

Is Having Inflammatory Bowel Disease a Risk Factor for Severe Acute Respiratory Syndrome Coronavirus 2?

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ABSTRACT

Background: The severe acute respiratory syndrome coronavirus 2 virus was found to have effects not only in the lungs but also in many different organs. We aimed to evaluate the management of our patients with inflammatory bowel disease in this pandemic, the incidence of coronavirus disease 2019 in terms of clinical, medical treatment, and features of inflammatory bowel disease, and to investigate the effects of the severe acute respiratory syndrome coronavirus 2 on this particular group of patients.

Methods: During the coronavirus disease 2019 pandemic, 207 patients who had inflammatory bowel disease for at least 6 months were questioned for coronavirus disease 2019 at their outpatient clinic admissions, and their medical records were evaluated prospectively.

Results: Of the 207 patients, 146 had Crohn's disease. The mean disease duration was determined as 118.15 ± 72.85 months. Of the patients, 127 (61.4%) were using mesalazine, 110 (53.1%) azathioprine, and 148 (71.5%) biological agents. It was found that 66 (31.9%) patients changed their medications during the coronavirus disease 2019 pandemic. As a medication change, anti-Tumor Necrosis Factor (TNF) dose was observed to be omitted most frequently at a rate of 80%. Diarrhea was present in 20.8%, abdominal pain in 20.3%, nausea in 10.6%, anorexia in 13.5%, and weight loss in 15.9% of the patients. Twelve (5.79%) patients were diagnosed with coronavirus disease 2019. Lung involvement was present in 11 (91.7%) of the patients diagnosed with coronavirus disease 2019. Of the patients diagnosed and not diagnosed with coronavirus disease 2019, 75% vs. 71.6% were using biological agents ($P = .80$), respectively. Half of the patients diagnosed with coronavirus disease 2019 were active in terms of inflammatory bowel disease at the time of diagnosis, and 2 of these patients were severely active.

Conclusion: The incidence of coronavirus disease 2019 infection in patients with inflammatory bowel disease was not different from the general population during the severe acute respiratory syndrome coronavirus 2 pandemic. Coronavirus disease 2019 infection does not progress with poor prognosis in patients with inflammatory bowel disease who receive immunosuppressive therapy including biological agents.

Keywords: COVID-19 infection, immunosuppressive therapy, inflammatory bowel disease

INTRODUCTION

In the clinical manifestations encountered after the World Health Organization declared coronavirus disease 2019 (COVID-19) infection as a pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on March 11, 2020, it became apparent that the virus had effects not only on the lungs but also on many different organs. The clinical course of the SARS-CoV-2 virus, which has a complex relationship with the immune system, has also been observed to differ in individuals who have chronic diseases and use immunosuppressive therapy.¹ Patient groups at risk of SARS-CoV-2 virus causing serious disease have been reported by the Centers for Disease Control and Prevention as individuals

with asthma, chronic lung disease, diabetes, severe heart disease, chronic kidney failure, morbid obesity, those aged 65 years and over, immunocompromised individuals, and liver disease patients.² The differentiation caused by the SARS-CoV-2 virus on the host immune system and the increase in cytokine release due to the activation of the host immune system are the main mechanisms in the pathophysiology of this virus.³ In addition, the SARS-CoV-2 virus has been found to use Angiotensin Converting Enzyme (ACE2), the human mono-carboxypeptidase, as the host receptor. ACE2 receptors have been found to be expressed by the epithelial cells of the lung, intestine, kidney, and blood vessels in the body and to be found to the largest extent in the terminal ileum

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and colon.^{4,5} Inflammatory bowel disease (IBD) constitutes a group of disease requiring special attention during the SARS-CoV-2 pandemic due to the intensity of ACE2 receptors in the intestine and the imbalance in the immune system involved in the pathophysiology of the disease, as well as the immunomodulator and biological agents required for the treatment.⁶ In the SARS-CoV-2 pandemic period, it has been concluded from the data obtained that it is not possible to mention an increased risk for COVID-19 infection in IBD patients, but each patient should be evaluated in terms of medical treatments and precautions to be taken.^{4,7}

In this study in which we aimed to evaluate whether IBD poses a risk for COVID-19 infection according to the general population, along with the clinical features of IBD, the immunosuppressants used, and the disease management and course of patients in this particular patient group with regard to the characteristics of the patient group diagnosed with COVID-19 infection, we shared our data in order to contribute to the literature.

MATERIALS AND METHODS

Patients

Inflammatory bowel disease patients, who were admitted to the Gastroenterohepatology Department of the Faculty of Medicine, between March 11, 2020 and July 1, 2020, and who were followed up by the Department with a diagnosis duration of at least 6 months, were questioned at their outpatient clinic admissions and evaluated prospectively.

Study Design and Setting

The study was designed as a single-center, prospective study in the Gastroenterohepatology Department of the Faculty of Medicine. The study protocol abided by the ethical guidelines of the Declaration of Helsinki from 1975 and was approved by the local ethics committee. For this study, ethical approval was obtained from the Ministry of Health with the number 2020-05-05T16_22_16.

