

ORIGINAL PAPER

Infectious diseases

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) /Hepatitis B virus (HBV) Co-infected Patients: A case series and review of the literature

Muhammed Bekçibaşı  | Eyüp Arslan

Department of Infectious Diseases and Clinical Microbiology, Bismil State Hospital, Diyarbakır, Turkey

Correspondence

Muhammed Bekçibaşı, Department of Infectious Diseases and Clinical Microbiology, Bismil State Hospital, 21500 Bismil, Diyarbakır, Turkey.
Email: m_bekcibas@hotmail.com

Abstract

Objective: We aimed to determine whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/hepatitis B virus (HBV) coinfection affects liver function and the outcome of the disease.

Methods: One hundred fifty-six laboratories confirmed SARS-CoV-2 positive patients were followed up between 1 July and 31 December 2020 and analysed retrospectively. Continuous variables were compared with the independent samples t-test. Categorical variables were compared using the Pearson's chi-square or Fisher's exact test. A *P* value of less than .05 was considered statistically significant.

Results: The age range of the cohort was from 40 to 78 and 73 (46.8%) of 156 patients were male. There was no significant difference in age and gender distribution between 20 patients (12.8%) with SARS-CoV-2/HBV coinfection and 136 patients without HBV infection (87.2%) (*P* > .05). Liver function tests were higher in the SARS-CoV-2/HBV coinfecting patient group but were not statistically significant. The levels of creatine kinase (CK) were significantly higher in coronavirus disease 2019 (COVID-19) patients without HBV infection compared with the SARS-CoV-2/HBV coinfecting patient group (*P* = .0047). Severe/critical illness was less common in the SARS-CoV-2/HBV coinfecting patient group, and no deaths were observed.

Conclusions: SARS-CoV-2/HBV coinfection did not change the severity and outcome of COVID-19. However, the patients with SARS-CoV-2/HBV coinfection should be closely monitored for liver complications.

1 | INTRODUCTION

Chronic hepatitis B virus (HBV) infection is a global public health problem, which causes significant liver-related morbidity and mortality.¹ HBV and virus coinfections lead to rapid progression of liver disease and an increased rate of liver-related mortality when compared with only HBV infection.²

Abnormal liver functions have been observed to be caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).³ Mild and moderate liver damage is common in patients with coronavirus disease 2019 (COVID-19).^{4,5} In addition, liver damage is common

in cases with severe COVID-19 compared with mild cases.⁶ SARS-CoV-2/HBV coinfections are inevitable in the areas where HBV infection is endemically observed.

Although there are data in the literature indicating that SARS-CoV-2/HBV coinfections worsen liver function and the course of the disease in the cases with COVID-19, there is limited information on the significance of this finding and reactivation status.^{7,8} Turkey is the one of the countries that has been seriously affected by the COVID-19 pandemic, and 3 357 988 current confirmed cases and 31 713 deaths have been reported (1 April 2021). Southeastern Anatolia, where our study was planned, is the region with the highest

HBsAg seropositivity rate (7.3%) in the country.⁹ We aimed to evaluate whether SARS-CoV-2/HBV coinfection affects liver function and the outcome of the disease.

2 | METHODS

2.1 | Study design and participants

This is a retrospective and single-centre study. The data of 410 patients who were followed up between 1 July and 31 December 2020 at the Bismil State Hospital with the diagnosis of COVID-19 were analysed retrospectively. One hundred seventy patients were excluded due to without serum HBV test results during hospitalisation, and 84 patients were excluded due to the negativity of SARS-CoV-2 PCR tests. One hundred fifty-six laboratories confirmed SARS-CoV-2 positive patients were included in the study. Clinical diagnosis, treatment and discharge criteria were determined according to the Ministry of Health of the Republic of Turkey COVID-19 reference guide.¹⁰ Chronic HBV infection was defined as a laboratory confirmed group of the patients known to be HBsAg positive for more than 6 months. Eleven patients were carriers of inactive hepatitis B, and three patients were receiving oral antiviral therapy. Because the HBV-DNA status was not known, the disease stage of six patients could not be determined. The patients with coinfection with hepatitis delta virus, hepatitis C virus, human immunodeficiency virus (HIV) and/or chronic liver diseases such as primary biliary cirrhosis, liver cirrhosis, autoimmune hepatitis and alcoholic hepatitis were excluded from the study. The stories, clinical findings, laboratory tests, radiological outcomes, microbiological tests and clinical course of the patients were analysed retrospectively.

