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Depression, Anxiety and Stress Among a Sample of Chronic Hepatitis C Patients in AL-Najaf Province /Iraq

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ABSTRACT

Previous studies in Euro-American countries have shown that patients with chronic hepatitis C virus infection have increased levels of neuropsychiatric symptoms. While chronic hepatitis C virus infection has been reported in Arab countries such as Iraq, there are little studies about the neuropsychological burden associated with chronic hepatitis C among patients in the Arab region. The aim of the current study was to measure the prevalence and level of severity of depression, anxiety and stress among a sample of chronic hepatitis C patients in AL-Najaf province /Iraq. The current study was cross-sectional study carried out on (110) already diagnosed chronic viral hepatitis C patients who attended the Gastroenterology and Hepatology Center/Al-Sader Medical City/Najaf/Iraq during November 2018 to May 2019. In addition, (100) apparently healthy subjects were included as a control group. The Arabic version of the Depression Anxiety Stress Scale (DASS-21) was used to assess mental health. Both the prevalence rates and severity levels of depression, anxiety and stress were significantly higher in chronic hepatitis C patients compared to the control group (P<0.001). Stress level is negatively correlated with age and is significantly more in single. Anxiety level is less with a higher level of education. Depression was significantly higher in those having children. The study indicates that the presence of chronic hepatitis C infection is associated with a higher risk of psychological burden. Accordingly, meeting the psychological needs of such patients would need to be addressed.

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INTRODUCTION

Hepatitis C virus (HCV) is a major blood-borne infection. There are about 120-130 million or 3% of the world population that is infected with HCV. According to the World Health Organization (WHO), there are approximately 3-4 million new cases of HCV infection annually (Morozov and Lagaye, 2018). It is a leading cause of hepatic morbidity and mortality by its predisposition to liver cirrhosis, fibrosis, and hepatocellular carcinoma (HCC). Yearly, hepatitis C causes about 399,000 deaths worldwide, mostly from cirrhosis and HCC (Renau and Berenguer, 2018). In Iraq, hepatitis C is considered of low endemicity. The prevalence of anti-HCV was low (0.4%) (Tarky *et al.*, 2005).

Rates of depression have been reported in the range of 22 – 59% of patients with hepatitis C (Majeed *et al.*, 2009; Gill *et al.*, 2005; Gleason *et al.*, 2005; Memon *et al.*, 2011).

Anxiety is another problem experienced by many patients with HCV. One study showed that 24% of patients with HCV had anxiety (Golden *et al.*, 2005). Most researches regarding anxiety show that it is at least as common as depression (Fontana *et al.*, 2002; Loftis *et al.*, 2006; Yovtcheva *et al.*, 2001; El-Serag *et al.*, 2002). Knowing that one has acquired a serious infection such as HCV, with its complications is a major life stressor, and will produce emotional stress in most, and neuropsychiatric disorder in many (Wessely and Pariante, 2002).

Psychiatric disorders are important in patients with hepatitis virus infection for their influence on daily function of hepatitis positive patients by increasing their extrahepatic manifestations (Obhrai *et al.*, 2001). They also can decrease health-related quality of life (HRQOL) (Fontana, 2001; Hussain, 2001), increase the risk of cancer, mortality (Garssen and Goodkin, 1999) and suicide attack probability (Dieperink, 2000; Alavian and Hajarizadeh, 2004) 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 (Bernstein *et al.*, 2002; Kraus *et al.*, 2001).

Evaluation for psychiatric symptoms in hepatitis is important because they have an adverse effect upon the course of the disease (Gadit, 2010). These psychiatric symptoms are the major reason for delay or stopping of treatment (Zdilar *et al.*, 2000). Successful medical treatment, therefore, requires detection and management of depression and other psychiatric issues before and during the treatment (Dogar *et al.*, 2009).

The aim of the current study was to measure the prevalence and level of severity of depression, anxiety and stress among a sample of chronic hepatitis C patients in AL-Najaf province/Iraq.

PATIENTS AND METHOD

Patients

The current cross-sectional study was carried out on (110) already diagnosed chronic viral hepatitis C patients who attended the Gastroenterology and Hepatology center/Al-Sader Medical City/Najaf during November 2018 to May 2019. In addition, 100 apparently healthy subjects were included as a control group.

Inclusion criteria

The inclusion criteria for the current study were:

1. Patients having chronic hepatitis C alone, who are aged 18 years or more of either sex who are accepted to participate in the study.
2. Disease duration (since diagnosis) of at least six months or more.

