

**Journal Pre-proof**

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**DOI:** <https://doi.org/10.22365/jpsych.2025.019>

**To appear in:** Psychiatriki Journal

**Received date:** 29 July 2024

**Accepted date:** 7 July 2025

**Please cite this article as:** Tatyana Vasiliyevna Polukchi, Prevalence and severity of depression in patients with chronic viral hepatitis in Kazakhstan, Psychiatriki (2025), doi: <https://doi.org/10.22365/jpsych.2025.019>

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## RESEARCH ARTICLE

### Prevalence and severity of depression in patients with chronic viral hepatitis in Kazakhstan

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**ARTICLE HISTORY:** Received 29 July 2024 / Revised 31 January 2025/ Published Online 5 August 2025

#### ----- ABSTRACT -----

Depression is a common issue among patients with chronic viral hepatitis. Living with chronic hepatitis can create chronic stress, which is a known risk factor for developing or exacerbating depression. This stress can be related to concerns about health, the effectiveness of treatment, and the social implications of the illness. Neuropsychological scales and assessments can objectively measure the severity of depression and other mental health issues in these patients. The presence of depression was studied in 233 patients with chronic viral hepatitis, who were treated in the Infectious Disease Hospital of Shymkent and the Regional Hepatology Centre of Shymkent in the period from March 2021 to January 2022. All patients were examined using the Hamilton Depression Rating Scale (HDRS) to identify the presence of depression. Of the 233 patients with chronic viral hepatitis, 38.3% had mild depressive disorder, 2.7% of patients had scores indicating moderate depressive disorder, and 2.7% of patients were found to have major depressive disorder. Multivariate analysis showed that older age, the form of chronic viral hepatitis, higher viral load, and female gender were most strongly associated with depression. Depression is a common manifestation in patients with chronic viral hepatitis and can lead to cognitive impairments such as difficulties with concentration, memory problems, and decreased executive function. In the context of chronic hepatitis, which may already affect liver function and metabolic processes, untreated depression can exacerbate these cognitive deficits.

**KEYWORDS:** Chronic viral hepatitis, fibrosis, cirrhosis, depression, Kazakhstan.

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### Introduction

Chronic viral hepatitis, particularly hepatitis B (HBV) and hepatitis C (HCV), is recognized as a systemic disease that can manifest with a variety of extrahepatic manifestations. These manifestations can affect different organ systems and develop at various times after the initial infection. Chronic viral hepatitis can lead to neurological symptoms and disorders involving the central nervous system (CNS).<sup>1</sup> Extrahepatic manifestations of chronic viral hepatitis can develop at different times after infection. Some may present early in the course of the disease, while others may manifest later, often in the context of advanced liver disease or as immune-

mediated complications.<sup>1</sup> Studies have indicated that approximately 50% of individuals chronically infected with HCV may experience cognitive dysfunction. This can range from mild cognitive impairment to more severe cognitive deficits.<sup>1</sup> The most common associated symptoms observed in patients with chronic viral hepatitis are anxiety and depression, chronic fatigue, mood changes, cognitive impairment, and sleep disturbances.<sup>2,3</sup> Depression is a significant concern among patients with chronic viral hepatitis, particularly hepatitis B and hepatitis C. The prevalence of depression in this patient population can vary widely across studies and regions, as noted by different authors. Some studies indicate that approximately 37% to 83% of patients with chronic hepatitis C may experience symptoms of depression.<sup>2</sup> In another study, after excluding inactive HBsAg carriers, a significantly higher prevalence of depression was found among patients with HCV (35.9%) compared to patients with HBV (19.8%) and healthy participants (11.3%).<sup>4</sup> However, after excluding inactive HBsAg carriers, no differences in the prevalence of depression were observed between patients with HBV and HCV. Among patients with HCV, smoking and alcohol consumption increased the frequency of depression, whereas factors such as viral load, fibrosis stage, HCV genotype, and sex did not have a significant impact. These data suggest that depression in patients with chronic viral hepatitis may be related not only to the infection itself but also to the chronic nature of the disease, stigmatization, and perceptions of adverse outcomes.<sup>4</sup> It has been found that unemployment is associated with more pronounced symptoms of depression and anxiety. However, no association was found between the duration of the disease, the mode of hepatitis C transmission, the presence of cirrhosis, and the levels of depression or anxiety.<sup>5</sup>

One study assessed liver fibrosis using elastography. It was found that patients with mild depression had varying degrees of liver fibrosis, including F<sub>0</sub> (no fibrosis), F<sub>1</sub> (mild fibrosis), and F<sub>2</sub> (moderate fibrosis). Meanwhile, all patients with moderate depression exhibited advanced fibrosis (F<sub>3</sub> — significant thickening of liver tissue with possible signs of cirrhosis). The F<sub>4</sub> stage of fibrosis, indicating cirrhosis, was also noted, representing a severe stage of the disease with irreversible tissue damage. According to the multiple regression model, the degree of liver fibrosis was a statistically significant independent predictor of depression.<sup>6</sup> In another similar study, a higher prevalence of depression was also found in patients with chronic hepatitis B compared to healthy individuals who were not HBsAg carriers.<sup>7</sup> Chronic hepatitis C is accompanied by a variety of extrahepatic manifestations, with the central nervous system often being involved. However, the pathophysiological mechanisms of this process are not yet fully understood.<sup>8</sup> HCV infection is often associated with depression and cognitive impairments, which may be due to HCV neuroinvasion and/or chronic inflammation. Proteins have previously been identified in the brain, and it has been suggested that blood leukocytes capable of crossing the blood-brain barrier may provide the virus with access to the CNS.<sup>8</sup> The results suggest that chronic hepatitis C virus infection negatively affects brain functions, with both viral replication in the mononuclear cells of peripheral blood and the state of immune activation playing an important role in this process.<sup>1,9</sup>