Severe/critical illness was defined by the presence of any one of the following:

1. respiratory distress with respiratory rate > 30 breaths per minute,
2. severe respiratory distress (dyspnoea, use of extra respiratory muscles) or
3. mean oxygen saturation (SpO₂) < 90% on room air (arterial blood oxygen (PaO₂)/oxygen concentration (FiO₂) < 300 in oxygen receiving patient).¹⁰

2.2 | Ethical approval

First, the study was approved by the Republic of Turkey Ministry of Health, the Scientific Research Platform (Approval No: 2020-11-30T14_47_55). Afterwards, our study protocol was reviewed and approved by the Clinical Research Ethics Committee of Health Sciences University Gazi Yaşargil Training and Research Hospital. (Date: 26/03/2021, Issue No. 726).

What's known

- The majority of studies show that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/hepatitis B virus (HBV) coinfection does not exacerbate liver damage. However, whether it affects the severity and outcome of coronavirus disease 2019 (COVID-19) has been controversial.

What's new

- SARS-CoV-2/HBV coinfection does not change the severity and the outcome of COVID-19.
- Clinicians should closely monitor liver function of the patients with SARS-CoV-2/HBV coinfection.

2.3 | Statistical analysis

Continuous variables were expressed as the median (interquartile range [IQR]). Categorical variables were shown as numbers and percentages. Continuous variables were compared with the independent samples t-test. Categorical variables were compared using the Pearson's chi-square or Fisher's exact test. All calculations were performed by using SPSS for Windows, version 18.0 software (SPSS Inc Chicago, IL, USA). A *P* value of less than .05 was considered statistically significant.

3 | RESULTS

3.1 | Demographic and epidemiologic characteristics

The age range of the cohort was from 40 to 78, and 73 (46.8%) of 156 patients were male. There was no significant difference in age and gender distribution between 20 patients (12.8%) with SARS-CoV-2/HBV coinfection and 136 patients without HBV infection (87.2%) (*P* > .05).

3.2 | Clinical outcomes and laboratory abnormalities

There was no statistically significant difference in the level of liver function tests, such as alkaline phosphatase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), alkaline phosphatase (ALP), gamma-glutamyltransferase (GGT) and albumin, and haematological parameters. However, creatine kinase (CK) levels were observed to be significantly higher in COVID-19 patients without HBV infection compared with the SARS-CoV-2/HBV coinfecting patient group (*P* = .0047). SARS-CoV-2 infection led to severe/critical illness in 1 (5%) case, and no death was observed in

the HBV coinfection patient group. However, in the patient group without HBV infection, severe/critical illness was observed in 33 (24.3%) cases and death in 13 (9.6%) patients (Table 1).

4 | DISCUSSION

Because chronic HBV infection can progress with reactivations, the guidelines recommend that the patients with SARS-CoV-2/HBV coinfection should continue their treatment without disruption and carefully monitored for reactivation.¹¹ The majority of studies show that SARS-CoV-2/HBV coinfection does not exacerbate liver damage. However, whether it affects the severity and outcome of COVID-19 disease has been controversial.¹² In our study, liver function tests of SARS-CoV-2/HBV coinfection patients were observed

to be slightly higher compared with the control group at the time of admission and during hospitalisation. Nevertheless, coinfection did not have a negative effect on the course of COVID-19 disease. However, elevated liver enzymes or laboratory abnormalities indicating hepatic exacerbation were not detected in the follow-up of SARS-CoV-2/HBV coinfection patients.

Serum CK levels are the most sensitive indicator of muscle damage.¹³ It is common for COVID-19 patients to show signs of dehydration. In the case of severe disease, hypovolaemia may contribute to renal failure and thus a slight increase in CK levels.¹⁴ In our study, serum CK levels in COVID-19 patients without HBV infection were significantly higher compared with the SARS-CoV-2/HBV coinfection patient group. In a recently published COVID-19 case series, it was concluded that high CK levels may be an early warning indicator for severe disease, consistent with our study.¹⁵ Serum CK

