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The impacts of the COVID-19 pandemic on patients with viral hepatitis B infection: follow-up, compliance with antiviral treatment, and vaccine preferences

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Abstract. – OBJECTIVE: Elimination programs and interventions for patients with viral hepatitis B (HBV) have been disrupted during the COVID-19 pandemic. This study aimed to evaluate the effects of the COVID-19 pandemic on patients with HBV infection in terms of COVID-19 vaccine preferences, follow-up visits, and antiviral treatment compliance.

PATIENTS AND METHODS: In this retrospective single-center cross-sectional study, 129 patients with viral hepatitis B infection were evaluated. The patients were surveyed at the time of admission. A special form was created for patients with viral hepatitis B infection, and the form contained information about the patients at admission to collect the study data.

RESULTS: A total of 129 participants were included in the study. Of the participants, 49.6% were males and the median age was 50 years. In total, 73 (56.6%) patients had their follow-up visits disrupted because of the COVID-19 pandemic. No newly diagnosed case of HBV infection was detected. Among the 129 patients, 46 had inactive hepatitis B, and 83 had chronic hepatitis B infection and were receiving antiviral treatment. None of the patients had trouble reaching antiviral treatments during the COVID-19 pandemic. A liver biopsy was recommended for 8 patients. Half of these 8 patients did not have follow-up visits during the COVID-19 pandemic. Most of the patients (123/129, 95.3%) received the COVID-19 vaccine and the most frequent vaccine that was used was the Pfizer-BioNTech (n: 92, 71.3%) vaccine. Serious side effects of the COVID-19 vaccines were not detected. Mild side effects were found in 41.9% (13/31) of the patients. The COVID antibody level was found to be statistically and significantly higher in the patients who received the Pfizer-BioNTech vaccine than in those that received the CoronoVac vaccine.

CONCLUSIONS: It was reported that elimination programs and interventions for HBV infection decreased or stopped because of the COVID-19 pandemic. In the present study, no newly diagnosed case of HBV infection was detected. Most of the patients had their follow-up visits disrupted. There were no patients who could not receive antiviral treatment, the vaccination rate of the patients was high, and the vaccines were well tolerated.

Key Words:
COVID-19, Hepatitis B virus, Pandemics, COVID-19 vaccine, Antibodies.

Introduction

The coronavirus disease 2019 (COVID-19) caused a pandemic, and in this process, healthcare services were disrupted in many countries. Additionally, several hepatitis B virus (HBV) infections are among the chronic diseases in which follow-up was delayed during the pandemic[1,2]. To prevent the progression of HBV infection to cirrhosis and liver cancer, treatment must be started when regular follow-up of patients is necessary.

Studies[3,4] have reported that SARS-CoV-2 affects not only the lungs but also other organs, such as the heart, kidney, and liver. Vaccination is an effective intervention in preventing SARS-CoV-2 infection, severe symptoms, and death. Recently,

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there have been several studies on the safety and immunogenicity of COVID-19 vaccination in patients with liver disease[5-7].

Since HBV is an important public health care issue worldwide, this study aimed to evaluate the effects of the COVID-19 pandemic on patients with HBV infection in terms of COVID-19 vaccine preferences, follow-up visits, and antiviral treatment compliance.

Patients and Methods

Study Design and Participants

In this retrospective single-center cross-sectional study, the impacts of the COVID-19 pandemic were evaluated in 129 patients with HBV infection who were older than 18 years and admitted to the Ankara City Hospital Infectious Diseases Outpatient Clinic between 1 and 31 March 2022. The patients were surveyed at the time of admission.

Collection of Data

A special form was created for patients with viral hepatitis B infection, and the form contained information about the patients at admission to collect the study data. The parameters included in this form were age, sex, comorbid diseases, COVID-19 vaccine history (vaccine name, dose), vaccine side effects, follow-up visits to outpatient clinics, antiviral treatment, and disruption of the treatment during the COVID-19 pandemic. The forms also included the following laboratory and radiological tests: serum biochemistry [alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, albumin, urea, creatinine, glomerular filtration rate (GFR), Hepatitis B surface antigen (HBsAg), anti-Hbe, hepatitis B e antigen (HBeAg), HBV-DNA polymerase chain reaction (PCR), Covid antibody and liver ultrasonography]. All the laboratory records in the patient files were completed from the hospital database.

