

Clinical Features and Lab Values of Patients with Chronic Hepatitis after Covid-19

Sherzod Zakirhodjaev, Malika Pattakhova*

Department of Internal Medicine, Tashkent Medical Academy, Tashkent, Uzbekistan

Abstract In scientific studies on the study of COVID-19, the researchers have reported that 14-53% of the cases showed signs of mild to moderate liver damage: increased levels of aminotransferases, hypoproteinemia, and an increase in prothrombin time. The severe course of the disease was associated with signs of liver damage. Exacerbation of pre-existing chronic liver disease leads to a more severe course of COVID-19 infection. The direct action of the SARS-CoV-2 virus can directly affect liver cells, as evidenced by the detection of increased expression of ACE-2 receptors in cholangiocytes [1,2]. Patients with advanced stages of chronic diffuse liver disease have a higher risk of infection due to immune disorders associated with the presence of cirrhosis [3]. The aim of the study was to study the clinical, functional and metabolic characteristics of patients with chronic hepatitis who had Covid-19.

Keywords Chronic hepatitis, Covid-19, Inflammation, Damage

1. Introduction

Up to now, scientific data have shown that the risk group with an increased likelihood of infection and severe course of coronavirus infection includes elderly patients and patients with chronic cardiovascular diseases such as hypertension, coronary artery disease and diabetes mellitus. Less is known about the impact of the virus on other chronic diseases, and in particular liver disease. But today it is already clear that patients with severe fibrosis and cirrhosis of the liver, patients who have undergone liver transplantation also represent a vulnerable group with an increased risk of infection and a severe course of COVID-19 [4,5,6,7]. In scientific studies on the study of COVID-19, it is reported that 14-53% of the cases showed signs of mild to moderate liver damage: increased levels of aminotransferases, hypoproteinemia, and an increase in prothrombin time. The severe course of the disease was associated with liver damage [8,9,10,11,12,13]. There are various mechanisms of liver damage as a result of direct cytotoxic action of the virus; toxic effects of drugs in the complex management of COVID-19 infection; increased activation of the immune system (cytokine storm) or hypoxia due to lung and myocardial damage [5]. Critically ill COVID-19 patients often show signs of liver dysfunction, according to Chinese doctors. Therefore, patients with cirrhosis and COVID-19 are at higher risk of decompensation

and liver failure.

In addition, scientists have found that the SARS-CoV-2 virus can directly infect liver cells and cells lining the intra- and extrahepatic bile ducts (cholangiocytes), since they contain, although in low concentrations, a special enzyme (angiotensin-converting enzyme 2), which the SARS-CoV-2 utilizes to enter the cell. This can explain the detection of the virus in feces. The same enzyme is found in the cell membranes of the intestines, kidneys, and lungs, which may play a key role in the risk of developing severe respiratory impairment (acute respiratory distress syndrome). Comorbidity also plays an important role, notably alcoholic or non-alcoholic fatty liver disease, chronic hepatitis of various etiologies, toxic (including drug) and autoimmune liver diseases, as well as cirrhosis of the liver are on the top. Exacerbation of pre-existing chronic liver disease leads to a more severe course of COVID-19 infection [6]. When we study the effect of other coronaviruses on organs, then SARS's direct lesion to the organs was established - SARS viral nucleic acids were found in the hepatic tissue of patients. When liver biopsies were analyzed, an increase in the number of mitoses of hepatocytes, apoptotic bodies, signs of ballooning (hydropic dystrophy) of hepatocytes and a lobular component (Jinyang Gu) were revealed. Surprising results were obtained from RNA sequencing in two independent studies of patients with COVID-19 infection. A significant increase in ACE2 expression in cholangiocytes (59.7%) compared to hepatocytes (2.6%) was proven. This suggests that in some patients, intrahepatic bile duct cholangiocytes are targeted by COVID-19, and this may lead to their direct damage during or after the disease [6]. Currently, literature data on the pathogenesis of chronic liver diseases after

* Corresponding author:

malikapattahova@gmail.com (Malika Pattakhova)

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Covid-19 is very scarce and requires further research.

2. Research Objective

Study of clinical and laboratory parameters in patients with chronic hepatitis and history of Covid-19.

3. Materials and Research Methods

The study was conducted in 2021-2022 years and involved 50 patients with a diagnosis of chronic hepatitis who were hospitalized in the department of 2-general therapy of the multidisciplinary clinic of the Tashkent Medical Academy. The patients were divided into 2 groups. Group 1 included the patients with chronic hepatitis, group 2 - patients with chronic hepatitis who have had Covid-19. Also, 15 apparently healthy study participants were matched for the control group. The diagnosis of chronic hepatitis was made according to the history and clinical manifestations of the disease, the laboratory data and instrumental methods.

The laboratory examination plan included a set of biochemical assays (AlAT, AsAT, bilirubin, total protein), coagulation study, clinical and laboratory studies of hematological parameters (hemoglobin, erythrocytes, leukocytes, platelets, leukocyte formula), urinalysis. Also, all patients underwent PCR for the coronavirus, and conducted a test for the determination of specific IgG, IgM.

The study materials were statistically processed using Student's t-test using the standard Microsoft Office 2019 and Prism 8 software package.

The 1st group included 25 patients with chronic hepatitis

in the relapse stage, (men - 14, 44.0%, women - 11, 56.0%). The age of patients ranged from 40 to 75 years, the mean age was 64.4 years. Patients received standard pharmacotherapy and diet.