TABLE 1 Clinical characteristics in patients with SARS-CoV-2/HBV coinfection

Characteristics	SARS-CoV-2 + HBV (n = 20)	SARS-CoV-2 (n = 136)	P value
Age, median (IQR) (years)	65.5 (52.2-70.5)	64.0 (57.0-71.0)	.868
Sex, male (%)	9 (45.0%)	64 (47.1%)	.863
Laboratory tests, median (IQR)			
White blood cells ($\times 10^9/L$)	6.53 (4.69-8.53)	6.30 (5.25-8.31)	.725
Neutrophil ($\times 10^9/L$)	4.15 (3.18-6.32)	4.60 (3.40-5.90)	.802
Lymphocyte ($\times 10^9/L$)	1.41 (0.75-1.80)	4.60 (3.40-5.90)	.784
Neutrophil to lymphocyte ratio	3.98 (1.91-5.73)	3.46 (2.44-5.66)	.364
Platelet ($\times 10^9/L$)	160.0 (119.0-265.5)	191.0 (149.2-229.5)	.805
CRP (mg/L)	66.0 (29.0-147.1)	83.4 (39.0-122.0)	.907
Serum creatinine (mg/dL)	0.91 (0.76-1.13)	0.96 (0.80-1.21)	.387
ALT (U/L)	35.0 (21.2-58.2)	26.5 (19.0-36.0)	.154
Peak ALT (U/L)	53.5 (35.5-75.5)	46.0 (28.0-76.0)	.662
AST (U/L)	47.5 (32.2-69.0)	36.0 (28.0-54.0)	.709
Peak AST (U/L)	56.0 (36.2-71.0)	52.0 (34.0-76.0)	.587
TBIL (mg/dL)	0.44 (0.34-0.75)	0.44 (0.31-0.61)	.570
Peak TBIL (mg/dL)	0.64 (0.48-0.96)	0.59 (0.45-0.84)	.661
ALP (U/L)	58.0 (36.0-66.0)	59.0 (46.0-72.2)	.099
GGT (U/L)	22.0 (15.2-58.2)	35.0 (23.0-68.0)	.885
LDH (U/L)	329.0 (255.2-364.7)	291.0 (224.0-363.0)	.956
Albumin (g/L)	36.1 (33.9-41.1)	35.9 (33.2-37.6)	.234
Creatine kinase (U/L)	112.9 (57.4-177.2)	123.3 (74.7-248.0)	.005
D-Dimer (ng/mL)	741 (587-1400)	842 (578-1292)	.625
Ferritin ($\mu g/L$)	335.7 (177.8-496.6)	295.6 (166.1-514.1)	.625
Outcome			
Hospital stays, median (IQR) (days)	6.5 (5.0-8.5)	7.0 (5.0-12.0)	.894
Severe/critically ill, n (%)	1 (5%)	33 (24.3%)	.078
Death, n (%)	0	13 (9.6%)	.221

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, c-reactive protein; GGT, gamma-glutamyltransferase; HBV, hepatitis B virus; IQR, interquartile range; LDH, lactate dehydrogenase; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TBIL, total bilirubin.

TABLE 2 Characteristics of liver injury and clinical outcomes in patients with SARS-CoV-2/HBV coinfection

Reference	Total cases	HBV cases, n (%)	ALT (U/L)	AST (U/L)	TBIL (μ mol/L)	ALP (U/L)	GGT (U/L)	Severe/critical ill, n (%)	Death, n (%)	Note
Lin et al ⁷	133	17 (12.8)	33.0	31.2	15.10	75.00	36.00	NA	0	Inactive HBV carriers with SARS-CoV-2 coinfection are at risk of greater liver injury
Yu et al ⁸	67	7 (10.4)	NA	NA	NA	NA	NA	2 (28.6)	0	SARS-CoV-2 would not cause of HBV reactivation
Li et al ²¹	342	7 (2)	31.0	31.0	12.7	NA	NA	0	0	The abnormalities of liver function are not uncommon
Chen et al ²²	326	20 (6.1)	28.00	27.5	10.55	60	23.50	2 (10.0)	0	No evidence showed coexistence of HBV infection increases the liver injury in COVID-19 patients
Wu et al ²³	620	70 (11.3)	50	40	NA	NA	NA	23 (32.8)	0	Higher rate of liver injury, coagulation disorders and severe/critical tendency and increased susceptibility
Zou et al ²⁴	105	105 (100)	23	28	8.3	62	24	56 (53.3)	7 (6.67)	Liver injury in patients with SARS-CoV-2/HBV coinfection was associated with severity and poor prognosis of disease
Liu et al ²⁵	347	21 (6.4)	30.40	34.15	12.60	NA	28.50	1 (5.0)	0	Three patients had HBV reactivation. The median levels of liver biochemistries were no significant difference between two groups
Chen et al ²⁹	123	15 (12.2)	25.0	28.0	13.2	76.0	20.0	7 (46.7)	2 (13.3)	The level of TBIL was higher in patients with SARS-CoV-2/HBV coinfection ($P < .05$)
Zhang et al ³⁰	23	23 (100)	38.6	31.6	24.9	73	32.3	5 (21.7)	0	26% of HBV carriers with COVID-19 had abnormal liver function test results at admission
Yip et al ³¹	5639	353 ^b	28	32	8.62 ^a	NA	NA	NA	8 (2.3)	Current and past HBV infections were not associated with more liver injury and mortality in COVID-19
Current study	156	20 (12.8)	35.0	47.5	7.52 ^a	58.0	22.0	1 (5.0)	0	Elevated liver enzymes or laboratory abnormalities indicating hepatic exacerbation were not detected