In chronic hepatitis C infection, the innate immune system remains persistently activated, accompanied by elevated levels of proinflammatory cytokines (IL-6, TNF- $\alpha$ , IL-1 $\beta$ ) in peripheral blood.<sup>10</sup> These mediators either cross the blood-brain barrier or transmit signals via the vagus nerve, triggering microglial activation. The resulting neuroinflammatory response within the central nervous system shifts tryptophan metabolism toward the kynurenine pathway, leading to a decrease in serotonin levels and an increase in the concentration of the neurotoxic metabolite quinolinic acid. This biochemical shift disrupts the functioning of prefrontal-limbic networks responsible for emotional regulation and cognitive processes. Clinically, this manifests as “brain fog,” pronounced fatigue, and sleep disturbances, while the cumulative effect of these factors significantly increases the risk of depression even in the early stages of liver fibrosis. Conversely, depressive symptoms may exacerbate systemic inflammation and reduce treatment adherence, negatively impacting the course of chronic hepatitis C. This

underscores the bidirectional relationship between mood disorders and chronic HCV infection.<sup>10</sup>

Studies show that depression and/or anxiety disorders associated with human immunodeficiency virus (HIV) or HBV infection may be due to common biological mechanisms. Specifically, microglial activation and cytokine release have been identified as potential pathogenetic mechanisms. Patients with HIV and depression also show an altered balance between quinolinic and kynurenic acids, indicating glutamatergic dysfunction.<sup>11</sup> The production of inflammatory cytokines and impaired regulation of the cellular immune response contribute to chronic inflammation, delayed healing, and reduced functional abilities in patients with chronic hepatitis B.<sup>11</sup> A shift in the balance of type 1 and type 2 cytokines may play a role in the immune pathogenesis associated with HBV, with depression and anxiety being considered immune-modulating factors. Cytokines also provoke hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, which is often observed in patients with HIV/HBV suffering from depression or anxiety disorders.<sup>11</sup>

In patients with chronic viral hepatitis, depression can arise from a combination of factors related to the disease itself, its physical manifestations, and the psychosocial impact it imposes.<sup>12</sup> Researchers have observed that patients with chronic viral hepatitis, even in the early stages with minimal liver inflammation and few comorbidities, may experience more severe symptoms of depression and fatigue compared to the general population.<sup>13,14</sup> The prevalence of depression in chronic HCV infection is estimated to be 1.5 to 4.0 times higher than in patients with chronic HBV infection.<sup>15</sup>

Gender also plays a significant role in the development of mental disorders, including depression. Research consistently shows that women have a higher incidence of depression compared to men. This may be due to biological differences, sociocultural factors, and differences in stress reactions and ways of coping. It is important to consider gender specificity in the assessment and treatment of psychological problems in this category of patients.<sup>16,17</sup> Patients with mental disorders, including depression, may engage in behaviors that increase their risk of HCV infection. Individuals with depression may face challenges in adhering to treatment regimens for HCV, such as antiviral therapy. Poor adherence increases the risk of treatment failure or relapse after achieving a sustained virologic response, which can lead to reinfection.<sup>18</sup> Research indicates that patients with chronic hepatitis B often experience a higher intensity of depression compared to healthy individuals, and this burden tends to increase as the disease progresses. Elderly patients with chronic HBV may experience the greatest severity of depression. Aging itself can bring additional challenges such as comorbidities, social isolation, and changes in physical health, which can further exacerbate depressive symptoms.<sup>19</sup> One study examined the relationship between maternal HBV infection and postpartum depression. In a cohort of women with no personal or family history of mental illnesses, the presence of HBV infection was not statistically significantly associated with depression compared to the absence of this infection.<sup>20</sup>

It was also found that Chinese ethnicity and lack of physical activity are associated with a higher risk of depression, regardless of antiviral treatment status. At the same time, physical activity has a protective effect, especially in patients receiving such treatment. Employment was associated with a lower risk of depression among Asian Americans taking medication, while among those not taking medication, younger age and being married reduced the risk of depression. These findings highlight the importance of physical activity as a protective factor for patients with chronic hepatitis B, particularly among those receiving antiviral treatment.<sup>21</sup>

