



# Predictors of Anxiety and Depression in Patients with Chronic Viral Hepatitis in Kazakhstan

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## Keywords

Anxiety; depression; hepatitis, chronic; fibrosis; psychiatric status rating scales

## Abstract

**Aim:** Anxiety and depressive disorders are commonly reported comorbidities in patients with chronic viral hepatitis. The burden of living with a chronic illness like hepatitis can significantly impact a person's mental health. The aim of the study is to explore several key aspects related to anxiety and depression in patients with chronic viral hepatitis in Kazakhstan. **Subjects and Methods:** A prospective cohort study was conducted involving 233 patients with chronic viral hepatitis. Socio-demographic data were collected, a comprehensive clinical examination was conducted, including assessment of complaints, clinical parameters, and anamnesis data. Laboratory methods were employed, and the severity of anxiety and depressive symptoms was measured using the Hospital anxiety and depression scale (HADS). **Results:** The analysis of the total scores from HADS in patients with chronic viral hepatitis revealed that 32.6 % of patients had sub-clinical expressed anxiety or depression, while 5.8 % exhibited clinically significant levels of anxiety or depression. The study identified several significant predictors of anxiety and depressive disorders in patients with chronic viral hepatitis are age ( $p < 0.000$ ), sex ( $p < 0.015$ ), dura-

tion of disease ( $p < 0.002$ ), aetiology of chronic viral hepatitis ( $p < 0.030$ ). **Conclusion:** Integrating the identified predictors into clinical practice allows healthcare providers to improve the early detection and diagnosis of anxiety and depression in patients with chronic viral hepatitis. This proactive approach not only enhances mental health outcomes but also supports overall disease management and patient well-being.

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## Introduction

Chronic viral hepatitis has been extensively associated with depression and cognitive dysfunction in clinical research [1,2]. Over the past decade, there has been a significant increase in research dedicated to understanding and addressing mental health disorders in patients with chronic viral hepatitis [3-5]. According to various researchers, the prevalence of anxiety and depression among patients with hepatitis C virus (HCV) ranges from 37 % to 83 % [1,6,7]. Patients with chronic viral hepatitis often exhibit a range of psychological and social challenges, which can significantly affect their quality of life. Individuals with chronic viral hepatitis may experience a higher prevalence of negative emotions such as anxiety, depression, and stress. The chronic nature of

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the disease, uncertainty about the future, and potential stigma associated with it can contribute to these feelings [8]. Patients may find it challenging to communicate openly about their condition. This could be due to fear of judgment, lack of understanding from others, or discomfort in discussing a potentially stigmatized illness [9].

Depressive disorders in patients with chronic viral hepatitis can arise from various factors related to both the disease itself and its impact on the patient's life. The diagnosis of chronic viral hepatitis and its chronic nature can lead to significant psychosocial stress. Patients may experience anxiety and worry about the progression of the disease, treatment outcomes, financial implications, and social stigma. This chronic stress can contribute to the development or exacerbation of depressive symptoms [10]. Patients with chronic viral hepatitis, even in the early stages or with minimal disease activity, often experience more pronounced symptoms of depression and chronic fatigue compared to the general population [11-13]. Many patients with chronic viral hepatitis may have other concomitant diseases or conditions, such as other chronic medical illnesses or substance use disorders. Managing multiple health conditions can be overwhelming and increase the risk of developing depressive symptoms [11-13].

The pathogenesis of depressive disorders in the context of chronic viral hepatitis is complex and multifactorial. Viral agents such as hepatitis C virus can have direct neurotoxic effects. These effects can lead to inflammation in the brain (neuroinflammation), altered neurotransmitter levels (such as serotonin and dopamine), and changes in neuronal function. These neurobiological changes are implicated in the development of depressive symptoms [14,15]. Viral agents such as HCV have been found to have the ability to cross the blood-brain barrier, which separates the bloodstream from the brain and cerebrospinal fluid [15]. Psychiatric disorders, including depression, can be observed in patients with chronic viral hepatitis, particularly in cases where there is disease progression or high viral activity. Elevated levels of alanine aminotransferase (ALT), an enzyme released into the bloodstream when the liver is damaged, can indicate active liver inflammation and damage in chronic viral hepatitis. Higher ALT levels are associated with more severe liver disease and can contribute to psychological distress. This marker of disease activity may serve as a psychological stressor for patients, increasing anxiety and depressive symptoms [15].

