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A Review: Link between Chronic Liver Disease and COVID-19

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ABSTRACT

COVID-19 is characterized by the recently identified SARS-CoV-2 coronavirus, that was originally surfaced at Wuhan, China, but soon expanded globally, posing a huge public health threat. In the same way as with severe acute respiratory is mostly a respiratory illness with symptoms such as cough, dyspnea and fever being the most often reported. Causes of acute syndrome (ARDS), septic shock, and death are all possible outcomes for patients who get pneumonia in the most extreme circumstances. Additionally, liver dysfunction has been noted as a frequent symptom, but its clinical importance is unknown, especially in individuals with underlying chronic liver illness. In the wake of the pandemic surge and subsequent lockdown, numerous medical ailments and illnesses have been impacted. Patient care for those with pre-existing liver illness, hepatocellular carcinoma, and those who have undergone or are scheduled to get a liver transplant has been altered because of the early ambiguity and concern about SARS-CoV-2 cross transmission. COVID-19 is a multisystem illness caused by the SARS-CoV-2 virus strain. Pre-existing liver illness may reappear and produce acute liver damage. There have been several studies looking at the effects of COVID-19 on the liver and how it may be used to treat those who already have liver disease. This article summarizes the findings of such investigations.

Keywords: Severe acute respiratory syndrome (SARS), Middle east respiratory syndrome (MERS-CoV), Coronavirus, Acute respiratory distress syndrome (ARDS), GGT (gamma-glutamyl transferase), SARS-CoV.

INTRODUCTION

Coronavirus is a single-stranded RNA virus that is enclosed. Coronavirae family, Orthocoronavirinae subfamily coronaviruses responsible for SARS and MERS epidemics in 2012 and 2003, respectively. Atypical pneumonia patients in Wuhan, China, were identified with coronavirus disease 2019 (COVID-19), which was produced by the SARS-CoV-2 virus at the end of December.10% - 15% of patients may need

hospitalization and respiratory assistance due to severe and critical symptoms such as hypoxemia (SpO2 less than 95%), shock, ADRS and multiorgan failure. Senior citizens (65 and older) have an increased risk of serious illness and death, particularly if they also have diabetes, chronic liver disease (CLD), cardiovascular disease (CVD), or high blood pressure (Hypertension).

COVID-19 and risk of Hepatic Damage

Numerous investigations have shown varying degrees of increased serum liver biochemistry in COVID-19 individuals. This is mostly manifested by aberrant alanine transferase and aspartate aminotransferase levels, along with modestly raised total bilirubin levels. Indeed, the prevalence of increased ALT and AST was 2.5%-50.0% to 2.5%-61.1% respectively. In the case of tuberculosis, research have shown elevated levels in between 0 to 35.3 percent of patients. Most studies did not detect significant increases in alkaline phosphatase or Gamma glutamyl transferase levels. He investigated 202 individuals with confirmed COVID19, 37.6% of whom had nonalcoholic fatty liver disease, and demonstrated that increased Gamma-glutamyl transferase levels indicate a more serious course of the illness.

It's unclear whether the bad prognostic is linked to the aberrant blood test findings. Indeed, the literature demonstrates inconsistent findings. Guan and colleagues discovered increased AST levels in 112 (18.2 percent) of patients with non-severe illness and 56 (38.4 percent) of the patients with severe sickness in a large cohort of 1099 patients from 552 hospitals. Additionally, the percentage of elevated ALT was higher in severe cases (28.1 percent) than in mild ones (19.8 percent). Huang et al. discovered that intensive care unit (ICU) patients had more risk of liver injury (61.5 percent) than non-ICU patients (25.0 percent).