The 2nd group included 25 patients with chronic hepatitis who received treatment in a multidisciplinary clinic of the Tashkent Medical Academy in department 2 - general therapy. This group consisted of 15 male patients (60.0%), and 10 female patients (40.0%). The age of patients ranged from 40 to 75 years, the mean age was 61.8 years. They were treated in October-December 2020 and received standard therapy.

The major symptoms of the patients included heartburn, nausea, pain and heaviness in the right subcostal area, fatigue, maldigestion, and decreased ability to work.

4. Results of the Study and Their Discussion

The clinical features included weakness, loss of appetite, nausea, pain in the right subcostal area. Vomiting was observed in 88%, loss of appetite in 96%, weakness in 96% of patients with chronic hepatitis who had Covid-19, which was significantly higher compared with the rates of patients with chronic hepatitis who did not have Covid-19. In addition, 5 patients had icterus accompanied by intense skin itching. Pain in the right hypochondrium was noted by 88% of patients of the 2nd group, which was higher by 30% compared with the 1st group. Hepatomegaly was determined in the vast majority of patients. Characteristics of the symptoms of the disease are given in table 1.

Table 1

Clinical features	Group 1 Patients with chronic hepatitis (n=25)		Group 2 Patients with chronic hepatitis and history of Covid-19 (n=25)	
Pain in left subcostal area	17	68%	22	88%
Jaundice	1	4%	5	20%
Poor appetite	18	72%	24	96%
Constipation	8	32%	8	32%
Fatigue	19	76%	23	92%
Pruritus	3	12%	4	16%
Nausea	15	60%	18	72%
Vomiting	3	12%	4	16%
Decrease in working capacity	18	72%	21	84%

Comparison of complete blood count between patients with chronic hepatitis alone and patients with chronic hepatitis and history of Covid-19

What is measured	Controls (n=15)	Group 1 (n=25) Chronic hepatitis	Group 2 (n=25) Chronic hepatitis and Covid-19	Unit	P-value
Red blood cells	4,4±0,9	4,0 ± 0,7	3,5 ± 0,4	10 ¹² /л	0.0032*
Hemoglobin	125,5±25,9	109,4 ± 19,7	92,3 ± 20,5	г/л	0.0042*
White blood cells	5,3±2,8	8,9 ± 1,7	4,8 ± 1,4	10 ⁹ /л	0.0001*

What is measured	Controls (n=15)	Group 1 (n=25) Chronic hepatitis	Group 2 (n=25) Chronic hepatitis and Covid-19	Unit	P-value
Color index	0,9±1,9	0,8±1,1	0,8±1,3		1.0000
Hematocrit	43,0±6,8	48,4 ± 6,1	51,3 ± 7,9	%	0.1528
Reticulocytes	1,1±0,2	1,0±0,1	1,1±0,2	%	0.0300*
Platelets	175,2±69,4	202,1 ± 76,4	194,3 ± 78,4	10 ⁹ /л	0.7232
ESR	8,9±2,8	9,1±2,7	8,5±2,1	мм/час	0.3848
White blood cells					
Eosinophils	4,0±1,7	3,8±1,2	2,8±0,3	%	0.0002*
Bands	6,4±1,1	3,9±1,03	4,4±1,4	%	0.1568
Segmented	49,4±19,4	65,1±25,1	53,0±17,8	%	0.0551
Lymphocytes	27,4±11,0	24,4±7,4	21,1±1,6	%	0.0342*
Monocytes	7,9±0,9	8,2±0,7	9,5±1,03	%	0.0001*

* - Statistically significant ($P \leq 0,05$)

Liver damage in coronavirus disease also occurs due to hypoxia, which develops due to pulmonary distress. Hypoxia associated with pneumonia is the cause of ischemic liver damage in patients with coronavirus infection. Decrease in oxygen content during hypoxic conditions can lead to the death of liver cells.

Also, damage to the liver after coronavirus infection is caused by drugs: antibiotics, antiviral, antipyretic, hormonal, anti-inflammatory and drugs of other groups used in the management of COVID-19. Many of the drugs that are recommended in the treatment of coronavirus have a toxic effect on the liver, thereby causing damage to it. Liver function test components, such as bilirubin (direct and indirect) and liver enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and alkaline phosphatase) indicate the liver functional capacity during the infection. Thus, a significant increase in bilirubin in the blood (hyperbilirubinemia) is often observed in patients with coronavirus infection.

AST is one of the main indicators in the detection of liver pathologies. The ratio of AST / ALT is clinically useful as well, which is normally equal to 1.33 ± 0.42 . Thus, in patients with various forms of coronavirus infection, a significant increase in the activity of ALT and AST was noted. Usually, a mild or asymptomatic course of coronavirus infection causes a transient increase in ALT levels without significant impairment of liver function.

There was an increase in ALT levels in patients with chronic hepatitis who had Covid-19 compared to patients who did not have Covid-19 (47.1 ± 33.0 and 30.5 ± 19.0 , respectively).

5. Conclusions

1. A severe manifestation of some symptoms was noted in the group of patients with chronic hepatitis and history of Covid-19 compared to the control group.
2. It was found that the group of patients with chronic

liver diseases and history of Covid-19 has a more severe anemia compared to the group of patients with chronic hepatitis alone. In the group 1 hemoglobin decreases by 15%, and erythrocytes by 12.5%.

3. Patients with chronic hepatitis and history of Covid-19, ALT, AST and bilirubin levels increased by 16%, 35% and 16.3%, respectively, compared with the control group, which indicates the cytotoxic effect of the virus on liver cells.

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