OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2024;9(1):21-26 *Online Türk Sağlık Bilimleri Dergisi 2024;9(1):21-26*

Prevalence of HBV, HCV, HIV and Effect on Clinical Course in COVID-19 Patients

COVID-19 Hastalarında HBV, HCV, HIV Prevalansı ve Klinik Seyre Etkisi

[1]Dilek YEKENKURUL, [1]Ali Rıza GÜRBÜZ, [1]Nevin İNCE, [2]Emel ÇALIŞKAN

[1]Düzce University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Düzce, Türkiye
[2]Düzce University Faculty of Medicine, Department of Medical Microbiology, Düzce, Türkiye

Dilek Yekenkurul: https://orcid.org/0000-0002-4456-7485
Ali Rıza Gürbüz: https://orcid.org/0000-0002-0106-9582
Nevin İnce: https://orcid.org/0000-0002-0129-4536
Emel Çalışkan: https://orcid.org/0000-0002-9451-7865

ABSTRACT

Objective: COVID-19 may progress with hepatic exacerbation in viral infections such as hepatitis B. It was aimed to investigate the prevalence and clinical course of HBV, HCV, and HIV in COVID-19 patients.

Materials and Methods: Patients who were hospitalized due to COVID-19 and requested hepatitis and HIV serological tests were included in the study. Demographic data, HBV, HCV, HIV serologies, ALT, and AST results of patients were recorded.

Results: Out of 226 patients included in the study, 118 (52%) were male, 108(48%) were female, and the average age was 63.47±16.09 years. HBsAg positivity was found in six (3%), isolated Anti-HBcIgG positivity in six (3%), and Anti-HCV positivity in seven (3%) patients. Anti-HIV positivity wasn't detected. In two HBsAg-positive patients, HBV-DNA was negative, and in four, it was positive. In anti-HCV-positive patients, HCV-RNA was negative. Although not statistically significant, the median age of HBsAg-positive patients was lower, and the median ALT and AST were higher. However, the length of hospital stay, transfer rate to the intensive care unit, and discharge status were similar in all groups.

Conclusions: Liver enzymes were high in the HBsAg-positive patient group. Therefore, it was considered that COVID-19 may cause hepatic exacerbation in HBsAg-positive patients.

Keywords: COVID-19, HBV, HCV, HIV

ÖZ

Amaç: COVID-19, hepatit B gibi viral enfeksiyonlarda hepatik alevlenmeyle seyredebilir. COVID-19 hastalarında HBV, HCV, HIV prevalansının ve klinik seyrinin araştırılması amaçlanmıştır.

Materyal ve Metot: COVID-19 nedeniyle yatarak takip edilen, hepatit ve HIV serolojik tetkikleri istenen hastalar çalışmaya dahil edildi. Hastaların demografik verileri; HBV, HCV, HIV serolojileri; ALT, AST sonuçları kaydedildi.

Bulgular: Çalışmaya alınan 226 hastanın 118'i (%52) erkek, 108'i (%48) kadındı, yaş ortalaması 63,47±16,09 yıldı. HBsAg pozitifliği altı (%3), izole Anti-HBcIgG pozitifliği altı (%3), Anti-HCV pozitifliği yedi (%3) hastada mevcuttu. Anti-HIV pozitifliği saptanmadı. HBsAg pozitif hastaların ikisinde HBV-DNA negatif, dördünde pozitifti. Anti-HCV pozitif hastalarda HCV-RNA negatifti. İstatistiksel olarak anlamlı olmasa da HBsAg pozitif hastaların yaş ortancası daha düşük; ALT, AST ortancası daha yüksekti. Ancak yatış süresi ile yoğun bakıma devir ve taburcu olma durumu tüm gruplarda benzerdi.

Sonuç: HBsAg pozitif hasta grubunda karaciğer enzimlerinin yüksek olduğu saptanmıştır. Bu nedenle COVID-19'un HBsAg pozitif hastalarda hepatik alevlenmeye sebep olabileceği düşünülmüştür.