Other investigations revealed that their findings were contradictory. For example, when mild/moderate patients were compared to severe patients. According to Wu et al., there have been no major changes in liver function tests. Additionally, Wang along with his colleagues examined 339 elderly COVID19 patients and in them they found no discernible difference in alanine transaminase (ALT) levels among survivors and those who died. Severe ALI (acute liver injury) has also only been reported in a small number of people. The majority of current research believe that COVID19-induced liver damage is often transient and modest in severity, with little clinical importance. As a result, it was suggested that careful monitoring be performed and that no particular therapy be administered.

It is unknown if liver harm is induced by the novel corona virus or it is a result of a strong inflammatory response that results in liver damage. SARSCoV2 may infect liver cells directly since the virus's receptor and angiotensin converting enzyme are expressed in liver cells and bile duct cells. ACE-2 expression was detected in 2.6 percent of hepatocytes and 59.7 percent of cholangiocytes in two separate cohorts. SARSCoV2 may directly affect the liver's normal function by binding to ACE2-positive cholangiocytes, according to the theory. Those who have undergone liver biopsies may have liver cell death as a result of infection with the coronavirus or the SARS virus. Infection with SARSCoV2, hypoxia, or drug-induced liver injury might all be responsible for these non-specific changes. This point must be emphasized: none of the samples tested had viral inclusions in the nucleus or intracytoplasmic vesicle.

COVID-19 and Chronic Liver Disease

A possible link in corelating CLD and COVID-19 has yet to be explored, even though infection risk is higher in the case of people suffering from chronic liver disease, specifically autoimmune liver disease and those on immunosuppressive treatment after transplant. Patients with cirrhosis who get viral, bacterial or fungal infection are at risk for developing chronic and acute liver failure. COVID-19 people are more prone to have health problems than the general public. However, no large-scale clinical research has been conducted to determine the complication rate in COVID-19 patients. According to the Covid Cirrhosis Register at the University of North Carolina, it is encouraged that verified cases be submitted to the registry. Patients with major or minor scarring cholangitis, which is characterized by increased expression of the angiotensin converting enzyme (ACE-2) receptor in cholangiocytes, may experience worsening cholestasis as a result of an infection with SARS-CoV-2. Immunosuppressive medications have an effect on both the adaptive and innate immune responses, increasing the probability of developing more severe or complex infections caused by viruses that are often encountered (e.g., influenza). The body's reaction to a coronavirus infection is an important factor in the progression of sickness. In reality,

infections may cause tissue damage and cellular compromise if the innate immune system is out of whack. When an immunocompromised host is infected, it may be shielded from the infectious agent by a lower immune response. Experience with coronavirus epidemics backs up this assertion. At the conclusion of the 2002-2003 epidemic of SARS-CoV-caused SARS, no transplant patients had died, despite the projected dismal prognosis for these patients. The outbreak was defined by an uncommon kind of acute viral pneumonia. The coronavirus MERS-CoV is responsible for the deadly zoonotic disease that was most prevalent in Saudi Arabia in 2018. Researchers found a number of risk variables for poor outcomes such as older age and the existence of comorbid conditions. Immunosuppression, on the other hand, was not thought to be a risk factor. Children's Papa Giovanni XXIII Hospital in Bergamo is one of Europe's leading liver transplant centres which was located at the "red zone" of Italy's epidemic. COVID-19 In spite of the fact that three of the transplant recipients tested positive for SARS, no clinical respiratory disease has been reported in any of the approximately 200 those who have had transplants, including 10 present patients. This suggests that patients on immune suppression are not at greater risk of severe consequences from COVID-19 than the population in general. While the consequences of immune suppression on COVID-19 remain unknown, clinics must communicate their knowledge of immune compromised patients as soon as possible.

CLD has been reported to occur in individuals with COVID-19 at a rate ranging from 0.6% to 37.6% in the literature. It is difficult to assess the influence of coronavirus on the various causes of chronic liver disease since the actual etiology of people who already have liver problems have not been specified in most of these case studies.

