FEATURES OF THE COURSE OF DIFFUSE LIVER DISEASES DURING THE BACKGROUND OF COVID-19.

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Abstarct*: It is known that coronavirus infection COVID-19 occurs in multiple organs of the body. The review article reveals the mechanisms of liver damage during coronavirus infection COVID-19, the impact of chronic liver diseases on the course and prognosis of COVID-19 disease. The studies conducted on liver damage in COVID-19 are summarized.*

Keywords*: COVID–19, chronic liver diseases, disease caused by the new coronavirus, liver damage.*

Introduction. In recent years, humanity has experienced a difficult period - the pandemic of the new coronavirus SARS-Cov-2 (severe acute respiratory syndrome coronavirus), called COVID - 19 (CoronaVirus Disease - 2019). During the pandemic, the priority task of medicine around the world was to combat this infection; various temporary recommendations were developed for the management of patients and treatment of COVID-19 disease, which was characterized by a course that was difficult to treat with pharmacotherapy and severe complications.

The diagnosis of COVID-19 is confirmed by detecting SARS-CoV-2 coronavirus RNA in biological media and antibodies in blood serum. Using molecular genetic research methods, the SARS-CoV-2 genome is determined not only in smears from the throat, nose, and lung tissue, but also in parenchymal cells, vascular endothelium of other organs, including hepatocytes [15]. Scientists around the world have noted the diversity of coronavirus damage, its course and the wide scale of involvement of organs and systems in the pathological process.

Lung damage in the form of pneumonia and bronchitis turned out to be the leading clinical manifestations of COVID-19 disease. It was found that, along with a high neutrophil/lymphocyte ratio, low numbers of lymphocytes, monocytes and platelets, high levels of muscle enzymes, ferritin and IL-6, elevated liver enzymes on admission were associated with a severe course, poor prognosis and the development of acute respiratory distress syndrome (ARDS) [7]. But neurological

disorders, skin changes, eye lesions, bone changes, damage to the heart and other internal organs are also described.

Machhi J. et al. COVID-19 is classified not as an acute respiratory infection, but as a systemic viral disease with multiple organ damage, including, in addition to the lungs, the kidneys and liver [1]. Laboratory studies have also shown liver damage in patients with COVID-19 [2]. Moreover, scientists have observed the progression of chronic liver diseases (CLD) against the background of coronavirus infection and a more severe course of COVID-19 against the background of CKD [3].

Bertolini A et al. [11] reported that changes in liver parameters are frequently reported in hospitalized patients with coronavirus infection. Thus, 46% of hospitalized patients with COVID-19 had elevated plasma aspartate aminotransferase (AST) levels upon admission and 35% had increased alanine aminotransferase (ALT) activity. The observed increase in liver enzymes (AST, ALT) was below 5-fold normal and correlated with the severity of the disease and elevated inflammatory markers. However, significant impairment of liver function or overt liver failure as a cause of death in COVID-19 was rare [5].

In modern literature, analyzing the condition of the liver in Chinese patients with COVID-19 from Wuhan (People's Republic of China), scientists noted that in 14-53% of patients changes in biochemical parameters were recorded [20, 22], in 2-11% of cases the infection developed in background of CKD [23]. Similar studies were conducted by Cholankeril G. et al (2020) in California.

Also, Shengliang Xin et al. [9] in 7,467 patients with COVID-19 compared biochemical blood test data - ALT, AST, total bilirubin and lactate dehydrogenase (LDH) in patients with severe infection compared with mild cases. Elevated levels of liver enzymes were more often recorded in patients with severe SARS-CoV-2 infection (37.1% - ALT, 47.4% - AST). Elevated bilirubin and LDH levels were observed in 19.8% and 77.8% of patients with severe disease, respectively. It was found that in patients with severe COVID-19, the risk of increased liver biochemical parameters (ALT, AST, total bilirubin concentration in the blood, LDH) was much higher compared to mild infection. In other words, patients with severe COVID-19 were more susceptible to liver damage [18].

The proportion of liver damage in patients with severe COVID-19 was significantly higher than in patients with mild disease. In a number of cases, a violation of protein synthetic function was noted - the albumin level decreased to 30.9-26.3 g/l [13].