In patients with chronic HCV infection undergoing antiviral therapy, several factors interplay in the development of symptoms of depression, including immune activation [16]. There are documented instances where patients with chronic HCV infection undergoing antiviral therapy experience mental and emotional disturbances early in the course of treatment. Importantly, many of these disturbances are reversible with appropriate management [17].

The chronic nature of hepatitis C and its variable disease activity can contribute to persistent stress in patients. Fluctuations in symptoms, uncertainty about disease progression, and the need for ongoing medical management can all contribute to chronic stress. This prolonged stress can predispose individuals to developing anxiety and depression over time [18]. Neuro-psychological assessments and tools are used to evaluate the cognitive and emotional functions of patients. These tools provide objective measures that demonstrate the severity of anxiety and depression experienced by patients with chronic hepatitis C. Such assessments help quantify the impact of the disease on mental health and guide appropriate interventions [18].

The aim of our study was to evaluate the presence of anxiety and depression in patients with chronic viral hepatitis and to establish its relationship with the aetiology of the disease, age, sex, duration of the disease, stage of liver fibrosis, and degree of inflammation.

## Subjects and Methods

For this study, we examined 233 patients with chronic viral hepatitis, who were either receiving inpatient treatment at the Shymkent City Infectious Diseases Hospital or on outpatient registration at the Shymkent Regional Hepatological Center, provides a substantial cohort for studying the relationship between depression and various clinical factors associated with the disease. The approval of your study protocol by the Local Ethics Committee of the Kazakh National Medical University named after S.D. Asfendiyarov. The collection of basic information, along with the analysis of demographic, clinical, laboratory, and instrumental data, was conducted following the receipt of written informed consent from each patient. Patients were surveyed from September 2020 through March 2022. The structure of our study involved the inclusion of patients with specific diagnoses related to chronic viral hepatitis and liver cirrhosis of viral aetiology. Patients included in our study confirmed diagnosis of chronic viral hepatitis B, chronic viral hepatitis C, or chronic viral hepatitis B + D. Only adult patients aged 18 years and older were included in your study. All patients with chronic viral hepatitis were categorized by stage of liver fibrosis ( $F_0$ ,  $F_1$ ,  $F_2$ ,  $F_3$ ,  $F_4$ ), age (18 - 80 years), sex (male, female), disease duration (from 1 month to 30 years), ALT and AST levels (norm, more than 40 U/L).

The Hospital Anxiety and Depression Scale (HADS) was used to assess the presence of anxiety and depression in patients with chronic viral hepatitis. The HADS is a self-report questionnaire designed to detect the presence and severity of anxiety and depression symptoms in non-psychiatric hospital settings. It consists of 14 items divided into two subscales - Anxiety subscale (HADS - A): measures symptoms of generalized anxiety disorder; - Depression subscale (HADS - D): assesses symptoms of depression. Each item on the HADS is scored on a 4-point scale (0-3), with higher scores indicating

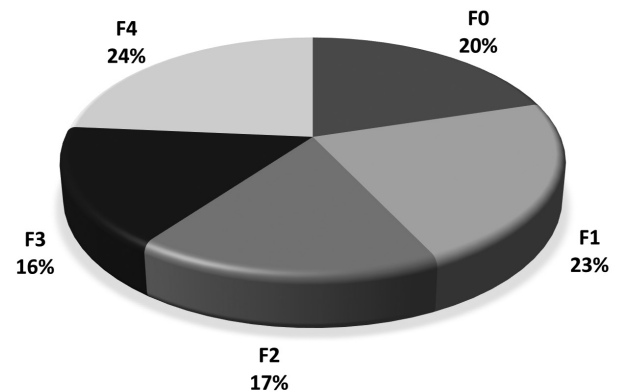
higher levels of anxiety or depression. Scores from 0 to 7 points indicate normal levels of anxiety or depression. Scores from 8 to 10 points suggest subclinical levels of anxiety or depression. Scores of 11 points and above indicate clinically significant levels of anxiety or depression. Scores for each subscale (HADS - A and HADS - D) are calculated separately and cut-off scores are used to classify participants as having normal, borderline or clinically significant levels of anxiety or depression.

The data were analysed using SPSS statistical software (version 27.0, SPSS Inc., Chicago, IL, USA) for Windows. Summary statistics for all variables were calculated, and the normal distribution of data was assessed using analytical methods (Kolmogorov-Smirnov test). Data were analysed using one-way analysis of variance (ANOVA), chi-square test, and Pearson correlation. All p-values were two-tailed, and indicators were considered statistically significant at  $p < 0.05$ . Quantitative variables were expressed as mean  $\pm$  standard deviation.