Overwhelming inflammatory reactions in liver cirrhosis patients that may lead to acute or chronic liver disease. Indeed, individuals with liver cirrhosis are at greater risk of bacterial infection and influenza complications, including organ failure and the development of secondary infections, as well as mortality. When a conservative approach was taken, including preventative measures for outpatients, hospital staff training, enhanced diagnosis and treatment methodologies, and emergency preparations, none of the 111 decompensated cirrhotics in Wuhan exhibited clinical symptoms consistent with SARS-CoV-2 infection. COVID-19 was detected in 16.8% of 101 cirrhotic patients at five more hospitals that did not use prophylactic measures. Liver cirrhosis along with SARS-CoV-2 infection is rare, but it could likely increase the probability of a severe course of COVID-19 infection. SARS-CoV-2 prevention methods and early warnings of cirrhotic consequences are thus essential.

In a study of 1099 hospitalized and outpatient, patients with laboratory-confirmed COVID-19 by Guan et al, 2.1% had chronic hepatitis B (CHB), an illness that is far more common in China than in Europe. CHB seems to have little effect on the outcome of COVID-19, since just one patient developed severe illness.

Diabetic ketoacidosis, hypertension, and obesity are all linked to a serious course of COVID-19 in patients with steatohepatitis (NASH) and NAFLD. Patients who have SARS-CoV-2 infection with preexisting NAFLD was examined by Cai et al. Six of these patients exhibited severe illness and had poorer outcomes. When it came to viral shedding and development to severe COVID-19, individuals with NAFLD had an increased probability of developing the disease, according to Ji and colleagues. Understanding the role of COVID-19 in NAFLD requires more investigation.

Cancer patients may have a worse prognosis and maybe at a greater risk for developing COVID-19 which further will lead severe respiratory illness. According to many studies, because of the systemic immunosuppressive condition they are in, as well as therapies like chemotherapy and surgery. Patients with cancer were shown to have a greater incidence of COVID-19 and a worse prognosis than those without cancer. Among the 28 COVID-19-infected cancer patients investigated by Zhang and his colleagues in Wuhan, China, two had hepatocellular carcinoma (HCC). Approximately half of the patients experienced serious episodes, and there was a 28.6 percent fatality rate as a result. Even more substantially, anti-cancer treatment during the past 14 days greatly elevated the probability of serious incidents. Patients with HCC have a bad prognosis and should be monitored more closely and admitted earlier if they have COVID-19 co-infection. Additional therapy and assessment for liver transplantation must be carried out in accordance with recommendations, we feel. Nevertheless, some precautions must be taken. These include, among other things, limiting

patients' exposure to medical personnel who use telemedicine and checking for signs such as fever before administering medication. COVID-19 patients should temporarily discontinue locoregional and immune-checkpoint inhibitor therapy. Depending on the circumstances, the choice to maintain or lower the kinase inhibitor dosage must be made.

Patients with autoimmune liver disease may have flares if their immunosuppressive medication is reduced or stopped. SARS-CoV-2 infection is rare in these individuals since there are no documented examples of COVID-19 in autoimmune hepatitis in the literature. Only in the event of severe COVID-19 and under rare conditions (i.e., bacterial/fungal super-infection or Drug-induced lymphopenia) should immunosuppressive medication be reduced, according to the current recommendations of the EASL and ESCMID. Maintaining mild doses of prednisone to prevent adrenal insufficiency is recommended by the World Health Organization (WHO).