Exclusion criteria

The exclusion criteria for this study were

1. Patient who had a hearing, speech or cognitive deficits that would impair understanding of the questions.
2. Patient who had liver cancer or clinical evidence of decompensated liver cirrhosis (ascites, history of hepatic encephalopathy, or history of variceal bleeding).
3. Concomitant significant medical illness (such as chronic renal failure, chronic lung disease, hypertension, heart disease, diabetes mellitus, stroke).
4. Patient who take antidepressant drugs, or being on treatment for any neurological or psychological diseases.
5. Pregnant women.
6. Patients providing incomplete information during completion of the questionnaire also will excluded from the study.

Method

The questionnaires

The Depression Anxiety Stress Scale (DASS-21) was used to assess mental health. DASS-21 is a 21-item self-reported tool developed to measure the 3 related negative emotional problems, including depression, anxiety, and stress. It has 21-items, with 7 items for each domain. Patients scored each item from 0-3, where zero meant (did not apply to me at all) and 3 meant (applied to me very much). All scores of each subscale were added and multiplied by 2. The normal score for stress was 0-14, for anxiety 0-7, and for depression 0-9. The mild score for stress was 15-18, for anxiety 8-9, and depression 10-13. The moderate score for stress 19-25, for anxiety 10-14, and for depression 14-20. The severe score for stress was 26-33, for anxiety 15-19, and for depressions 21-27. The extremely severe score for stress was 34+, for anxiety 20+, and for depression 28+ (Lovibond and Lovibond, 1995). The Arabic

Table 1: Sociodemographic characteristics of chronic hepatitis C patients compared to that of the control group

Characteristics		Control		Hepatitis C		P value
		N	Mean±SD	N	Mean±SD	
Age		100	40.8±11.6	110	42.2±15.6	0.454 †NS
Gender		N	%	N	%	P value
	Male	53	53.0%	60	54.5%	0.822 ¥ NS
	Female	47	47.0%	50	45.5%	
Education Level	Illiterate	19	19.0%	26	23.6%	0.69 ¥ NS
	Primary	32	32.0%	49	44.5%	
	Secondary	32	32.0%	20	18.2%	
	University	17	17.0%	15	13.6%	
Social status	Single	11	11.0%	14	12.7%	0.822 ¥ NS
	Married	79	79.0%	83	75.5%	
	Divorced	4	4.0%	6	5.5%	
	Widow	6	6.0%	7	6.4%	
Children	Yes	83	83.0%	91	82.7%	0.958 ¥ NS
	No	17	17.0%	19	17.3%	
Residency	Urban	75	75.0%	82	74.5%	0.940 ¥ NS
	Rural	25	25.0%	28	25.5%	

Data were expressed as either mean ± standard deviation (SD) or number (%); †: independent samples t-test; ¥: Chi-square test; NS: not significant at P >0.05

version of this tool has been psychometrically validated.

Administration of questionnaires

The data related to the study were collected by the researcher herself. When the patients arrived to the hospital to made their programmed laboratory data and received their treatment, they were asked if they accept to participate in the study, if they accepted to participate, a complete explanation to the questions in the questionnaire was done and each patient spent about 5 minutes to fill the research questionnaire completely.

Statistical analysis

Data were collected, summarized, analyzed using two software programs, statistical package for social sciences (SPSS) version 23 and Microsoft Office Excel 2010. Categorical variables were presented as number and percentage. Quantitative variables were initially analyzed for normality distribution Kolmogorov-Smirnov test. Therefore, quantitative variables were described as mean ± standard deviation or median (interquartile range). Comparison of mean values between any two groups carried out using independent sample t-test. Association between any two categorical variables was done using Chi-square test. Spearman correlation test was used to assess variables. P-value was considered significant when it is equal or less than 0.05 and highly significant when it is equal or less than 0.01.

RESULTS AND DISCUSSION

Demographic characteristics of patients with hepatitis C and control subjects are shown in Table 1. While the disease characteristics and investigations in patients with HCV infection are shown in Table 2.

The prevalence rates of depression, anxiety and stress in control and HCV groups are shown in Table 3. For depression, anxiety and stress, the differences were highly significant between hepatitis c group and control group (P<0.001).

The levels of severity of depression, anxiety and stress among study groups are shown in Table 4. For depression, anxiety and stress, the differences were highly significant between hepatitis c group and control group (P<0.001).

Correlations of DASS domain to demographic characteristics of patients with HCV are shown in Table 5. Stress level is negatively correlated with age, and is significantly more in single. Anxiety level is less with higher level of education. Depression was significantly higher in those having children.

Correlations of DASS domain to disease characteristics of patients with HCV are shown in Table 6.

