

# Quality of life assessment in chronic viral hepatitis

Tatyana Polukchi<sup>1,3</sup>, Zulfiya Zhankalova<sup>2</sup>, Gulzhan Abuova<sup>3</sup>, Akhmedova Muborakhon<sup>4</sup>

<sup>1</sup>Department of Gastroenterology, S.D. Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan

<sup>2</sup>Department of General Medical Practice, S.D. Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan.

<sup>3</sup>Department of Infectious Diseases and Dermatovenereology, South Kazakhstan Medical Academy, Shymkent, Kazakhstan

<sup>4</sup>Department of Infectious and Children Infectious Diseases, Tashkent Medical Academy, Tashkent, Uzbekistan

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Corresponding author:

Tatyana Polukchi.

Email: [tatyana\\_polukchi@mail.ru](mailto:tatyana_polukchi@mail.ru).

ORCID: 0000-0002-6134-884X

## Abstract

Chronic viral hepatitis has a significant impact on morbidity, quality of life and mortality and is characterized by a growing economic and social burden in the context of disability of the population and an increase in life expectancy. Chronic viral hepatitis can significantly worsen health-related quality of life indicators (HRQoL), which are a reflection of the influence of the disease and therapy on the physical and emotional components of the patient's health, especially in patients with progressive liver disease and/or active viral activity. To assess the quality of life related to health, you can use general tools and tools for specific diseases. Common tools available in the scientific literature include the Short Form 36 questionnaire (SF-36) and the Euroqol five-point questionnaire (EQ-5D). However, since general instruments cannot always detect the subtle effects of a particular condition on the quality of life, the use of special instruments is of great value, due to their ability to clinically characterize the quality of life in patients with chronic viral hepatitis. The use of recently developed special tools for assessing the quality of life will greatly assist in the verification of preventive and therapeutic interventions in this area. One of the priorities of any measures for the prevention and treatment of chronic viral hepatitis is to improve the quality of life in this category of patients.

**Key words:** chronic viral hepatitis, health-related quality of life, mental disorder, depression, antiviral treatment

## Introduction

Viral hepatitis plays a significant role in the structure of diseases of the digestive system, characterized as one of the global socially significant problems that affects the lives of hundreds of millions of people around the world and is a source of steadily progressive morbidity and mortality. Most of the burden of hepatitis falls on viral hepatitis B and viral hepatitis C, which tend to chronic infection and are characterized by inflammatory processes in the liver, capable of eventually transformation into fibrotic and cirrhotic changes [1,2]. According to the latest estimates, more than 257 million people in the world have active HBV infection, and according to some researchers, the number of infected patients reaches 350 million, from 71 to 185 million people have HCV infection [1,3,4]. One of the most severe forms of chronic viral hepatitis is chronic viral hepatitis D, which can often develop to liver cirrhosis and hepatocellular carcinoma [5]. A necessary condition for the manifestation of pathogenicity in chronic viral hepatitis D is the simultaneous presence of HBV infection [6]. Thus, according to the latest data,

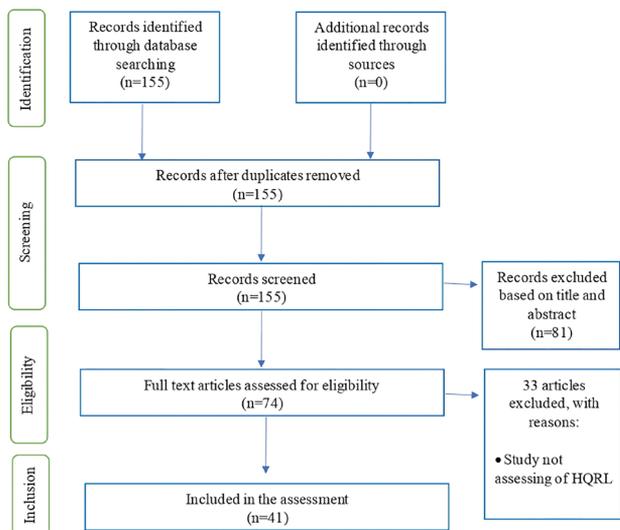
worldwide 5% of chronically infected patients with HBV are also infected chronic viral hepatitis D, which is estimated to be 20 million people with HDV infection [7].

