

Depression, anxiety and quality of life in patients with chronic hepatitis C virus infection in Vojvodina

Item Type	Journal article
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Citation	Kačavenda-Babović, D., Đurić, P., Babović, R., Fabri, M., Ružić, M. i Bugarski Ignjatović, V. (2021) Depression, Anxiety and Quality of Life in Patients with Chronic Hepatitis C Virus Infection in Vojvodina. <i>Acta clinica Croatica</i> , 60(4), pp. 579-589. https://doi.org/10.20471/acc.2021.60.04.03
DOI	10.20471/acc.2021.60.04.03
Publisher	Sestre Milosrdnice University Hospital and Institute of Clinical Medical Research
Journal	Acta Clinica Croatica
Rights	Licence for published version: Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International
Download date	2026-06-18 14:07:26
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Link to Item	http://hdl.handle.net/2436/625513



DEPRESSION, ANXIETY AND QUALITY OF LIFE IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION IN VOJVODINA

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SUMMARY - The objective of this study was to investigate the prevalence of depression and anxiety among patients with chronic hepatitis C and how depression and anxiety correlate with respective health-related quality of life (HRQoL) domains, sociodemographic factors, and clinico-epidemiological characteristics. This prospective study involved 150 patients with chronic hepatitis C awaiting interferon treatment for hepatitis C and 150 healthy subjects. All individuals enrolled in the study completed the Short Form 36 (SF-36) questionnaire and Hospital Anxiety Depression Scale. The symptoms showed greater severity/score among patients with chronic hepatitis C for both depression ($t=3.37$; $p<0.01$) and anxiety ($t=2.35$; $p<0.05$). Regression analysis was used for estimating the relationship between depression and the set of predictors (domains of the SF-36 questionnaire). Three HRQoL domains (Physical Functioning, Vitality, and Mental Health) were found to have the strongest predictive contribution to the occurrence of depression. A series of Kruskal-Wallis and Mann-Whitney tests showed a significant difference in depression level between marital status categories ($\chi^2(2)=7.86$, $p<0.05$). Divorced participants had significantly higher scores compared to married participants ($Z=-2.40$, $p<0.05$) and single participants ($Z=-2.75$, $p<0.01$). Unemployment was associated with a higher degree of depression and anxiety. There was no association identified between duration of the disease, route of hepatitis C virus transmission, existence of cirrhosis, and depression or anxiety. The findings of this study can assist in developing a standard protocol for the management of chronic hepatitis C that will include psychological assessment and support.

Key words: *Chronic hepatitis C; Quality of life; Depression; Anxiety; Socioeconomic factors*

Introduction

Chronic hepatitis C virus (HCV) infection is one of the significant public health problems affecting about 3% of the population worldwide¹. There are no precise data on the prevalence of chronic HCV infec-

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Received June 19, 2018, accepted February 20, 2019

tion in Serbia, but it is estimated that 1.5% of the general population have anti-HCV antibodies².

According to the latest World Health Organization (WHO) data, 71 million people across the globe suffer from chronic HCV infection, and many of them will develop liver cirrhosis or hepatocellular carcinoma in the future³. Additionally, there is a considerable public health and economic burden of HCV disease due to the inability to work, social marginalization, and changed lifestyle in this group of patients⁴. Chronic HCV infection is associated with a number of extrahepatic conditions, including neurological and psychiatric disorders. Recent review articles report that chronic hepatitis C was associated with neurological and psychiatric disorders in up to 50% of patients. Neurological conditions commonly linked with chronic HCV infection are peripheral neuropathy, cognitive impairment and cerebrovascular accidents, and common psychiatric disorders include depression, anxiety, and fatigue^{5,6}.

Some of the studies were focused on depression only, but not on anxiety, which can also significantly correlate with health-related quality of life (HRQoL)⁷⁻⁹. HRQoL is defined as a person's subjective perception of own physical, mental and social well-being. Different disease-specific and generic HRQoL questionnaires have been used to measure quality of life of HCV infected patients and the effects of anti-viral therapy⁵.

The presence of depression and anxiety affects the clinical course of HCV infection with poorer outcome of treatment and reduced functional ability. Therefore, the diagnosis of these disorders at the right time in patients with chronic hepatitis C may contribute to improvement of the subjective well-being and HRQoL^{5,7}. The relationship between quality of life, depression and anxiety is not clear. There is still a question whether depression and anxiety are just some of the extrahepatic manifestations of HCV infection, or they are a psychological reaction to decreased quality of life caused by chronic liver deterioration¹⁰.

