better clarification of the differences in the incidence of cognitive disorders in patients suffering from hepatitis B or C virus contamination and healthy controls seems to be beneficial. Evaluation of the accuracy of the third hypothesis needs more investigations to compare anxiety level of patients after diagnosis of hepatitis C contamination in comparison with diagnosis of hepatitis B contamination. Reports demonstrating that patients suffering from anxiety and depression show more high risk behaviors which impose them to acquire hepatitis viruses are in line with the forth hypothesis (2,16,17,37). For instance, intravenous drug use as the leading cause of hepatitis C virus transmission in our country (odds ratio of intravenous drug use for hepatitis C virus contamination is 50) (38-39) accompanies by

psychiatric disorders including anxiety and depression (40). Assessing the accuracy of this hypothesis needs more investigations evaluating the relationship between psychiatric status and transmission causes of hepatitis C virus. The fact that presence of somatic diseases (41) and their aggravation (42) can increase anxiety and depression, also bearing in mind that in this study patients with hepatitis C virus contamination showed to have more somatic comorbidities in comparison with patients with hepatitis B virus contamination, this may be in line with the fifth hypothesis.

In our study, absence of a significant difference between the severity of depression and type of therapy may be due to the few sample size since many investigations have reported the association between interferon alpha therapy and the incidence of psychological side effects (2,16,37,43) as depression, anxiety, psychosis, cognitive disorders, delirium, fatigue and excitability (2,17,37). Diagnosis of the psychiatric disorders at the commencement of interferon therapy seems much more vital by taking into consideration that some severe psychiatric disorders like depression has been introduced as a contraindication for prescribing this drug and necessitates more precise monitoring of the patients or dose adjustment (2,17,37,44,45). Inattention to theses psychiatric disorders has been reported to result in patients` suicide and mortality (2,22,46). Incidence of depression and mortality following interferon consumption has been reported to be as high as 17% and 0.02% to 3.4%, respectively (47). Although, some investigators believe that the incidence of depression is associated with the interferon dose (11) and suggest that patients receiving higher doses of interferon should be monitored more precisely and others introduce alcohol dependency and presence of depression before receiving interferon as risk factors for higher incidence of depression in patients taking interferon (22,48); some others recommend that all patients receiving interferon, independent of history of depression or interferon dose, should be monitored well (48-50). Taking into consideration that psychiatric disorders usually occur in the first month following commencement of interferon therapy (51,52), early assessment of patients` mental health seems to be acceptable in most cases. Still, there are many questions waiting to be answered in this field. For instance, there is no unanimous agreement whether the beginning of anti-viral treatment with interferon in patients suffering from major depressive disorder which is under control by using anti-depression therapy would be favorite or not (45).

Finally we should mention that in various investigations, different methods and diagnostic tools have been applied for identifying psychiatric disorders. Structured interviews (14,53) and various questionnaires like Symptom Checklist 90-R (SCL-90-R) (54) and Beck Depression Inventory (BDI-sf) (14) are among these tools. HADS questionnaire, albeit has acceptable sensitivity and specificity for the detection of anxiety and depression disorders besides symptoms, was used in this study to stratify our patients regarding the probable diagnosis of anxiety and depression (47). It also worth to say that as considering patients` liver enzymes and bilirubin levels, comorbidities and grade of liver histopathologic damage seems to be vital for comparison of depression and anxiety in patients suffering from hepatitis B and C and analysis of this study, psychological aspects should also be considered in treating these patients. This necessitates further investigations in this field. Inequality of sample size in different groups, few patients with viral hepatitis C and inattentiveness to the effect, type and duration of therapy as confounding variables should also be mentioned as some limitations of this study. All these should be considered before generalizing the results of this study; although, using standard questionnaire and the case control type of this study are among its rewarding features.

In conclusion, higher prevalence of anxiety and depression in patients with viral hepatitis C in comparison with patients with viral hepatitis B and normal controls indicates more attention to psychiatric consultation, monitoring and therapies of these patients; nevertheless, further investigations seems to be necessary.

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