Anahtar Kelimeler: COVID-19, HBV, HCV, HIV

Sorumlu Yazar / Corresponding Author:
Dilek Yekenkurul
Düzce University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology. Konuralp Campus, 81620, Düzce/Türkiye
Tel: +90 5059255425
E-mail: dr.dilekakinci@gmail.com

Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 19/07/2023
Kabul Tarihi/ Accepted: 22/12/2023
Online Yayın Tarihi/ Published: 11/03/2024

Atıf / Cited: Yekenkurul D and et al. Prevalence of HBV, HCV, HIV and Effect on Clinical Course in COVID-19 Patients. *Online Türk Sağlık Bilimleri Dergisi* 2024;9(1):21-26. doi: 10.26453/otjhs.1329992

INTRODUCTION

In December 2019, a disease clinically similar to viral pneumonia was observed in Wuhan, China. This disease's causative agent, defined as coronavirus disease 2019 (COVID-19) by the World Health Organization in February 2020, was named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1] COVID-19 is a disease that can occur with different clinical symptoms, such as mild respiratory infection, severe pneumonia, respiratory failure, or multiple organ dysfunction.[2] While the virus causes more respiratory symptoms through the angiotensin-converting enzyme 2 (ACE2) receptor on the cell surface, it also affects the liver, heart, pancreas and intestines.[3] In the studies, it has been reported that liver enzyme elevation is observed at 16.1-53.1% rates in COVID-19 infection.[4] Especially in studies examining the prevalence of liver disease in COVID -19 patients, severe liver disease is a moderate risk factor for COVID-19 infection.[5,6]

The prevalence of hepatitis C virus (HCV) infection is approximately 1% in the world. Turkey is among the low-prevalence countries with a prevalence rate between 0.6%-0.8%. However, HCV infection is a disease in which 85% of cases can become chronic disease, 20% of chronic hepatitis C cases progress to cirrhosis, and 1-4% of cirrhosis cases progress to hepatocellular carcinoma.[7] Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) is a global problem. According to the United Nations 2021 report, since the beginning of the HIV epidemic, approximately 73 million HIV infections and 36 million deaths from AIDS-related diseases have occurred. In our country, it was reported that there were about 30 thousand people with confirmed HIV and two thousand AIDS cases between 1985-2021.[8] Hepatitis B virus (HBV) infection is an important cause of mortality and morbidity worldwide. Our country is among the middle-endemic countries. The approximate prevalence is 4-6%. There are many causes of acute flare-ups in chronic hepatitis B infection. Immunosuppressive therapy, pregnancy, drug resistance and other infections are some.[9]

Viral or bacterial infections such as COVID-19 may lead to hepatic flare-ups of infections such as HBV, HCV, and HIV. For this reason, in addition to respiratory problems, patients with elevated liver enzymes or chronic HBV, HCV, and HIV infections should also be evaluated primarily in terms of hospitalization. It was aimed to investigate the prevalence and clinical course of HBV, HCV and HIV infection in patients followed up with COVID-19 infection.

MATERIALS AND METHODS

Ethics Committee Approval: Approval for the study was obtained from the Clinical Research Ethics Committee of Düzce University with the ethics committee decision dated 20.06.2022 and numbered 2022/122. All procedures have been carried out following the Helsinki Declaration.

Study Design and Participants: The data of 460 patients who were followed up with the diagnosis of COVID-19 infection in the Infectious Diseases and Clinical Microbiology Clinic of Düzce University Research and Application Hospital between 15.03.2020-15.03.2022 were retrospectively analyzed. However, 226 patients who requested serological tests for hepatitis B, hepatitis C and HIV were included in the study. Demographic data such as age and gender of the patients, HBV, HCV, HIV serologies (HBsAg, Anti-HBs, Anti-HBcIgG, Anti-HCV, Anti-HIV-studied by ELISA method), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) results were recorded. Prevalence of HBV, HCV, HIV and isolated Anti HBcIgG, COVID-19 polymerase chain reaction (PCR) results, length of stay, last clinical status, ALT and AST levels were examined. ALT 0-41U/mL, AST 0-50IU/L (male) and 0-35IU/L (female) values were considered normal. AntiHBs values of 10 mIU/mL and above were considered positive. The effect of COVID-19 infection on elevated liver enzymes and length of hospital stay in patients with HBV, HCV and HIV infection was investigated.