However, the presence of depression and anxiety symptoms can have an important role in compliance with direct-acting antiviral drug (DAA) therapy regimens⁹⁻¹¹ and in adherence to interferon (IFN) based treatments¹². IFN has been widely considered as able to induce depression and suicidal ideas, consequently causing discontinuation of treatment^{9,12}. Despite many

benefits of DAA treatment, including undetectability of the virus in 90% or more patients and in most cases less negative impact on their quality of life when compared with IFN-based regimens, in some European countries, this therapy is not yet available for all patients with chronic hepatitis C¹³. The high price of this new anti-HCV treatment has contributed to its inaccessibility to some chronic HCV-infected patients in Serbia. In addition, a large number of elderly patients with advanced stage disease that requires immediate therapeutic treatment has been identified; hence, there is a high risk of IFN-induced depression and poorer adherence to therapy regimen¹⁴.

Unfortunately, standardized diagnostic protocols for chronic hepatitis C do not include psychological assessment, so depression and anxiety mainly remain unrecognized by routine clinical examination¹⁵. Therefore, the aim of this study was to assess the occurrence of anxiety and depression and their relation with respective HRQoL domains, sociodemographic factors, epidemiological and clinical characteristics of patients with chronic hepatitis C who were awaiting IFN therapy. This is the first study of the quality of life of patients with chronic hepatitis C in the Autonomous Province (AP) of Vojvodina, which is located in the northern part of Serbia, with a population of around two million people.

Subjects and Methods

Sample

A prospective study was conducted during a period of two years (2015-2017) in the AP of Vojvodina. Three hundred participants of both sexes, aged 18 and above, were included in the study and divided into two groups. The study group included 150 naive chronic hepatitis infected patients waiting for therapy at the Department of Infectious Diseases, University Clinical Centre of Vojvodina, Novi Sad. Most of the patients had a diagnosis of chronic hepatitis C established for more than five years ($n=58$; 39%), and a similar number of patients had a diagnosis established less than a year ($n=48$; 32%) before the study. Thirty-five (23%) patients were diagnosed with chronic hepatitis C one to five years before the study, and for 9 (6.0%) patients, the information on the time of chronic hepatitis C diagnosis remained unknown. The diag-

nosis of chronic hepatitis C was confirmed by serum HCV RNA polymerase chain reaction and histopathologic criteria (aspiration biopsy of the liver).

Exclusion criteria for the study group were hepatocellular carcinoma or other malignancies, liver transplantation, co-infection with hepatitis B virus/human immunodeficiency virus, ongoing therapy for chronic hepatitis C, dementia or psychosis, presence of depressive and anxiety disorders in medical records, abstinence from psychoactive substance shorter than six months, language misunderstanding, and severe cognitive impairments that disable proper communication with the patient.

The control group included 150 healthy volunteers during voluntary blood donation at the General Hospital Sombor, Serbia. They had HCV infection excluded by mandatory anti-HCV and HCV RNA screening of blood donations. Both groups were matched by basic sociodemographic characteristics.

Research instruments

The Short Form health survey-36 (SF-36) measures the subjective feeling of health through eight respective health domains: Physical functioning (PF), Role limitation due to physical problems (RP), Role limitation due to emotional problems (RE), Vitality/Energy (VT), Mental health (MH), Social functioning (SF), Bodily pain (BP), and General health (GH). The scores for eight domains are ranked between 0 and 100, with a higher score signifying better quality of life for the studied domain and *vice versa*¹⁶. The reliability expressed by the Cronbach alpha coefficient ranged from 0.774 to 0.923 for all domains of SF-36.

Hospital Anxiety and Depression Scale (HADS) is a specially designed scale for assessing depressive and anxiety symptoms in individuals suffering from a physical illness. The advantage of this scale is simple application in assessing the degree of anxiety and depression. Since HADS does not include the items on somatic symptoms of depression (such as loss of appetite or fatigue), which may also result from physical disease, it is regarded as the most appropriate screening tool for mental disorders in somatic medicine¹⁷. The questionnaire consists of 14 questions, i.e. seven for depression and seven for anxiety. Answers are scored at four levels: from 0 to 3 (0 – not at all, 3 – all the time), and results vary between 0 and 21 for both depression and anxiety. Scores are categorized as fol-

lows: 0-7 no depression/anxiety, 8-10 mild depression/anxiety, and 11-21 moderate/severe depression/anxiety. HADS is comprised of two subscales, i.e. anxiety subscale (HADS-A) and depression subscale (HADS-D)¹⁸. As a self-assessment inventory, HADS is used to record (screening) the presence of certain anxiety and depressive symptoms, but not to diagnose a disorder. The reliability expressed by the Cronbach's alpha coefficient was 0.786 for HADS-D and 0.830 for HADS-A subscale.

