CLINICAL MANIFESTATIONS IN COVID-19 WITH HDV INFECTION

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Annotation: In the context of liver involvement in patients with COVID-19, many key aspects need to be addressed in both native and transplanted organs. This review focuses on the clinical presentations and laboratory abnormalities of liver function tests in patients with COVID-19 with no prior liver disease, patients with pre-existing liver diseases and liver transplant recipients. A brief overview of the history of COVID-19 and etiopathogenesis of the liver injury will also be described as a prelude to better understanding the above aspects.

Keywords: COVID-19, liver injury, SARS-CoV-2, clinical manifestations, liver function tests, cirrhosis

Relevance

Many patients with severe disease may die from multiorgan failure. In this review, we described liver involvement in COVID-19, which can be studied from many aspects. The focus of this review, however, was on clinical and laboratory manifestations of liver disease in COVID-19 patients, in the native healthy liver, native diseased liver and in the transplanted liver.In the Republic of Uzbekistan, the introduction of the HBV vaccination into the preventive vaccination schedule has resulted in nearly a 40-fold reduction in cases. However, despite effective measures, the number of mixed HBV infections identified with the delta agent is increasing, and Uzbekistan remains one of the countries with moderate endemicity on the global map [4].

In the literature reviewed, we did not find information regarding the course of COVID-19 infection against the background of chronic HDV infection. Therefore, the aim of this study was to determine the clinical and laboratory characteristics of COVID-19 infection in the context of HDV infection.

“Livomed” tablets, a well-balanced combination of pure herbs, is a very useful remedy for jaundice, liver enlargement and cirrhosis, loss of appetite, anemia, alcoholism, etc. It protects the liver from various hepatotoxins, corrects liver dysfunction and damage. Promotes appetite and controls jaundice. It helps the liver eliminate toxins and restore cell growth while protecting them from the harmful effects of alcohol, drugs and environmental toxins. Restores the functional efficiency of the

liver by protecting the liver parenchyma and promoting liver cell regeneration. Its antiperoxidant activity prevents the loss of functional integrity of the cell membrane, supports and ensures early restoration of liver function in infectious hepatitis.

Materials and methods. A total of 143 patients with HDV+COVID-19 infection and 50 patients with only COVID-19 infection, treated at the Zangiota Specialized Hospital from 2021 to 2023, were selected using a randomized method. The main clinical signs of the disease and a comparative analysis of certain laboratory indicators were conducted for these patients.

Inclusion criteria for the study: Patient consent to participate in the study. Male or female patients aged 18 years and older. Patients with confirmed COVID-19 and HDV infection by PCR.

Exclusion criteria for the study: Pregnant or lactating women. Non-compliance with the requirements and procedures of the study. Patients younger than 18 years. Patients with chronic somatic, oncological, or hematological diseases.

Specific IgM and IgG for chronic viral hepatitis B and D were determined in serum by the IFT method, along with D-dimer, C-reactive protein, and interleukin-6 (IL-6). The test kits developed by HUMAN (Germany) and NPO "Diagnostic Systems" (Nizhny Novgorod, Russia) were used for this purpose. The quantity of viral hepatitis B DNA and D RNA in the serum was determined by the PCR method, using test kits developed by InterLabServis (Moscow, Russia) and Vektor-Best (Novosibirsk, Russia).

Results. In the course of the study, we observed 120 patients who received treatment at Zangiota Specialized Hospital No. 2 between 2021 and 2023, and 43 of them were found to have HDV infection, representing 1.1% of the total number of patients studied. Accordingly, we divided the patients into two groups: the main group, consisting of 43 patients with HDV+COVID-19 infection, and the comparison group, which included 50 patients with COVID-19 infection only. Among patients in the main group with HDV+COVID-19 infection, 26 (60.5%) were women and 17 (39.5%) were men. In the comparison group, 62.0% (31) of the patients were women and 38.0% (19) were men. The average age of patients in the main group was 41.6±2.1 years, while in the comparison group, it was 38.9±1.7 years. As can be seen, there were no significant differences between the groups in terms of age ($p=0.987622$) or gender (OR=1.8; CI=0.9-3.1; $\chi 2=0.328$), meaning the groups were comparable.

Among the 93 patients in the study group, 15 (16.1%) had a mild course of COVID-19, 51 (54.8%) had a moderate course, and 27 (29.0%) had a severe course. In the main group of patients with COVID-19 on the background of HDV infection, mild cases of the disease were observed less frequently compared to patients in the comparison group, and the difference between the groups was statistically significant (OR=5.7; CI=1.5-21.4; $p<0.05$ by Fisher's exact test). In the study group, the

probability of moderate and severe COVID-19 courses was nearly the same, with no statistically significant differences between the groups.

Results. This finding is significant as it aligns with existing research that highlights sex differences in immune responses and disease outcomes, particularly in infections like COVID-19 [15].

Patients in the main group exhibited more pronounced signs of intoxication, such as headache, dizziness, and respiratory symptoms. Dyspeptic symptoms (nausea, vomiting) were significantly more common in the HDV+COVID-19 group, highlighting the gastrointestinal impact of HDV infection. The frequency of jaundice and hepatosplenomegaly was also notably higher in the HDV+COVID-19 group, indicating a more severe effect on liver function. According to diarrhea and loss of appetite are also reported, with gastrointestinal symptoms linked to increased severity of COVID-19 [16]. The combination of HDV and COVID-19 exacerbates liver damage, leading to higher rates of jaundice and hepatosplenomegaly [17]

Conversely, some studies suggest that gastrointestinal symptoms may correlate with milder COVID-19 outcomes, indicating a complex relationship between these symptoms and disease severity(Canakis et al., 2022).

Mild cases of COVID-19 were less frequent in the HDV+COVID-19 group compared to the COVID-19-only group, indicating that HDV infection may contribute to a more severe disease course. Among patients with moderate and severe forms of the disease, there were no significant differences between the two groups, suggesting that while HDV co-infection affects the incidence of mild cases, it does not appear to impact the distribution of moderate and severe cases.

Conclusion

In conclusion, liver involvement is common in patients with COVID-19 infection, particularly in those with moderate to severe disease. It is mostly asymptomatic or mild in nature. Conversely, patients with pre-existing liver disease are prone to serious COVID-19. Data on the impact of COVID-19 infection on patients with pre-existing diseases or liver transplants is either conflicting or scarce. Hence, large collaborative studies with prolonged follow-up are needed to fully comprehend the impact of this challenging infection on patients with liver diseases.

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