Statistical Analysis

The data obtained were analyzed using SPSS software for Windows, version 24 for Windows (IBM Corp., Armonk, NY, USA). Quantitative variables were presented with the mean, standard deviation, and median values, while continuous data were presented with the median, minimum, and maximum values because of skewed distributions. Categorical data were described with frequencies and percentages. Relationships between categorical variables were evaluated using Fisher's exact test. Mann-Whitney or Kruskal-Wallis tests were applied to compare continuous variables. Two-tailed p-values <0.05 were defined as statistically significant.

Results

A total of 129 participants were included in the study. Of the participants, 49.6% were male. The median age of the participants was 50 years, and 50.4% were over 50 years of age.

Among the 129 patients, 46 had inactive hepatitis B, and 83 had chronic hepatitis B infection and were receiving antiviral treatment. No newly diagnosed HBV infection was detected in the patients. Most of the chronic viral hepatitis B patients received tenofovir disoproxil fumarate or entecavir treatment. Elevated ALT was detected in 4.7% (6/126) of the patients. These patients were not followed-up during the COVID-19 pandemic, and most (83.3%, 5/6) were receiving antiviral treatment. Other laboratory parameters are given in Table I.

Most of the patients were negative for HBV-DNA (76/125, 60.8%). The median HBV-DNA level was 689 IU/mL (min-max: 32-396,079,855). Among 49 HBV-DNA-positive patients, 13 had chronic hepatitis B and received antiviral treatment, and 36 had inactive hepatitis B infections. Liver biopsy was recommended for 8 patients with inactive hepatitis B because their HBV-DNA levels were >2,000 IU/mL. Half of these 8 patients did not attend follow-up visits. Liver ultrasonography was performed in 97 of 129 patients. Liver ultrasonography results were normal in 34 patients, and the abnormal liver ultrasound findings in 63 patients are shown in Table I.

In total, 73 (56.6%) patients had their follow-up visits disrupted because of the COVID-19 pandemic. Most of the patients with inactive hepatitis B (31/46, 67.4%) did not come to the follow-up visits. Among the 83 patients with chronic hepatitis B who received antiviral treatment, 42 (50.6%) were not admitted for follow-up visits. All patients received antiviral treatment. However, treatment interruption was seen in only six patients with chronic viral hepatitis B. HBV-DNA was found to be elevated in 5 of 6 patients who stated that they disrupted their treatment. According to follow-up status, the demographic, laboratory, and liver ultrasonography results of the patients are compared

in Table II. No statistically significant differences were found between the groups (p>0.05).

It was found that 95.3% (123/129) of the patients received the COVID-19 vaccine, and the Pfizer-BioNTech (n: 92, 71.3%) vaccine was the most preferred. Among the patients who received the Pfizer-BioNTech vaccine, 44 had 2 doses, and 48 had 3 doses. A total of 31 (24%) patients received the CoronaVac vaccine, 20 received 2 doses, 7 received 3 doses, and 4 received 4 doses. Twenty patients preferred different types of vaccines. Most of these patients (90%, 18/20) preferred Pfizer-BioNTech after CoronaVac. One patient preferred CoronaVac and Turcovac after 2 doses of Pfizer-BioNTech, and 1 patient preferred CoronaVac after Pfizer-BioNTech.

When the vaccine side effects were questioned, no serious side effects were detected in any of the patients. Mild side effects were detected in 41.9% (13/31) of the patients. Most of the patients (12/13, 92.3%) with mild side effects took the Pfizer-BioNTech vaccine. Headache was detected as a side effect in only 1 of the patients who received the CoronaVac vaccine (Table III).

Table I. Characteristic features of patients with viral hepatitis B infection.

