

# Assessment of Depression, Anxiety and Stress among a Sample of patients with Chronic Hepatitis B in Gastroenterology and Hepatology Center/ AL-Najaf Province

Hanan N. Najaf<sup>1</sup>, Dheyaa J. Kadhim<sup>2</sup>, Helen F. Marzooq<sup>3</sup>

<sup>1</sup>Department of clinical pharmacy, College of Pharmacy, University of Kufa, Najaf, Iraq.

<sup>2</sup>Department of clinical pharmacy, College of Pharmacy, University of Baghdad, Baghdad, Iraq.

<sup>3</sup>Department of clinical pharmacy, College of Pharmacy, University of Kufa, Najaf, Iraq.

Email: han173004@gmail.com

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## Abstract

**Objective:** Hepatitis B has recently been identified as the primary cause of cirrhosis, chronic hepatitis, and hepatocellular cancer (HCC) (1). stress, depression, anxiety, and other psychological problems accompanied with decay in social and work functionality along may occur in patients with CHB (2). The study's objective was to assess the prevalence and severity of depression, anxiety, and stress in a sampling of chronic hepatitis B patients at the gastroenterology and hepatology center in the Iraqi province of Al-Najaf.

**Subjects and method:** The Gastroenterology and Hepatology Center/Al-Sader Medical City/Najaf treated 104 patients with chronic viral hepatitis B who had already been diagnosed with the disease between November 2018 and May 2019. 100 people who appeared to be in good health were also added as a control group. To evaluate mental health, the Depression, Anxiety, Stress scale (DASS-21) in Arabic was employed.

**Results:** Depression, anxiety and stress which associated in patients with hepatitis B were significantly affected on quality of life of those patients where the prevalence rate of depression, anxiety and stress was significantly high in compared with healthy control group and within extremely severe stage.

**Conclusion:** In conclusion, chronic hepatitis B patients have a higher significantly prevalence rate and level of severity of depression, anxiety and stress which consequently greatly affected on quality of life in comparison to healthy control individuals at the province of AL-gastroenterology Najaf's and hepatology center .

**Keywords:** hepatitis B virus, DASS questionnaire, Al-Najaf, Iraq.

## INTRODUCTION

As a persistent infection linked to cirrhosis, hepatocellular cancer, and mortality, chronic hepatitis B poses a worldwide health concern (3). According to WHO estimates, 3.5% of people had chronic HBV infection in 2015 (4). Hepatitis B surface antigen was prevalent in Iraq at 1.6% (5). Hepatitis B virus transmission is caused by contact with infected blood or bodily fluids that include blood. Unprotected sexual contact, blood transfusions, reusing contaminated needles and syringes, and vertical transmission from mother to child during childbirth are only a few examples of possible transmission routes. Without treatment, there is a 20% chance that a mother who tests positive for HBsAg would infect her unborn child. If the mother also tests positive for HBeAg, the risk might be as high as 90% . Within families, the hepatitis B virus can spread through contact with non-intact skin or mucous membranes that have come into touch with fluids or saliva that contain the virus. About 30% of adult cases of Hepatitis B, however, cannot be linked to a specific risk factor. Working in the medical field, receiving blood transfusions or dialysis, getting acupuncture, and getting tattoos are additional risk factors for contracting the hepatitis B virus. (6). Diagnostic standards for long-term hepatitis B (CHB) The existence of detectable HBsAg and serum HBV-DNA for more than 6 months

is a sign of infection (7). Hepatocellular carcinoma incidence is greatly increased by cirrhosis, which is brought on by chronic hepatitis B virus infection. Cirrhosis is a consequence of chronic liver inflammation (HCC) (8). Up to 40% of people with chronic HBV infection who are not treated go on to develop liver cirrhosis (9). 3% of cirrhotic patients have decompensation each year. Patients with cirrhosis have a 2% to 3% annual chance of developing HCC, whereas those without it have a risk of less than 1% (10). The serological tests that used to determine chronic HBV infection consist of the presence or absence of HBeAg and anti-HBe, the level of HBV-DNA, level of alanine amino transferase (ALT), and the presence or absence of intra hepatic necro inflammation and fibrosis (9).