The general questionnaire was tailor-made for this study, and it included questions regarding basic sociodemographic characteristics such as sex, age, level of education, marital status, employment status, place of residence, route of HCV transmission, duration of the disease, and presence of cirrhosis.

Ethical aspects of the study

Participants from both groups signed an informed consent form and were informed verbally and in writing about study objectives and all information on the relevance of the research process. The study was approved by the boards of ethics of the responsible health institutions (General Hospital Sombor, University Clinical Centre Vojvodina and Faculty of Medicine, University of Novi Sad) in accordance with the Helsinki Declaration.

Statistical analysis

The SPSS v. 21 for Windows software was used to enter and process data. Statistical data processing was carried out in line with data analysis, which was divided into several parts. In descriptive statistics, data were expressed as arithmetic mean (AM), standard deviation (SD), absolute numbers, and percentages. Correlation between depression (HADS-D) and anxiety (HADS-A) and quality of life measured with SF-36 was done by a series of multiple regression analysis. The set of predictors consisted of average scores on respective domains of SF-36. Criterion variables included average scores on HADS subscales. The analysis was carried out separately for each group of participants.

To test differences between the groups, both parametric and non-parametric tests were applied. The t-test was applied in a situation with nearly equal groups (similar number of participants *per* group) for measures that were normally distributed (skewness and

Table 1. Sociodemographic characteristics of both groups and clinical-epidemiological characteristics of the study group

Characteristic	Group				
	Study group		Control group		
Gender:	n	%	n	%	p=0.723
Male	93	62.0	90	60.0	
Female	57	38.0	60	40.0	
Age (years):	AM=42.01		AM=41.49		p=0.189
18-30	29	19.3	26	17.3	
31-50	75	50.0	90	60.0	
51+	46	30.7	34	22.7	
Education:					
Elementary school	28	18.7	7	4.7	
High school	92	61.3	102	68.0	
College	9	6.0	16	10.7	
University	21	14.0	25	16.6	
Employment status:					p=0.000
Employed	39	26.0	113	75.3	
Unemployed	84	56.0	25	16.7	
Retiree	27	18.0	12	8.0	
Marital status:					p=0.001
Married	66	44.0	95	63.3	
Divorced	25	16.7	14	9.3	
Widowed	10	6.7	1	0.7	
Single	49	32.6	40	26.7	
Place of residence:					p=0.892
Rural	36	24.0	35	23.3	
Urban	114	76.0	115	76.7	
Route of transmission:					
Drug injection	62	41.3			
Blood transfusion	25	16.7			
Medical intervention	4	2.7			
Sexual intercourse	2	1.3			
Other or unknown	57	38.0			
Duration of infection:					
Less than a year	48	32.0			
1-5 years	35	23.0			
Over 5 years	58	39.0			
Unknown	9	6.0			
Cirrhosis:					
Yes	23	15.3			
No	127	84.7			

AM = arithmetic mean; n = number of participants

Table 2. Scores on HADS subscales

Group		N	AM	SD	Sk	Ku	t	DF	p
Depression (HADS-D)	Study	150	1.05	0.57	0.51	-0.52	3.37	298.00	0.001
	Control	150	0.84	0.49	0.69	-0.35			
Anxiety (HADS-A)	Study	150	0.78	0.55	0.42	-0.52	2.35	298.00	0.020
	Control	150	0.64	0.50	0.87	-0.35			

HADS = Hospital Anxiety and Depression Scale; HADS-D = HADS depression subscale; HADS-A = HADS anxiety subscale; AM = arithmetic mean; SD = standard deviation; t = t test value; Sk = skewness; Ku = kurtosis; DF = degree of freedom; p = statistical significance; N = number of participants

kurtosis) within the ± 1.5 range as proposed by Tabachnick and Fidell¹⁹. A series of Kruskal-Wallis and Mann-Whitney tests were conducted in situations with non-equal group size and/or non-normal distribution of dependent variables. In each result section, we describe the analysis in more detail. The implemented analytical method used $p < 0.05$ as the criterion for statistical significance.