Total Participants	
Gender (n, %)	129
Male	64 (49.6)
Female	65 (50.4)
Age, years, (n, %)	
18-30	8 (6.2)
31-40	21 (16.3)
41-50	35 (27.1)
>50	65 (50.4)
Treatment (n, %)	
Tenofovir disoproxil fumarate	38 (45.7)
Entecavir	31 (37.3)
Tenofovir-alafenamide	13 (15.6)
Combined tenofovir-alafenamide with entecavir	1 (1.2)
Laboratory	
HbsAg positive (n, %)	129 (100)
HbeAg positive (n, %)	11 (8.5)
Anti Hbe positive (n, %)	106 (82.1)
HBV-DNA IU/mL (median, min-max)	689 (32-396,079,855)
ALT U/L (median, min-max)	23 (7-125)
AST U/L (median, min-max)	23 (11-102)
Total bilirubin g/L (median, min-max)	0.6 (01-23)
Albumin mg/dL (median, min-max)	45 (32-51)
Urea mg/dL (median, min-max)	30 (13-69)
Creatinine mg/dL (median, min-max)	0.8 (0.4-1.6)
GFR ml/dk/1.73 m^2	98 (9-129)
Ultrasonography of liver finding (n, %)	
Normal	34
Grade 1 steatosis	16
Grade 2 steatosis	12
Chronic liver disease	1
Fine granular	9
Diffuse heterogenic granular	2
Hepatomegaly	12
Hemangioma	4
Parenchyma minimal heterogenic	7
Total	63

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), glomerular filtration rate (GFR), Hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg).

Table II. Comparison of demographic, laboratory, and liver ultrasonography results according to their follow-up visits during COVID-19 pandemic.

Follow-up visits	Not follow-up visits		*p*
Chronic Hepatitis B	41 (73.2)	42 (57.5)	0.065
Inactive Hepatitis B	15 (26.8)	31 (42.5)	
Age	47.79±10.44	49.56±11.77	0.374
Age group			
18-30	4 (7.1)	4 (5.5)	0.872
31-40	10 (17.9)	11 (15.1)	
41-50	16 (28.6)	19 (26)	
50 and above	26 (46.4)	39 (53.4)	
Gender			
Female	27 (48.2)	38 (52.1)	0.665
Male	29 (51.8)	35 (47.9)	
Comorbidity			
Yes	4 (66.7)	9 (69.2)	1.000
No	2 (33.3)	4 (30.8)	
Disruption in treatment			
Yes	1 (2.4)	5 (11.9)	0.202
No	40 (97.6)	37 (88.1)	
Liver ultrasonography			
Normal	14 (25)	20 (27.4)	0.759
Anormal	42 (75)	53 (72.6)	
Laboratory			
Urea mg/dL	29.41±7.73	31.98±10.09	0.159
Cr mg/dL	0.78±0.17	0.82±0.2	0.267
ALT U/L	23.58±10.18	29.01±18.01	0.058
AST U/L	22.58±6.76	24.94±12.16	0.328
HBV-DNA			
Positive	17 (31.5)	32 (45.1)	0.123
Negative	37 (68.5)	39 (54.9)	
HBV-DNA	9,015,010.96±55,067,537.53	939.38±3,129.56	0.212

Alanine aminotransferase (ALT), aspartate aminotransferase (AST).

COVID antibodies were tested in 69 patients. Fifty had Pfizer-BioNTech, 16 had CoronaVac, and 3 were unvaccinated. The median COVID antibody level of the patients was 91 (min-max: 0-150). When the distribution of the clinical characteristics according to the vaccine type was examined, statistically significant differences were detected between the groups in terms of age, sex, and COVID-19 antibody levels ($p<0.05$). It was determined that the average age of those who preferred the Pfizer-BioNTech vaccine was lower than that of those who preferred the CoronaVac vaccine, and women preferred it more. The COVID antibody level was statistically and significantly higher in those who received Pfizer-BioNTech vaccine. There was no statistically significant difference between the groups in terms of other variables ($p>0.05$) (Table III).

Discussion

The World Health Organization[8] developed a plan in 2016 to eradicate viral hepatitis by 2030. As a result of a survey[9] conducted in the clinical centers of 44 countries (32 European and 12 non-European), it was reported that elimination programs and interventions (screening, diagnosis, and treatment) for hepatitis B virus infection decreased or stopped because of the COVID-19 pandemic. In the present study, 56.6% of the HBV-infected patients were never followed up

during the pandemic. In the present study, no newly diagnosed case of HBV infection was detected. In 2 similar studies[10,11], a significant decrease was found in hepatitis B applications by 49.45% and 71-95%. In the current study, liver biopsy (because HBV-DNA >2,000 IU/mL) was recommended for 8 (17.4%) of the 46 patients with inactive hepatitis B infection, half of whom were not followed up during the COVID-19 pandemic. In a similar study[11] that was conducted in our country, it was reported that there was a 63.63% decrease in liver biopsies during the COVID-19 pandemic. Not having a liver biopsy also leads to the inability to identify patients who need to be treated and results in delays in treatment.