Main Points

- Inflammatory bowel disease (IBD) does not appear to be an increased risk factor for coronavirus disease 2019 (COVID-19) infection.
- Taking biological agents in IBD does not seem to increase the risk for COVID-19 infection.
- COVID-19 infection is not more severe in IBD.

Statistical Analysis

The conformity of the data to normal distribution was tested by the Shapiro–Wilk test. The Student's *t*-test was used for comparison of normally distributed variables in 2 independent groups, while the Mann–Whitney *U* test was used for comparison of non-normally distributed variables in 2 independent groups. The Kruskal–Wallis test was used for comparisons of more than 2 non-normally distributed independent groups, while Dunn's test was used as a post hoc test. The descriptive statistics were given as mean \pm standard deviation for numerical variables and as numbers and % values for categorical variables. The Statistical Package for the Social Sciences (SPSS) Windows version 21.0 software package (IBM Corp.; Armonk, NY, USA) was used for statistical analyses, and a *P* value of $<.05$ was considered statistically significant.

RESULTS

The data of 207 patients with IBD who were followed up by the University Medical Faculty Department of Gastroenterohepatology were evaluated. Of the 207 patients, 146 had Crohn's disease and 61 had ulcerative colitis (UC) (Figure 1). The mean age of the patients was 41.75 ± 13.58 years. Of the patients, 133 (64.3%) were males and 74 were females. The mean body mass index (BMI) of the patients was 25.18 ± 2.65 kg/m². The mean disease duration was 118.15 ± 72.85 months. Extraintestinal involvement was present in 61 (29.6%) patients.

Medications used by the patients were evaluated, 127 (61.4%) of the patients were using mesalazine,

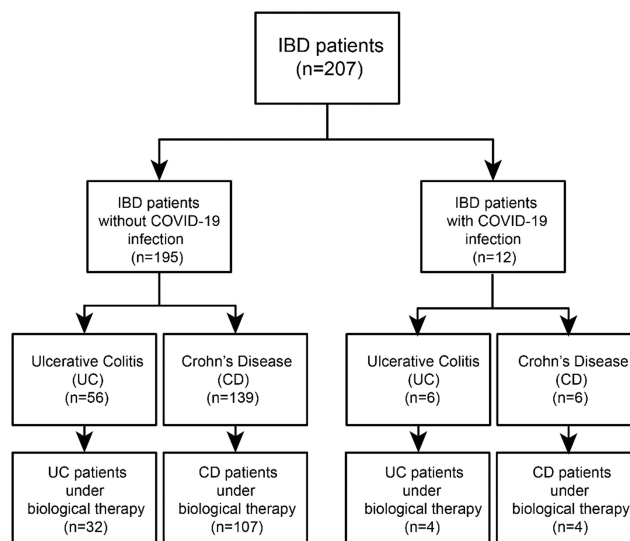


Figure 1. Patients' distribution in the study.

110 (53.1%) azathioprine (AZA), and 148 (71.5%) biological agents. Of those using biological agents, 103 (69.5%) were on infliximab, 26 (17.5%) on adalimumab, 18 (12.1%) on vedolizumab, and 1 (0.6%) on secukinumab.

While the medication use status of the patients was evaluated during the COVID-19 pandemic, 66 (31.9%) patients were found to have changed their medications due to the pandemic. Of the medication changes, 58.8% was made upon the recommendation of a physician. As a medication change, anti-TNF dose was observed to be omitted most frequently at a rate of 80%. In other medication changes, it was determined that anti-TNF was discontinued in 4.6%, anti-TNF was switched to vedolizumab in 4.6%, AZA dose was decreased in 3.1%, AZA was discontinued in 3.1%, and mesalazine was discontinued in 3.1% of the patients. Anti-TNF dose was observed to be discontinued for an average of 2.38 ± 2.03 months.

Gastrointestinal symptoms of IBD were evaluated during the COVID-19 pandemic, diarrhea was detected in 20.8%, abdominal pain in 20.3%, nausea in 10.6%, anorexia in 13.5%, and weight loss in 15.9% of the patients. The mean weight loss was 6.03 ± 5.32 kg.

Twenty-three (11.1%) patients were admitted to the hospital with the suspicion of COVID-19. Twelve (5.79%) patients were diagnosed with COVID-19. Of the patients diagnosed with COVID-19, 11 (91.7%) had lung involvement and 6 (50%) had SARS-CoV-2 PCR positivity in the swab sample taken from the oropharyngeal region. Six (50%) of the patients diagnosed with COVID-19 had Crohn's disease and 6 of them had UC. One of the patients with UC diagnosed with COVID-19 infection was diagnosed in the post-op period after total colectomy. Another patient with UC, also diagnosed with COVID-19 infection, received azithromycin, hydroxychloroquine, and anakinra treatments for SARS-Cov-2 infection. Although the patient, who was diagnosed with Cytomegalovirus (CMV) colitis, was treated with ganciclovir treatment, total colectomy was performed since the disease activation could not be controlled with biological agents such as infliximab and vedolizumab. Table 1 shows the characteristics of the patients diagnosed with COVID-19.