The persistence of significant depressive disorders in patients even during successful 12-month antiviral therapy highlights a crucial aspect of managing chronic hepatitis, particularly hepatitis B and hepatitis C. Despite achieving sustained virological response (SVR), some patients may continue to experience significant depressive symptoms. This suggests that the psychological impact of chronic hepatitis, its treatment, and associated factors may persist

beyond viral suppression.<sup>22</sup> Studies have reported a wide range of incidence rates of depression during interferon treatment, ranging from 0% to 37%.<sup>18</sup> Nearly half of patients undergoing antiviral therapy may experience transient depression during treatment. This form of depression is directly linked to the use of interferon-based therapies, which were historically associated with neuropsychiatric side effects, including mood disturbances. Despite discontinuation of therapy, treatment-induced depression may persist beyond six months in approximately one in ten patients. Factors contributing to prolonged depression in these cases may include pre-existing mental health conditions, underlying psychosocial stressors, and the residual impact of interferon treatment on the CNS.<sup>14,23,24,25</sup> This study aimed to analyze the factors contributing to the development of depression in patients with chronic viral hepatitis, as well as to investigate potential relationships between depression, stages of liver fibrosis, and the treatment of chronic viral hepatitis (including interferon and other therapeutic interventions). This study provides new insights into the psychosocial aspects of chronic viral hepatitis, such as the impact of depression on treatment adherence, viral resistance, and treatment success. We also examine the duration of depression, which persists even after achieving an SVR and successful completion of antiviral therapy.

## **Materials and methods**

### ***Sample***

The study protocol was approved by the Experimental Ethics Committee of the Kazakh Medical University of Continuing Education and Asfendiyarov Kazakh National Medical University (Protocol № 3 of 17.03.2020, Protocol № 3 of 16.03.2021) and Asfendiyarov Kazakh National Medical University (Protocol № 7 of 30.05.2022).

The study included 233 individuals with chronic viral hepatitis who were receiving inpatient treatment at the Infectious Disease Hospital in Shymkent city and visiting the Shymkent Regional Hepatology Centre during routine outpatient visits. Patients were aged over 18 years, and all participants provided written informed consent before participating in the study. The study took place between March 2021 and January 2022.

Participants in the study were aged over 18 years. The reasons for exclusion of patients from the study on chronic viral hepatitis were clearly defined and aimed at ensuring the integrity and focus of the research. Exclusion criteria based on our description: age less than 18 years, pregnancy, cancer, acute viral hepatitis, mental disorders, intoxication with psychotropic drugs, and alcoholism. These exclusion criteria are designed to enhance the study's internal validity by controlling for factors that could confound the relationship between chronic viral hepatitis and its clinical outcomes.

### ***Tools***

To assess the severity of depressive symptoms, the 17-item Hamilton Depression Rating Scale (HDRS) was used. The scale includes the following ranges for depressive severity: 0-7 points: normal (no depressive symptoms), 8-13 points: mild depressive disorder, 14-18 points: moderate depressive disorder, 19-22 points: severe depressive disorder, and more than 23 points: extremely severe depressive disorder. In the present study, we employed the Russian-language version of the Hamilton Depression Rating Scale (HDRS), which is traditionally applied in clinical practice throughout Russia and other Russian-speaking CIS countries. At this time, however, no publication detailing a formal validation of this Russian-language HDRS version is available in international scientific databases. There is, nevertheless, a study that examined the HDRS in a Belarusian population and utilized a Belarusian version of the scale.<sup>26</sup> Given the linguistic and cultural proximity of Belarusian and Russian, as well as the historically shared clinical diagnostic approaches, the findings of this work can be partially extrapolated to Russian-language practice. Nevertheless, we acknowledge the need for further research

aimed at formally validating the Russian-language HDRS and identifying this issue as a limitation of our study.

### **Statistical analysis**

Data analysis was conducted using SPSS statistical software, version 22.0, developed by SPSS Inc., Chicago, IL, USA. Summary statistics, such as mean and standard deviation, were calculated for quantitative variables. This provides a concise overview of the central tendency and variability of the data. We used non-parametric tests (Kruskal-Wallis and Mann-Whitney U-test) since the preliminary analysis indicated that the data did not follow a normal distribution. A multiple regression analysis was also conducted to assess the influence of independent variables on the severity of depressive symptoms. All p-values were two-tailed, and statistical significance was defined as  $p < 0.05$ .

## **Results**

Demographic data: Most participants in the study were female, comprising 52.4% (N=222) of the total sample. The average age of the participants was 47.14 years, with a standard deviation of  $\pm 14.1$  years. Types of chronic viral hepatitis: 42.1% of participants (98 individuals) had chronic hepatitis C virus, 16.7% of participants (41 individuals) had chronic HBV infection, and 17.1% of participants (40 individuals) had chronic hepatitis D virus. Liver Cirrhosis: A subset of participants had liver cirrhosis, categorized by etiology: 2.1% (5 patients) had liver cirrhosis due to HBV infection, 14.2% (33 patients) had liver cirrhosis due to HCV infection, 7.7% (18 patients) had liver cirrhosis due to co-infection with HBV and HDV. The study included 233 individuals with chronic viral hepatitis: 66 people, which accounts for 28.3% of the total participants, were residents of Shymkent city; the majority of participants, 167 people (71.6%), came from various districts within Turkestan oblast: Suzak, Sairam, Kazygurt, Arys, Saryagash, Maktaral, Tolebi, and Baudibek. Based on the age distribution of patients with chronic viral hepatitis in your study, here's the breakdown: 18-19 years: 4 patients (1.7%), 20-29 years: 25 patients (10.7%), 30-39 years: 50 patients (21.5%), 40-49 years: 52 patients (22.3%), 50-59 years: 38 patients (16.3%), 60-69 years: 59 patients (25.3%), 70-79 years: 5 patients (2.2%). Patients had varying durations of chronic viral hepatitis, ranging from 1 month to 20 years or more. The patients were divided into stages of liver fibrosis: group F<sub>0</sub> included 47 patients (20.2%), group F<sub>1</sub> - 52 patients (22.7%), group F<sub>2</sub> - 40 people (17.2%), group F<sub>3</sub> - 38 patients (16.3%), group F<sub>4</sub> comprised 56 examined patients (23.6%).

