

## Depression, Anxiety, Stress and Social Isolation in Hepatitis Patients

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### Abstract

Hepatitis is a complex and chronic liver disorder. Due to the nature of the disease, these patients experience various levels of social isolation, anxiety, and depression. Therefore, this study was conducted to evaluate depression, anxiety, stress, and social isolation in patients with hepatitis B and C in Kermanshah. This study is descriptive-analytic research, the participants were the patients with hepatitis, who referred to liver disease center. Data collection was with Russell social isolation questionnaire and DASS-21 questionnaire. The questionnaires were completed by the patients. 67.3% of the patients were male. The mean age was  $41.02 \pm 12.4$  years, and the majority of the participants were married (143; 67.8%). The results showed that there is a direct and significant relationship between social isolation with depression, anxiety, and stress ( $P=0.001$ ,  $P=0.001$ ,  $P=0.001$ ). In addition, results showed that there is a significant difference between the mean depression scores and age ( $P=0.048$ ). Also, the results showed that there is a significant difference in the mean score of social isolation and education level ( $P=0.038$ ). There is no significant difference between the other variables with depression, anxiety, stress, and social isolation ( $P>0.05$ ). These results showed that there is a relationship between social isolation with anxiety, stress, and depression. Also, anxiety, stress, and depression in hepatitis patients are related to age and education level. So, it is suggested to provide effective programs in the care of these patients.

**Keywords:** Hepatitis; Depression; Anxiety; Stress; Social Isolation.

### 1. Introduction

Among the chronic diseases, hepatitis is one of the most important diseases in the world, that there are more than 350 million hepatitis patients in the world, which causes more than 500,000 deaths annually, especially in developing countries [1]. Hepatitis can be caused by infectious and non-infectious agents such as viruses, bacteria, fungi, parasites, alcohol, drugs, autoimmune diseases, and metabolic diseases [2]. Chronic hepatitis is a complex liver disorder with different causes and severity, and the inflammatory process and necrosis of the liver cells in hepatitis are lasted for at least 6 months [3]. During 2015–2018 in the US, the prevalence of hepatitis B virus (HBV) infection was 4.3% [4] and was higher among men (5.3%) than women (3.4%). Also, the prevalence of hepatitis in EU/EEA country, reported between 0.0 – 7.5% and 0.0 – 27.6% for HBV and hepatitis C virus (HCV) respectively [5, 6]. So, an estimated 185 million people are infected with the HCV virus around the world and 3-4 million new infections are diagnosed annually [7]. This rate in hepatitis B patients estimated almost 400 million people all over the world [8]. Chronic hepatitis has often no symptoms, but it can be with several common symptoms such as fatigue, reduced ability in work, home, and school, loss of appetite, and mood changes [1, 9]. Hepatitis B causes progressive liver damage; about 25% die prematurely from cirrhosis or hepatocellular carcinoma (HCC) [10]. Hepatitis disease can be a reason for depression, anxiety, and stress as well as a feeling of frustration and disappointment in patients [1, 11, 12]. Also, social

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isolation and social stigma are other complications that occur in hepatitis patients [13, 14]. The prevalence of negative emotions in patients with chronic hepatitis has been reported between 1.51 to 38.1%, that of these, 47% experience anxiety disorders and 68% a mild to moderate depression [8]. Depression, feeling emptiness and frivolity, feeling ineffective, and worthless in hepatitis patients have an effect on self-care activities [3].

In Kesen et al. study, the mean anxiety score was 7.56 and the depression score was 6.84 in hepatitis C patients [15]. The incidence of depression in chronic hepatitis C patients was estimated at almost 25-44% [7, 16]. A study on 264 patients with chronic hepatitis C, reported that 85.7% of them had no depression, 8.9% mild depression, and 4.5% moderate depression, and the anxiety in patients was 17.9% and 17% for mild to moderate anxiety and 0.9% for severe anxiety [17]. Depression in patients with hepatitis B can also affect the quality of life, diagnosis of disease and mortality rates [8].

Because the prevalence of psychological issues is high in hepatitis patients and due to their adverse consequences on the physiological and social status of patients, and wherever the lack of information in this issue, especially in Iran, the current study was conducted to evaluate depression, anxiety, stress, and social isolation in hepatitis B and C patients in Kermanshah.