Note: The data in the laboratory results are expressed as the median.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; HBV, hepatitis B virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TBIL, total bilirubin.

^aData were converted from mg/dL to μ mol/L.

^bCurrent HBV infection.

^cPast HBV infection.

concentrations were found significantly higher in nonsurvivors compared with recovered patients in the cohort studies of COVID-19.¹⁶ The absence of death in the SARS-CoV-2/HBV coinfecting patient group in our study and the lower rate of serious/critical patients may explain this difference in CK levels.

Although liver damage is common in COVID-19, severe liver damage is rarely observed. Liver function gradually returns to normal as clinical findings improve in the majority of patients.¹² In a study comparing COVID-19 patients with and without liver cirrhosis, no significant difference was observed in terms of liver biochemical abnormality.¹⁷ Liver function tests are closely related to the severity and prognosis of COVID-19.¹⁸ Although severe liver dysfunction has been described in patients with severe COVID-19, the influence of other factors such as sepsis-associated cholestasis, ischaemic hepatitis from hypoxaemia and hypotension and drug-induced liver injury should not be ruled out.¹⁹ In a recent retrospective cohort study, ALT/AST elevation was commonly observed in COVID-19 patients and independently associated with adverse clinical outcomes. Use of ribavirin, interferon beta and/or lopinavir-ritonavir alone or in combination with corticosteroids has been independently associated with ALT/AST elevation.²⁰ However, it is recommended that off-label COVID-19 treatments be used with caution and close monitoring in patients with abnormal liver function. COVID-19 patients who are planned to use systemic high-dose corticosteroids or tocilizumab should be screened for HBV. Antiviral prophylaxis with nucleoside analogues is recommended in all of these patient groups with HBsAg positivity.¹⁹

In some retrospective studies evaluating patients with SARS-CoV-2/HBV coinfection, it was shown that liver damage in SARS-CoV-2/HBV coinfecting patients progressed with varying degrees of high function tests (AST, ALT, TBIL, ALP, GGT, etc), which is in accordance with our study. However, this difference was not found to be statistically significant when compared with the group of COVID-19 patients who were not infected with HBV.^{21,22} In a study involving a larger patient group, however, the levels of AST, ALT and APTT were significantly higher in the SARS-CoV-2/HBV coinfecting group compared with the control group.²³ In another study in which 105 SARS-CoV-2/HBV coinfecting patients were examined without forming a control group, liver damage was developed in 14 (13.3%) patients; four (28.6%) of these patients developed acute-on-chronic liver failure that resulted in death.²⁴ In the study conducted by Liu et al,²⁵ HBV reactivation was observed in three (15%) of 20 SARS-CoV-2/HBV coinfecting patients. The characteristics of liver injury in patients with SARS-CoV-2/HBV coinfection are summarised in Table 2.