The WHO defines QOL as "individual's view of their place in life in respect to their objectives, aspirations, standards and concerns and within the framework of the culture and value systems in which they live." (11). Especially significant in chronic disease, HRQOL may comprehensively analyze health outcomes to help healthcare professionals better understand patients' requirements and deliver high-quality medical treatment (12). Chronic hepatitis B patients tend to experience psychological and emotional issues more frequently than the general population (7). Patients with hepatitis infection need to be monitored for psychiatric illnesses since they can affect everyday living and lower quality of life (13,14,15), rise in the likelihood of suicide attacks, cancer, and death (16,17) among these patients. The least compliance to pharmacological therapy is found in those with psychiatric problems, which raises the chance of treatment failure in those individuals (16,18). The current study's objective was to assess the prevalence and severity of stress, anxiety, and depression in a sample of chronic hepatitis C patients in AL-Najaf, Iraq.

## Patients and methods

### Patients

The Gastroenterology and Hepatology center/Al-Sader Medical City/Najaf welcomed (104) chronic hepatitis B patients who had already been diagnosed between November 2018 and May 2019. Additionally, a control group of (100) people who appeared to be in good health was included.

### Inclusion criteria

The following were the inclusion criteria for this study

- 1-Patients with chronic hepatitis B who were admitted into the trial and were at least 18 years old and of either sex
- 2-A disease that has been present for at least six months or longer following diagnosis.

### Exclusion criteria

The following were the study's exclusion criteria:

- 1- a patient whose hearing, speech, or cognitive impairments would make it difficult for them to grasp the inquiries.
- 2- Patient with clinical signs of decompensated liver cirrhosis or liver cancer (ascites, history of hepatic encephalopathy, or history of variceal bleeding).
- 3- concurrent medical conditions (such as chronic renal failure, chronic lung disease, hypertension, heart disease, DM, stroke).
- 4- Antidepressant users or those receiving therapy for any neurological or psychiatric conditions.
- 5-Pregnant women
- 6- Patients who provided inaccurate information when filling out the questionnaire will also be disqualified from the trial.

## Method

### The questionnaires

The Arabic version of the Depression, Anxiety, Stress Scale (DASS) was utilized in the current study to measure quality of life and evaluate mental health. The DASS-21 questionnaire features 21 items that each assess one of the three scales—anxiety, stress, and depression—separately. Patients gave each of the 113 items a score between 0 and 3, with 3 representing "completely did not apply to me" (applied to me very much). Each subscale's total scores were summed together and multiplied by two. Anxiety and sadness each had normal scores of 0-7, 0-14, and 0-9. The moderate scale ranged from 8 to 13 for depression, anxiety, and tension. The moderate range is 10–14 for anxiety, 19–25 for stress, and 14–20 for depression. The severe scale ranged from 26 to 33 for stress, 15 to 19 for anxiety, and 21 to 27 for depression. For stress, anxiety, and depression, the extremely severe score was 34+, 20+, and 28+ respectively (19). This instrument's Arabic version has undergone psychometric validation.

### Administration of questionnaires

The researcher, who visited the hospital five days a week, was the one who gathered the study's data. Patients were asked whether they were approved to participate in the study when they arrived at the hospital. If they consented, a thorough explanation of the questionnaire's questions was given, and each patient took around 5 minutes to complete it.

### Statistical analysis

The statistical package for social sciences (SPSS) version 23 and Microsoft Office Excel 2010 were used to gather, summarize, and analyze data. Categorical variables were shown as percentages and numbers. Initial analyses of quantitative variables focused on the Kolmogorov-Smirnov test for normalcy distribution. Consequently, the mean, standard deviation, and median were used to characterize quantitative quantities (interquartile range). Using an independent sample t-test, mean values between any two groups were compared. Using the Chi square test, associations between any two category variables were determined. To evaluate the variables, the Spearman correlation test was utilized. When the P-value was 0.05 or less, it was deemed significant, and when it was 0.01 or less, it was deemed very significant.

## Results

Table 1 displays the demographic details of hepatitis B patients and healthy volunteers. Table 2 displays the illness features and tests performed on HBV patients.

