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Health–Related Quality of Life and Factors Affecting It in Patients with Liver Cirrhosis of HBV, HDV and HCV Etiology

Allabergan Kadirovich Bayjanov[1], Aziza Saydullaevna Khikmatullaeva[1], Nodira Khusanovna Ibadova[2], Charos Bakhtiyorovna Turaeva[3]

[1]Doctor of Medical Sciences, Senior Research Fellow, Scientific Research Institute of Virology of the Republican Specialized Scientific and Practical Medical Center of Epidemiology, Microbiology, Infectious and Parasitic Diseases, Tashkent, Uzbekistan
[2]Head of Department, Clinic of the Scientific Research Institute of Virology, Tashkent, Uzbekistan
[3]Independent Researcher, Scientific Research Institute of Virology of the Republican Specialized Scientific and Practical Medical Center of Epidemiology, Microbiology, Infectious and Parasitic Diseases, Tashkent, Uzbekistan

Abstract Determining the health–related quality of life of patients with liver cirrhosis has become one of the main areas of hepatology in recent years. By identifying and eliminating factors that contribute to the deterioration of health–related quality of life, patients' lifestyles can be improved. There are currently a number of scales (questionnaires) available to measure this indicator. This article summarizes the results of an analysis of available scientific sources on the identification of health–related quality of life in patients and the factors affecting it. It provides information on the advantages and disadvantages of existing methods, modern assessment methods, and the possibilities of their practical application.

Keywords Health–related quality of life (HRQOL), Patient, Liver cirrhosis (LC), Hepatology, Factor, Method, Hepatitis B Virus (HBV), Hepatitis D Virus (HDV), Hepatitis C Virus (HCV), Viral etiology, Body mass index (BMI), Chronic hepatitis, Hepatic encephalopathy (HE), Chronic liver disease (CLD), Fatty liver disease, Autoimmune diseases

1. Introduction

Liver cirrhosis (LC) has a long history of development and is characterized by a significant negative impact on patients, especially as the disease progresses. The global prevalence of the disease increased by 74.53% from 1990 to 2017. Today, the mortality rate from LC is on average 4%, and 2 million people die from this disease every year [11,25]. The pathogenesis of the disease is associated with alcohol abuse, the development of autoimmune diseases or fatty liver disease, and chronic hepatitis of viral etiology. A 2017 study in UK clinics found that patients' awareness of cirrhosis was very low: only half of patients undergoing endoscopy understood the seriousness of the diagnosis. In addition, 10% of patients who presented to the clinic were unaware that they had cirrhosis [14]. Women with cirrhosis of the liver are at increased risk of developing pregnancy complications. According to various scientific sources, up to 50% of women with this diagnosis experience various complications of the disease [3].

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Studies conducted by the American Association for the Study of Liver Diseases show that a woman with liver disease has a 6% higher chance of having a baby with various defects, and an 8.8% higher chance of having a baby with a smaller weight and height for gestational age [17]. Another study showed that in patients with cirrhosis of the liver, the incidence of postpartum hemorrhage was 13.8%, cesarean section was performed in 73.6% of cases, the appearance or exacerbation of ascites was observed in 73.6% of cases, and admission to the intensive care unit was 24.1%. A high rate of complications was observed in newborns, with asphyxia occurring in 10.2% of cases [13]. The main cause of death in pregnant women with cirrhosis (according to some reports, from 15% to 50%) is bleeding from esophageal varices, especially in the second and third trimesters of pregnancy [3]. Liver cirrhosis in children is a rare but very serious pathology. Among non–infectious liver diseases, autoimmune hepatitis is most often diagnosed, with cirrhosis developing in 15.9% of cases (most often in adolescent girls). Among metabolic diseases, liver cirrhosis is the most common (7.7% of cases), and in Wilson's disease, the first clinical manifestations are accompanied by damage to the central nervous system [1]. There is a strong

association between liver cirrhosis and poor health–related quality of life (HRQOL). Identifying factors that contribute to poor HRQOL in patients with liver cirrhosis is essential to improve healthcare and therapeutic approaches. In addition, physical exercise, liver transplantation, stem cell therapy, probiotics, rifaximin, and lactulose have been associated with improved HRQOL. Older age, female gender, low body mass index (BMI), anxiety and depression, complications of liver cirrhosis including ascites and hepatic encephalopathy (HE), severe illness, sarcopenia, sleep disturbance, muscle spasms, increased bilirubin levels, prothrombin time, and albumin–bilirubin ratio are factors associated with poor HRQOL [30].