Results

The mean age was 42 (AM=42.01) years in the study group and 41 (AM=41.49) years in the control group ($p=0.189$). On average, both samples were predominated by middle-aged subjects (aged 31-50), with high school, married, males, and from urban environment. In the study group, 41.3% of patients were infected by injection drug use (based on self-reporting). As for the duration of infection, 39.0% of the patients had been infected for over five years. Most of the study group patients (84.7%) did not suffer from liver cirrhosis (Table 1).

According to the HADS (average scores on the HADS-D and HADS-A subscales), these symptoms showed greater severity/score in the study group than in the control group. The difference was statistically significant for both depression ($t=3.37$; $p < 0.01$) and anxiety ($t=2.35$; $p < 0.05$) (Table 2).

Anxiety (mild, moderate/severe) was recorded in 41% of study group patients and 27% of control group subjects, while depression (mild, moderate/severe) was recorded in 24% of study group patients and 21% of control group subjects (Table 3).

Multiple regression analysis was carried out in order to study the structure of correlation between depression and respective HRQoL domains measured with SF-36. The result in the study group showed that

Table 3. Anxiety and depression levels measured with HADS questionnaire

	Study group		Control group	
	n	%	n	%
Anxiety:				
No symptoms	88	58.60	109	72.70
Mild	34	22.70	26	17.30
Moderate/severe	28	18.70	15	10.00
Depression:				
No symptoms	114	76.00	118	78.70
Mild	19	12.70	24	16.00
Moderate/severe	17	11.30	8	5.30

HADS = Hospital Anxiety and Depression Scale; n = number of participants

the entire regression model was significant, whereby the value of the coefficient of multiple correlations indicated high intensity correlation between the predictor set and the criterion variable (72%). Three HRQoL domains from SF-36 were singled out as significant predictors for the occurrence of depression: Physical Functioning, Vitality, and Mental Health ($p < 0.001$). In the control group, HRQoL domains measured by SF-36 were also significantly correlated with depression but to a lesser extent than in the study group. The percentage of depression variance that was explained by the quality of life domains was 43.4%. The Social Functioning domain provided the only significant individual contribution to prediction ($p=0.047$) (Table 4).

Multiple regression analysis was also carried out in order to study the structure of correlation between anxiety and respective HRQoL domains measured with SF-36. The percentage of anxiety variance explained by domains of SF-36 questionnaire was 56.9% for the study group and 54.2% for the control group. In both groups, the Mental health domain provided the

Table 4. Correlation between depression and SF-36 domains

Predictor	Study group			Control group		
	β	p	R ²	β	p	R ²
PF	-0.243	0.000	0.72	-0.140	0.184	0.43
RP	0.116	0.139		0.122	0.498	
RE	-0.067	0.308		-0.146	0.712	
VT	-0.365	0.000		0.011	0.138	
MH	-0.316	0.000		-0.573	0.338	
SF	0.047	0.567		0.039	0.047	
BP	-0.087	0.142		-0.105	0.211	
GH	-0.079	0.198		-0.080	0.394	

Study group and control group: criterion-depression; predictors Short Form health survey-36 (SF-36) domains; PF = physical functioning; RP = role physical; RE = role emotional; VT = vitality; MH = mental health; SF = social functioning; BP = bodily pain; GH = general health; β = standardized regression coefficient; p = statistical significance; R² = coefficient of determination

Table 5. Correlation between anxiety and SF-36 domains

Predictor	Study group			Control group		
	β	p	R ²	β	p	R ²
PF	0.002	0.976	0.57	-0.140	0.053	0.54
RP	0.039	0.686		0.122	0.165	
RE	-0.072	0.372		-0.146	0.127	
VT	-0.191	0.114		0.011	0.934	
MH	-0.436	0.000		-0.573	0.000	
SF	-0.122	0.229		0.039	0.701	
BP	-0.095	0.194		-0.105	0.165	
GH	0.026	0.726		-0.080	0.308	

Study group and control group: criterion-anxiety; predictors Short Form health survey-36 (SF-36) domains; PF = physical functioning; RP = role physical; RE = role emotional; VT = vitality; MH = mental health; SF = social functioning; BP = bodily pain; GH = general health; β = standardized regression coefficient; p = statistical significance; R² = coefficient of determination

only significant individual contribution to prediction ($p < 0.001$) (Table 5).