Depression, anxiety and stress levels were not cor-

Table 2: Disease characteristics and investigations of chronic hepatitis C patients

Characteristic	N	%	Characteristic	N	%
Mode of transmission			Biopsy	2	1.8
Blood transfusion	32	29.1	Other family member	15	13.6
Surgery	33	30.0	Hospital admission	2	1.8
Dental procedure	19	17.3	Treatment experience		
Shaving	2	1.8	Naïve	52	47.3
Needle	2	1.8	Experienced	58	52.7
Tattoo	8	7.3	Treatment		
			Sofosbuvir + velpatasvir	1	0.9
Unknown	12	10.9	Sofosbuvir + ledipasvir	7	6.4
			Sofosbuvir + ledipasvir + Ribavirin	1	0.9
			Peg-INF + Ribavirin	3	2.7
Vertical	2	1.8	Peg-INF + Sofosbuvir	1	0.9
			Not treated	96	87.3
			Ribavirin	1	0.9
Characteristic	**Minimum**	**Maximum**	**Median**	**IQR**	
Duration of disease	0.50	10.00	1.50	2.00	
Duration of treatment	0.00	1.00	0.00	0.00	
HCV RNA (IU/ml)	0.00	171000000.0	264760.00	2870000.0	
ALT (U/L)	4.00	161.00	32.95	36.45	
AST (U/L)	4.00	240.00	28.00	31.72	
Albumin (g/dl)	0.80	43.00	4.35	1.50	
INR	1.00	2.00	1.20	0.40	
Bilirubin (mg/dl)	0.30	14.86	0.80	0.88	

ALT: alanine aminotransferase; AST: aspartate aminotransferase; HCV: hepatitis C virus; INR: international normalized ratio; Peg-INF: pegylated interferon; RNA: ribonucleic acid

Table 3: Prevalence rate of DASS-21 domains in control group and chronic hepatitis C patients

Characteristic	Control Group N=100	HCV n = 110	P
Depression	9	87	<0.001 ¥
Prevalence	9	79.1 %	HS
Anxiety	17	77	<0.001 ¥
Prevalence	17	70.0 %	HS
Stress	16	76	<0.001 ¥
Prevalence	16	69.1 %	HS

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

Table 4: Levels of DASS-21 domains in control group and chronic hepatitis C patients

Characteristic		Control n = 100		HCV n = 110		P value
		n	%	n	%	
Depression	No	91	91	23	20.9	<0.001 ¥
	Mild	7	7	8	7.3	HS
	Moderate	2	2	14	12.7	
	Severe	0	0	11	10.0	
	Extremely severe	0	0	54	49.1	
Anxiety	No Anxiety	83	83	33	30.0	<0.001 ¥
	Mild	6	6	5	4.5	HS
	Moderate	7	7	19	17.3	
	Severe	3	3	10	9.1	
	Extremely severe	1	1.0	43	39.1	
Stress	No Stress	84	84	34	30.9	<0.001 ¥
	Mild	7	7	11	10.0	HS
	Moderate	9	9	10	9.1	
	Severe	0	0	18	16.4	
	Extremely severe	0	0	37	33.6	

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

Table 5: Correlation of DASS-21 and demographic characteristics of chronic hepatitis C patients

Characteristic	Stress Level		Anxiety Level		Depression Level	
	r	P	r	P	r	p
Gender	0.073	0.446	0.165	0.085	0.006	0.949
Age	-0.197	0.039 *	0.070	0.465	-0.116	0.230
Education	-0.020	0.838	-0.269	0.005 *	-0.087	0.367
Social	-0.229	0.016 *	-0.030	0.756	-0.175	0.067
Children	0.081	0.398	-0.056	0.564	0.194	0.043 *
Residency	-0.023	0.812	0.035	0.715	0.005	0.956

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

related to any of disease characteristics.

Several studies had shown that patients with HCV infection tend to be associated with increased levels of emotional distress (Fontana *et al.*, 2002; Forton, 2002; Bonkovsky and Woolley, 1999). Most of the studies have generally conducted on Euro-American patients. To our knowledge, there are little studies from the Arabic-speaking countries. To fill this gap, this study was conducted to compare the prevalence and severity of depression, anxiety and stress as defined by DASS-21of those diagnosed with chronic HCV infection with those without.

Both the prevalence rates and severity levels of depression, anxiety and stress were significantly higher in chronic hepatitis C patients compared to control. In a cross-sectional study of eighty, one HCV-infected patient who were not treated by antiviral therapy, anxiety, depression, neuropsychiatric symptoms were assessed (Erim *et al.*, 2010). It was found that depression and anxiety scores were significantly higher among HCV patients compared to the healthy control group (Erim *et al.*, 2010).

In a previous Italian report, 36.7% of HCV patients were found to have a psychiatric disorder (Taruschio *et al.*, 1996). Another study (Hunt *et al.*, 1997), found the rate of depression to be 11%-30% in HCV patients. Almost 25% of HCV infected patients referred for treatment were found to suffer from depression, with 60% of them requiring treatment (Lee *et al.*, 1997).