Table1: Demographic characteristics of patients with chronic hepatitis B infection comparing to that of control group

Characteristics	Control		Hepatitis B		P value	
	N	Mean ± SD	N	Mean ± SD		
Age	100	40.81±11.6	104	42.6±15.8	0.368† NS	
Gender	N	%	N	%	P value	
	Male	53	53	57	54.8	0.796¥
	Female	47	47	47	45.2	NS
Education level	Illiterate	19	19	29	27.9	0.352¥ NS
	Primary	32	32	35	33.7	
	Secondary	32	32	28	26.9	
	University	17	17	12	11.5	
Social status	Single	11	11	10	9.6	0.881¥ NS
	Married	79	79	86	82.7	
	Divorced	4	4	4	3.8	
	Widow	6	6	4	3.8	
Children	Yes	83	83	84	80.8	0.679¥
	No	17	17	20	19.2	NS
Residency	Urban	75	75	75	72.1	0.640¥
	Rural	25	25	29	27.9	NS

Data was expressed as either mean  $\pm$  standard deviation (SD) or numbers (%); †: independent samples t-test; ¥: Chi-square test; NS: not significant at  $P \leq 0.05$ .

Table 2: Diseases characteristic and investigation in patients with chronic hepatitis B infection.

Characteristic	N	%	Characteristic	N	%
Biopsy	2	1.9	<b>Treatment</b>		
Other family member	17	16.3	Entecavir	28	26.9
<b>Mode of transmission</b>			Peg-INF	1	1
Blood transfusion	19	18.3	Peg-INF + Ribavirin	41	39.4
Surgery	23	22.1	Not treated	24	23.1
Dental procedure	18	17.3	Tenofovir	10	9.6
Shaving	4	3.8	<b>Treatment experience</b>		
Needle	5	4.8	Naïve	29	27.9
Tattoo	14	13.5	Experienced	75	72.1
Unknown	3	2.9	<b>Hospital admission</b>	5	4.8
Vertical	16	15.4			
Sexual	2	1.9			
<b>Characteristic</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Median</b>	<b>IQR</b>	
Duration of disease	0.50	7.00	1.25	2.50	
Duration of treatment	0.00	3.50	0.00	1.00	
HBV DNA (IU/ml)	0.00	200000000.00	4140.0	2910000.00	
ALT (U/l)	5.00	179.00	17.25	15.12	
AST (U/l)	3.00	95.00	15.00	13.65	
Albumin (g/dl)	3.60	39.00	4.64	1.32	
INR	1.00	2.30	1.15	0.42	
Total bilirubin (mg/dl)	0.40	42.10	0.75	0.45	

HBV: hepatitis B virus; DNA: deoxyribonucleic acid; ALT: alanine aminotransferase normal range (up to 12) U/l; AST: aspartate aminotransferase normal range (up to 12) U/l; INR: international normalized ratio (1.0); Total bilirubin normal range (0.3-1.2) mg/dl; Serum albumin (35-52) g/l; Peg-INF: pegylated interferon.

The prevalence rates of depression, anxiety and stress in control and HBV groups are shown in table 3. The prevalence rate of depression was 9 % and 75.0 % in control and HBV groups, respectively; the difference between control and hepatitis B groups was highly significant ( $P < 0.001$ ). The prevalence rate of anxiety was 17 % and 70.2 % in control and HBV groups, respectively; the difference between control and hepatitis B groups was highly significant ( $P < 0.001$ ). The prevalence rate of stress was 16 % and 64.4 % in control and HBV groups, respectively; the difference between control and hepatitis B groups was highly significant ( $P < 0.001$ ).

Table 3: Prevalence rate of DASS domains in control group and patients with HBV

Characteristic	Control Group n = 100	HBV n = 104	P Control vs HBV
Depression	9	78	<0.001¥ HS
Prevalence	9	75.0	
Anxiety	17	73	<0.001¥ HS
Prevalence	17	70.2	
Stress	16	67	<0.001¥ HS
Prevalence	16	64.4	

Data were expressed as number and %; ¥: Chi-square test; HS: highly significant at  $P \leq 0.01$

The levels of severity of depression, anxiety and stress among study groups are shown in table 4. Mild, moderate, severe and extremely severe depression was seen in 7(7.0), 2 (2.0), 0 (0.0) and 0 (0.0) cases of control group, in 2 (1.9), 14 (13.5), 14 (13.5) and 47 (45.2) of HBV group and the difference was highly significant between hepatitis B groups and control group ( $P < 0.001$ ).