The results of the study show that, regardless of the etiology of diseases preceding liver cirrhosis, the quality of life of patients with their final stage deteriorates significantly. Decompensated patients have more unsatisfactory indicators of health–related quality of life than patients with compensated liver cirrhosis [22,27,29,34]. The most common symptoms in patients with liver cirrhosis are: pain (prevalence 30–79%), shortness of breath (20–88%), muscle spasms (56–68%), sleep disturbances (insomnia 26–77%, daytime sleepiness 29.5–71%), and mental illness (depression 4.5–64%) [27].

According to a study conducted by Baranova E.N., asthenic syndrome is often detected in patients with liver cirrhosis of viral etiology, which is manifested by the inability to take care of oneself due to weakness, fatigue (70.87%), decreased work capacity (44.66%), and sleep disorders (40%). Sleep disorders were observed in 32.04%. Alternating manifestations of constipation and diarrhea were observed in 29.13% and urinary disorders in 33.98% of cases. In all patients with cirrhosis of the liver, symptoms characteristic of varying degrees of autonomic nervous system disorders have been identified [2].

In studying the quality of life of patients with liver cirrhosis, which includes the main areas of human life: physical, mental, social, and spiritual, the relationships of patients with their relatives also play an important role. Taking into account modern realities, these criteria were assessed both before and after quarantine measures related to the COVID–19 pandemic, and varying degrees of deterioration in the quality of life were observed in patients [24].

The issue of introducing changes to the current principles of care for patients with liver cirrhosis is being actively studied. At the same time, quality of life should be considered as a differential criterion for the effectiveness of rehabilitation within the framework of the algorithm for the diagnosis and treatment of compensated and decompensated liver cirrhosis [28]. Communication between the patient and the attending physician based on medical principles is also important. Educational programs have been developed in this regard, and its positive effect on clinical and functional indicators in patients has been justified [16,21].

One of the emerging trends in medicine today is the individualization of treatment. This is confirmed by legislation in many countries. These documents provide for individual approaches to the provision of medical care and rehabilitation for each patient. According to him, today's medicine follows the 4P principle: individualized (individual approach to the patient), predictive (predicting the risk of developing a disease based on research), preventive (reducing or completely preventing the risk of developing a disease), and participatory (patient participation in the treatment process, patient cooperation with the doctor) [4].

In recent years, the SF–36 questionnaire has been widely used to study the quality of life of patients with liver cirrhosis. The results of one study show that patients with liver cirrhosis have significantly decreased scores on 7 of the 8 scales of the SF–36 questionnaire. The most reduced indicators were general health (GH) and physical activity (PF), which were associated with high pain intensity (BP). Indeed, according to foreign sources, 82% of patients with liver cirrhosis have severe pain, and more than half of them are chronic pain affecting all areas of life [19]. Women have higher quality of life indicators than men, which may be explained by their lower prevalence of alcoholism and smoking, which are factors that exacerbate the course of the disease [8]. At the same time, despite moderate social and physical activity, patients with cirrhosis experience a decrease in their quality of life (VL) and mental health (MH). 60% of patients experience mental disorders. In 40–50% of cases, patients with cirrhosis of the liver of various etiologies experience a decrease in their quality of life due to the disease and associated reduced income [5].

Low levels of social support and poor relationships with family members are strongly associated with poor quality of life and increased risk of death from cirrhosis [24]. In these cases, the risk of suicide is also increased, especially when cirrhosis has progressed to the decompensated stage [9].

A study by Abureesh M. to assess the risk of depression in patients with liver cirrhosis in the US collected data from 1999 to 2019 from 26 major integrated healthcare systems consisting of 360 hospitals in the United States using electronic health records. Of the 293,150 people diagnosed with cirrhosis, 23.93% had depression, compared to 7.61% (95% II, 16.1836%) in the control group without cirrhosis. Using a multivariate analysis model, it was found that patients with cirrhosis were more likely to develop depression compared with patients without cirrhosis (odds ratio=2.172; 95%, CI2.159–2.185; 16.477%, $p<0.001$) [6].

In a study conducted by Seo G.H. to assess the dynamics of depression detection in patients before and after the diagnosis of liver cirrhosis, the proportion of patients with depression detected after the diagnosis increased sharply, indicating the need to diagnose depression within the first three months after the diagnosis of liver cirrhosis [32]. Fatigue is the most common clinical symptom in patients with chronic liver disease (CLD), and the reduced quality of life in these patients results in fatigue–related societal costs. In addition, fatigue is associated with social dysfunction, increased daytime sleepiness, decreased work capacity, and an increased risk of mortality [20]. The mechanism of fatigue development is associated with peripheral (local–muscle) and central (as a result of changes in synaptic transmission