Cognitive function disorders and neuropsychiatric disorders are registered in almost 50% of patients with HCV infection, which do not depend on the severity of liver disease or the rate of replication of HCV infection [8]. In addition, symptoms such as chronic fatigue, sleep disturbance, depression and decreased quality of life are usually associated with neurocognitive changes in patients with non-cirrhotic chronic HCV infection, regardless of the stage of fibrosis, the infecting genotype and in the absence of structural brain damage or signal abnormalities with conventional magnetic resonance imaging of the brain [9].

The present review aims to investigate the quality of life of patients with chronic viral hepatitis. A systematic literature search of English-language studies was performed in Medline, Embase, Web of Science, Scopus and The Cochrane Library from January 2016 to February 2022. The systematic literature search resulted

in 155 hits. The screening of titles and abstracts identified 74 potentially eligible articles. Finally, 41 studies were included in this review. The selection algorithm is shown in Figure 1.

**Figure 1** - Flow diagram of the of the literature search



## Health-related quality of life and fatigue in patients with chronic hepatitis

The presence of chronic diseases in patients can have a negative impact on the well-being of patients, both psychologically and physically. Thus, chronic HCV-infection can significantly worsen the indicators of health-related quality of life (HRQoL), which are a reflection of the influence of the disease and therapy on the physical and emotional components of patient’s health, especially those with advance liver disease and/or active viral activity [10,11]. According to researchers, patients with chronic viral hepatitis develop symptoms of anxiety and/or depression, which also has a strong impact on their health-related quality of life [11]. In a study conducted in Greece, high levels of anxiety and depression were recorded among patients with cholemic viral hepatitis, as well as the overall health-related quality of life ( $p < 0.001$ ). At the same time, female sex and damage to the liver parenchyma were associated with a higher level of anxiety ( $p < 0.05$ ) [11]. In a recent study, it was found that the most common extrahepatic manifestations are diabetes mellitus (in 15% of patients) and depression (in 25% of patients). These HRQL data showed that chronic viral hepatitis has a negative impact on overall physical and mental health [12]. It has been established that patients with chronic HCV infection may experience other symptoms that worsen the quality of life, such as fatigue and neurocognitive disorders. In the early stages of HCV disease with minimal inflammation of the liver, patients may have pronounced symptoms of depression, fatigue, neurocognitive deficiency than in the general population [12].

Depression is a frequent disorder reported in one third of patients with HCV infection and may be a reaction to increased psychosocial stress, as well as physical symptoms of progressive chronic viral hepatitis C or concomitant diseases [13,14]. Thus, the prevalence of depression is estimated to be 1.5-4.0 times higher than in patients with chronic viral hepatitis B [14]. Researchers report that the non-modern diagnosis of mental disorders can not only significantly reduce the already rather poor quality of life, but lead to non-compliance with recommendations and drug therapy regimens, which can lead to poor treatment results. These disorders, in the absence of their therapy, contribute to a higher level of risky behavior among

patients, which can pose a danger both to the patients themselves and to the healthy population [15]. In patients with chronic viral hepatitis B, depression is also considered one of the most common mental disorders that has an adverse effect on the progression of the disease. Although, there are currently limited studies on the assessment of depression in patients with chronic HBV-infection [16]. The results of a recent study showed that 37.5% of patients with chronic hepatitis had depressive symptoms, 31.4% of patients had minimal depressive symptoms. According to the multivariate logistic regression, it was found that higher age, lower income, unemployment, living with a spouse/partners had a positive association with the presence of depression. At the same time, the presence of physical health problems and a lower quality of life associated with health were closely associated with a higher risk of depression [16]. Data of researchers from China have shown that the quality of life in patients with chronic viral hepatitis B depends on the presence of cirrhosis. Thus, the results showed that the physiological quality of life of HRQoL in the group with cirrhosis was significantly lower than in the group without cirrhosis ( $P = 0.003$ ), while psychological HRQoL was also lower ( $P = 0.006$ ) and had a significant negative correlation with liver stiffness ( $P = 0.001$ ). Additional independent factors associated with poor quality of life HRQoL in patients with HBV-related cirrhosis were positive HBV DNA viral load ( $OR = 6,296$ ,  $P = 0.041$ ), family history of hepatocellular carcinoma ( $OR = 36,211$ ,  $P = 0.001$ ) [17]. Comparing the quality of life in patients with chronic viral hepatitis C and chronic viral hepatitis B, researchers found that patients with HCV have lower indicators when using the SF-36 quality of life questionnaire, indicators of memorization of words, in recognition of figures and in terms of alertness and working memory [18]. The patients with chronic viral hepatitis C have lower life indicators and these data are confirmed by the results of other researchers. Thus, in the conducted study, it was found that 85% of patients with chronic viral hepatitis C had chronic fatigue, 50-60% of patients had mild depression or anxiety, 45% memory deficit and 30% attention deficit, regardless of their HCV viremia status or treatment history [19].