COVID-19 Infection Diagnosis: In our country, the diagnosis of COVID-19 infection is made according to the COVID-19 guidelines published and revised by the Ministry of Health. Therefore, patients with a positive COVID-19 PCR test and/or signs of COVID-19 pneumonia on thorax computed tomography that cannot be explained for any other reason were considered COVID-19 infections during the pandemic.[10]

Study Groups

Group 1: HBsAg, anti-HCV, anti-HIV negative 207 patients were determined as group 1. Of these 207 patients, 28 were naturally immune to HBV (anti-HBcIgG positive, anti-HBs positive), 70 were negative for anti-HBcIgG, and 109 were not tested for anti-HBcIgG, but HBsAg results were negative.

Group 2: HBsAg-positive six patients were determined as group 2. Patients with negative anti-HCV and anti-HIV results but positive HBsAg test were evaluated in this group.

Group 3: Isolated anti-HBcIgG positive six patients were determined as group 3. Patients who have negative HBsAg, anti-HBs, anti-HIV and anti-HCV results but positive anti-HBcIgG test were evaluated in this group.

Group 4: Anti-HCV positive seven patients were determined as group 4. Patients who have negative

HBsAg, anti-HBcIgG and anti-HIV results but positive anti-HCV tests were evaluated in this group.

Group 5: Anti-HIV positive patients were determined. However, this group was excluded from the study because there were no patients with positive anti-HIV tests

Statistical Analysis: Statistical analysis was performed between the groups regarding gender, age, COVID-19 PCR, number and proportion of patients with elevated ALT and AST levels, median of ALT and AST, length of hospital stay, and clinical outcomes. SPSS 23 package program was used for statistical evaluation of the data. Chi-Square and Fisher Freeman Halton Test were used to analyse categorical variables, and the Kruskal-Wallis Test was used to evaluate the relationship between the mean values of numerical values between groups; $p<0.05$ was considered significant.

RESULTS

Out of 226 patients included in the study, 118 (52%) were male, and 108 (48%) were female; the mean age was 63.47±16.09 years. HBsAg positivity in six (3%) patients, isolated anti-HBcIgG positivity in six (3%, from 116 patients) patients, anti-HBs positivity in 74 (33%) patients, anti-HCV positivity in seven (3%) patients were present. Anti-HBcIgG positivity in 42 (19%) patients was present (28 were naturally immune to HBV, six HBsAg positive, six isolated anti-HBcIgG positive, and two anti-HCV positive). Anti-HIV positivity was not detected. Two HBsAg-positive patients had negative HBV DNA results; the other four were positive with 360, 470, 1000 and 5010 IU/mL, respectively. Only one of those with isolated anti-HBcIgG positivity had HBV-DNA tested, and that was negative. HCV-RNA results were negative in all patients who were anti-HCV positive. The number of patients with high ALT levels was 79 (35%), and the number of patients with high AST levels was 89 (39%) in all patients. The overall mortality rate was 2% (4/226), and the rate of admission to the intensive care unit was 14% (31/226). Although it was not statistically significant in the intergroup analysis, the median age of HBsAg-positive patients was lower, and the median of ALT and AST was higher compared to other groups ($p=0.149$, $p=0.177$ and $p=0.229$, respectively). The ALT and AST medians of patients with HBsAg positive were determined respectively as 23.55 and 20.95 before COVID-19 infection. Still, the ALT median was 62.8, and the AST median was 71.4 in COVID-19 infection. ALT (median 27.0) and AST (median 32.8) levels decreased after COVID-19 infection in HBsAg-positive patients with liver enzyme elevation. However, the median length of hospitalization ($p=0.117$), need for intensive care, and discharge status ($p=0.954$) were similar (Table 1).

DISCUSSION AND CONCLUSION

Hepatic damage in COVID-19 can occur by various mechanisms. Some of these are the side effects of the drugs used in the treatment, hepatic immunology and the direct cytotoxic effect of the virus. The virus causes overexpression in hepatocytes via the ACE2 receptor. It initiates replication in the cell with the same receptor, stimulates the synthesis and release of a new viral RNA, and makes protein synthesis.[11] The effect of ACE2 receptors on hepatocytes is limited. Therefore, hepatitis does not develop in every patient; however, patients who developed acute hepatitis due to COVID-19 have also been reported.[12,13] Especially in patients with COVID-19 pneumonia, SARS-CoV-2 infection may trigger hepatic failure.[14] For this reason, even in those who do not

Table 1. Results of patients diagnosed with COVID-19 and requested serological tests (n:226).

