Research Article

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Examination of COVID-19 and Vaccines in Patients with Chronic Hepatitis B

Kronik Hepatit B Hastalarında COVID-19 Hastalığının ve Aşılarının İncelenmesi

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ABSTRACT

Objectives: Coronavirus disease-2019 (COVID-19) has affected more than 16 million people around the worldwide so far. Simultaneously, it has made the follow-up of chronic diseases difficult. We examined the course of co-infection with COVID-19 and chronic hepatitis B in this article and to reveal the vaccination status of these patients.

Materials and Methods: Patients requiring oxygen therapy were classified as severe. Also, patients' demographic and vaccination information was scanned using the hospital data system.

Results: A total of 100 patients with chronic hepatitis B were included. There were 53 patients with polymerase chain reaction-confirmed COVID-19. Since these patients needed oxygen, 9 were admitted to clinics and 4 to the intensive care unit. Of 13 patients with severe disease, 5 had Sinovac, 2 had Pfizer-BioNTech, 1 had mixed vaccine, and 5 were unvaccinated. Severe disease was significantly lower in the Pfizer-BioNTech vaccinated group. Similarly, the longest interval between vaccine and COVID-19 disease was found in this group.

Conclusion: The effect of COVID-19 and hepatitis B co-infection on the severity of COVID-19 and the long-term effects of vaccine-induced immunity in these patients will be guided by epidemiological studies. According to our study, it can be said that the type of vaccine is one of the factors affecting the severity of the disease. Although the number of patients is small, severe acute respiratory syndrome-coronavirus-2 and hepatitis B co-infection do not affect the more severe outcomes.

Keywords: Chronic HBV infection, COVID-19, COVID-19 vaccines, HBV

ÖZ

Amaç: Koronavirüs hastalığı-2019 (COVID-19) şimdiye kadar dünya çapında 16 milyondan fazla insanı etkilemiştir. Aynı zamanda COVID-19 pandemisi sürecinde kronik hastalıkların takibi zorlaşmıştır. Bu yazımızda COVID-19 ve kronik hepatit B ko-enfeksiyonunun seyrini ve bu hastaların aşılanma durumlarını irdelemeyi amaçladık.

Gereç ve Yöntemler: Kronik hepatit B'si mevcut olup COVID-19 geçiren hastalardan oksijen tedavisi gerektiren hastalar şiddetli olarak sınıflandırıldı. Ayrıca hastane veri sistemi kullanılarak hastaların demografik ve aşı bilgileri tarandı.

Bulgular: Kronik hepatit B'li toplam 100 hasta dahil edildi. Polimeraz zincir reaksiyonu ile doğrulanmış COVID-19 olan 53 hasta vardı. Bu hastaların oksijene ihtiyacı olduğu için 9'u kliniklere, 4'ü de yoğun bakıma yatırıldı. Şiddetli hastalığı olan 13 hastanın 5'inde Sinovac, 2'sinde Pfizer-BioNTech, 1'inde karma aşı vardı ve 5'inde aşı yoktu. Şiddetli hastalık, Pfizer-BioNTech ile aşılanmış grupta önemli ölçüde daha düşüktü. Benzer şekilde aşı ile aşı sonrası COVID-19 geçirme arasındaki en uzun aralık da bu grupta bulundu.

Sonuç: COVID-19 ve hepatit B ko-enfeksiyonunun COVID-19'un ciddiyeti üzerindeki etkisi ve bu hastalarda aşı kaynaklı bağışıklığın uzun vadeli etkileri epidemiyolojik çalışmalara ışık tutacaktır. Çalışmamıza göre hastalığın şiddetini etkileyen faktörlerin birinin aşı türü olduğu söylenebilir. Hasta sayısı az olsa da COVID-19 ve hepatit B ko-enfeksiyonu kliniğin daha ciddi olmasına yol açmamıştır.

Anahtar Kelimeler: Kronik HBV enfeksiyonu, COVID-19, COVID-19 aşıları, HBV

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Introduction

A coronavirus strain known as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has spread throughout the worldwide and emerged as a significant cause of morbidity and mortality. The outbreak of coronavirus disease-2019 (COVID-19) has been declared a pandemic on March 11, 2020 (1). On the other hand, with approximately 300 million people chronically infected worldwide, the hepatitis B virus (HBV) is a serious threat to public health (2). There have been problems in the follow-up of chronic diseases due to the quarantine of countries, the overcapacity of hospitals with COVID-19. Regarding chronic hepatitis B, Turkey is a middle -endemic region, because of that co-infection with COVID-19 and chronic hepatitis B is also common (3).