It has been shown in meta-analysis studies that the prevalence of chronic liver disease in COVID-19 patients is as low as 3.0%.²⁶ However, COVID-19 disease progression is significantly higher in patients with chronic liver disease compared with those without chronic liver disease, and acute-on-chronic liver failure may also occur in patients with compensated chronic liver disease.²⁷ In most retrospective analyses comparing SARS-CoV-2/HBV coinfecting patients with the patients who has SARS-CoV-2 infection alone, no significant difference was shown between these two groups in terms of hospital stay, critical illness and prognosis.^{7,21,22,28} Also in

our study, SARS-CoV-2/HBV coinfection was not associated with the severity of COVID-19 or poor prognosis. However, some studies also reported contradictory results. In the study conducted by Wu et al,²³ the rate of severe/critical patients in 70 SARS-CoV-2/HBV coinfecting patients was found to be significantly higher than the group without HBV (32.9% vs. 15.3%). However, all patients with SARS-CoV-2/HBV coinfecting were discharged, and there was no significant difference between the two groups in terms of hospital stay and mortality. In another study conducted with 15 SARS-CoV-2/HBV coinfecting patients, it was reported that almost half of the HBV patients had a severe COVID-19 disease and had higher mortality rates.²⁹ The comparison of COVID-19 disease severity and clinical outcomes in SARS-CoV-2/HBV coinfecting patients are summarised in Table 2.

There are some limitations in our study. First, our study was limited to a single-centre, retrospective study, and we had a small number of patients. In addition, there may be selection bias in our study because we could only reach HBV serology results in half of the patients hospitalised due to COVID-19. Second, serum HBV-DNA levels of SARS-CoV-2/HBV coinfecting patients could not be followed during the disease, and we were not able to determine whether there is HBV reactivation. Finally, the patients were not grouped according to chronic HBV infection stages due to the lack of HBeAg and HBV-DNA levels of some patients.

As a result, SARS-CoV-2/HBV coinfection does not change the severity and the outcome of COVID-19 disease. Clinicians should closely monitor liver function of the patients with SARS-CoV-2/HBV coinfection. These findings need confirmation in future studies with a larger number of patient groups, including chronic hepatitis B patients, according to infection stages.

DISCLOSURES

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

First, the study was approved by the Republic of Turkey Ministry of Health, the Scientific Research Platform (Approval No: 2020-11-30T14_47_55). Afterwards, our study protocol was reviewed and approved by the Clinical Research Ethics Committee of Health Sciences University Gazi Yaşargil Training and Research Hospital. (Date: 26/03/2021, Issue No. 726).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Muhammed Bekçibaşı  <https://orcid.org/0000-0003-0230-9127>