Mild, moderate, severe and extremely severe anxiety was seen in 6 (6.0), 7 (7.0), 3 (3.0) and 1 (1.0) cases of control group, in 10 (9.6), 16 (15.4), 10 (9.6) and 37 (35.6) of HBV group and the difference was highly significant between hepatitis B groups and control group ( $P < 0.001$ ).

Mild, moderate, severe and extremely severe stress was seen in 7 (7.0), 9 (9.0), 0 (0.0) and 0 (0.0) cases of control group, in 9 (8.7), 7 (6.7), 18 (17.3) and 33 (31.7) of HBV group and the difference was highly significant between hepatitis B groups and control group ( $P < 0.001$ ).

Table 4: levels of DASS domains in control group and patients with HBV

Characteristic		Control n = 100		HBV n = 104		P values
		N	%	N	%	Control vs HBV
<b>Depression</b>	No	91	91	27	26	<0.001¥ HS
	Mild	7	7	2	1.9	
	Moderate	2	2	14	13.5	
	Severe	0	0	14	13.5	
	Extremely severe	0	0	47	45.2	
<b>Anxiety</b>	No Anxiety	83	83.	31	29.8	<0.001¥ HS
	Mild	6	6	10	9.6	
	Moderate	7	7	16	15.4	
	Severe	3	3	10	9.6	
	Extremely severe	1	1.0	37	35.6	
<b>Stress</b>	No Stress	84	84	37	35.6	<0.001¥ HS
	Mild	7	7	9	8.7	
	Moderate	9	9	7	6.7	
	Severe	0	0	18	17.3	
	Extremely severe	0	0	33	31.7	

Data were expressed as number and %; ¥: Chi-square test; HS: highly significant at  $P \leq 0.01$

Correlations of DASS domain to demographic characteristics of patients with HBV are shown in table 5. Stress level is negatively correlated with age (higher in younger age). Anxiety level is positively correlated with gender and negatively correlated with level of education. Depression was not correlated to any of demographic characteristics.

Table 5: Correlation of DASS to demographic characteristics of patients with HBV

Characteristic	Stress Level		Anxiety Level		Depression Level	
	<i>R</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Gender	0.110	0.265	0.247	0.011*	0.108	0.274
Age	-0.318	0.001**	-0.106	0.282	-0.126	0.203
Education	-0.128	0.197	-0.222	0.023*	-0.111	0.261
Social status	-0.125	0.208	0.047	0.636	-0.029	0.766
Children	0.014	0.891	-0.156	0.113	-0.027	0.787
Residency	0.105	0.290	0.084	0.394	0.152	0.122

Correlation was carried out using Spearman correlation test; \*: significant at  $P \leq 0.05$ ; \*\*: highly significant at  $P \leq 0.01$ .

Table 6 displays correlations between DASS domain and HBV patient illness characteristics. There was no relationship between stress level and any illness features. Anxiety level was negatively correlated to serum ALT. Depression was positively correlated to viral load.

Table 6: Correlation of DASS to Disease characteristics of patients with HBV

Characteristic	Stress Level		Anxiety Level		Depression Level	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Duration of disease	0.029	0.771	0.003	0.975	0.064	0.519
Biopsy	-0.005	0.961	-0.074	0.455	0.137	0.164
Other family member	-0.017	0.863	-0.050	0.617	-0.030	0.763
Mode of transmission	0.056	0.570	-0.047	0.635	0.103	0.298
Treatment	-0.022	0.821	-0.022	0.822	-0.031	0.756
Duration of treatment	0.005	0.962	-0.079	0.428	0.043	0.661
Treatment experience	0.125	0.205	0.033	0.742	0.046	0.641
Hospital admission	0.158	0.109	-0.006	0.950	-0.048	0.631
HBV DNA (IU/ml)	0.146	0.139	0.129	0.190	0.251	0.010**
ALT (U/l)	0.005	0.957	-0.254	0.009**	-0.148	0.135
AST (U/l)	0.040	0.688	-0.176	0.074	-0.055	0.577
Albumin (g/dl)	-0.018	0.944	0.157	0.533	0.022	0.932
INR	0.006	0.950	-0.069	0.490	0.039	0.691
Total bilirubin (mg/dl)	0.138	0.162	-0.034	0.733	0.121	0.221

Correlation was carried out using Spearman correlation test; \*: significant at  $P \leq 0.05$ ; \*\*: highly significant at  $P \leq 0.01$ ; HBV: hepatitis B virus; DNA: deoxyribonucleic acid; ALT: alanine aminotransferase normal range (up to 12) U/l; AST: aspartate

aminotransferase normal range (up to 12) U/l; INR: international normalized ratio (1.0); Total bilirubin normal range (0.3-1.2) mg/dl; Serum albumin (35-52) g/l.