## 2. Materials and Method

### 2.1. Study Participants

In this descriptive-analytical study, evaluated the level of depression, stress, anxiety and social isolation of patients with hepatitis B and C and their relation factors. The project was approved by the ethics committee affiliated with the Department of Research and Technology of Kermanshah University of Medical Sciences (Grant Number: 96231).

The participants were 211 patients with hepatitis B and C who referred to the hospitals of Kermanshah University of Medical Sciences, who had been diagnosed for at least 3 months. Patients with other chronic physical/psychological disease, patients who use of psychiatry medications, patients who did not willing to cooperate in the study after stating the research goals, and incomplete questionnaires were excluded. Patients were recruited as convenience sampling. The minimum number of patients according to the previous studies (Ataei et al. [17]) with a depression rate of 14.7%, with 95% confidence level was estimated 185, so with considering an attrition rate of 12% [18] Finally, 204 people were calculated and eventually we enrolled 211 patients.

### 2.2. Data Collection

The patients were assessed during the last eight months of 2019. The data were collected by a demographic check list and the 21-item questionnaire for depression, anxiety, and stress (DASS-21) as well as Russell social isolation questionnaire. The demographic checklist included 13 items that are reviewed by 12 faculty members of Kermanshah University of Medical Sciences as content validity and their comments were considered in the checklist.

DASS-21 is a standard and self-report tool developed by Antony et al. (1998) to measure the severity of a range of symptoms related to depression, anxiety and stress among individuals without a depression, anxiety, and stress diagnosis [19]. The DASS-21 questionnaire was used to assess the level of depression, anxiety, and stress. Content validity was sued to measure the validity of this scale [20, 21]. Covic et al. studied the internal consistency of the questionnaire using Cronbach's alpha, and reported the reliability index of 0.94 for depression and 0.87 for anxiety [20]. In other study, Cronbach's alpha was obtained for each individual and total scale was high (0.88), and the sensitivity of the questionnaire was 79.1% and its specialty was 77% [18]. The Persian version of the questionnaire was studied in a Sahebi et al. study, with a Cronbach's alpha levels of 0.7, 0.67, and 0.49 for depression, anxiety, and stress dimensions, respectively [21].

DASS-21 has 21 items and three subscales of depression, anxiety, and stress. Each subscale includes 7 items. The lowest score for each question is zero and the highest score is 3, in each dimension of depression, anxiety, and stress, the total score is between 0 - 4 (mild), 5 - 11 (moderate), and  $\geq 12$  (severe).

For evaluating the social isolation, Russell questionnaire was used. this questionnaire was developed in 1980 by Russell et al. [22]. Reliability of the test was reported by Russell using test-retest (0.78) and Cronbach's alpha (0.96). Validity and reliability of the Persian version of the questionnaire were evaluated by Zarei et al. in 2016 [23]. The Cronbach's alpha was 0.91. Russell questionnaire has 20 self-reported questions. The scoring of this questionnaire is conducted as Likert with options of never (1), rarely (2), sometimes (3) and often (4). The overall score of the questionnaire is between 20 and 80, and the higher score, indicating greater isolation and loneliness.

### 2.3. Research Hypothesis

It was hypothesized that evaluation of depression, anxiety, and stress and relation with social isolation and demographic characteristics in hepatitis patients.

### 2.4. Data Analysis

Data were analysed by the Statistical Package for Social Sciences (SPSS v.18.0; SPSS Inc., Chicago, IL, USA) using descriptive statistics (mean and standard deviation) and inferential statistics (Kolmogrov-Smirnov, Spearman correlation test, and Mann-Whitney). In terms of education, the participants were subdivided into three categories: under diploma, diploma, and college education. In terms of economic status, the participants were classified into one of the poor and middle income ( $\leq \$1400$ ), and good income ( $> \$1400$ ) classes, based on their monthly income. In terms of age, the patients were subdivided in two categories: under 40 years and above 40 years. To analyse the data, the distribution of depression, anxiety, and stress variables was analysed by the Kolmogorov-Smirnov test, which showed they were abnormally distributed. Then, the Spearman correlation test was run to assess the relation between depression, anxiety, and stress variables and independent variables. The Spearman correlation test used to assess relation between social isolation and depression, anxiety, and stress. The Mann Whitney was applied to analyse the concurrent relationship between demographic variables and depression, anxiety, and stress. The level of significance was set at  $p < 0.05$ .