In studies by Portincasa P et al. [16] note that the mechanisms of liver damage during a new coronavirus infection are complex and include both direct damage to cholangiocytes and other associated conditions (use of antiviral drugs, systemic inflammatory response, respiratory distress syndrome, hypoxia, sepsis, multiple organ dysfunction and etc.). The authors emphasize that additional attention is required if patients have a history of CKD, which worsens the prognosis and prolongs the length of hospital stay. In decompensated cirrhosis, liver damage was progressive in 57% of patients with a 43% mortality rate. Increased bilirubin and level of AST/ALT change had predictive power for mortality among patients with cirrhosis [6].

The authors come to a clear conclusion: SARS-Cov-2 infection causes significant additional liver damage in patients with CKD, leading to decompensation in 1/5 of patients with cirrhosis and a significant deterioration in the clinical status of already decompensated cirrhosis [8]. Cai et al. in their work [14] found that primary damage to cholangiocytes can lead to subsequent abnormalities of hepatocytes. They described an increase in the level of alkaline phosphatase (ALP) in 0.34% of patients during the initial study and in 11% of patients again, and glutamyl transpeptidase (GGT) in 17.1% initially and in 48.7% during the entire period of hospitalization. Thus, the authors suggest that cholangiocyte damage occurs in the early stages of COVID-19 [2].

Another pathogenetic mechanism of hepatocyte damage caused by SARS-CoV-2 is associated with liver ischemia, hypoxia and hypovolemia, to which it is especially sensitive. Severe infection leads to a decrease in the delivery and/or utilization of oxygen by the liver and a significant increase in aminotransferase levels. However, some researchers describe that in patients with respiratory failure and decreased blood saturation, venous congestion in the liver is observed, which can also cause damage to hepatocytes. Moderate microvascular steatosis with mild liver inflammation in patients with COVID-19 indicates the possibility of drug-induced liver injury [21].

The authors conclude that dynamic changes in liver function may correlate with the severity and, most importantly, the prognosis of COVID-19. The degree of liver damage is closely related to mortality and the need for mechanical ventilation, so biochemical parameters

must be closely monitored throughout the entire period of hospitalization. [4].

Under the microscope, the liver demonstrates moderate dilatation of the sinusoids, with slightly increased infiltration of small lymphocytes in the sinusoidal spaces. Mild to moderate steatosis was reported in one case but not in the other

cases. More significant findings are multifocal hepatic necrosis without obvious inflammatory cell infiltration. Tubular cholestasis can rarely be observed [12].

Meanwhile, the described histological changes may be largely due to drug-induced liver damage rather than SARS-CoV-2 [1].

Analyzing the results obtained, scientists put forward the following assumptions regarding liver damage in COVID-19:

- microscopic changes in the liver can be directly related to a viral attack;
- changes may be caused by drugs used in the treatment of COVID-19;
- predisposition to liver diseases in some patients with COVID-19 may provoke changes;
- a hyperinflammatory response to COVID-19 may contribute to liver damage [7].

COVID-19 continues to pose a threat to global public health. The pathogenesis of the new coronavirus infection has not been sufficiently studied; Information about the epidemiology, clinical features, prevention and treatment of COVID-19 is constantly updated [9, 12]. In particular, patients with liver cirrhosis have not only an increased risk of occurrence and development of more severe forms of COVID-19, but also often progression of chronic liver disease itself [19]. In real clinical practice, to achieve effective results in etiotropic and pathogenetic therapy of COVID-19, careful clinical monitoring, as well as a personalized approach to the treatment of each patient, taking into account comorbidity, immune status, and drug-drug interactions, are of critical importance [17].

Thus: with coronavirus infection COVID-19, multiple organ damage occurs, which, along with other organs, is characterized by liver damage and the presence of CKD adversely affects the course of the disease, aggravating the outcomes and prognosis. Current recommendations for the management of patients with COVID-19 disease in the presence of CKD are insufficient for the diagnosis and treatment of lesions. The study of liver damage in COVID-19 and the presence of CKD requires further targeted study to develop new recommendations. Studying these issues is an urgent task for further research.

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