

PERSPECTIVES

An Insight into Coronavirus Disease 2019 in Patients with Pre-Existing Viral Hepatitis

Mohammad K. Parvez*

Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

The emergence of a novel coronavirus called the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the third highly pathogenic coronavirus after the SARS-CoV-1 and Middle East respiratory syndrome coronavirus (MERS-CoV), at the end of 2019 has continued to cause massive devastation in the pandemic^[1]. The human-to-human direct transmission of SARS-CoV-2, which causes the coronavirus disease 2019 (COVID-19), can be spread through multiple modes, such as oro-/nasopharyngeal droplets, aerosols, and fomites^[1]. SARS-CoV-2 has an incubation period of 2–14 days with flu-like symptoms, which may progress to mild-to-severe pneumonia and death^[1]. Within a year of this crisis, we have a remarkable understanding of its epidemiology, clinical presentations, immune pathobiology, treatments, and preventive strategies. At present, serological or antibody-based diagnostic kits and reverse transcription polymerase chain reaction (RT-PCR) tests are available to identify COVID-19-positive cases. In the absence of specific therapeutics, several repurposed drugs are currently under final stages of clinical trials or approved for emergency use^[2]. Fortunately, of the leading vaccine candidates under final stages of trials, at least ten are now granted approval in some countries.

COVID-19 patients of the old age group or with comorbidity such as pulmonary, cardiac, renal, or hepatic disorders have shown higher mortality rate than those with pneumonia only^[1]. Of the known gastrointestinal manifestations of SARS-CoV-2, liver disease, including viral hepatitis, in a proportion of COVID-19 patients is an important clinical issue that should warrant our attention^[3]. In view of this, it is imperative to look into whether patients with pre-existing viral hepatitis caused by hepatitis B or C viruses (HBV or HCV) are more susceptible to COVID-19 and have a worse prognosis and increased mortality. Another major concern is whether SARS-CoV-2 coinfection enhances the replication of active hepatitis virus or reactivates the quiescent or suppressed virus.

Notwithstanding, the available literature on this issue is based on retrospective or prospective observational studies, small case series, or case studies mainly reported in the Chinese subjects. Chen *et al.* in a retrospective analysis of hospitalized COVID-19 patients have reported about 12.2% of the COVID-19 patients with pre-existing HBV infection, of which ~46.7% progressed to severe outcomes with a mortality rate of ~13.3%^[4]. As reported by Wu *et al.*, 32.86% of COVID-19 patients with HBV coinfection have more severe forms of the disease with a mortality rate of 2.26% when compared to COVID-19 patients alone^[5]. Moreover, in another Chinese report, 30% of hepatitis B comorbid cases progressed to severe form of COVID-19 as evidenced by abnormal alanine aminotransferase (ALT) levels^[6]. Interestingly, three patients had hepatitis B reactivation, which indicated that SARS-CoV-2 may induce HBV replication. In line with this, a case of HBV reactivation in a young adult with COVID-19 has been recently reported in the United Arab Emirates^[7]. In the United States, a case series study has shown that ~0.1%

Received: March 29, 2021

Accepted: April 28, 2021

Published Online: May 10, 2021

***CORRESPONDING AUTHOR**

Mohammad K. Parvez

Email: khalid_parvez@yahoo.com

CITATION

Parvez MK, 2021, An Insight into Coronavirus Disease 2019 in Patients with Pre-Existing Viral Hepatitis, *Gastroenterol Hepatol Lett*, 3(1):17-19.
DOI: [10.18063/ghl.v3i1.266](https://doi.org/10.18063/ghl.v3i1.266)

Copyright: © 2021 Parvez.

This is an Open-Access article distributed under the terms of the Creative Commons Attribution-Non-Commercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

and <0.1% of hospitalized COVID-19 patients had pre-existing HBV and HCV infections, respectively^[8]. Notably, this appears to be the only known case study reporting the coinfection of HCV and SARS-CoV-2^[8]. Therefore, it is recommended to monitor liver function, especially ALT levels, as well as perform quantitative HBV DNA test in such patients during the whole course of disease.