### 3. Results

In this study, 211 patients with hepatitis B and C were evaluated (Table 1). The mean and standard deviation (SD) of age was  $41.02 \pm 12.40$  years. 67.3% of patients were male, 67.8 were married, 65.4% had under diploma education, 68.7% had a job, and 69.7% lived in urban areas (Table 1). 97.6% of patients had a poor to middle income and 58.8% had a history of smoking. Most of the patients (70.6%), were diagnosed as hepatitis B and only 14.2% had a family history of hepatitis (Table 1).

The Mean  $\pm$  SD duration of disease was  $1.90 \pm 1.13$  years which ranged from 3 months to 6 years. Mean and SD duration of disease was  $1.86 \pm 1.10$  years ranged from 3 months to 6 years (Table 1).

**Table 1. The frequency of demographic variables**

Variable	N (%)
Gender	Male 142 (67.3)
	Female 69 (32.7)
Age	<40 115 (54.5)
	$\geq 40$ 96 (45.5)
Marital status	Single 68 (32.2)
	Married 143 (67.8)
Education	Under diploma 138 (65.4)
	Diploma 65 (30.8)
	College 8 (3.8)
Job	Unemployed 66 (31.3)
	Employed 145 (68.7)
Location	Urban 147 (69.7)
	Rural 64 (30.3)
Income	Poor and middle 206 (97.6)
	Good 5 (2.4)
Smoking	Yes 124 (58.8)
	No 87 (41.2)
Hepatitis type	Type B 149 (70.6)
	Type C 62 (29.4)
Family history	Yes 30 (14.2)
	No 181 (85.8)

The mean  $\pm$  SD of DASS and Russell social isolation scale reported in Table 2 and also, Kolmogrov-Smirnov test showed that they are abnormal ( $P < 0.05$ ) except for stress ( $P = 0.058$ ) (Table 2).

The Mean of depression, anxiety, and stress were  $10.94 \pm 3.93$ ,  $10.96 \pm 3.45$ , and  $10.02 \pm 3.94$  respectively. And, the Mean of social isolation score was  $51.41 \pm 7.92$  (Table 2).

**Table 2. Kolmogrov-Smirnov to distribution of depression, anxiety, and stress, and social isolation**

	Mean ± SD	Potential range	Calculated range	Test statistic	P-value*
Total DASS	31.93±9.91	0-63	5-56	0.078	0.003
Depression	10.94±3.93	0-21	0-20	0.077	0.004
Anxiety	10.96±3.45	0-21	2-19	0.070	0.013
Stress	10.02±3.94	0-21	0-21	0.061	0.058
Total Russell	51.41±7.92	20-80	21-67	0.115	0.001

\* Normal distribution in P-value > 0.05.

Results showed that 43.6% of patients had severe depression, 34.6% had severe anxiety and 43.6% had severe stress. Also, of patients 50.2, 56.9, and 52.1% of patients had moderate depression, anxiety, and stress, respectively (Table 3). Depression, anxiety, stress, and social isolation was higher in male than female. Similarly, patients with type B had higher levels than type C patients (Table 4).

**Table 3. Frequency of depression, anxiety and stress**

DASS		Depression	Anxiety	Stress
		N (%)	N (%)	N (%)
Mild	0-4	13 (6.2)	18 (8.5)	9 (4.3)
Middle	5-11	106 (50.2)	120 (56.9)	110 (52.1)
Severe	>12	92 (43.6)	73 (34.6)	92 (43.6)

