



Review Article

Hepatic involvement in COVID 19 infection

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Abstract

Background: Severe Acute Respiratory Distress Syndrome Coronavirus -2 (SARS -CoV-2) outbreak is a significant public health threat since December 2019. Lung is the most common organ involved by COVID 19 followed by gastrointestinal tract and liver. This review article discusses hepatic involvement and monitoring in this outbreak.

Methods: Recently published studies from PubMed, Red Cross, and Copernicus were reviewed to prepare this review article.

Conclusions: Hepatic involvement is common in COVID 19 infection and it is the second most common organ involved after lung. Most of the hepatic involvements are mild and self limiting. However close monitoring is required.

Introduction

Coronavirus disease 2019 (COVID-19), is a highly infectious respiratory virus that emerged in Wuhan, China and has posed a serious threat to human health worldwide since December 2019. coronavirus disease 2019 (COVID-19), is a highly infectious respiratory virus that emerged in Wuhan, China and has posed a serious threat to human health worldwide since December 2019. coronavirus disease 2019 (COVID-19), is a highly infectious respiratory virus that emerged in Wuhan, China and has posed a serious threat to human health worldwide since December 2019.

Corona virus disease 2019 (COVID-19) is a highly infectious respiratory virus that is a serious threat to human health worldwide since December 2019. It has been declared public health emergency of international concern by the World Health Organization (WHO). It is firmly a disease of droplet transmission and contact transmission however it may be an airborne disease in poorly ventilated and closed area. Majority of COVID-19 affected patients are asymptomatic but most common presentations of symptomatic patients include fever and respiratory symptoms, such as cough, shortness of breath and dyspnoea. This virus enters through angiotensin converting enzyme II (ACE2)-expressing cells and this cell is expressed not only in lung, but also seen in gastrointestinal system. Patients who experience gastrointestinal (GI) symptoms

(nausea, vomiting, or diarrhea) are more likely to suffer from severe pneumonia. Three-stage classification system is proposed for COVID19 infection: stage I (early infection), stage II (pulmonary phase), and stage III (hyperinflammation phase) [1,2]. After lung involvement, liver appears to be the second organ involved [3,4].

Manifestation of liver injury

Hepatic injury in mild COVID-19 infection is often transient and can return to normal without any special management. Overall 39.6% to 53% COVID 19 infected patients show elevation of alanine Aminotransferase (ALT) and aspartate Aminotransferase (AST) levels [5,6]; however hyperbilirubinemia or clinically detected jaundice is seen in only 11% to 18% patients [7,8]. Few studies also reported a decrease in serum albumin, suggesting hepatic synthetic function impairment in COVID 19. Gamma-glutamyl transferase (GGT) is elevated in 54% patients, whereas only 1.8% of patients (1/56) showed elevated alkaline phosphatase (ALP) level [9]. Prevalence of AST elevation is higher in men (66%) than women (35%) [10] and Probability of hepatic injury increases with older age [11].

Mechanisms of liver involvement

Currently, the underlying mechanisms for hepatic injury



in patients with COVID-19 are still unclear however following mechanism of hepatic injury has been described.

First: ACE2 receptors in the liver are expressed mainly in cholangiocytes (60% of cells), minimally expressed in hepatocytes (3% of cells) [12,13] and presence of these receptors, together with the local effects of systemic inflammation seem to be the main mechanisms involved in the onset of liver damage in COVID-19 patients.

Second: Secondary to drugs used in COVID 19 treatment. Antiviral medications (lopinavir and ritonavir), acetaminophen, steroids, hydroxychloroquine and azithromycin have been used in some patients and may cause hepatotoxicity to various degrees. Presence of hypoxic state increases hepatotoxic potential of these drugs results in liver injury and elevate hepatic enzymes [14].

Third: Immune-mediated inflammation in COVID-19 infected patients may be the contributing factor of hepatic injury. Elevated plasma levels of cytokine and other inflammatory substances, such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor results in cytokine storm in some patients, and may cause multiorgan failure and severe elevation of liver enzymes [15]. Use of remdesivir also can elevate liver enzymes [16].

Fourth: High levels of positive end expiratory pressure that can cause hepatic congestion by increasing right atrial pressure and impeding venous return may be a possible aetiology of hepatic injury in COVID 19 patients.

Fifth: Presence of pre-existing liver disease is also a contributing factor of elevated liver injury [17] or acute on chronic liver failure in COVID 19 infected patients. Liver cirrhosis patients are more susceptible to infections due to their systemic immunocompromised status [18]. Therefore, preventing infection with SARS-CoV-2 is of utmost importance.

Histopathology

The histology only showed moderate microvascular steatosis and mild lobular and portal activity. Pathological analysis of hepatocytes from patients who died from COVID-19 shows there is no viral inclusion in the liver [19].

Monitoring

According to the recent AASLD guidelines, regular liver function should be monitored in all hospitalized COVID-19 patients, in particular in those treated with remdesivir or tocilizumab, irrespective of baseline value of liver function test result [20].

Management

Till now there is no specific treatment for COVID 19 infection and no guidelines for management of hepatic injury in COVID-19 patients. The key is in prevention, that is, to help patients to avoid chances of being infected by SARS-CoV-2. High risk populations such as elderly population, patients with end stage liver disease and liver transplant recipients require

close monitoring. There is no need of specific treatment for patients with mild abnormalities in liver function tests, however close monitoring is required. However, when severe liver damage occurs, liver protective drugs have usually been given to such patients in our unit. Avoidance of non-steroidal anti-inflammatory drugs is recommended.

Conclusion

Hepatic involvements in COVID-19 infected patients are common which can be due to direct effect of COVID-19 on hepatocytes and cholangiocytes, adverse effect of antiviral medications used for this infection, immune-mediated inflammation and high levels of positive end expiratory pressure. Pre-existing liver disease has to be excluded. In most of the cases hepatic involvement is self limiting but close monitoring is required.

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