## Discussion

Up to 90% of those patients who were diagnosed with HBV infection reported experiencing severe stress as a result of the virus. (20). Social isolation during chronic disease consider as predisposing factor for development anxiety and depression (2). Tables 3 and 4 in the current study demonstrate this, the prevalence rate of depression is 75 % in patients with HBV as compared with control group 9%, and 58.7% of HBV patients at sever and extremely sever of depression. Hepatitis B patients exhibited higher rates of sadness than healthy individuals, according to a research conducted in Islamabad (58.6% in the HBV group and 37.8% in the control group) (21). Depression in hepatitis patients is considered to be brought on by the complexity of the disease, the inability to forecast how the sickness will progress, changes in brain metabolites that may be seen by MRI, emotional variables, and the experience of stigma (21,22). Also found that the prevalence rate of anxiety in patients with HBV is 70% as compared to control group 17% and 45.2% of HBV at sever and extremely sever of anxiety. A study in Iran showed that mean anxiety score in HBV was higher ( $7.4 \pm 4.5$ ) than control group ( $4.8 \pm 2.8$ ) (16). High follow-up frequency, evaluation needs, treatment needs, and information needs for CHB patients who experience high levels of anxiety might all be contributing factors. (2). According to a study conducted in Turkey, individuals with chronic active hepatitis B experience exaggerated physical sensations and anxiety-depression problems, both of which have an effect on functioning (2). Another Australian research also clarified the spectrum of concerns and fears associated with hepatitis B that affected people's outlooks and attitudes about life (23).

Furthermore, this study revealed that the prevalence rate of stress in patients with HBV is 64.6% as compared to control group 16% and 49% of HBV patients at sever and extremely sever level of stress. A study in china, showed that Psychological stress lead to anxiety, Therefore, the degree of stress and anxiety are related, and patients with large stress have immunological responses that are less severe from those with moderate stress. (20). Also, this study was showed the prevalence ratee of depression 75% is higher than that of anxiety 70.2% and stress 64.6%. similar finding found in Iranian study which showed that depression has been meet more than other psychiatric illnesses in patients with hepatitis B (24,25). So, patients withing hepatitis B are lesser health and wellness from the normal people (26). The diagnosis of people with HBV especially during the first 3 months leads to fear, worries about stigma and depression which lead to decline the quality of life of infected patients (27). Fear of transmit the disease to family, close friends also colleagues as well as fear of the stigma lead to isolation, stay away from them and depression are the most negative impact of hepatitis B virus (28).

The current study also, showed the correlation between DASS domains and demographic characteristics as in table 5, which revealed that stress level is negatively correlated with age (higher in younger age) and without any correlation with other characteristics. Also, anxiety level is positively correlated with gender and negatively correlated with education, without correlation with other characteristics. While a research conducted in China found no discernible difference between high and low stress/anxiety levels in sociodemographic factors (gender, age, marital state, and economic state, and disease duration.) While there was a correlation between education and state anxiety and the proportion of those with a college degree was higher in the low stress group, it was substantially lower in the high stress group (20). Furthermore, the depression level has no correlation with all demographic characteristics. According to a study conducted in Iran, the mean age of patients in the groups without depression was 48.76 years, that of those with mild depression was 39.48 years, that of those with moderate depression was 35.37 years, and that of those with severe depression was 30.07 years ( $p < 0.05$ ). Additionally, 72.7% of men and 75% of women in the study had depression (29).

While table 6, showed the correlation between DASS domains and disease characteristics, in which stress level has no correlation with all characteristics, while anxiety level is negatively correlated with serum ALT level but without correlations of other characteristics and depression level is positively correlate with HBV-DNA level, also, without correlation with other characteristics.