In order to determine differences between the level of depression and anxiety related to certain sociodemographic factors (sex, age, level of education, marital status, employment status, place of residence) within the study group, a series of Kruskal-Wallis and Mann-Whitney tests were conducted. The results from the Kruskal-Wallis test (Table 6) suggested three statistically significant differences, and for all of them, we applied three Man-Whitney U tests for the purpose of testing differences between the two groups (Table 7). The first significant difference was found in depression level between marital status categories ($\chi^2(2) = 7.86$, $p < 0.05$). Divorced participants (M rank = 56.76) had

significantly higher scores ($Z = -2.40$, $p < 0.05$) compared to those who were married (M rank = 41.92). Very similar, participants that were divorced (M rank = 47.06) had significantly higher scores ($Z = -2.75$, $p < 0.01$) compared to participants who were not married (M rank = 32.62). The second significant difference was found in both depression and anxiety levels in the context of employment status. On the anxiety scale ($\chi^2(2) = 8.44$, $p < 0.05$), the group of employed participants (M rank = 48.44) had significantly lower scores ($Z = -2.88$, $p < 0.01$) in comparison with participants that were not employed (M rank = 68.30). The same pattern was present on the depression scale ($\chi^2(2) = 13.84$, $p < 0.01$). The group of employed participants (M rank = 44.96) had significantly lower scores ($Z =$

Table 6. Differences between categories of sociodemographic factors in the context of anxiety and depression level in study group

Variable	Category	n	Anxiety			Depression		
			MR	Z test	p	MR	Z test	p
Gender	Male	93	75.32			76.40		
	Female	57	75.79	-0.06	0.949	74.04	-0.32	0.745
Place of living	Rural	36	79.83			69.63		
	Urban	114	74.13	-0.68	0.491	77.36	-0.93	0.350
		n	MR	χ^2 (DF)	p	MR	χ^2 (DF)	p
Education	Elementary school	28	76.95			79.70		
	High school	92	78.73			76.10		
	College/university degree	30	64.23	2.57 (2)	0.276	69.75	0.81	0.666
Marital status	Married	66	67.98			64.86		
	Divorced	25	84.16			90.82		
	Single	49	66.93	3.49 (2)	0.174	67.73	7.86(2)	0.020
Employment status	Employed	39	60.17			54.92		
	Unemployed	84	84.04			85.95		
	Retired	27	71.07	8.44 (2)	0.015	72.72	13.84 (2)	0.001

n = number of participants; MR = mean rank; Z test = test statistic from Mann-Whitney analysis; p = p value; χ^2 = test statistic from Kruskal-Wallis analysis. There were no statistically significant correlations between age and anxiety/depression; DF = degree of freedom

-3.63, $p < 0.01$) when compared with those that were not employed (M rank=68.30).

There was no relationship between the duration of the disease, route of transmission, existence of cirrhosis, and depression or anxiety.

Discussion

Chronic hepatitis C is a slow-progressing disease with a well-known negative influence on all dimensions of HRQoL, even in patients with the absence of significant liver damage and clinical symptoms²⁰. Also, reduced HRQoL was found to be independently associated with depressive disorders in patients living with chronic hepatitis C regardless of the severity of liver disease, and therefore the implementation of screening and appropriate multidisciplinary health care is encouraged^{10,21}.

The relationship between HCV infection and depression is complex and not fully understood. Several mechanisms have been proposed to explain the pathogenesis of neuropsychiatric disorders observed in chronic HCV infection, including direct neuroinvasion, changes in metabolic pathways, and cerebral and systemic invasion⁶.

On the one hand, the symptoms of depression and anxiety in chronic hepatitis C can be related to the awareness of the diagnosis and prognosis of the disease, whereas on the other hand, they can occur due to the pathological process of the disease^{6,22}. It has been indicated that the virus can pass the blood-brain barrier, and HCV RNA sequences have been detected in the brain and cerebrospinal fluid. In addition, the immune response of a host associated with cytokine activation plays an important role in the emergence of these processes²³. Proton magnetic resonance spectroscopy of the brain (a technique that provides information on brain metabolism) has demonstrated the presence of abnormal metabolites in the HCV infected. An increased cerebral relationship of choline-creatine in the basal ganglia and white brain mass has been found²⁴. Furthermore, it is believed that the psychological changes that occurred in some patients were due to the previous narcotic use as the leading route of transmission of HCV infection²⁵.