**Table 4. Comparison mean of depression, anxiety, stress, and social isolation in terms of demographic variables**

		Depression	Anxiety	Stress	Total DASS	Social isolation
		mean± SD	mean±SD	mean±SD	mean±SD	mean±SD
Gender	Male	11.17±4.01	10.05±4.12	11.04±3.36	32.27±10.26	51.66±8.20
	Female	10.94±3.93	10.02±3.94	10.96±3.45	31.93±9.91	50.89±7.36
	P-value	0.282	0.694	0.650	0.538	0.226
Age	<40	10.46±3.67	9.69±3.83	10.87±3.45	31.03±9.33	50.81±8.03
	≥40	11.52±4.17	10.42±4.06	11.07±3.45	33.02±10.51	52.13±7.78
	P-value	0.048*	0.684	0.201	0.173	0.133
Marital status	Single	10.75±3.35	10±3.71	10.97±3.30	31.72±8.61	50.86±7.34
	Married	11.03±4.19	10.02±3.94	10.96±3.45	31.93±9.91	51.41±7.92
	P-value	0.532	0.991	0.991	0.693	0.545
Education	Under diploma	11.11±4.03	10.14±3.92	10.82±3.48	32.08±10.20	51.83±7.97
	Diploma	10.36±3.68	9.66±4.01	10.96±3.42	31±9.31	49.95±7.64
	University	10.94±3.93	10.02±3.94	10.96±3.45	31.93±9.91	51.41±7.92
	P-value	0.337	0.577	0.127	0.357	0.038*
Job	Employed	11.02±3.93	10.15±3.93	11.02±3.58	32.19±9.94	51.8±8.05
	Unemployed	10.77±3.97	75.9±3.99	10.84±3.16	31.37±9.89	50.56±7.63
	P-value	0.927	0.612	0.738	0.718	0.274
Location	Urban	10.66±3.87	9.91±3.86	10.95±3.41	31.53±9.56	51.27±7.80
	Rural	11.57±4.03	10.29±4.13	11±3.56	32.87±10.69	51.73±8.25
	P-value	0.069	0.598	0.927	0.351	0.801
Income	Poor-middle	10.93±3.95	10.01±3.93	10.90±3.46	31.85±9.93	51.35±7.90
	Good	11.20±3.83	10.60±5.02	13.40±2.07	35.20±9.57	54±9.19
	P-value	0.879	0.738	0.111	0.609	0.518
Smoking	Yes	11.15±3.97	10.37±3.90	11.32±3.38	32.85±9.80	52.18±7.52
	No	10.64±3.89	9.52±3.97	10.45±3.50	30.63±9.98	50.32±8.39
	P-value	0.217	0.218	0.074	0.119	0.183
Hepatitis type	B	11.07±3.84	10.20±3.80	11.14±3.34	32.43±9.43	51.93±7.93
	C	10.59±4.17	9.59±4.25	10.54±3.68	30.74±10.97	50.17±7.83
	P-value	0.341	0.474	0.257	0.350	0.069
Family history of hepatitis	Yes	10.73±3.95	9.93±3.99	11.33±3.74	32±9.91	50.06±8.46
	No	10.97±3.94	10.04±3.94	10.90±3.40	31.92±9.94	51.64±7.83
	P-value	0.714	0.751	0.531	0.929	0.280

\* Significant at the level of 0.05

The Spearman correlation test between DASS components and social isolation showed that there was a direct and significant relationship between social isolation and depression (P=0.001), social isolation and anxiety scales (P=0.001) and social isolation scale and stress (P=0.001). Although the difference between DASS components are not clear, but results showed that depression was stronger factor for social isolation ( $r^2=0.245$ ) (Table 5).

**Table 5. Correlation between depression, anxiety and stress with social isolation**

	Depression		Anxiety		Stress		Total Score	
	r (r <sup>2</sup> )	P-value	r (r <sup>2</sup> )	P-value	r (r <sup>2</sup> )	P-value	r (r <sup>2</sup> )	P-value
<b>Social isolation scale</b>	0.495 (0.245)	0.001	0.360 (0.129)	0.001	0.469 (0.219)	0.001	0.518 (0.268)	0.001

As shown in Table 4, the results of the Mann-Whitney test showed that there was a significant difference between the mean depression scores and their age. A comparison of means showed that the mean of depression is higher in patient over 40 years of age. Also, the results of this test showed that there was a significant difference in the mean of social isolation of patients based on their education. There was no significant difference between the other variables with depression, anxiety, stress, and social isolation.

#### 4. Discussion

Hepatitis is global health-treat that speared in whole of the world and causes many complications in patients and deaths annually. Cost of hepatitis treatment in china is 37 598.6 Yuan per Quality Adjusted Life Year (QALY) and in USA is \$6000-\$21000 pre QALY [24, 25]. HBV is referred to as a “Silent Killer” because infected persons can live 20–40 years before developing liver complications [25]. Psychiatric disorders can be occur in chronic patients like hepatitis. Hepatitis patients experience different levels of depression, anxiety, and social isolation [26-30]. Social isolation is higher in chronic patients and can cause other psychiatric disorders [31, 32]. In this study, we aimed to evaluate depression, anxiety, and stress in hepatitis patients, and calculate their relation with social isolation and demographic variables. Results showed 67.3% of patients were male and the mean age of the patients were 41.02%. Other studies reported that most of patients were men and mean age was between 42 – 57 years [8, 16, 33].