A study in China showed that a negative association between ALT and stress and anxiety were but, not correlated with viral load and virus genotype (20). Another research in Lahore found that the prevalence of depression was 70.6%, 26.2%, and 3.1% among patients with diseases lasting less than two years, between two and four years, and more than four years. Depression and the length of the illness were significantly correlated ( $p$ -value = 0.001) (30).

Future research may benefit from highlighting some of our study's shortcomings in relation to the planning process. This study's cross-sectional design, which does not allow for prospective analysis of the treatment's impact on patients' HRQOL, is one of its limitations. Future research on the same issue can be done as multi-center studies to include participants from other Iraqi centers.

## Conclusion:

When compared to control healthy participants, our sample of chronic hepatitis B patients had considerably poorer HRQOL due to the high incidence of depression, anxiety, and stress. The majority of patients also had moderate to severe disease.

## REFERENCES

1. Saim Dayan, Alicem Tekin, Recep Tekin, et al. HBsAg, anti-HCV, anti-HIV 1/2 and syphilis seroprevalence in healthy volunteer blood donors in southeastern Anatolia. *J Infect Dev Ctries* 2013; 7(9): 665-669.
2. Ahmet Yilmaz, MD, Feyzullah Ucmak, MD, Su`leyman Do`nmezgil, MD, et al. Somatosensory Amplification, Anxiety, and Depression in Patients With Hepatitis B: Impact on Functionality. *Medicine Journal*2016; 95(21):e3779.
3. Sun Young Yim and Ji Hoon Kim. The epidemiology of hepatitis B virus infection in Korea. *The Korean Journal of Internal Medicine* 2019; Mar 29.
4. GLOBAL HEPATITIS REPORT. World Health Organization 2017.
5. Ata Allah M. Tarky, Wijdan Akram, Ahmed S. Al-Naaimi, et al. Epidemiology of viral hepatitis B and C in Iraq: a national survey 2005-2006. *Zanco J. Med. Sci.*, 17(1), 2013.
6. Dieter Glebe, Stephan Urban. Viral and cellular determinants involved in hepadnaviral entry. *World J Gastroenterology* 2007 January 7; 13(1): 22-38.
7. Abdurrahman Altindag, MD, Dursun Cadirci, MD, CCFP, Fatma Sirmatel, MD. Depression and health related quality of life in non-cirrhotic chronic hepatitis B patients and hepatitis B carriers. *Neurosciences* 2009; Vol. 14 (1): 56-59.
8. PATRICK ARBUTHNOT and MICHAEL KEW. Hepatitis B virus and hepatocellular carcinoma. *International Journal of Experimental Pathology* 2001; 82: 77-100.
9. Lydia S. Y. Tang, MBChB; Emily Covertt, BS; Eleanor Wilson, MD, MS, et al. Chronic Hepatitis B Infection A Review. *The Journal of the American Medical Association* 2018 May; 8;319(17):1802-1813.
10. Bo Hyun Kim, M.D. and W. Ray Kim, M.D.. Epidemiology of Hepatitis B Virus Infection in the United States. *CLINICAL LIVER DISEASE* 2018; 12(1).
11. MEASURING QUALITY OF LIFE. THE WORLD HEALTH ORGANIZATION 1997.
12. MARCIA A. TESTA, M.P.H., PH.D., AND DONALD C. SIMONSON, M.D.. ASSESSMENT OF QUALITY-OF-LIFE OUTCOMES A review. *THE NEW ENGLAND JOURNAL OF MEDICINE* 1996; 334 (13): 835-840.
13. Jagdeep Obhrai, M.D., Yoshio Hall, and B.S. Anand, M.D.. Assessment of Fatigue and Psychologic Disturbances in Patients with Hepatitis C Virus Infection. *J Clin Gastroenterol* 2001;32(5):413-417.
14. Robert J. Fontana, M.D., Cheryl A. Moyer, M.S., Seema Sonnad, Ph.D, et al. Comorbidities and Quality of Life in Patients With Interferon-Refractory Chronic Hepatitis C. *Am J Gastroenterol* 2001;96:170-178.