Contrarily, in a Chinese study, about 6% of hospitalized COVID-19 patients with pre-existing hepatitis B did not show any significant differences in liver function parameters compared to those with HBV infection only^[9]. Moreover, in a multicenter analysis by He *et al.*, ~2.63% of COVID-19 patients showed a history of HBV infection but had a lower risk of severe consequences of coinfection^[10]. Furthermore, in a case study by Zhang *et al.*, 17.4% of COVID-19 patients were found to have been chronically infected with HBV and 26% had a history of HBV seropositivity which did not progress to severe illness^[11]. In a very recent analysis by Yu *et al.*, markers of HBV replication did not extensively fluctuate during the acute course of COVID-19^[12]. Therein, HBV did not extend the viral shedding cycle or incubation periods of SARS-CoV-2. Taken together, these data do not imply that chronic hepatitis B has a significant impact on the severity and progression of COVID-19.

Recent clinical analyses have demonstrated that chronic hepatitis B or C infection leads to a suboptimal or absent virus-specific T lymphocytes reactivity. This phenomenon known as “immune exhaustion” is a result of impaired ability of T-cells to efficiently produce the cytokines. In view of SARS-CoV-2 coinfection, it is possible that the T-cell exhaustion may affect their ability to respond to HBV or HCV and reduce the degree of “cytokine storm” as observed in COVID-19 patients, resulting in a less severe outcome. In line with this, Zhao *et al.* have demonstrated a differentially impaired immune response during the course of COVID-19 in patients with pre-existing chronic hepatitis C^[13]. Notably, in cases of hepatitis B patients undergoing immunosuppressive treatment, low risk of HBV reactivation and resolved viremia in severe COVID-19 cases has been observed^[14]. In addition, corticosteroid treatment has been implicated in prolonged clearance of SARS-CoV-2 in about 6.5% of COVID-19 patients with pre-existing hepatitis B^[15]. Nonetheless, the previous studies have shown the reactivation of HBV infection following treatment with immunosuppressive drugs such as tocilizumab or baricitinib^[16] and corticosteroids, emphasizing the cautionary choice of using these agents in COVID-19 patients with chronic hepatitis B. Moreover, treatment with certain hepatotoxic immunosuppressive drugs might also elevate disease severity in such comorbid cases. Notably, in HBV seropositive COVID-19 patients who are not on nucleoside analogs-based antivirals, prophylaxis with tenofovir or entecavir is needed in the case of prolonged corticosteroid or immunosuppressive therapy to decrease the risk of HBV reactivation or liver failure.

Since SARS-CoV-2 can also cause liver dysfunction and hepatitis similar to HBV or HCV, it is of paramount importance to determine whether SARS-CoV-2 coinfection has significant impact on the progression of chronic liver disease. The limited studies on this issue restrict our understanding of epidemiological and clinical characteristics of the comorbidity. While some studies support that comorbidity leads to worse prognosis and high mortality rate, others do not envisage that the comorbid cases are more susceptible to SARS-CoV-2 or more severe form of disease. Furthermore, the increased risk for HBV reactivation as a result of taking COVID-19 drugs as well as the low incidence of HCV coinfection further makes the data inconclusive. Therefore, unique considerations in such cases should involve meticulous selection of antiviral treatment and continuous monitoring of abnormal liver function. Nonetheless, longitudinal studies involving larger cohorts are needed to conclusively demonstrate the impact of COVID-19 on viral hepatitis or *vice versa* that could help elucidate the underlying mechanisms of liver immunopathology and select proper treatment.