Based on the results of our study involving 233 patients with chronic viral hepatitis and their Hamilton Depression Rating Scale (HDRS) scores, the breakdown of depressive disorder severity: 89 patients (38.3%) had HDRS scores indicating mild depressive disorder, 6 patients (2.7%) were found to have moderate depressive disorder, 6 patients (2.7%) had HDRS scores indicating severe depressive disorder.

The data presented shows the prevalence of depressive disorders at different stages (F<sub>0</sub> to F<sub>4</sub>) in a group of patients: mild depressive disorder: stage F<sub>0</sub>- 10.6%, stage F<sub>1</sub>- 12.3%, stage F<sub>2</sub>-25%, stage F<sub>3</sub>-31.6%, stage F<sub>4</sub>- 45.5%; moderate depressive disorder: stage F<sub>0</sub>- 2.1%; stage F<sub>1</sub>- 3.5%, stage F<sub>2</sub>- 5%, stage F<sub>3</sub>- 23.7%, stage F<sub>4</sub>- 18.2%; severe depressive disorder: stage F<sub>2</sub>- 2.5%, stage F<sub>3</sub>- 5.3%, stage F<sub>4</sub>-5.3%. These percentages indicate the proportion of patients at each stage of liver fibrosis (F<sub>0</sub> to F<sub>4</sub>) who were observed to have different severity levels of depressive disorder.

The mean Hamilton Depression Rating Scale (HDRS) scores for patients at each stage of fibrosis are as follows: stage F<sub>0</sub>-  $5.1 \pm 2.1$ ; stage F<sub>1</sub>-  $6.4 \pm 2.8$ ; stage F<sub>2</sub>-  $7.7 \pm 3.7$ ; stage F<sub>3</sub>-  $10.3 \pm 5.0$ ; stage F<sub>4</sub>-  $11.2 \pm 5.4$  (Table 1). These scores indicate the average severity of depressive symptoms among patients at different stages of liver fibrosis. As the fibrosis stage progresses

from F<sub>0</sub> to F<sub>4</sub>, there is a noticeable increase in the mean HDRS score, suggesting a higher severity of depressive symptoms associated with more advanced liver disease.

The results of the analyses indicate that several factors significantly influence the total scores of the Hamilton Depression Rating Scale (HDRS) in patients with chronic viral hepatitis. Age was found to be significantly associated with HDRS scores ( $p < 0.000$ ). This suggests that older patients may have different levels of depressive symptoms compared to younger patients. The specific form of chronic viral hepatitis (hepatitis B and hepatitis C) was also significantly associated with HDRS scores ( $p < 0.000$ ). The stage of fibrosis, as categorized by F<sub>0</sub> to F<sub>4</sub>, was significantly associated with HDRS scores ( $p < 0.000$ ). This indicates that as liver fibrosis progresses, depressive symptoms tend to increase. Gender was found to be significantly associated with HDRS scores ( $p < 0.000$ ). This suggests that there may be differences in depressive symptomatology between male and female patients with chronic viral hepatitis. These results highlight that age, type of chronic viral hepatitis, stage of fibrosis, and gender are important factors that influence the severity of depressive symptoms in patients with chronic viral hepatitis (Table 2).

The multiple regression analysis revealed that several variables are correlated with the presence of depression in patients with chronic viral hepatitis. Age ( $p < 0.001$ ) was identified as a significant factor associated with the presence of depression. This suggests that older age may contribute to higher levels of depressive symptoms in these patients. The specific form of chronic viral hepatitis (such as hepatitis B and hepatitis C) ( $p < 0.000$ ) was found to be significantly correlated with depression. Different forms of hepatitis may have varying impacts on mental health, potentially influencing the presence and severity of depressive symptoms. Viral load ( $p < 0.000$ ), a measure of the amount of virus present in the blood, was also identified as a significant variable related to depression. Higher viral loads may be associated with increased likelihood or severity of depressive symptoms in patients with chronic viral hepatitis. These findings indicate that age, the type of chronic viral hepatitis, and viral load are important factors to consider when assessing and managing depression in patients with chronic viral hepatitis (Table 3).

## Discussion

There have been several studies investigating depression in patients with chronic hepatitis, but most of them have assessed quality of life in conjunction with depressive disorders.<sup>27,28</sup> Given the limited data available in existing literature, the objective of the present study was to conduct a cross-sectional screening for depression among patients with chronic viral hepatitis. In this prospective cohort study, the primary focus was to investigate the prevalence of depression symptoms among patients with chronic viral hepatitis who were receiving treatment at the Shymkent City Infectious Diseases Hospital and the Shymkent Regional Hepatology Center. When considering a large sample size in a study investigating depression symptoms among patients with chronic viral hepatitis were several clinical significances.