Chronic viral hepatitis D is the most severe form of chronic hepatitis, which is characterized by the most rapid development of liver cirrhosis, liver failure and hepatocellular carcinoma compared to HBV mono-infection. Despite all this, there are still difficulties in its diagnosis and in the absence of its standardized treatment [20,21]. As a result of a review of the existing literature, we found reports of health-related quality of life in chronic hepatitis B and HCV-infection, but no studies of outcomes reported by patients with chronic viral hepatitis D. But few studies have shown that HDV infected patients reported worse outcomes in psychological areas, such as anxiety and emotional well-being, as well as in physical areas, such as abdominal symptoms, physical well-being and impaired activity, compared with patients with chronic viral hepatitis D [22].

Another of the common and main signs of chronic viral hepatitis affecting the quality of life is sleep disturbance. Other researchers also confirm the fact that the violation of the quality of life is more pronounced with the progression of the disease [23]. According to the latest data, 60-80% of patients with chronic liver diseases have problems with sleep, which manifest themselves in the form of insomnia, a decrease in the quality and time of sleep, an increase in the duration of latent sleep, prolonged daytime drowsiness, restless legs syndrome [23].

The quality of life of HRQoL in patients with chronic viral hepatitis remains low and depends on many factors, such as the presence of cirrhosis, viral load, concomitant pathology.

HRQoL can be improved through the use of antiviral therapy, which prevents the progression of cirrhosis [24]. In addition, the eradication of hepatitis viruses improves a wide range of extrahepatic manifestations and improves the quality of life [25]. Elimination of the hepatitis virus with the use of antiviral drugs leads to a significant and long-term improvement in the quality of life of HRQoL in patients [26]. Although, according to some researchers, the quality of life of patients with chronic viral hepatitis still remains lower than that of the general population. Despite the elimination of the virus, patients still have primary problems in normal activities and anxiety/depression. Therefore, the study of information about these ongoing problems, despite treatment, serves as a guide for medical interventions and follow-up of the patient [27].

## Assessment of quality of life in chronic viral hepatitis

Currently, it is believed that health-related quality of life (HRQoL) serves as a subjective assessment of the impact of illness and treatment on the physical, psychological, social and somatic spheres of functioning and well-being in patients [28]. Currently, HRQoL general tools are actively used in clinical practice, which are intended for use in a wide range of population groups and interventions. The main feature of these tools is simplicity and efficiency. All of these tools are designed to explore areas of quality of life that are expected to be affected by medical interventions. According to this quality, they are widely used in observational and clinical studies, because they allow comparing, for example, different groups of the population suffering from the same disease or comparing the effect of the disease on the quality of life depending on the condition of the disease [29].

One of the publicly available tools in the scientific literature is the short form 36 questionnaire (SF-36) and the Euroqol five item questionnaire (EQ-5D), which are the two most popular questionnaires used to quantify the quality of life associated with health in patients with chronic viral hepatitis [30,31]. The SF-36 questionnaire consists of 36 items, in which 8 health-related areas of health quality are measured (physical functioning, role restriction due to physical problems, bodily pain, general health, vitality, social functioning, role restriction due to emotional problems and mental health) [30]. Using the EQ-5D questionnaire, it is possible to register the level of problems reported by patients themselves in accordance with five parameters (mobility, self-care, normal activity, pain/discomfort and anxiety/depression) [31].

Studies using SF-36 were conducted in patients with chronic hepatitis B on the background of antiviral treatment and without treatment [32], in patients with chronic hepatitis C receiving interferon-free therapy [33], after treatment of chronic hepatitis C viral infection with direct-acting antiviral drugs [34]. In a study involving 102 patients with chronic viral hepatitis B, the quality of life associated with health was assessed against the background of antiviral treatment and without treatment. Thus, the results showed that in the treatment group SF-36 showed that physical functions improved significantly compared to the treatment discontinuation group [32]. EQ-5D was used in the treatment of direct-acting antiviral drugs in patients with chronic hepatitis C [35], when studying the real impact of direct-acting antiviral therapy on the health-related quality of life of people with HIV and chronic viral hepatitis C co-infection [36]. In the Canadian cohort study of HIV and HCV coinfection, in which 1795 participants from 18 centers participated prospectively, participants initiated oral responses of the using direct acting

antiviral therapy. The results showed improvements in HRQoL in sustained viral response [36].