15. Khozema B. Hussain, M.D., Robert J. Fontana, M.D., Cheryl A. Moyer, M.S. Comorbid Illness Is an Important Determinant of Health-Related Quality of Life in Patients With Chronic Hepatitis C. *THE AMERICAN JOURNAL OF GASTROENTEROLOGY* Vol2001; 96(90): 2737-2744.
16. Seyed M. Alavian, Seyed A. Tavallaii, Mahdi A. Farahani, et al. Evaluation of the severity of depression and anxiety in hepatitis B and hepatitis C patients: a case control study. *Iranian Journal of Clinical Infectious Diseases* 2007;2(3):113-119.
17. Seyed-Moayed Alavian MD., Behzad Hajarizadeh MD.. Attempted suicide in two patients with chronic hepatitis C while being treated with Interferon-alpha. *Hepatitis Monthly* (2004) 4, 20-22.
18. David Bernstein, Leah Kleinman, Chris M. Barker, et al. Relationship of Health-Related Quality of Life to Treatment Adherence and Sustained Response in Chronic Hepatitis C Patients. *HEPATOLOGY*2002; 35(3): 704-708.
19. Naglaa F. A. Youssef, Mohamed El Kassas, Amany Farag, et al. Health-related quality of Life in patients with chronic hepatitis C receiving Sofosbuvir-based treatment, with and without Interferon: a prospective observational study in Egypt. *BMC Gastroenterology* (2017); 17: 18.
20. YingLi He, Heng Gao, XiaoMei Li, et al. Psychological Stress Exerts Effects on Pathogenesis of Hepatitis B via Type-1/Type-2 Cytokines Shift toward Type-2 Cytokine Response. *www.plosone.org* August 2014; 9(8).
21. Muhammad O. Qureshi, Nasir Kh. and Farzana Sh.. Severity of Depression in Hepatitis B and Hepatitis C Patients. *Journal of the College of Physicians and Surgeons Pakistan* 2012, Vol. 22 (10): 632-634.
22. E. Amy Janke, Ph.D., Sarah McGraw, Ph.D., Liana Fraenkel, MD, MPH. Psychosocial Correlates of Hepatitis C: Interaction and impact on quality of life. *Psychosomatics*. 2008 ; 49(6): 494-501.
23. Behzad Hajarizadeh, Jacqui Richmond, Naomi Ngo, et al. Hepatitis B-Related Concerns and Anxieties Among People With Chronic Hepatitis B in Australia. *Hepat Mon.* 2016 June; 16(6):e35566.
24. Jinous Arvand, Abdollah Shafiabadi, Mohammad R. Falsafinejad, et al. Depression in patients with chronic hepatitis B: an experience on individual solution- focused therapy. *Gastroenterol Hepatol Bed Bench* 2012;5(3):166-168.
25. CHRISTINE M. HUNT, MD, JASON A. DOMINITZ, MD, MHS, et al. Effect of Interferon-a Treatment of Chronic Hepatitis C on Health-Related Quality of Life. *Digestive Diseases and Sciences* 1997; 42(12): 2482-2486.
26. Amirhossein Modabbernia MD, Mandana Ashrafi MD, Reza Malekzadeh MD, et al. A Review of Psychosocial Issues in Patients with Chronic Hepatitis B. *Archives of Iranian Medicine* 2013; 16(2): 114-122.
27. AURELIA ENESCU, P. MITRUT, MARIA BALASOIU, et al. Psychosocial Issues in Patients with Chronic Hepatitis B and C. *Current Health Sciences Journal* 2014; 40(2): 93-96.
28. Leila Valizadeh, Vahid Zamanzadeh, Reza Negarandeh, et al. Psychological Reactions among Patients with Chronic Hepatitis B: a Qualitative Study.

Journal of Caring Sciences, 2016, 5(1), 57-66.

29. Shahriar Alian MD, Abbas Masoudzadeh MD, Talayeh Khoddad MD, et al. Depression in Hepatitis B and C, and Its Correlation With Hepatitis Drugs Consumption (Interfron/Lamivodin/Ribaverin). Iran J Psychiatry Behav Sci 2013; 7(1): 24-29.
30. JEHANGIR AHMED, NASIR FAROOQBUTT, RABIA RATHORE, et al. Prevalence of Depression in patients of Chronic Hepatitis B & C Presenting to Mayo Hospital Lahore. P J M H S 2017; 11(2): 690-694.