## Results

The patients were distributed by sex as follows: 111 patients were men (47.6 %) and 122 patients were women (52.4 %). From the total number of patients, 66 people (28.3 %) were residents of Shymkent, and 167 people (71.6 %) were residents of various districts in the Turkestan region. In the current study, the average age of patients was  $47.14 \pm 14.1$  years, with disease duration ranging from 1 month to 30 years. According to the nosological structure, patients were categorized as follows: chronic viral hepatitis B - 44 patients (18.9 %), chronic viral hepatitis C - 132 patients (56.7 %) and chronic viral hepatitis D - 57 patients (24.4 %). The patients were also classified by fibrosis stages: F0 - 47 patients (20.2 %), F1 - 52 patients (22.7 %), F2 - 40 patients (17.2 %), F3 - 38

**Figure 1.** The distribution of patients with chronic viral hepatitis according to fibrosis stage



patients (16.3 %), and F4 - 56 patients (23.6 %) (Figure 1). The mean age of the total number of patients with chronic viral hepatitis was  $47.1 \pm 14.1$  years. The mean duration of disease in the total number of patients was  $5.5 \pm 4.6$  years. The mean fibrosis score in the total number of patients was  $10.7 \pm 7.9$  kPa. The mean ALT level in the total number of patients was  $56.1 \pm 49.4$  U/L, mean AST level- $49.5 \pm 41.3$  U/L (Table 1).

The viral load was determined in patients with chronic viral hepatitis. In chronic viral hepatitis B, a high viral load was defined as greater than  $2 \times 10^3$  copies/ml, while in chronic viral hepatitis C, it was defined as more than  $2 \times 10^6$  copies/ml. A high viral load was found in 9 % of patients with stage F0, 13.6 % with stage F1, 6.8 % with stage F2, 11.3 % with stage F3 and 9 % with stage F4 fibrosis. In patients with chronic viral hepatitis C, high viral load was diagnosed in 3.8 % with stage F0,

**Table 1.** Clinical and demographic characteristics of patients with chronic viral hepatitis

Characteristics	Total number (N = 233)	F0 (N = 47)	F1 (N = 53)	F2 (N = 40)	F3 (N = 38)	F4 (N = 55)
Age (years)	18 - 75	19 - 66	25 - 72	25 - 72	26 - 70	20 - 75
Mean $\pm$ standard deviation	$47.1 \pm 14.1$	$40.0 \pm 13.5$	$47.4 \pm 13.8$	$46.1 \pm 14.0$	$48.2 \pm 14.3$	$52.6 \pm 12.9$
Sex N (%)						
Male	111 (47.6)	27 (57.4)	21 (39.6)	21 (52.5)	17 (44.7)	25 (45.5)
Female	122 (52.4)	20 (42.6)	32 (60.4)	19 (47.5)	21 (55.3)	30 (54.5)
Duration of the disease						
Mean $\pm$ standard deviation	$5.5 \pm 4.6$	$5.0 \pm 4.1$	$4.6 \pm 2.9$	$6.3 \pm 5.5$	$5.1 \pm 5.5$	$6.6 \pm 4.9$
Fibrosis (kPa)						
Mean $\pm$ standard deviation	$10.7 \pm 7.9$	$4.8 \pm 0.6$	$6.6 \pm 0.3$	$8.1 \pm 0.7$	$10.7 \pm 0.8$	$21.8 \pm 9.6$
ALT level						
Mean $\pm$ standard deviation	$56.1 \pm 49.4$	$31.3 \pm 19.9$	$54.8 \pm 50.5$	$51.7 \pm 38.9$	$62.7 \pm 50.6$	$77.1 \pm 61.8$
AST level						
Mean $\pm$ standard deviation	$49.5 \pm 41.3$	$29.4 \pm 17.7$	$43.4 \pm 31.0$	$46.6 \pm 30.1$	$54.3 \pm 44.6$	$71.5 \pm 57.0$