in the brain) components. The pathogenesis of fatigue in chronic liver diseases is multifactorial [7,20]. Muscle dysfunction has been shown to be a major mechanism of fatigue in CLL. Ekerfors U. et al. demonstrated that fatigue in outpatients with chronic liver disease is directly related to muscle function. Fatigue scores were studied in outpatients (49 patients with autoimmune hepatitis, 45 with primary biliary cholangitis, 46 with primary sclerosing cholangitis, 57 with chronic hepatitis B, and 73 with chronic hepatitis C). The mean age of the patients was 52±15 years. Fatigue was assessed using the Fatigue Impact Scale (FIS) questionnaire. Physical activity levels were assessed based on subjective data from patients. Muscle function was assessed using four tests: walking speed, grip strength, standing heel–lift test (SHT), and Timed Up and Go (TUG). The mean total FIS score was 30 (40% had FIS>40, which is considered high fatigue). Decreased muscle performance was observed in SHT (predicted value: 53±26%) and maximum grip strength (85 ± 20%). The level of fatigue was lower in subjects with high physical activity ($p<0.001$). Based on the data obtained, it was concluded that fatigue in patients with chronic liver disease is associated with poor muscle function and a decrease in physical activity levels [10].

One study by Gabr R.M. et al. aimed to assess the relationship between the severity of HF and neurological symptoms, detect subclinical neuropathic damage by examining neuromuscular conduction and counting motor units, and found that 45 (80.3%) of 56 patients with HF had neurological symptoms. Muscle spasms are the most common symptom, followed by fatigue and insomnia. The progression of CKD is also associated with impaired nerve conduction, which can occur even in the absence of clinical symptoms. In turn, a decrease in the number of motor units leads to fatigue in patients with liver cirrhosis [12].

Sarcopenia and severe weakness are of great importance in patients with liver cirrhosis. In hepatology, sarcopenia is defined as the loss of muscle mass due to decreased protein synthesis, and severe weakness is defined as the loss of muscle function as a phenotypic manifestation [18,35]. Early detection and accurate assessment of these parameters are important because they are closely associated with morbidity, mortality, and poor quality of life in patients with liver cirrhosis [35]. One study by Geladari E. et al. examined the physical frailty of patients with cirrhosis and predicted their risk of death over an 18–month period. The results showed that frail patients had a higher mortality rate than patients without severe frailty [15]. Hsieh H.C. et al. studied the effects of physical exercise on body composition, physical performance, fatigue, and quality of life in patients with liver cirrhosis. According to the results of the meta–analysis, exercise increased the six–minute walk distance (6MWD) by 68.93 meters (95% CI 14.29–123.57 meters), hip circumference by 1.26 cm (MD=1.26 cm, 95% CI 0.12–2.39 cm), and mean ultrasound hip compression index by 0.07 (MD=0.07, 95% CI 0.00–0.14) compared to the control group. In addition, physical activity reduced fatigue scores by 0.7 points (95% CI 0.38–1.03) in patients with cirrhosis. However, there was no significant effect on body mass index (BMI) or fat mass or quality of life. In conclusion, the authors concluded that increasing physical exercise can increase thigh muscle thickness and reduce fatigue in patients with liver cirrhosis, but it does not significantly affect the patient's quality of life [18].

The quality of life of patients with cirrhosis largely depends on the severity of the disease. HRQOL decreases significantly with the progression of the disease and the development of complications. Thus, ascites, which is taken into account to calculate the severity of cirrhosis according to the Child–Pugh system, is one of the factors that leads to a deterioration in the quality of life with the development of cirrhosis [33]. Hepatic encephalopathy (HE) also has a significant impact on health-related quality of life. Impairments include activities of daily living, changes in sleep-wake cycles, and work capacity [23]. Studies have shown that patients with higher cognitive reserve are better able to tolerate cirrhotic patients and their impact on quality of life than those with lower cognitive reserve. The deterioration in quality of life in patients with cirrhosis affects both the patients themselves and their caregivers [26,33]. Salih Z.M. et al. examined the stressors affecting caregivers of patients with liver cirrhosis. The results of the study showed increased anxiety, fear, guilt, and hopelessness among caregivers [31].

2. Conclusions

The above points determine the practical importance of studying this area, the urgency of improving approaches to evaluating rehabilitation interventions as part of the provision of medical care to patients with liver cirrhosis. In patients diagnosed with cirrhosis of the liver of various etiologies, many indicators of the quality of life decrease sharply, in particular, the level of subjective assessment of physical and social activity, emotional state, health and overall vitality is significantly reduced, all of which causes a decrease in the effectiveness of treatment. Early identification and elimination of factors that affect the health–related quality of life of patients leads to activation of liver cell regeneration.

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