The differences in the incidence of depressive symptoms between our study (32.6%) and the study by Li et al. (53.1%) are attributed to several factors, including sample size and possibly other methodological differences. As noted, the study by Li et al. had a larger sample size of 1995 patients compared to our study. Differences in the characteristics of the study populations between the two studies could also contribute to variations in the reported rates of depression symptoms. The use of different assessment tools to measure depression symptoms can lead to variability in reported rates. Our study used the Hamilton Depression Rating Scale (HDRS), while Li et al. have used a different tool or criteria.<sup>28</sup>

In another similar study by Jiang et al, which included 517 patients with chronic viral hepatitis, the incidence of depression in patients with chronic viral hepatitis was 58.3%, which was also related to the large number of patients included in the study.<sup>27</sup> It is likely that the

differences in the final results of the study are due to the use of different tools to assess depression. The Hamilton Depression Rating Scale (HDRS), which is the most common tool for assessing depression, was used in this study.

In the study by Sarkar et al. involving 181 patients with chronic hepatitis C, the findings indicated that women were significantly affected by clinically significant depression.<sup>29</sup> In the study conducted by researchers from Greece, several significant associations were identified regarding depression in patients with chronic viral hepatitis. Similar to findings in other studies, being female was strongly associated with depression. Women may experience different psychosocial stressors, societal pressures, and hormonal influences that contribute to higher rates of depression compared to men with chronic viral hepatitis. The study found that advanced stages of liver disease were linked to higher rates of depression. Patients with more severe liver disease may also face greater uncertainty about prognosis and treatment outcomes, which can contribute to psychological distress. Elevated viral load was also identified as a significant factor associated with depression.<sup>30</sup>

Depression, in addition to affecting treatment adherence, can have a significant impact on treatment response and the effectiveness of therapeutic regimens, including through neuropathological mechanisms.<sup>31</sup> Studies show that depression can disrupt the neurochemical balance in the CNS, which, in turn, may influence the immune response and reparative processes in the body. For example, activation of inflammatory pathways and changes in neurotransmitter levels, such as serotonin, dopamine, and glutamate, can affect the perception and effectiveness of therapy. Neuropathological changes associated with chronic inflammation may impair the body's ability to respond effectively to antiviral therapy, reducing its clinical effectiveness. Furthermore, depression may contribute to increased stress levels and activation of the hypothalamic-pituitary-adrenal (HPA) axis, which, as shown in several studies, can also negatively affect treatment outcomes. Therefore, it is important to consider depression not only as a factor affecting treatment adherence but also as a potential barrier to achieving optimal therapeutic results, requiring a comprehensive approach in the treatment of patients with chronic viral infections.<sup>31,32,33</sup>

One of the significant limitations of the present study is the lack of direct assessment of cognitive impairment in patients with chronic viral hepatitis. Although associations between the degree of liver fibrosis and the severity of depressive symptoms were identified, standardized neuropsychological tests were not employed in this study. Such tools could have revealed cognitive impairments, which are frequently associated with both depression and chronic somatic conditions. Incorporating assessment instruments such as the MoCA (Montreal Cognitive Assessment) or the MMSE (Mini-Mental State Examination) in future research would allow for a more comprehensive evaluation of patients' neuropsychological status and provide a clearer understanding of the relationship between depression and cognitive functioning in the context of chronic viral hepatitis.

## **Conclusion**

Depression is a common manifestation among patients with chronic viral hepatitis, significantly affecting their quality of life and overall well-being. Our study highlights several factors associated with depression in patients with chronic viral hepatitis, such as advanced age, female gender, hepatitis type, and viral load. These findings underscore the importance of addressing both the physical and psychological health of patients, emphasizing the need for screening, early detection, and appropriate management of depression. It is important to recognize that while antidepressants are commonly used for treating depression in these patients, clinicians must be cautious about potential hepatotoxicity. Some antidepressants may cause liver injury, and while there is no guaranteed way to prevent this, early detection and prompt cessation of the medication can minimize the severity of the reaction.



Antidepressants are not associated with an increased risk of liver cancer, and may even correlate with a reduced risk, although more robust evidence is needed. The management of chronic viral hepatitis should include a comprehensive approach that addresses both mental and physical health to improve patient outcomes.