**Table 2.** Viral load levels in patients with chronic viral hepatitis C depending on the stage of fibrosis

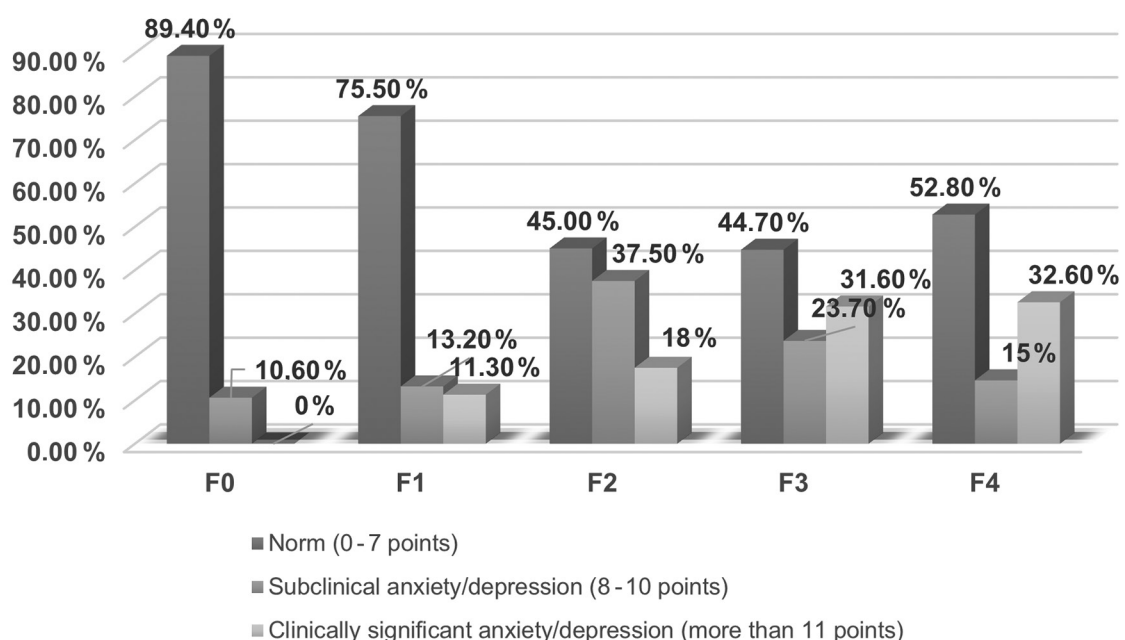
Fibrosis stage	Chronic viral hepatitis B (N = 44)		Chronic viral hepatitis D (N = 57)		Chronic viral hepatitis C (N = 132)	
	Norm	More than 2 x 10 <sup>3</sup> copies/ml	Norm	More than 2 x 10 <sup>3</sup> copies/ml	Norm	More than 2 x 10 <sup>6</sup> copies/ml
F0	25 % (N = 11)	9 % (N = 4)	1.7 % (N = 1)	7 % (N = 4)	18.1 % (N = 24)	3.8 % (N = 5)
F1	11.3 % (N = 5)	13.6 % (N = 6)	7 % (N = 4)	5.3 % (N = 3)	20.5 % (N = 27)	6.1 % (N = 8)
F2	6.8 % (N = 3)	6.8 % (N = 3)	19.3 % (N = 11)	10.5 % (N = 6)	6.1 % (N = 8)	6.1 % (N = 8)
F3	6.8 % (N = 3)	11.3 % (N = 5)	8.8 % (N = 5)	8.8 % (N = 5)	6.8 % (N = 9)	7.6 % (N = 10)
F4	4.5 % (N = 2)	9 % (N = 4)	7 % (N = 4)	27.3 % (N = 12)	10.6 % (N = 14)	13.6 % (N = 18)

6.1 % with stage F1, 6.1 % with stage F2, 7.6 % with stage F3, and 13.6 % with stage F4 fibrosis (Table 2).

The Hospital Anxiety and Depression Scale (HADS) was used to assess the presence of anxiety and depression in patients with chronic viral hepatitis. Analysis of the total scores on the HADS revealed that 76 people (32.6 %) out of 233 patients had subclinical expressed anxiety or depression, and 13 people (5.8 %) had clinically significant anxiety or depression. Subclinical anxiety or depression was reported in 10.6 % of patients at stage F0, 13.2 % at stage F1, 37.5 % at stage F2, 23.7 % at stage F3, and 14.6 % at stage F4. Clinically significant anxiety or depression was found in 11.3 % of patients at stage F1, 17.5 % at stage F2, 31.6 % at stage F3, and 32.6 % at stage F4 (Figure 2).