Specifications		**Group 1 (n:207)***	**Group 2 (n:6)****	**Group 3 (n:6)*****	**Group 4 (n:7)******	**p**
Age (year)	Median/IQR	65.00 (21.00)	53.00 (17.00)	67.00 (28.25)	70.00 (17.00)	0.149
Gender n (%)	Male	106 (51%)	4 (67%)	5 (83%)	3 (43%)	
	Female	101 (49%)	2 (33%)	1 (17%)	4 (57%)	0.441
COVID-19 PCR,	Positive	179 (86%)	5 (83%)	5 (83%)	6 (86%)	1.000
[a]n(%)	Negative	28 (14%)	1 (17%)	1 (17%)	1 (14%)	
Length of hospitalization (day), Median/IQR		7.00 (6.00)	4.00 (10.00)	7.50 (9.00)	5.00 (5.00)	0.117
Last clinical status,	Healing	174 (84%)	5 (83%)	6 (100%)	6 (86%)	
n (%)	Intensive care	29 (14%)	1 (17%)	0	1 (14%)	0.954
	Discharge status	4 (2%)	0	0	0	
ALT, Median/IQR		32.20 (38.40)	62.80 (54.10)	34.85(36.63)	31.40 (30.40)	0.177
AST, Median/IQR		34.70 (29.40)	71.40 (58.13)	40.00 (21.23)	36.10 (28.80)	0.229
High-level ALT, [b]n (%)		72 (35%)	4 (67%)	2 (33%)	1 (14%)	0.285
High-level AST, [c]n (%)		82 (40%)	4 (67%)	1 (17%)	2 (29%)	0.343

*: HBsAg, anti-HCV, anti-HIV negative patients; **: HBsAg positive patients; ***: Anti-HBcIgG positive, HBsAg and anti-HBs negative patients; ****: Anti-HCV positive patients; [a]: Number of patients with signs of COVID-19 pneumonia on thorax computed tomography; [b]: Number of patients with high ALT level; [c]: Number of patients with high AST level.

have any chronic disease, COVID-19 disease can cause hepatic dysfunction. In studies conducted in China in patients with a diagnosis of COVID-19 and predisposed to hepatic disease, it has been reported that hepatic functions were impaired at a rate of 14-50%.[1,15] In the study of Phipps et al.[16], it was found that baseline and peak ALT levels were higher in those with positive SARS-CoV-2 test than those with negative results. It has been reported that 45% of positive cases have mild, 21% moderate, and 6.4% severe hepatic damage, and severe damage was associated with a higher rate of mortality and intensive care hospitalization. On the other hand, Wang et al.[14] reported that 41% of their patients had elevated hepatic enzymes, and these patients had higher radiology scores. However, they stated no difference in mortality and hospitalization days between those with and without hepatic damage. In our study, 35% of our patients had elevated ALT, and 39% had elevated AST. It was concluded that this rate is low due to the low number of hepatitis B patients and the absence of chronic hepatitis C and HIV-positive patients. Although not statistically significant, the median ALT and AST of HBsAg-positive patients were higher than those of other groups.