In a survey that was conducted by the World Hepatitis Alliance (WHA)[12], it was determined that 52% of the patients with viral hepatitis could not reach treatment during the COVID-19 pandemic. One of the measures taken within the scope of COVID-19 infection control measures in our country was that people who regularly took drugs because of chronic diseases could obtain their drugs directly from the pharmacy without going to a healthcare institution[13]. With this precaution, access to treatment became easy. All patients who received antiviral treatment in this study could receive treatment during the COVID-19 pandemic period. However, 6 (7.2%) of the 83 patients who received antiviral treatment said that they interrupted their treatment, and 5 of these 6 patients were positive for HBV-DNA. Elevated ALT was detected in 4.7% (6/126) of the patients, not all of these patients had followed-up visits, and most (83.3%, 5/6) were receiving antiviral treatment. Even if the patient obtained the treatment, it was important to use telemedicine visits for patient follow-up during the pandemic period so that the treatment is not disrupted. We must accept that the pandemic is a part of our lives and be prepared for new pandemics in the future.

In Turkey, three types of COVID-19 vaccines, CoronaVac (an inactivated SARS-CoV-2 vaccine of Sinovac, China), Pfizer-BioNTech, and Turcovac, were put into use and are still in use. Turcovac, on the other hand, is an inactivated virus vaccine developed by the Presidency of Turkish Health Institutes (TUSEB), and it started to be used in Turkey at the end of 2021 after obtaining emergency use approval[14]. In the present study, it was found that the patients more frequently preferred the Pfizer-BioNTech (71.3%) vaccine. It

Table III. The distribution of the clinical characteristics according to vaccine types.

	Pfizer-BioNTech	CoronaVac	*p*
Age	47.04±9.44	55.48±13.65	0.000
Age group			
18-30	5 (5.4)	2 (6.5)	0.023
31-40	17 (18.5)	2 (6.5)	
41-50	29 (31.5)	4 (12.9)	
50 and above	41 (44.6)	23 (74.2)	
Gender			
Female	41 (44.6)	22 (71)	0.011
Male	51 (55.4)	9 (29)	
COVID status			
Past COVID history	36 (39.1)	14 (45.2)	0.554
No past COVID history	56 (60.9)	17 (54.8)	
Covid antibody	106.2±53.72	72.19±54.19	0.015
Side effects of the vaccine			
Yes	12 (52.2)	1 (12.5)	0.095
No	11 (47.8)	7 (87.5)	
Fever	3 (25)	0 (0)	1.000
Weakness	6 (50)	0 (0)	1.000
Myalgia	4 (33.3)	0 (0)	1.000
Brachialgia	3 (25)	0 (0)	1.000
Arthralgia	3 (25)	0 (0)	1.000
Menstrual irregularity	2 (28.6)	0 (0)	1.000
Headache	1 (8.3)	1 (100)	0.154

was determined that younger people and women preferred the Pfizer-BioNTech vaccine more than the CoronaVac. The first CoronaVac vaccine became available in our country, and it was first used in patients over the age of 65. For this reason, it was considered that the higher average age of those who preferred CoronaVac was related to this. It was also determined that most of the patients (58%) who had the first dose of CoronaVac preferred the next dose of Pfizer-BioNTech. It was reported in a similar study[15] that the majority of the participants (81.4%) had taken the vaccine developed by Pfizer-BioNTech. Most of the world population (68.4%) had received at least one dose of the COVID-19 vaccine as of October 21, 2022. However, only 23.3% of the population in the developing world received at least one dose[16]. A total of 95.3% of the patients that were included in the present study had at least 2 doses of vaccine, 47.8% of the patients who had the Pfizer-BioNTech vaccine had 2 doses, and 52.1% had 3 doses. The vaccination rate was found to be high in patients with viral hepatitis B infection.

In the present study, the inactivated CoronaVac vaccine was well tolerated, and no serious side effects were observed. Headache was determined in only one (12.5%) of the 31 patients who received the CoronaVac vaccine. According to the results of phase 3 clinical studies[17] on the CoronaVac vaccine, in which more than 10,000 participants between the ages of 18-59 participated in Turkey, the effectiveness against COVID-19 was found to be 83.5%, and 90% of the participants had a strong neutralizing antibody response in a subgroup of 1,400 participants. It was also reported[17] that no serious side effects were detected in the study, most of the side effects (90%) were mild, and the most common side effects were reported to be fatigue, injection site pain, and muscle pain. A study[18] investigated the safety and immunogenicity of inactivated COVID-19 vaccines in patients with viral hepatitis B infection. It was well tolerated and safe for patients with viral hepatitis B infection, and the antibody rate after vaccination was similar to that of healthy individuals. The most common side effects were local pain (5.8%, 21/362) and fatigue (4.7%, 17/362)[18].