COVID-19 does not only affect the respiratory system. The cause of hepatic manifestations is unclear at this stage. Cholangiocytes and hepatocytes have entry cell receptors for SARS-CoV-2 known as angiotensin-converting enzyme 2 receptors (4). According to a recent study, asymptomatic liver function tests are elevated in 50% of patients hospitalized for COVID-19 (5). Possible causes of liver impairment are the direct cytopathic effect of the virus, ischemic liver injury due to hypoxia developing during the disease, and immune-mediated liver injury (6). Additionally, hepatitis B reactivation and drug hepatotoxicity may develop because of the drugs used for treating COVID-19. The management of SARS-CoV-2 and hepatitis B co-infection is challenging because of them (7).

There are many studies have evaluating the severity of COVID-19 in patients with chronic hepatitis B patients. Several studies have shown that COVID-19 is not severe in patients with chronic hepatitis B (7). However, the mortality of COVID-19 is higher in patients with advanced liver disease. Also, patients with advanced liver disease have a poor immune system, and as a result, they are a vulnerable population that should prioritize COVID-19 vaccines. There are inactivated coronavirus vaccine (Sinovac) and mRNA vaccine (Phizer-BionTech) in our country. In this study, we determined the vaccination preference and vaccination rates of chronic hepatitis B patients, as well as to examine the effect of co-infection on the course of the COVID-19.

Materials and Methods

Subjects

One hundred people were included in the study who had chronic hepatitis B. The diagnosis of chronic hepatitis B was made according to the European Association for the Study of the Liver 2020 hepatitis B guideline. Patients' demographics and vaccination information were manually collected from electronic health records.

Ethical Approval

The study protocol was approved by the Ethics Committee of Kocaeli University (approval number GOKAEK-2022/10.10). Since the study was retrospective, informed consent was not obtained from the patients.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 20.0. The values $p<0.05$ were considered statistically significant. Data are presented as mean and percentages. The Kolmogorov-Smirnov test was used to assess the normality of the distribution of the investigated parameters. All parameters in our study were not distributed normally. Differences were tested by Mann-Whitney U test and Wilcoxon test.

Results

One-hundred patients with chronic hepatitis B were included in our study. Among these patients, males (n=56, 56%) predominated over females (n=44, 44%). The mean age of the individuals was calculated as 44 years (range: 12-78). All patients were taken antiviral treatment. Elevated aspartate aminotransferase and alanine aminotransferase were recorded in patients on 7/18 and 2/18, respectively, during COVID-19. The demographics and medical findings of the individuals are shown in Table 1.

Of all chronic hepatitis B patients, 50 were vaccinated with mRNA vaccine (Pfizer-BioNTech, 50%), and 22 with inactivated coronavirus vaccine (Sinovac, 22%). While 11 people (11%) had mixed immunotherapy, 17 (17%) were unvaccinated. In the Pfizer-BioNTech vaccinated group, 15 individuals had COVID-19 after vaccination. In the Sinovac vaccinated group, there were 7 patients after vaccination. Four people who vaccinated with mixed immunotherapy had also COVID-19 disease after vaccines. The time between the vaccination and polymerase chain reaction (PCR) positivity is shown in Table 2. The mean day count between the last vaccine date and SARS-CoV-2 PCR positivity date 127 (Pfizer-BioNTech group), 64 (Sinovac group), and 91 (mixed vaccine group) days, respectively. Those vaccinated with Pfizer-BioNTech were statistically significantly less infected with COVID-19 after vaccination ($p<0.05$).

There were 53 patients with PCR-confirmed COVID-19. Among them, 9 patients were admitted to clinics and 4 to the intensive care unit due to hypoxia. Of 13 patients with severe disease, 5 had Sinovac, 2 had Pfizer-BioNTech, one had mixed, and 5 were unvaccinated. When the 2 patients who died were examined, it was found that 1 of them was unvaccinated and the other was inactivated coronavirus vaccine. Forty patients (74%) had mild disease. On the other hand, among patients with severe diseases, 10 of them had negative current HBV-DNA values.