One of the disadvantages identified when using common questionnaires is that they are not sensitive enough to determine the quality of life of HRQoL to specific a particular disease. Researchers recommend to supplement general tools with questionnaires specific to this disease in order to obtain more accurate results of quality of life in patients with chronic viral hepatitis [10].

## Specific tools to assess quality of life in chronic viral hepatitis

Due to the fact that common instruments may not always detect subtle effects of a certain condition on the quality of life, the use of special tools can give more accurate results in assessing the quality of life associated with health in patients. There are already a number of tools in the field of health assessment in chronic viral hepatitis.

So, one of the important special tools for studying the quality of life is the questionnaire of chronic liver diseases (CLDQ), designed for specific liver diseases. It is a reliable and reliable tool for assessing the quality of life of HRQoL in patients with chronic viral hepatitis. The results of a study conducted in Japan indicate that HRQoL in patients with chronic viral hepatitis mainly worsens due to emotional factors, not somatic symptoms [37]. One of the subtypes of the questionnaire developed recently is CLDQ-HBV, which is a short, specific tool for assessing the quality of life in patients with chronic viral hepatitis B [38] and Chronic Liver Disease Questionnaire-Hepatitis C (CLDQ-HCV) the hepatitis C virus-specific quality-of-life instrument [39]. These tool models have been developed and validated using a large data set and an established methodology that demonstrates excellent psychometric characteristics and has excellent accuracy at the group level [38,39]. Another tool actively used in assessing the quality of life in patients with chronic viral hepatitis is the FACIT-F questionnaire. This questionnaire is a tool used to determine the outcomes reported by patients and is focused on fatigue, including 4 domains of well-being (physical, emotional, social and functional) and a fatigue subscale. It has the form of a scale from 0 to 160, in which the higher the score, the higher the HRQoL [40]. Thus, in a recent study, the overall FACIT-F score in patients with chronic viral hepatitis D was  $129.4 \pm 24.5$  and  $136.8 \pm 14.2$  in patients with chronic viral hepatitis B ( $p=0.4416$ ), which indicated poorer physical well-being ( $p=0.0036$ ) and emotional well-being ( $p=0.0541$ ) in patients with HDV-infection [22]. The WPAI questionnaire identifies specific health problems and is used to assess violations of patients' daily activities and labor productivity associated with HDV or HBV infections in patients. It includes two domains, the first domain «Violation of labor productivity» characterizes the sum of the domains "absenteeism" (loss of hours of work) and "presenteeism" (self-report on a decrease in productivity during work), it is evaluated only if the patient is working, the second domain «Violation of activity» determines the violation of daily activities in all participants, regardless of their employment status [22]. WPAI results are expressed as a percentage, with higher numbers indicating greater degradation and lower performance [22]. In many studies, the 5D-itch scale has been used, which includes a description of the perception of itching caused by the disease, as well as to monitor the results of the treatment [41]. This questionnaire is a one-page questionnaire that classifies patients with itching according to 5D, in particular with duration, degree, direction, distribution and disability. Scores below 5 mean no itching, while 25 points mean having the most severe itching [41].

All of the above special tools have the ability to most accurately characterize the quality of life in patients with chronic viral hepatitis and the ability to assess its changes over time. Another advantage of special tools is the ability to assess the quality of life of patients during therapy and its effectiveness. The disadvantage of specific tools is that they do not make it possible to compare the quality of life of patients with chronic viral hepatitis with other types of population.

## Conclusion

Chronic viral hepatitis are the main diseases that can affect morbidity, quality of life and mortality, which can lead to increased health care costs for society. Health-related quality of life (HRQoL) is an important indicator for evaluating the treatment and prognosis of patients with chronic viral hepatitis,

and it often has low indicators. The quality of life of patients with chronic viral hepatitis is affected by various factors, among which are the severity of the disease, clinical symptoms and low self-efficacy, affecting the quality of life of patients. Timely screening and treatment of patients with chronic viral hepatitis would be very cost-effective and would significantly reduce morbidity and mortality. The use of special tools designed to assess the quality of life associated with chronic viral hepatitis can significantly contribute to the verification of such interventions.

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