## References

1. Polukchi TV, Abuova GN, Slavko YA. The Neuropsychiatric Aspect of the Chronic Viral Hepatitis. *Prague Med Rep* 2023, 124:94-107, doi:10.14712/23362936.2023.8
2. Adinolfi LE, Nevola R, Lus G, et al. Chronic hepatitis C virus infection and neurological and psychiatric disorders: an overview. *World J Gastroenterol* 2015, 21:2269-2280, doi:10.3748/wjg.v21.i8.2269
3. Polukchi TV, Slavko YA. Viral hepatitis B and C and neurological impairment. *Ankara Med J* 2023, 23:468-477, doi:10.5505/amj.2023.73483
4. Mirabdolhagh Hazaveh M, Dormohammadi Toosi T, et al. Prevalence and severity of depression in chronic viral hepatitis in Iran. *Gastroenterol Rep (Oxf)* 2015, 3:234-237, doi: 10.1093/gastro/gou091
5. Kačavenda-Babović D, Đurić P, Babović R, et al. Depression, anxiety and quality of life in patients with chronic hepatitis C virus infection in Vojvodina. *Acta Clin Croat* 2021, 60:579-589, doi: 10.20471/acc.2021.60.04.03
6. Stoenescu AF, Popescu CP, Florescu SA, et al. The Prevalence of Depression and Its Potential Link to Liver Fibrosis in Patients Diagnosed With Chronic Hepatitis C Virus Infection Prior to the Initiation of Direct-Acting Antiviral Treatment. *Cureus* 2024, 16:e62970, doi:10.7759/cureus.62970
7. Rahman M, Noor-E-Alam SM, Rahim MA, et al. Depression among Patients with Chronic Hepatitis B: A Cross-sectional Study in a Tertiary Hospital of Bangladesh. *Euroasian J Hepatogastroenterol* 2023, 13:79-83, doi:10.5005/jp-journals-10018-1406
8. Tassi A, Gitto S, Piras C, et al. Cognitive, neurological and psychiatric disorders occurring in Hepatitis C Virus infection. *Minerva Med* 2021, 112:238-245, doi:10.23736/S0026-4806.21.07388-2
9. Radkowski M, Kryczka T, Szymańska-Kotwica B, et al. Depression and Cognitive Dysfunction in Patients with Chronic Hepatitis C: Correlation with Viral Replication in the Peripheral Blood Mononuclear Cells and Cytokines in Serum. *Int J Mol Sci* 2023, 24:15351, doi:10.3390/ijms242015351
10. Faccioli J, Nardelli S, Gioia S, et al. Neurological and psychiatric effects of hepatitis C virus infection. *World J Gastroenterol* 2021, 27:4846-4861, doi: 10.3748/wjg.v27.i29.4846
11. Fabrazzo M, Cipolla S, Pisaturo M, et al. Bidirectional Relationship between HIV/HBV Infection and Comorbid Depression and/or Anxiety: A Systematic Review on Shared Biological Mechanisms. *J Pers Med* 2023, 13:1689, doi: 10.3390/jpm13121689
12. Wedemeyer H, Manns MP. Epidemiology, pathogenesis and management of hepatitis D: update and challenges ahead. *Nat Rev Gastroenterol Hepatol* 2010, 7:31-40, doi: 10.1038/nrgastro.2009.205
13. Aktuğ Demir N, Çelik M, Kölgelir S, et al. [Comparison of the level of depression and anxiety in inactive hepatitis B carriers and chronic hepatitis B patients]. *Turk Psikiyatri Derg* 2013, 24:248-52, PMID: 24310091 (In Turkish)

14. Egmond E, Mariño Z, Navines R, et al. Incidence of depression in patients with hepatitis C treated with direct-acting antivirals. *Braz J Psychiatry*. 2020, 42:72-76, doi: 10.1590/1516-4446-2018-0336
15. Zayed HS, Amin A, Alsirafy S, et al. Psychiatric and functional neuroimaging abnormalities in chronic hepatitis C virus patients: Is vasculitis a contributing factor? *Arab J Gastroenterol* 2018, 19:71-75, doi: 10.1016/j.ajg.2018.06.003
16. Yeoh SW, Holmes ACN, Saling MM, et al. Depression, fatigue and neurocognitive deficits in chronic hepatitis C. *Hepatol Int* 2018, 12:294-304, doi: 10.1007/s12072-018-9879-5
17. Tagliapietra M, Monaco S. Neuroimaging Findings in Chronic Hepatitis C Virus Infection: Correlation with Neurocognitive and Neuropsychiatric Manifestations. *Int J Mol Sci* 2020, 21:2478, doi: 10.3390/ijms21072478
18. Yarlott L, Heald E, Forton D. Hepatitis C virus infection, and neurological and psychiatric disorders - A review. *J Adv Res* 2017, 8:139-148, doi: 10.1016/j.jare.2016.09.005
19. Darke S, Mills K, Teesson M, et al. Patterns of major depression and drug-related problems amongst heroin users across 36 months. *Psychiatry Res* 2009, 166:7-14, doi: 10.1016/j.psychres.2007.12.007
20. Erim Y, Tagay S, Beckmann M, Bein S, et al. Depression and protective factors of mental health in people with hepatitis C: a questionnaire survey. *Int J Nurs Stud*. 2010, 47:342-349, doi: 10.1016/j.ijnurstu.2009.08.002
21. Huang W, Wu X, Yao Z, et al. Investigating the relationship between hepatitis B virus infection and postpartum depression in Chinese women: a retrospective cohort study. *Front Public Health* 2023, 11:1214151, doi: 10.3389/fpubh.2023.1214151
22. Zhu L, Lu W, Gamoso W, et al. The Association between Modifiable Lifestyle Behaviors and Depression among Asian Americans with Chronic Hepatitis B by Medication Status. *Brain Sci*. 2022, 12:188, doi: 10.3390/brainsci12020188
23. Cunha EC, Behrendorf MF, Bavaresco V, et al. Genotype 1 of hepatitis C virus increases the risk of major depression: a 12-week prospective study. *Gen Hosp Psychiatry* 2015, 37:283-287, doi: 10.1016/j.genhosppsy.2015.03.016
24. Chiu WC, Su YP, Su KP, Chen PC. Recurrence of depressive disorders after interferon-induced depression. *Transl Psychiatry* 2017, 7:e1026, doi: 10.1038/tp.2016.274
25. Huckans M, Fuller B, Wheaton V, et al. A longitudinal study evaluating the effects of interferon-alpha therapy on cognitive and psychiatric function in adults with chronic hepatitis C. *J Psychosom Res* 2015, 78:184-192, doi: 10.1016/j.jpsychores.2014.07.020
26. Zimmerman M, Martinez JH, Young D, et al. Severity classification on the Hamilton Depression Rating Scale. *J Affect Disord* 2013, 150:384-388, doi: 10.1016/j.jad.2013.04.028
27. Assanovich M. Evaluation and improvement of the psychometric properties of the Hamilton Rating Scale for Depression using Rasch analysis for applying in Belarusian population. *Int J Appl Behav Sci* 2017, 4:40-46, doi:10.22037/ijabs.v4i1.16593
28. Jiang RH, Yu X, Ma H, et al. [The prevalence of depression and anxiety in gastrointestinal out-patients of tertiary general hospitals in Beijing]. *Zhonghua Nei Ke Za Zhi* 2009, 48:399-401, PMID: 19615159 (In Chinese)