Although no serious side effects were observed in the patients who received Pfizer-BioNTech in the present study, side effects were detected in 52.2% (12/23) of the patients. These side effects were fatigue, myalgia, arm pain, joint pain, fever, and menstrual irregularity. It was also reported[15,19] in other studies that individuals with the COVID-19 vaccine had changes in their menstrual cycles. However, it is still not possible to predict all the side effects of the Pfizer-BioNTech COVID-19 vaccine because it is a new vaccine[20]. Vaccines protect against death because of communicable diseases and save the lives of at least 2.5 million people every year[21]. Focusing on the benefits rather than the side effects will be a life-saving approach. In our study, none of the patients reported a serious side effect after vaccination. With increased vaccination and disease transmission rates, herd immunity develops, resulting in a significant decrease in mortality and hospitalization rates because of SARS-CoV-2.

In the present study, the COVID antibody level was found to be higher in patients who received Pfizer-BioNTech than in those who received CoronoVac. It can be considered that the decrease in neutralizing activity may occur earlier in inactivated vaccines because the initial production level of neutralizing antibodies is much lower than that of mRNA vaccines[22]. Out of 230 enrolled patients, all responded excellently to the mRNA Pfizer (BNT162b) vaccine[23]. Previous studies[7] that were conducted in patients with viral hepatitis B infection also reported that an inactivated COVID-19 vaccine seemed to be safe with good immunogenicity in patients with nonalcoholic fatty liver disease (NAFLD). However, it was also found that there was a normal humoral response and a weak T-cell response in 53 cirrhosis patients[24].

Study Limitations

A number of limitations of this study should be noted. First, the size of the sample was small. Second, the study included only patients with viral hepatitis B infection who were followed up in one single center. Further studies with large multi-center samples are needed.

Conclusions

Elimination programs and interventions for hepatitis B virus infection decreased or stopped because of the COVID-19 pandemic. In the present study, most HBV-infected patients who visited our clinic were never followed up during the pandemic. In the present study, no newly diagnosed case of HBV infection was detected. Liver biopsy was recommended for half of the patients who were not followed up during the COVID-19 pandemic. No liver biopsy also leads to the in-

ability to identify patients who need to be treated and delays the treatment. The patients could receive antiviral treatment during the COVID-19 pandemic period. The vaccination rates were found to be high in patients with viral hepatitis B. It was found that the patients most frequently preferred the Pfizer-BioNTech vaccine. No serious side effects were detected in the vaccines. It was observed that the inactivated vaccine was well tolerated.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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Ethics Approval
The study protocol and procedures of informed consent were approved by Ankara City Hospital Ethical Committee (approval number: E1-22-2817, date: 17/08/2022).

Authors' Contribution
Burcu Ozdemir contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article; validation and final approval of the version of the article to be published. Adalet Altunsoy, Rahmet Guner and Esragul Akinci contributed to the conception and design of the study, reviewing and editing the article; supervision; validation and final approval of the version of the article to be published.

Informed Consent
Informed consent was obtained from all subjects involved in the study.

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Availability of Data and Materials
The datasets generated and/or analyzed during the current study are available from the corresponding author upon request.

Informed Consent
Informed consent was waived due to the retrospective design of the study.