Higher prevalence of hepatitis in young patients need future program for these patients because they are active workers in society. Results showed the mean of depression, anxiety, and stress were 10.94, 10.96, and 10.02 respectively. In addition, mean of Depression, anxiety, stress, and social isolation was higher in male than female and in Type B hepatitis than Type C. This study sowed the direct relationship between social isolation with DASS components. And, stress was stronger factor for social isolation. In hepatitis patients, depression can be cause of treatment failure [34]. He et al., reported that stress induces a shift in the type-1/type-2 cytokine balance towards a type-2 response, which implicated a role of psychological stress in the course of HBV related immune-pathogenesis [35]. And, stresses have a continuing impact on hepatitis B antibody status [36]. A study, reported that patients with hepatitis B developed moderate to severe psychiatric including 22.4% with depression, 18.8% with anxiety, and 10.3% with both [27]. Vu et al. reported that, 37.5% of chronic hepatitis B patients, experienced depressive symptoms [37].

In other study diagnosis of depression was 29.8% in HCV, and 3.7% in HBV. In addition, in this study reported that the most consistent correlates of depression status in Chronic Liver Disease (CLD) patients are being female and excessive alcohol consumption [38]. In other study, the prevalence of depression in hepatitis C patients (35.9%) was higher than in hepatitis B patients (19.8%) [39]. Alian et al. study, reported the frequency of depression was 68% in hepatitis B and 86% in hepatitis C patients, and the frequency of mild depression was 14%, moderate depression was 57.3% and severe depression was 28.7% [40]. These results were not versus to our results. Because we calculate the mean of depression and anxiety and these studies calculated the prevalence of them. This means that the prevalence of depression is higher in hepatitis C patients than Hepatitis B, but the mean of depression score in hepatitis patients is higher than hepatitis C. This suggests that patients with type B hepatitis need more care than HCV patients about depression severity. A review study, prevalence of depression in HCV patients was 18.2-57.2% [28]. Stewart et al. shows prevalence rates of 41% for anxiety and 27% for depression in hepatitis C patients [41]. A study showed that prevalence of depression and anxiety was higher in hepatitis B patients than HBsAg-positive inactive carriers [42], that it can be due to the nature of disease. Psychiatric disorders can be caused by medications and/or nature of disease [27, 43], Medications such as interferon can be reason for psychiatric disorders [33]. The hepatitis C virus effect the brain tissue and brain metabolites and cause depression [44]. In our study, the mean of social isolation was 51.41. The mean of social isolation was higher in male than female and in hepatitis B than hepatitis C. in studies reported that social stigma is worse in first days after diagnosis [45]. Reducing the social isolation can be useful especially in young patients. Results show the relation between social isolation and DASS components. This need further studies to confirm and show an available score for prediction of social isolation based on DASS components. Higher depression in older patients and in low and high educated patients reported in this study, and needed further studies. Psychiatric

status in chronic hepatitis B and chronic hepatitis C patients may be beneficial in disease management and treatment. In Najaf et al. study, stress level was negatively correlated with age and was significantly more in single patients, and the anxiety level was less in patients with higher level of education [46].

#### **4.1. Limitation**

The studied participants were hospitalized patients, and the nature of hospitalization creates social isolation and shows a higher level of social isolation. This issue should be considered in future studies.

### **5. Conclusion**

Hepatitis has a clear effect on the mental status of patients, which can affect many aspects of their lives. The results reported that the mean of depression, anxiety, stress, and social isolation are higher in hepatitis B patients compared with hepatitis C patients that are a new result. Most of the patients were at young ages and co-occurrence of both hepatitis and Psychiatric disorders can cause failure treatment and adverse complications. Social isolation has a relation to depression, anxiety, and stress. And also, the results showed that social isolation has a relation with age and education. The higher age and less level of education have a negative relation to social isolation.

### **6. Availability of Data and Materials**

The identified datasets used during the current study are available from the corresponding author on reasonable request.

### **7. Funding**

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### **8. Acknowledgements**

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### **9. Authors' Contributions**

MJ and PAS, SB, and HM contributed in designing the study. PAS, MJ, and SB collected the data, and analysed by MJ and HM. the final report and manuscript were written by PAS, MJ, SB, and HM. All the authors read and approved the final version for submission.

All authors contributed to drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

### **10. Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### **11. Ethical Approval**

All procedures performed in studies involving human participants were in accordance with the ethics committee affiliated with the Department of Research and Technology of Kermanshah University of Medical Sciences (Approval Number 97786) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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