Patients were also divided according to the score obtained on the Hospital anxiety and depression scale (HADS). The mean HADS score by fibrosis stage was

**Figure 2.** Hospital anxiety and depression scale (HADS) results in patients with chronic viral hepatitis at different stages of fibrosis



**Table 3.** Mean scores on the Hospital anxiety and depression scale (HADS) in patients with chronic viral hepatitis

Characteristics	Total number (N = 233)	F0 (N = 47)	F1 (N = 53)	F2 (N = 40)	F3 (N = 38)	F4 (N = 55)
HADS (Mean $\pm$ standard deviation)	7.8 $\pm$ 3.9	5.0 $\pm$ 1.8	6.5 $\pm$ 2.5	7.8 $\pm$ 2.4	8.6 $\pm$ 3.5	10.8 $\pm$ 5.2

**Table 4.** Multiple regression analysis of factors influencing anxiety and depression in patients with chronic viral hepatitis at various stages of fibrosis (N = 233)

Variable	Multiple regression analysis	
	beta	p - value
Age	- 0.620	0.000
Sex	0.351	0.015
Duration of the disease	0.148	0.295
The form of chronic viral hepatitis	0.244	0.030
Serum ALT levels	0.367	0.098
Serum AST levels	0.124	0.150
Viral load	0.010	0.911
Stage of fibrosis	0.018	0.779
Regression Statistics	R Square Adjusted = 0.241	

as follows: 5.0  $\pm$  1.8 in patients at stage F0, 6.5  $\pm$  2.5 at stage F1, 7.8  $\pm$  2.4 at stage F2, 8.6  $\pm$  3.5 at stage F3 and 10.8  $\pm$  5.2 at stage F4 (Table 3).

Multiple regression analysis demonstrated that age ( $p < 0.000$ ), sex ( $p < 0.015$ ), disease duration ( $p < 0.002$ ) and aetiology of chronic viral hepatitis ( $p < 0.030$ ) were variables significantly correlated with the presence of anxiety and depression in patients (Table 4).

## Discussion

Several studies have investigated depression in patients with chronic hepatitis, with many of them assessing quality of life alongside anxiety and depressive disorders [1,19,20]. In a study conducted by researchers from China, which included 517 patients, 301 had HADS scores of 8 or higher. The prevalence of depressive disorders and anxiety disorders among outpatients with gastrointestinal diseases was reported as follows: depressive disorders were 12.0 %, anxiety disorders were 6.4 %, and depressive combined with anxiety disorder was 3.0 % [19]. In our study, anxiety and depression

scores were higher, likely because we focused exclusively on patients with chronic viral hepatitis. In another study, the prevalence of depressive disorders was 5.84 % in women and 1.64 % in men [20]. Our data are consistent with the results of this study, as in our study, anxiety and depressive disorders were more commonly observed in female subjects, similar to their findings.

Recent findings indicate, like our results, that more severe degrees of anxiety and depression are observed in advanced stages of the disease. The study found that physical well-being and role limitations due to physical health issues were associated with absenteeism, while cirrhosis, anxiety, depression, and fatigue were associated with work productivity impairment [21]. However, according to other authors, findings from the Hospital anxiety and depression scale in HCV infection suggest that anxiety and depression do not correlate with disease severity, mode of infection, loss to follow-up, or rates of sustained virological response [22]. In the study conducted by Sarkar and associates, which involved 181 patients diagnosed with chronic hepatitis C, the results revealed a significant impact of clinically significant depression specifically among women [23]. Our results are confirmed with their data.

Researchers from Greece identified several notable associations concerning depression among patients with chronic viral hepatitis. Consistent with findings from other studies, there was a strong correlation between being female and experiencing depression. Women may encounter distinct psychosocial stressors, societal expectations, and hormonal influences that contribute to higher rates of depression compared to their male counterparts with chronic viral hepatitis. The study also highlighted that more advanced stages of liver disease were linked to increased rates of depression. Patients facing more severe liver disease often grapple with heightened uncertainty regarding their prognosis and treatment outcomes, which can intensify psychological distress. Additionally, elevated viral load emerged as another significant factor associated with depression in their findings [5].

This study had several limitations because it did not compare anxiety and depression levels in patients with chronic viral hepatitis before and after receiving antiviral therapy.

In conclusion, anxiety and depression are commonly observed among patients suffering from chronic viral hepatitis. This psychological burden significantly affects

the quality of life and overall well-being of individuals coping with this condition. Our study has identified several key factors associated with depression in these patients, including older age, being female, longer duration of disease, and the specific type of hepatitis involved. Recognizing anxiety and depression as frequent issues in chronic viral hepatitis underscores the importance of comprehensive care that addresses both the physical and mental health needs of these individuals. Screening for anxiety and depression, early detection, and appropriate management are crucial aspects of ensuring holistic patient care and enhancing outcomes for those living with chronic hepatitis.

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### Conflicts of interest

None to declare.

### Funding Sources

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