References

1) Karimi-Sari H, Rezaee-Zavareh MS. COVID-19 and viral hepatitis elimination programs: A rewestepping backward? Liver International 2020; 40: 2042.
2) Gupta N, Desalegn H, Ocama P, Lacombe K, Njouom R, Afihene M, Cunha L, Spearman CW, Sonderup MW, Kateera F. Converging pandemics: implications of COVID-19 for the viral hepatitis response in sub-Saharan Africa. Lancet Gastroenterol Hepatol 2020; 5: 634-636.
3) Pesaresi M, Pirani F, Tagliabracci A, Valsecchi M, Procopio AD, Busardò FP, Graciotti L. SARS-CoV-2 identification in lungs, heart and kidney specimens by transmission and scanning electron microscopy. Eur Rev Med Pharmacol Sci 2020; 24: 5186-5188.
4) M. Pirisi, C. Rigamonti, S. D'Alfonso, M. Nebuloni, D. Fanni, C. Gerosa, G. Orrù, E. Venanzi Rullo, P. Pavone, G. Faa, L. Saba, R. Boldorini. Liver infection and COVID-19: the electron microscopy proof and revision of the literature. Eur Rev Med Pharmacol Sci 2021; 25: 2146-2151.
5) Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, Goepfert PA, Truyers C, Fennema H, Spiessens B, Offergeld K, Scheper G, Taylor KL, Robb ML, Treanor J, Barouch DH, Stoddard J, Ryser MF, Marovich MA, Neuzil KM, Corey L, Cauwenberghs N, Tanner T, Hardt K, Ruiz-Guiñazú J, Le Gars M, Schuitemaker H, Van Hoof J, Struyf F, Douoguih M; ENSEMBLE Study Group. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. N Engl J Med 2021; 384: 2187-2201.
6) Thompson MG, Burgess JL, Naleway AL, Tyner H, Yoon SK, Meece J, Olsho LEW, Caban-Martinez AJ, Fowlkes AL, Lutrick K, Groom HC, Dunnigan K, Odean MJ, Hegmann K, Stefanski E, Edwards LJ, Schaefer-Solle N, Grant L, Ellingson K, Kuntz JL, Zunie T, Thiese MS, Ivacic L, Wesley MG, Mayo Lamberte J, Sun X, Smith ME, Phillips AL, Groover KD, Yoo YM, Gerald J, Brown RT, Herring MK, Joseph G, Beitel S, Morrill TC, Mak J, Rivers P, Poe BP, Lynch B, Zhou Y, Zhang J, Kelleher A, Li Y, Dickerson M, Hanson E, Guenther K, Tong S, Bateman A, Reisdorf E, Barnes J, Azziz-Baumgartner E, Hunt DR, Arvay ML, Kutty P, Fry AM, Gaglani M. Prevention and attenuation of Covid-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med 2021; 385: 320-329.
7) Wang J, Hou Z, Liu J, Gu Y, Wu Y, Chen Z, Ji J, Diao S, Qiu Y, Zou S, Zhang A, Zhang N, Wang F, Li X, Wang Y, Liu X, Lv C, Chen S, Liu D, Ji X, Liu C, Ren T, Sun J, Zhao Z, Wu F, Li F, Wang R,

Yan Y, Zhang S, Ge G, Shao J, Yang S, Liu C, Huang Y, Xu D, Li X, Ai J, He Q, Zheng MH, Zhang L, Xie Q, Rockey DC, Fallowfield JA, Zhang W, Qi X. Safety and immunogenicity of COVID-19 vaccination in patients with non-alcoholic fatty liver disease (CHESS 2101): a multicenter study. J Hepatol 2021; 75: 439-441.

8) World Health Organization (WHO). Global health sector strategy on viral hepatitis 2016-2021. Available at: https:// apps.who.int /iris/ handle/10665/246177, (accessed October 31, 2022).

9) Kondili LA, Buti M, Riveiro-Barciela M. Impact of the COVID-19 pandemic on hepatitis B and C elimination: An EASL survey. JHEP Reports 2022; 4: 100531.

10) Lemoine M, Kim JU, Ndow G, Bah S, Forrest K, Rwegasha J, Bouyou M, Napon D, Somda S, Sawadogo A, Sombie R, Shimakawa Y. Effect of the COVID-19 pandemic on viral hepatitis services in sub-Saharan Africa. Lancet Gastroenterol Hepatol 2020; 5: 966-967.

11) İskender G. Effect of the COVID-19 Pandemic on chronic viral hepatitis Services. The Journal of Kesit Academy 2020; 6: 685-693.

12) Wingrove C, Ferrier L, James C, Wang S. The impact of COVID-19 on hepatitis elimination. Lancet Gastroenterol Hepatol 2020; 5: 792-794.

13) COVID-19 Tedbiri: Kronik Hastalıklarda Sona Eren Sağlık Raproları Geçerli: Aile, Çalışma ve Sosyal Hizmetler Bakanlığı; 2020. Available at: https:// www.ailevecalisma .gov.tr/tr-tr/haberler/bakan-selcuk-kronik-hastaligi-bulunan-sigortalilarimizin-saglik-raporlari-ve-receteleri-ikinci-bir-duyuraya-kadar-gecerli-sayilacak/.