29. Li XJ, He YL, Ma H, et al. Prevalence of depressive and anxiety disorders in Chinese gastroenterological outpatients. *World J Gastroenterol* 2012, 18:2561-2568, doi: 10.3748/wjg.v18.i20.2561
30. Sarkar S, Kemper J, Sarkar R, et al. Influence of gender on cytokine induced depression and treatment: Gender aspects of IFN- $\alpha$ -induced depression. *J Affect Disord* 2021, 292:766-772, doi: 10.1016/j.jad.2021.05.087
31. Fotos NV, Elefsiniotis I, Patelarou A, et al. Psychological Disorders and Quality of Life Among Patients With Chronic Viral Hepatitis: A Single-Center Cross-Sectional Study With Pair-Matched Healthy Controls. *Gastroenterol Nurs* 2018, 41:206-218, doi: 10.1097/SGA.0000000000000339
32. DeSanty KP, Amabile CM. Antidepressant-induced liver injury. *Ann Pharmacother* 2007, 41:1201-1211, doi: 10.1345/aph.1K114
33. Chen X, Wang Y, Lu T, et al. Antidepressants and Risk of Liver Cancer: A Systematic Review and Meta-Analysis. *Ann Pharmacother*. 2023, 57:1398-1409, doi: 10.1177/10600280221143512

**Table 1:** Prevalence of depressive disorders and mean scores on the Hamilton Depression Rating Scale (HDRS) at different stages of liver fibrosis (F<sub>0</sub> to F<sub>4</sub>) among patients with chronic viral hepatitis

Fibrosis Stage	Mild Depressive Disorder (%)	Moderate Depressive Disorder (%)	Severe Depressive Disorder (%)	N (233)	Mean HDRS Score ( $\pm$ SD)	ANOVA F (df)	p (HDRS)
F <sub>0</sub>	10.6	2.1	-	47	5,1 $\pm$ 2,1	12.35 (4, 228)	<0.001
F <sub>1</sub>	12.3	3.5	-	53	6,4 $\pm$ 2,8		
F <sub>2</sub>	25.0	5.0	2.5	40	7,7 $\pm$ 3,7		
F <sub>3</sub>	31.6	23.7	5.3	38	10,3 $\pm$ 5,0		
F <sub>4</sub>	45.5	18.2	5.3	55	11,2 $\pm$ 5,4		

**Table 2:** Mean Hamilton Depression Rating Scale (HDRS) scores in patients with chronic viral hepatitis

Variable	N	Mean	HDRS t / F	df (between/within)	p
Age (years)			4.402	6 / 226	0.000
-18-19	4	4,0 $\pm$ 1,2			
-20-29	25	6,0 $\pm$ 3,2			
-30-39	50	6,8 $\pm$ 3,2			
-40-49	52	8,4 $\pm$ 5,1			
-50-59	38	9,2 $\pm$ 5,0			
-60-69	59	9,7 $\pm$ 4,0			
-70-79	5	7,6 $\pm$ 3,1			