Graft loss occurs as a result of rejection when immunosuppression is insufficient, and severe infections may occur when immunosuppression is excessive. The post-transplant treatment is complicated. COVID-19 infection in liver transplant patients has just a little of clinical evidence to support it. In a case documented by Qin et al., a patient had a liver transplant and had COVID-19 infection during the perioperative phase. Gradually the dosage of tacrolimus and glucocorticoids was decreased while maintaining the medication's effectiveness. When the patient was discharged from the hospital, SARS-CoV-2 RT-PCR results were negative. SARS-CoV-2 was found in a 50-year-old man who had just had liver transplantation, according to a report by Bin et al. Patients with severe COVID-19 pneumonia may be helped by temporarily discontinuing immunosuppression and administering a systemic low-dose corticosteroid to the body. COVID-19 was found in a patient who had had a liver transplant for HCC three years before, despite repeated intensive treatment approaches, and Huang and colleagues reported this case. Multiple nosocomial infections and organ failure accelerated the disease's progression from moderate to serious. In an Italian trans-plant facility in Lombardy, Bhoori et al. detailed their experiences. Three of the 111 long-term liver transplant recipients have passed away. However, their immunosuppressive regimen had been steadily reduced, and all three patients died within three weeks of each other. Post-transplant metabolic issues may surpass immunosuppression as a potential cause for severe COVID-19 disease, according to the authors finding. Only in certain cases (e.g., bacterial/fungal superinfection, medication-induced lymphopenia) does EASL-ESCMID recommend reducing immunosuppressive treatment in post-transplant patients with severe COVID-19.

Damage to the liver in children caused by COVID-19

SARS-CoV-2 may infect persons of all ages. Children, regardless of how they became sick, seem to have a better prognosis and a milder course of illness than adults. Children, on the other hand, have a unique immune response system characterized by COVID-19's particular clinical characteristics.

Researchers from three hospitals in Zhejiang identified elevated liver enzymes in just two of 36 pediatric patients (from aged 0 to 16 years) with laboratory-confirmed COVID-19. Researchers from six northern Chinese provinces conducted a study involving 32 children with SARS-CoV2 infection and found that 22.2% of them had elevated transamine levels in their blood. The highest values were recorded in their study, which was published in the New England Journal of Medicine in 2013. Only two of the 10 infants were born who suffered COVID-19 pneumonia and had abnormal liver function tests, according to research by Zhu et al. It is strongly recommended that children with abnormal liver enzymesareto be tested for underlying liver illnesses and not suggest that they have COVID19, since COVID19 in children is associated within a limited and with no increase or minimal increase in AST and ALT levels in children.

COVID vaccinations and their interaction with Chronic Liver Disease

Indians began receiving the COVID-19 vaccines COVISHIELD and COVAXIN on January 16, 2021, as part of the country's COVID-19 immunization campaign. The first recommendation was for a 4-to-6-week gap between the two doses. It was declared by the Indian government on 22 March 2021. For COVISHIELD, the gap has been extended to 6–8 weeks instead of the standard four. As recent studies have shown an improvement in effectiveness at this point in time. There is, however a COVAXIN timetable stays the same as it was before. Antibody

measurement is not suggested at this time titers after immunization. Only a few studies have examined the safety of COVID vaccinations in people with Chronic liver disease (CLD). We don't know yet if COVID vaccinations will produce a sufficient and long-lasting immune response against this virus in patients with CLD who have lower immunogenicity to non-COVID vaccines. The effect of an increase intensity of liver disease on the immunological response to the COVID vaccination is also unknown at this time. While immunizations did not cause significant hepatotoxicity in the studies, the number of patients with liver disease included was inadequate to make conclusions regarding the vaccine's efficacy in this group. Post-marketing monitoring is anticipated to provide more data on patients with CLD. Many studies are now taking place in people with liver disease across the globe.

CONCLUSION

This disease has expanded all over the world and created a number of questions and public health issues. A variety of aberrant liver function tests, most notably triglycerides, are frequently observed as the result of SARS-CoV-2 infection. There appears to be little indication that people with chronic liver disease (CLD) are at risk of contracting SARS-CoV-2. There is also a chance that those who have cirrhosis or NAFLD may be more prone to severe COVID-19 than others. As there are limited healthcare resources, it is suggested to keep a close check on these patients and devise feasible ways for prioritizing their treatment, particularly in the elderly and those with numerous comorbidities, during times of resource constraints. COVID-19 therapy and outcome should be investigated in the future, as should any existing liver-related comorbid conditions and their influence on treatment and result.

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