Table 1. Demographic and medical findings of the patients

Characteristic	Patient
Age, mean	44
Gender, M/F, n	56/44
SARS-CoV-2 PCR positivity, n	53
Mild disease, n (%)	40 (75)
Severe disease, n (%)	13 (25)
Pfizer-BioNTech vaccinated, n (%)	43 (54)
Sinovac vaccinated, n (%)	17 (21)
No vaccinated, n (%)	13 (16)
Mixed vaccinated, n (%)	7 (9)

M: Male F: Female, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, PCR: Polymerase chain reaction

Table 2. The time between the vaccination and PCR positivity

	SARS-CoV-2 PCR positivity
Pfizer-BioNTech, day (range)	127 (29-333)
Sinovac, day (range)	64 (7-149)
Mixed, day (range)	91 (51-129)

SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, PCR: Polymerase chain reaction

Discussion

Data on the prevalence of COVID-19 and chronic hepatitis B confection are limited. In a meta-analysis conducted in China where chronic hepatitis B is hyperendemic, approximately 25,000 COVID-19 patients were examined, and the prevalence of co-infection was found to be 3% (8). Recent reports showed that about 2-11% of patients with COVID-19 had underlying chronic liver disease (9). Hepatic involvement in COVID-19 is multi-factorial. Many reasons such as the direct cytopathic effect of the virus, uncontrolled immune reaction, drug-related injury, sepsis, and hypoxia can cause damage in the spectrum from asymptomatic liver enzyme abnormalities to fatal acute liver injury. During this pandemic, hepatic dysfunction has been seen in 14-53% of patients (10).

In our study, although the number of patients is small, SARS-CoV-2 and hepatitis B co-infection do not affect the severe outcomes. Similar findings were found by Lv et al. (11), who discovered that COVID-19 patients with HBV infection had a lower risk of serious events such as intensive care unit admission or death. However, Jothimani et al. (10) said that COVID-19 may cause worsening of underlying chronic liver disease, leading to hepatic decompensation and acute-on-chronic liver failure, with higher mortality. In a study from China, where hepatitis B is highly endemic, COVID-19 is related to more severe outcomes in patients with chronic liver disease (8).

The administration of vaccines against SARS-CoV-2 will help control the pandemic, especially to populations at high risk of developing severe COVID-19. Although it varied according to the variants, the efficacy of CoronaVac and Pfizer-BioNTech vaccines was found to be 60% and 90%, respectively (12).

Study Limitations

Main limitations are the small number of our patients and the inability to do subgroup analyses.

Conclusion

The effect of COVID-19 and hepatitis B co-infection on the severity of COVID-19 and the long-term effects of vaccine-induced immunity in these patients will be guided by epidemiological studies. In our study post-vaccine COVID-19 disease and severity of disease are less in Pfizer-BioNTech vaccinated group. Additionally, co-infection with SARS-CoV-2 and hepatitis B has no impact on the more serious outcomes.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Kocaeli University (approval number GOKAEK-2022/10.10).

Informed Consent: Since the study was retrospective, informed consent was not obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.M.K., Concept: S.A., Design: S.A., Data Collection and Processing: M.T.D., Analysis or Interpretation: S.A., Literature Search: M.T.D., Writing: M.T.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020;91:157-160.
2. Xia Y, Liang TJ. Development of Direct-acting Antiviral and Host-targeting Agents for Treatment of Hepatitis B Virus Infection. Gastroenterology. 2019;156:311-324.
3. Tozun N, Ozdogan O, Cakaloglu Y, Idilman R, Karasu Z, Akarca U, Kaymakoglu S, Ergonul O. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect. 2015;21:1020-1026.
4. Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. Liver Int. 2020;40:998-1004.
5. Clark R, Waters B, Stanfill AG. Elevated liver function tests in COVID-19: Causes, clinical evidence, and potential treatments. Nurse Pract. 2021;46:21-26.
6. Reddy KR. SARS-CoV-2 and the Liver: Considerations in Hepatitis B and Hepatitis C Infections. Clin Liver Dis (Hoboken). 2020;15:191-194.
7. Alqahtani SA, Buti M. COVID-19 and hepatitis B infection. Antivir Ther. 2020;25:389-397.
8. Kovalic AJ, Satapathy SK, Thuluvath PJ. Prevalence of chronic liver disease in patients with COVID-19 and their clinical outcomes: a systematic review and meta-analysis. Hepatol Int. 2020;14:612-620.
9. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5:428-430.
10. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. J Hepatol. 2020;73:1231-1240.
11. Lv XH, Yang JL, Deng K. COVID-19 Patients with Hepatitis B Virus Infection. Am J Gastroenterol. 2021;116:1357-1358.
12. Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clin Microbiol Infect. 2022;28:202-221.