References

1. Parvez MK, Jagirdar RM, Purty RS, *et al.*, 2020, COVID-19 Pandemic: Understanding the Emergence, Pathogenesis and Containment. *World Acad Sci J*, 2:18. DOI: 10.3892/wasj.2020.59.
2. Parvez MK, Padhan K, 2021, Current Advances in Novel SARS-CoV-2 Disease Treatment and Intervention Strategies. *Coronaviruses*, 2:1–6. DOI: 10.2174/2666796701999201116125249.
3. Parvez MK, 2020, COVID-19 and Coronaviral Hepatitis: Evidence of Collateral Damage. *Future Virol*, 6:325–9. DOI: 10.2217/fvl-2020-0065.
4. Chen X, Jiang Q, Ma Z, *et al.*, 2020, Clinical Characteristics of Hospitalized Patients with SARS-CoV-2 and Hepatitis B Virus Co-infection. *Virol Sin*, 35:842–5. DOI: 10.1007/s12250-020-00276-5.
5. Wu J, Yu J, Shi X, *et al.*, 2021, Epidemiological and Clinical Characteristics of 70 Cases of Coronavirus Disease and Concomitant Hepatitis B Virus Infection: A Multicentre Descriptive Study. *J Viral Hepat*, 28:80–8. DOI: 10.1111/jvh.13404.
6. Liu J, Wang T, Cai Q, *et al.*, 2020, Longitudinal Changes of Liver Function and Hepatitis B Reactivation in COVID-19 Patients with Pre-existing Chronic Hepatitis B Virus Infection. *Hepatol Res*, 50:1211–21. DOI: 10.1111/hepr.13553.
7. Aldhaleei WA, Alnuaimi A, Bhagavathula AS, 2020, COVID-19 Induced Hepatitis B Virus Reactivation: A Novel Case from the United Arab Emirates. *Cureus*,

- 12:e8645. DOI: 10.7759/cureus.8645.
8. Richardson S, Hirsch JS, Narasimhan M, *et al.*, 2020, Presenting Characteristics, Comorbidities, and Outcomes among 5700 Patients Hospitalized with COVID-19 in the New York city area. *JAMA*, 323:2052–9. DOI: 10.3410/f.737797860.793574198.
 9. Chen L, Huang S, Yang J, *et al.*, 2020, Clinical Characteristics in Patients with SARS-CoV-2/HBV Coinfection. *J Viral Hepat*, 27:1504–7.
 10. He Q, Zhang G, Gu Y, *et al.*, 2020, Clinical Characteristics of COVID-19 Patients with Pre-existing Hepatitis B Virus Infection: A Multicenter Report. *Am J Gastroenterol*, 116:420–1.
 11. Zhang B, Huang W, Zhang S, 2020, Clinical Features and Outcomes of Coronavirus Disease 2019 (COVID-19) Patients with Chronic Hepatitis B Virus Infection. *Clin Gastroenterol Hepatol*, 18:2633–7. DOI: 10.1016/j.cgh.2020.06.011.
 12. Yu R, Tan S, Dan Y, *et al.*, 2021, Effect of SARS-CoV-2 Coinfection was not Apparent on the Dynamics of Chronic Hepatitis B Infection. *Virology*, 553:131–4. DOI: 10.1016/j.virol.2020.11.012.
 13. Zhao J, Liao X, Wang H, *et al.*, 2020, Early Virus Clearance and Delayed Antibody Response in a Case of COVID-19 with a History of Co-infection with HIV-1 and HCV. *Clin Infect*, 72:180–2.
 14. Rodríguez-Tajes S, Miralpeix A, Costa J, *et al.*, 2021, Low Risk of Hepatitis B Reactivation in Patients with Severe COVID-19 who Receive Immunosuppressive Therapy. *J Viral Hepat*, 28:89–94. DOI: 10.1111/jvh.13410.
 15. Zha L, Li S, Pan L, *et al.*, 2020, Corticosteroid Treatment of Patients with Coronavirus Disease (COVID-19). *Med J Australia*, 212:416–20.
 16. Reddy KR, Beavers KL, Hammond SP, *et al.*, 2015. American Gastroenterological Association Institute Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation during Immunosuppressive Drug Therapy. *Gastroenterology*, 148:215–9. DOI: 10.1053/j.gastro.2014.10.039.