However, some studies found the prevalence of depression to be between 20% and 30%^{7,8,26}, and it is consistent with our results. The study group patients showed a higher level of depressive and anxiety symp-

Table 7. Post-hoc tests

Independent variable	Group	n	Depression			
			M _{rank}	Z	p	
Marital status	Married	66	41.92	-2.40	0.016	
	Divorced	25	56.76			
	Married	66	56.43	-0.59	0.556	
	Single	49	60.11			
Employment status	Divorced	25	47.06	-2.75	0.006	
	Single	49	32.62			
	Employed	39	44.96	-3.63	0.000	
	Unemployed	84	69.91			
Anxiety	Employed	39	29.96	-1.81	0.070	
	Retired	27	38.61			
	Employment status	Unemployed	84	58.54	-1.47	0.142
		Retired	27	48.11		
			Anxiety			
		n	M _{rank}	Z	p value	
Employment status	Employed	39	48.44	-2.88	0.004	
	Unemployed	84	68.30			
	Employed	39	31.73	-0.90	0.366	
	Retired	27	36.06			
Employment status	Unemployed	84	58.24	-1.30	0.193	
	Retired	27	49.02			

M_{rank} = mean rank; Z = Z test statistic; p = p value; n = number of participants

toms than control group subjects. Depression was verified in 24% of chronic HCV-infected patients and 21% of control group subjects. The prevalence of depression in the group of HCV-infected patients largely depends on the sampling method, which can be seen through the results of various studies. Compared to our study, Batista-Neves *et al.* found a lower prevalence of depression and anxiety (18.9% and 15%, respectively)²⁷. Using the interview as a diagnostic tool, Carta *et al.*²² found the prevalence of 32.6% among HCV-positive patients, with a significant correlation between chronic hepatitis C and major depressive disorder when compared to healthy controls, which is in accordance with our results.

Previous studies showed the existence of correlation between psychological symptoms and HCV infection, with the effect being reflected on changes in the quality of life^{10,26,28}. The results obtained in this study using multiple regression analysis indicated that the high percentage of depression in the study group

was significantly explained with a set of predictors comprised of HRQoL domains in the SF-36 questionnaire. Three domains, i.e. Physical Functioning, Vitality, and Mental Health, were found to have the strongest contribution to the prevalence of depression. The higher degree of depression in chronic HCV-infected patients was associated with lower quality of life, particularly regarding these three domains. In the control group, the correlation between SF-36 domains and depression subscale was somewhat lower than that in the study group. The SF-36 Social Functioning domain was singled out as a factor that significantly contributed to the individual prediction of depression. This result suggests that the prevalence of depression in the study group greatly depended on the physical aspects that may be affected due to chronic HCV infection, as well as all those aspects that comprise the Mental Health domain, along with Vitality that may also be affected by the disease. The control group differed since the Social Functioning domain stands out

as the only significant predictor of the occurrence of depression. Therefore, it can be indirectly assumed that depression in patients with chronic hepatitis C is more determined by the effect of the disease itself and can primarily be regarded as an expression of pathophysiological mechanisms, whereas in the control group, it is more determined by psychosocial factors and has reactive etiology. The results obtained in this study are consistent with the previous study by Fábregas *et al.*, who used the WHO short scale to assess the quality of life²⁰.

Several studies have addressed the significant presence of anxiety symptoms. The necessity of their detection and monitoring in patients with chronic HCV infection can improve their quality of life and ensure an adequate response to therapy^{8,9,20}. The results observed in our study are consistent with the results of previous investigations, where the prevalence of anxiety ranged from 15.6%²⁰ to 41%⁸, with the exception that we found a statistically significantly higher presence of anxiety in chronic HCV-infected patients compared to the healthy control group. This can be related to different inclusion criteria in different studies. A recent study performed in Egypt showed that the presence of anxiety prior to anti-viral treatment was remarkably associated with impaired HRQoL among patients with chronic HCV before initiation of treatment⁹.

Employed patients with chronic hepatitis C exhibited a lower level of depression and anxiety than those who were unemployed, which is consistent with other studies that found a correlation between lower family income and prevalence of these disorders in chronic HCV infected patients²⁹.