Gender			71.87	- / 11.42	0.000
-Male	111	7,0±4,1			
-Female	122	9,0±4,5			
Disease			19.61	2 / 230	0.000
-Chronic viral hepatitis B	44	6,4±2,8			
-Chronic viral hepatitis C	132	7,5±4,0			
-Chronic viral hepatitis D	57	11,0±5,0			
Duration of the disease			2.154	4 / 228	0.096
-Up to 1 year	28	7,4±4,3			
-Up to 5 years	109	7,9±4,1			
-6-10 years	73	8,1±4,2			
-11-20 years	19	10,7±5,2			
-More 20 years	4	9,8±5,4			
Serum ALT levels			96.00	- / 19.45	0.464
-Less than 40 U/L	34	7,7±4,5			
-More than 40 U/L	199	8,2±4,4			
Serum AST levels			96.39	- / 16.30	0.391
-Less than 40 U/L	47	7,6±4,1			
-More than 40 U/L	186	8,3±4,4			
Viral load			55.39	- / 10.96	0.005
-Norm	131	7,2±3,5			
-Excessive	102	9,4±5,1			
Fibrosis (kPa)			20.25	4 / 228	0.000
-F <sub>0</sub>	47	5,1±2,1			
-F <sub>1</sub>	53	6,4±2,8			
-F <sub>2</sub>	40	7,7±3,7			
-F <sub>3</sub>	38	10,3±5,0			
-F <sub>4</sub>	55	11,2±5,4			

**Table 3:** Multiple regression analysis of factors affecting depression in patients with chronic viral hepatitis at different stages of fibrosis (N=233)

Variable	$\beta$	SE	t	df	p
Age	-0.125	0.110	-1.136	224	0.001
Gender	0.451	0.121	3.727	224	0.828
Duration of the disease	0.232	0.052	4.462	224	0.835
The form of chronic viral hepatitis	0.099	0.147	0.673	224	0.000
Serum ALT levels	-0.344	0.133	-2.586	224	0.820
Serum AST levels	-0.344	0.071	-4.845	224	0.464
Viral load	-0.442	0.068	-6.500	224	0.000
Stage of fibrosis	0.366	0.068	5.382	224	0.277

Adjusted R<sup>2</sup> = 0.293

## ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

### Επικράτηση και βαρύτητα της κατάθλιψης σε ασθενής με χρόνια ηπατίτιδα στο Καζακστάν

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**ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ:** Παραλήφθηκε 29 Ιουλίου 2024/ Αναθεωρήθηκε 31 Ιανουαρίου 2025 / Δημοσιεύθηκε Διαδικτυακά 5 Αυγούστου 2025

#### ΠΕΡΙΛΗΨΗ

Η κατάθλιψη είναι ένα κοινό πρόβλημα μεταξύ των ασθενών με χρόνια ιογενή ηπατίτιδα. Η διαδρομή μιας χρόνιας ηπατίτιδας μπορεί να πυροδοτήσει χρόνιο stress, το οποίο είναι γνωστός παράγοντας κινδύνου για την ανάπτυξη ή την επιδείνωση της κατάθλιψης. Αυτό το stress μπορεί να σχετίζεται με ανησυχίες για την υγεία, την αποτελεσματικότητα της θεραπείας και τις κοινωνικές επιπτώσεις της ασθένειας. Νευροψυχολογικές κλίμακες και αξιολογήσεις μπορούν να μετρήσουν αντικειμενικά τη βαρύτητα της κατάθλιψης και άλλων ψυχικών προβλημάτων σε αυτούς τους ασθενείς. Η παρουσία κατάθλιψης μελετήθηκε σε 233 ασθενείς με χρόνια ιογενή ηπατίτιδα, οι οποίοι θεραπεύτηκαν στο Νοσοκομείο Λοιμωδών Νόσων Shymkent και στο Περιφερειακό Κέντρο Ηπατολογίας Shymkent την περίοδο από Μάρτιο 2021 έως Ιανουάριο 2022. Όλοι οι ασθενείς εξετάστηκαν με την Κλίμακα Αξιολόγησης Κατάθλιψης Χάμιλτον (HDRS) για την ανίχνευση της κατάθλιψης. Από τους 233 ασθενείς με χρόνια ιογενή ηπατίτιδα, το 38,3% είχε ήπιο καταθλιπτικό επεισόδιο, το 2,7% των ασθενών παρουσίασε βαθμολογίες που υποδηλώνουν μέτριο καταθλιπτικό επεισόδιο, και το 2,7% των ασθενών βρέθηκε να έχει σοβαρή καταθλιπτική διαταραχή. Η πολυπαραγοντική ανάλυση έδειξε ότι η μεγαλύτερη ηλικία, η μορφή της χρόνιας ιογενούς ηπατίτιδας, το υϊκό φορτίο και το φύλο (θήλυ) ήταν οι παράγοντες που σχετίζονταν πιο έντονα με την κατάθλιψη. Η κατάθλιψη είναι μια κοινή εκδήλωση σε ασθενείς με χρόνια ιογενή ηπατίτιδα και μπορεί να οδηγήσει σε νοητικές διαταραχές όπως δυσκολίες στην προσοχή, προβλήματα μνήμης και μειωμένη εκτελεστική λειτουργία. Στο πλαίσιο της χρόνιας ηπατίτιδας, η οποία μπορεί ήδη να επηρεάσει τη λειτουργία του ήπατος και τις μεταβολικές διαδικασίες, η αθεράπευτη κατάθλιψη μπορεί να επιδεινώσει αυτές τις νοητικές ανεπάρκειες.

**ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ:** Χρόνια ιογενής ηπατίτιδα, ίνωση, κίρρωση, κατάθλιψη, Καζακστάν.

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