Two distinct types of evidence support the association between depression and HCV infection. First,

Table 6: Correlation of DASS-21 to disease characteristics of chronic hepatitis C patients

Characteristic	Stress Level		Anxiety Level		Depression Level	
	r	P	r	P	r	P
Duration of disease	0.072	0.456	0.084	0.381	0.081	0.403
Biopsy	-0.009	0.926	-0.058	0.544	0.078	0.417
Other family member	0.022	0.819	0.042	0.663	-0.021	0.824
Mode of transmission	-0.072	0.456	-0.124	0.198	-0.121	0.210
Treatment	-0.081	0.398	0.064	0.507	0.032	0.737
Duration of treatment	0.030	0.760	-0.070	0.467	-0.085	0.377
Treatment experience	0.021	0.829	0.054	0.576	0.007	0.939
Hospital admission	-0.101	0.292	-0.151	0.116	-0.129	0.180
HCV RNA (IU/ml)	0.097	0.311	0.092	0.338	0.093	0.335
ALT (U/L)	0.154	0.108	0.122	0.204	0.118	0.218
AST (U/L)	0.043	0.657	0.043	0.659	0.009	0.926
Albumin (g/dl)	0.108	0.554	0.056	0.761	0.106	0.562
INR	-0.099	0.304	-0.025	0.798	-0.037	0.698
Bilirubin (mg/dl)	0.021	0.829	-0.157	0.102	0.045	0.639

Correlation was carried out using Spearman correlation test;ALT: alanine aminotransferase; AST: aspartate aminotransferase; HCV: hepatitis C virus; INR:international normalized; RNA: ribonucleic acid

patients with neuropsychiatric disorders have a higher rate of HCV infection. Second, patients with chronic HCV infection may have a higher rate of neuropsychiatric disorders, including depression. The prevalence of HCV is higher in patients with neuropsychiatric disorders than in healthy control. In intravenous drug users, 74% -100% of individuals are infected with HCV (Bell *et al.*, 1990; Fingerhood, 1993; Woodfield *et al.*, 1994; Fisher *et al.*, 1997).

The reasons for the high prevalence of depression in HCV infected patients are not fully understood, but two factors are important. First, HCV-infected patients are relatively younger age (the highest rate is in the 3^{rd} and 4^{th} decades of life) (Sarbah and Younossi, 2000) and may suffer from depression related to excess fatigue or worries about the long-term prognosis; they have more somatic complaints than patients having other liver diseases (Singh *et al.*, 1997). Secondly, HCV-infected patients may have additional risk factors for depression, such as substance abuse (Johnson *et al.*, 1998). From these data, it is increasingly evident that HCV infection, depression, and substance abuse are intimately related and clinically important. Depression may impair the HRQOL of patients infected with HCV infection (Dusheiko, 1997). Also, Interferon (IFN) therapy may aggravate the symptoms of those with underlying depression, (Otsubo *et al.*, 1997) reducing adherence, and the preexisting depressive disorders may affect with the assessment of IFN-induced depression (Johnson *et al.*, 1998).

Regarding the correlation of DASS-21 with demographic characteristics of patients, the current study showed that stress level is significantly high in young, and single patients. Also, the anxiety level is significantly high in low educated patients. Benjamin *et al.* found that education and relationship status (partnered) were independent predictors of decreased anxiety while age was a significant predictor of decreased depression among chronic hepatitis C Australian patients (Stewart *et al.*, 2015).

Furthermore, in the current study, depression level was significantly high in patients with a high number of children, and this may be due to fearfulness of patients from disease transmission to their children. Also, there are no correlations between DASS-21 domains with disease characteristics. Seyed *et al.* found that in patients with viral hepatitis B or C, both anxiety and depression score were correlated with total serum bilirubin level, and AST level while depression score (but not anxiety score) was correlated with serum ALT level (Seyed *et al.*, 2007).

CONCLUSION

Showing attention to some limitations of our study regarding the planning process could be helpful for future studies. One limitation is the relatively small sample size collected from one Iraqi province (AL-Najaf) that could limit our ability to generalize the results to all chronic hepatitis C patients in Iraq. Future study about the same topic can be conducted as multi-center studies to enrol patients from different centers in Iraq. Another limitation

is the cross-sectional design of this study rather than prospective which allow studying the effect of treatment on neuropsychiatric symptoms associated with chronic hepatitis C. In conclusion, our sample of chronic hepatitis C patients show significantly higher prevalence rate and severity levels of depression, anxiety and stress compared to control healthy subjects. These results could prove useful for health-care providers treating chronic hepatitis C patients. In addition to medical treatments that aim to cure chronic hepatitis C infection, it is important to adopt psychological counseling to further improve the HRQOL of chronic hepatitis C patients.

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