In contrast to the study by Stewart *et al.*, which found older patients with chronic hepatitis C to have significantly lower levels of anxiety but not depression compared to younger patients⁸, the results of our study did not suggest any relationship between age and anxiety/depression, which is consistent with the results reported by Erim *et al.*³⁰. Divorced patients had significantly higher scores compared to those who were married or single. Marriage was found to be a protective factor in several studies^{8,20}. We did not find a significant relationship between depression/anxiety and gender, level of education, and place of residence. There was no statistically significant relationship between the route of HCV transmission, duration of the dis-

ease, and existence of cirrhosis with depression/anxiety either.

Limitations

The study was conducted during everyday routine medical practice, and we were unable to use psychiatric interview. Furthermore, HADS limited the identification of depression and anxiety to probable and possible clinical cases. Consequently, any implementation of self-assessment inventories and techniques should be considered with certain limitations. However, their importance is constantly increasing because of many advantages such as simple application and appropriate screening.

In conclusion, based on our research findings, unemployed people suffering from chronic hepatitis C should be monitored with more attention. It is necessary to identify the risk factors for this population, with special focus on economic and social factors. Also, the results showed that chronic hepatitis C patients, regardless of the severity of the disease, route of transmission and duration of the disease, have more pronounced symptoms of depression and anxiety than healthy control subjects. This indicates that HCV itself has a negative effect on the well-being of patients, and we believe that psychosocial screening and support for this group of patients is of paramount importance.

Psychological support would help chronic HCV-infected patients feel better and be more satisfied, which may increase therapeutic response. Without treatment, chronic hepatitis C patients cannot expect improvement in their HRQoL; therefore, all efforts and options should be focused on encouraging patients to accept the treatment and be compliant with medication until the end of therapy regimen^{5,31}. Moreover, these results urge the introduction of the DAA regimen as soon as possible as a standard treatment in our country in order to additionally avoid IFN induced depression and consequently increase the quality of life of chronic HCV-infected patients.

Acknowledgments

We would like to acknowledge all the participants of this study and Dr Sarah Barden, Approved Clinician and Specialty Doctor, Norfolk and Suffolk NHS Foundation Trust, who kindly helped us with English language revision.

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Sažetak

DEPRESIJA, ANKSIOZNOST I KVALITETA ŽIVOTA U BOLESNIKA S KRONIČNOM INFEKCIJOM VIRUSOM HEPATITISA C U VOJVODINI

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Cilj studije je bio utvrditi učestalost depresije i anksioznosti među bolesnicima s kroničnim hepatitisom C i povezanost depresije i anksioznosti s odgovarajućim domenama kvalitete života vezane za zdravlje (HRQoL), sociodemografskim čimbenicima i kliničko-epidemiološkim značajkama. Ova prospektivna studija uključila je 150 bolesnika s kroničnim hepatitisom C koji su čekali interferonsku terapiju za hepatitis C i 150 zdravih ispitanika u kontrolnoj skupini. Svi sudionici istraživanja popunili su upitnik SF-36 i Bolničku ljestvicu za procjenu anksioznosti i depresije. Bolesnici s kroničnim hepatitisom C imali su statistički značajno izraženiju depresiju ($t=3,37$, $p<0,01$) i anksioznost ($t=2,35$, $p<0,05$). Analizom višestrukih regresija visok postotak depresije objašnjen je skupom prediktora koji su činili domene upitnika SF-36. Tri domene (Fizičko funkcioniranje, Vitalnost i Mentalno zdravlje) imale su najjači prediktivni doprinos pojavi depresije. Serija Kruskal-Wallisovih i Mann-Whitneyevih testova pokazala je značajnu razliku u razini depresije između kategorija bračnog statusa ($\chi^2(2)=7,86$, $p<0,05$). Razvedeni sudionici imali su značajnije viši stupanj depresivnosti u usporedbi s onima koji su u braku ($Z=-2,40$, $p<0,05$) i neoženjenima ($Z=-2,75$, $p<0,01$). Nezaposlenost je bila povezana s višim stupnjem depresije i anksioznosti. Nije nađena veza između trajanja bolesti, načina prijenosa virusa hepatitisa C, postojanja ciroze i depresije ili anksioznosti. Rezultati ove studije mogu pomoći u razvijanju standardnog protokola za liječenje kroničnog hepatitisa C koji će uključivati psihološku procjenu i potporu.

Ključne riječi: *Kronični hepatitis C; Kvaliteta života; Depresija; Anksioznost; Socioekonomski čimbenici*