REFERENCES

1. Seto WK, Lo YR, Pawlotsky JM, Yuen MF. Chronic hepatitis B virus infection. *Lancet*. 2018;392:2313-2324.

2. Singh KP, Crane M, Audsley J, Avihingsanon A, Sasadeusz J, Lewin SR. HIV-hepatitis B virus coinfection: epidemiology, pathogenesis, and treatment. *AIDS*. 2017;31:2035-2052.
3. Liao FL, Peng DH, Chen W, et al. Evaluation of serum hepatic enzyme activities in different COVID-19 phenotypes. *J Med Virol*. 2021 Apr;93:2365-2373.
4. Wang J, Zhu L, Xue L, et al. Risk factors of liver injury in patients with coronavirus disease 2019 in Jiangsu, China: a retrospective, multi-center study. *J Med Virol*. 2021 Jun;93:3305-3311.
5. Yu X, He W, Wang L, et al. Profiles of liver function abnormalities in elderly patients with Coronavirus Disease 2019. *Int J Clin Pract*. 2021 Mar;75:e13632.
6. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol*. 2020 May;5:428-430.
7. Lin Y, Yuan J, Long Q, et al. Patients with SARS-CoV-2 and HBV co-infection are at risk of greater liver injury. *Genes Dis*. 2020 Nov 18. <https://doi.org/10.1016/j.gendis.2020.11.005>. Online ahead of print.
8. Yu R, Tan S, Dan Y, et al. Effect of SARS-CoV-2 coinfection was not apparent on the dynamics of chronic hepatitis B infection. *Virology*. 2021;553:131-134.
9. Tozun N, Ozdogan O, Cakaloglu Y, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. *Clin Microbiol Infect*. 2015 Nov;21:1020-1026.
10. Republic of Turkey Ministry of Health. <https://covid19.saglik.gov.tr/TR-66301/covid-19-rehberi.html>. Accessed September 3, 2020.
11. Reddy KR. SARS-CoV-2 and the liver: considerations in hepatitis B and hepatitis C infections. *Clin Liver Dis (Hoboken)*. 2020 May;15:191-194.
12. Xiang TD, Zheng X. Interaction between hepatitis B virus and SARS-CoV-2 infections. *World J Gastroenterol*. 2021;27:782-793.
13. Khan FY. Rhabdomyolysis: a review of the literature. *Neth J Med*. 2009 Oct;67:272-283.
14. Rivas-Garcia S, Bernal J, Bachiller-Corral J. Rhabdomyolysis as the main manifestation of coronavirus disease 2019. *Rheumatology (Oxford)*. 2020;59:2174-2176.
15. Wang Y, Hu Z, Luo J, et al. Clinical characteristics and abnormal parameters evolution in patients with novel coronavirus infection: a case series of 272 cases in Guangzhou. *Disaster Med Public Health Prep*. 2021 May 18:1-26. <https://doi.org/10.1017/dmp.2021.149>. Online ahead of print.
16. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. *Crit Rev Clin Lab Sci*. 2020 Sep;57:389-399.
17. An Y, Ma Z, Guo X, et al. Comparison of liver biochemical abnormality between COVID-19 patients with liver cirrhosis versus COVID-19 alone and liver cirrhosis alone A STROBE observational study. *Medicine*. 2021;100:e25497.
18. Wu Y, Li H, Guo X, et al. Incidence, risk factors, and prognosis of abnormal liver biochemical tests in COVID-19 patients: a systematic review and meta-analysis. *Hepatol Int*. 2020 Sep;14:621-637.
19. Wong GL, Wong VW, Thompson A, et al. Management of patients with liver derangement during the COVID-19 pandemic: an Asia-Pacific position statement. *Lancet Gastroenterol Hepatol*. 2020 Aug;5:776-787.
20. Yip TC, Lui GC, Wong VW, et al. Liver injury is independently associated with adverse clinical outcomes in patients with COVID-19. *Gut*. 2021 Apr;70:733-742.
21. Li Y, Li C, Wang J, et al. A case series of COVID-19 patients with chronic hepatitis B virus infection. *J Med Virol*. 2020 Nov;92:2785-2791.
22. Chen L, Huang S, Yang J, et al. Clinical characteristics in patients with SARS-CoV-2/HBV co-infection. *J Viral Hepat*. 2020 Dec;27:1504-1507.
23. Wu J, Yu J, Shi X, et al. Epidemiological and clinical characteristics of 70 cases of coronavirus disease and concomitant hepatitis B virus infection: a multicentre descriptive study. *J Viral Hepat*. 2021 Jan;28:80-88.
24. Zou X, Fang M, Li S, et al. Characteristics of liver function in patients with SARS-CoV-2 and chronic HBV coinfection. *Clin Gastroenterol Hepatol*. 2021 Mar;19:597-603.
25. Liu J, Wang T, Cai Q, et al. Longitudinal changes of liver function and hepatitis B reactivation in COVID-19 patients with pre-existing chronic hepatitis B virus infection. *Hepatol Res*. 2020 Nov;50:1211-1221.
26. Mantovani A, Beatrice G, Dalbeni A. Coronavirus disease 2019 and prevalence of chronic liver disease: a meta-analysis. *Liver Int*. 2020 Jun;40:1316-1320.
27. Ji D, Zhang D, Yang T, et al. Effect of COVID-19 on patients with compensated chronic liver diseases. *Hepatol Int*. 2020 Sep;14:701-710.
28. He Q, Zhang G, Gu Y, et al. Clinical characteristics of COVID-19 patients with pre-existing hepatitis B virus infection: a multicenter report. *Am J Gastroenterol*. 2021;116:420-421.
29. Chen X, Jiang Q, Ma Z, et al. Clinical Characteristics of hospitalized patients with SARS-CoV-2 and hepatitis B virus co-infection. *Viral Sin*. 2020 Dec;35:842-845.
30. Zhang B, Huang W, Zhang S. Clinical features and outcomes of coronavirus disease 2019 (COVID-19) patients with chronic hepatitis B virus infection. *Clin Gastroenterol Hepatol*. 2020 Oct;18:2633-2637.
31. Yip TC, Wong VW, Lui GC, et al. Current and past infections of hepatitis B virus do not increase mortality in patients with COVID-19. *Hepatology*. 2021 May 7. <https://doi.org/10.1002/hep.31890>. Online ahead of print.

How to cite this article: Bekçibaşı M, Arslan E. Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) /Hepatitis B virus (HBV) Co-infected Patients: A case series and review of the literature. *Int J Clin Pract*. 2021;75:e14412. <https://doi.org/10.1111/ijcp.14412>