In a meta-analysis, Kunutsor and Laukkanen[17] stated that acute hepatic injury, hepatic enzyme abnormality and hypoproteinemia were common hepatic complications in patients hospitalized due to coronavirus disease 2019. They also reported worse outcomes of COVID-19 pneumonia in those with a known hepatic disease. While the most common causes of chronic hepatic disease in Western countries are chronic alcohol consumption and HCV infection, HCV and HBV-related hepatitis are the most common causes in our country.[18] Studies on hepatic symptoms, signs and difficulties in SARS-CoV-2 infection continue. Observations and guidelines are important in multiple viral infections. In an early meta-analysis from China, the prevalence of chronic hepatic disease was reported to be 3% in people infected with COVID-19. However, no specific data was found for HCV and HBV infections. Chronic hepatitis B and C are still common infections worldwide. Therefore, the effect of COVID-19 infection on the course of HBV and HCV raises concerns.[19] In the United States, the rates were lower in 5700 patients hospitalized with the diagnosis of SARS-CoV-2, with the prevalence of HBV infection at 0.1% and HCV <0.1%.[20] In a study conducted with 20.133 inpatients diagnosed with COVID-19 infection in 208 care hospitals in England, Wales and Scotland, among the comorbid diseases, moderate-to-advanced hepatic disease as 1.8%, mild hepatic disease as 1.6% and HIV-positive patient rate as 0.5% were reported.[5] In the study of Jin et al.[21], 25 (3.8%) of 651 COVID-19 patients reported having a previous hepatic disease. In another study conducted in Wuhan, China, 23 (2.1%) of 1099 patients were reported to be infected with HBV, and this rate was 2.4% in mild cases and 0.6% in severe cases.[22] However, in another study conducted in the same country, 15 of 123 (12.2%) patients had HBV infection, and even HBV-positive patients had higher rates of severe COVID-19 (46.7%>24.1%) and death (13.3%>2.8%).[23] Zha et al.[24] reported the prevalence of HBV as 6.5% (2 in 31 patients) in their study and observed that HBV infection also delayed the clearance of the SARS-CoV-2 virus. In our study, our rate of HBsAg-positive patients was lower than the literature with 3%. However, anti-HBcIgG positivity was detected in 42 (19%) patients. Our rate of anti-HCV positive patients (3%) is higher than the literature. Since the HCV-RNA test was negative in all anti-HCV-positive patients, it was observed that there was no patient with a diagnosis of chronic hepatitis C in our study. In addition, immunity to hepatitis C or false positivity could not be differentiated in these patients.

From the studies on HIV and COVID-19 coinfection, Blanco et al.[25] reported that 0.9% (5/543) of hospitalized patients had HIV infection and viral pneumonia developed in three of these patients, but no death was observed. In our country, Altuntas Aydın et al.[26] stated that only four of the 1224 HIV-positive cases they followed were diagnosed with COVID-19. No HIV-positive patient was found in our study. This was thought to be due to the low number of HIV-positive patients followed in our city and some of them being followed in other cities due to social pressure. Docherty et al.[5], in their study with an overall mortality rate of 26%, found that apart from factors such as male gender and advanced age, some other diseases such as non-asthmatic chronic lung disease, obesity, and hepatic disease were associated with increased mortality. In our study, the mortality rate was 2%, lower than the literature, but the rate of admission to the intensive care unit was 14%. Since the intensive care patients were not included in the study, it was concluded that the mortality rate was low. The median length of hospitalization, need for intensive care, and discharge status were similar between the groups.

In conclusion, COVID-19 may cause hepatic flare-ups in HBsAg-positive patients, like other viral or bacterial infections. Hepatic enzymes were found to be high in the HBsAg-positive patient group. However, its insignificance was thought to be related to the low number of patients. Although elevated hepatic enzymes or the presence of chronic diseases such as hepatitis and immunodeficiency syndrome increase the possibility of hospitalization, our HBsAg-positive patient rate was found to be lower

than similar studies. Our anti-HCV positivity rate is higher than that of similar studies, but all of them are HCV-RNA negative. It is noteworthy that there are no anti-HIV-positive patients. In the literature, there are some studies on the presence of hepatic disease with other underlying diseases, but there are few studies on HBV, HCV, HIV and COVID-19 coinfection. More study on this subject is needed. To minimize the risk of hepatic failure in COVID-19 infection, chronic hepatitis B, C and HIV infections of the patient should be investigated, and individuals with the disease should be followed closely.

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of Düzce University (Date: 20.06.2022, decision no: 2022/122).

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

Author Contributions: Concept – DY; Supervision – DY, ARG, Nİ, EÇ; Materials –DY, ARG; Data Collection and/or Processing –ARG, Nİ, EÇ; Analysis and/ or Interpretation – DY, EÇ; Writing – DY, Nİ.

Peer-review: Externally peer-reviewed.

Other information: This study was presented as a poster at the 10th Türkiye EKMUD Scientific Congress (May 2022).

REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
2. Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discov Ther. 2020;14(1):58-60.
3. Téllez L, Martín Mateos RM. COVID-19 and liver disease: An update. Gastroenterología y Hepatología. 2020;43(8):472-480.
4. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: Management and challenges. Lancet Gastroenterol Hepatol. 2020;5(5):428-430.
5. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO clinical characterisation protocol: Prospective observational cohort study. BMJ. 2020;369:m1985.
6. Zhang H, Kang Z, Gong H, et al. Digestive system is a potential route of COVID19: An analysis of single-cell coexpression pattern of key proteins in viral entry process. Gut. 2020;69(6):1010-1018.
7. Dayan S. Hepatitis C virus infection. In: Infectious Diseases Diagnosis and Treatment Manual. 1st ed. Ankara, Hippocratic Publishing House; 2022:11-16.
8. Dayan S. HIV/AIDS. In: Infectious Diseases Diagnosis and Treatment Manual. 1st ed. Ankara, Hippocratic Publishing House; 2022:19-35.
9. Moroğlu Ç, Tülek N, Aktepe E, et al. Causes of acute exacerbation of chronic hepatitis B infection: A report of case series. Viral Hepatitis Journal. 2015;21(2):48-51.
10. T.C. Ministry of Health. COVID-19 Information Platform. COVID-19 (SARS-CoV-2 Infection) General Information, Epidemiology and Diagnosis 2020. https://covid19.saglik.gov.tr/TR-66337/genel-bilgiler-epidemioloji-ve-tani.html. Accessed June 6, 2022.
11. Bourgonje AR, Abdulle AE, Timens W, et al. Angiotensin-converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). J Pathol. 2020;251:228-248.
12. Bayrak M, Çadırcı K. A case of acute hepatitis associated with COVID-19 in a geriatric patient. J Med Palliat Care. 2021;2(3):102-104.
13. Tian S, Xiong Y, Liu H, Niu L, Guo J, Liao M, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. Modern Pathology. 2020;33:1007-1014.
14. Wang Y, Liu S, Liu H, et al. SARS-CoV-2 infection of the liver directly contributes to hepatic impairment in patients with COVID-19. J hepatol. 2020;73(4):807-816.
15. Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. Liver Int. 2020;40(5):998-1004.
16. Phipps MM, Barraza LH, LaSota ED, et al. Acute liver injury in COVID-19: Prevalence and association with clinical outcomes in a large US cohort. Hepatology. 2020;72(3):807-817.
17. Kunutsor SK, Laukkanen JA. Hepatic manifestations and complications of COVID-19: A systematic review and metanalysis. J Infect. 2020;81 (3):e72-e74.
18. T.C. Ministry of Health, General Directorate of Public Health. 2018-Ankara. Türkiye Viral Hepatitis Prevention and Control Program 2018-2023. https://hsgm.saglik.gov.tr/tr/bulasicihastaliklar-haberler/turkiye-viral-hepatit-onleme-ve-kontrol-programi.html. Accessed June 10, 2022.
19. Reddy KR. SARS-CoV-2 and the liver: Considerations in hepatitis B and hepatitis C infections. Clin Liver Dis. 2020;15(5):191-194.
20. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;323(20):2052-2059.
21. Jin X, Lian JS, Hu JH, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-

19) with gastrointestinal symptoms. Gut. 2020;69 (6):1002-1009.
22. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Eng J Med. 2020;382:1708-1720.
23. Chen X, Jiang Q, Ma Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 and hepatitis B virus co-infection. Virol Sin. 2020;35(6):842-845.
24. Zha L, Li S, Pan L, et al. Corticosteroid treatment of patients with coronavirus disease 2019 (COVID-19). Med J Aust. 2020;212(9):416-420.
25. Blanco JL, Ambrosioni J, Garcia F, et al. COVID -19 in patients with HIV: clinical case series. Lancet HIV. 2020;7(5):e314-e316.
26. Altuntas Aydin O, Kumbasar Karaosmanoglu H, Kart Yasar K. HIV/SARS-CoV-2 co-infected patients in Istanbul, Turkey. J Med Virol. 2020;92(11):2288-2290.