14) Türkiye Sağlık Enstitüleri Başkanlığı (TÜSEB). Available at: https://www.tuseb.gov.tr/ (accessed on 15 July 2022).

15) Akarsu GD. Determining the Health Problems Experienced by Young Adults in Turkey, Who Received the COVID-19 Vaccine. Vaccines 2022; 10: 1526.

16) Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Giattino C, Hasell J, Macdonald B, Dattani S, Beltekian D, Ortiz-Ospina E, Roser M. "Coronavirus Pandemic (COVID-19)". Published online at Our World In Data.org. Retrieved from: 'https:// ourworldindata.org/coronavirus' [Online Resource] (cited October 21, 2022). Available at: https://ourworldindata.org/covid-vaccinations.

17) Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, Köse Ş, Erdinç FŞ, Akalın EH, Tabak ÖF, Pullukçu H, Batum Ö, Şimşek Yavuz S, Turhan Ö, Yıldırmak MT, Köksal İ, Taşova Y, Korten V, Yılmaz G, Çelen MK, Altın S, Çelik İ, Bayındır Y, Karaoğlan İ, Yılmaz A, Özkul A, Gür H, Unal S; CoronaVac Study Group. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet 2021; 398: 213-222.

18) He T, Zhou Y, Xu P, Ling N, Chen M, Huang T, Zhang B, Yang Z, Ao L, Li H, Chen Z, Zhang D, Shi X, Lei Y, Wang Z, Zeng W, Hu P, Lan Y, Zhou Z, Kang J, Huang Y, Shi T, Pan Q, Zhu Q, Ran X, Zhang Y, Song R, Xiang D, Xiao S, Zhang G, Shen W, Peng M, Cai D, Ren H. Safety and antibody response to inactivated COVID-19 vaccine in patients with chronic hepatitis B virus infection. Liver Int 2022; 42: 1287-1296.

19) Male V. Menstrual changes after COVID-19 vaccination. BMJ 2021; 374: n2211.

20) Walsh EE, Frenck RW Jr, Falsey AR, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Mulligan MJ, Bailey R, Swanson KA, Li P, Koury K, Kalina W, Cooper D, Fontes-Garfias C, Shi PY, Türeci Ö, Tompkins KR, Lyke KE, Raabe V, Dormitzer PR, Jansen KU, Şahin U, Gruber WC. Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates. N Engl J Med 2020; 383: 2439-2450.

21) World Health Organization. Global Vaccine Action Plan; World Health Organization: Geneva, Switzerland, 2013. Available at: https://www.who.int/teams/immunization-vaccines-and-biologicals/strategies/global-vaccine-action-plan.

22) Anderson M, Stec M, Rewane A, Landay A, Cloherty G, Moy J. SARS-CoV-2 antibody responses in infection-naive or previously infected individuals after 1 and 2 doses of the BNT162b2 vaccine. JAMA Netw Open 2021; 4: e2119741.

23) Inchingolo AD, Malcangi G, Ceci S, Patano A, Corriero A, Azzollini D, Marinelli G, Coloccia G, Piras F, Barile G, Settanni V, Mancini A, De Leonardis N, Garofoli G, Palmieri G, Isacco CG, Rapone B, Jones M, Bordea IR, Tartaglia GM, Scarano A, Lorusso F, Macchia L, Larocca AMV, Tafuri S, Migliore G, Brienza N, Dipalma G, Inchingolo F. Antispike Immunoglobulin-G (IgG) Titer Response of SARS-CoV-2 mRNA-Vaccine (BNT162b2): A Monitoring Study on Healthcare Workers. Biomedicines 2022; 10: 2402.

24) Ruether DF, Schaub GM, Duengelhoef PM, Haag F, Brehm TT, Fathi A, Wehmeyer M, Jahnke-Triankowski J, Mayer L, Hoffmann A, Fischer L, Addo MM, Lütgehetmann M, Lohse AW, Schulze Zur Wiesch J, Sterneck M. SARS-CoV2-specific humoral and T-cell immune response after second vaccination in liver cirrhosis and transplant patients. Clin Gastroenterol Hepatol 2021; 20: 162-172.e9.