Of the patients diagnosed with and not diagnosed with COVID-19, 75% versus 71.6% were using biological agents ($P = .80$), 58.3% versus 61.3% were using mesalazine ($P = .83$), and 41.6% versus 54.1% were using AZA ($P = .401$), respectively. Among the patients with IBD who were diagnosed with COVID 19 infection, the drug dose

skipping was used as the most frequent drug change in the COVID19 infection process in patients using anti-TNF. Among these patients, anti-TNF treatment was interrupted, with an average dose (3 months) in those using infliximab and an average of 2 doses (1 month) in those using adalimumab. Of the patients with and without the diagnosis of COVID-19, 41.7% versus 29% had extraintestinal involvement ($P = .34$), 16.6% versus 2.6% had eye involvement ($P = .009$), and 25% versus 15.5% had joint involvement ($P = .41$), respectively. The rate of using Sulfasalazine (SZP) in the treatment and the rate of eye involvement of patients diagnosed with COVID-19 infection were higher than those with IBD who were not diagnosed with COVID-19 infection ($P = .040$, $P = .032$, and $P = .09$, respectively), and there was no difference in terms of biological agent use. In the patients diagnosed with and not diagnosed with COVID-19, the mean age was 49.5 ± 10.95 years versus 41.21 ± 13.61 ($P = .040$), the mean BMI was 23.78 ± 4.27 kg/m² versus 25.24 ± 4.67 kg/m² ($P = .292$), the mean disease duration was 119.75 ± 111.89 months versus 117.98 ± 81.31 months ($P = .943$), and the mean duration of biological agent use was 47.22 ± 47.75 months versus 45.15 ± 37.8 months ($P = .876$), respectively. Table 2 shows the comparison of the characteristics of the IBD patients diagnosed with and not diagnosed with COVID-19.

No patient diagnosed with COVID 19 infection with IBD needed endotracheal intubation during the course of their illness, and there is no need for hospitalization in the intensive care unit, and no patient died.

DISCUSSION

While it was unclear at the beginning of the pandemic how the course of the wide spectrum of clinical manifestations caused by SARS-CoV-2 would be in different disease groups compared to the normal population, and which disease groups were at higher risk, our knowledge on this subject has been enhanced by the observations during the process, as well as by the studies based on the analysis of findings. Throughout the process, the course of the disease in patients with IBD attracted attention in terms of both the presence of differentiated immunity in the pathogenesis of the disease and the treatments used for the disease.⁸ Regarding this, a study by Bezzio et al⁹ evaluating the incidence of COVID-19 infection in IBD during the pandemic in Italy found that there was no increased risk compared to the general population. In this study conducted with our own data, we found that patients with IBD do not have increased risk in terms of

Table 1. Characteristics of IBD Patients Diagnosed with COVID-19

| Patients | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | |
|---|---|---|---------------------------------|---|---|---|---------------------------------|----------------------------|---|---|---|---------------------------------------|---------------------------------------|
| Age (years) | 31 | 48 | 70 | 50 | 35 | 36 | 48 | 61 | 59 | 42 | 49 | 45 | |
| Gender | M | F | M | F | M | F | M | M | F | M | F | M | |
| BMI (kg/m ²) | 23 | 18 | 22 | 30 | 25 | 18 | 29 | 18 | 22 | 25 | 24 | 25 | |
| Smoking status | Ex-smoker | No | Yes | No | Ex-smoker | Smoking | No | Smoking | No | No | No | Yes | |
| IBD | UC | CD | CD | UC | UC | UC | UC | CD | CD | CD | UC | CD | |
| IBD duration (months) | 72 | 204 | 264 | 48 | 6 | 300 | 12 | 132 | 14 | 60 | 276 | 60 | |
| Biologic agent | IFX | IFX | IFX | VEDO | No | VEDO | ADA | No | ADA | No | Anti-IL17A | ADA | |
| Duration of biologic agent (months) | 26 | 96 | 60 | 12 | 3 | 3 | 12 | 14 | 14 | 144 | 144 | 60 | |
| Drugs for IBD | 5-ASA AZA | 5-ASA AZA | AZA | 5-ASA AZA | 5-ASA AZA | 5-ASA AZA | 5-ASA AZA | 5-ASA | 5-ASA | 5-ASA | 5-ASA | Sulfasalazine | |
| Other drugs | No | No | Insulin Doxazosin | No | No | Cymaven | No | Beta 2 agonist | Dexamethasone Colchicine | Tenofovir | Dexamethasone Colchicine | No | |
| Comorbidities | No | No | CRD HT DM | No | DM | ITP (CMV colitis) | No | Asthma | Ankylosing spondylitis | CHB | Ankylosing spondylitis, CRD | Behçet's disease | |
| Complaints | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Dyspnea Cough Anorexia Fever Weight loss | Dyspnea | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Vomiting Anorexia Diarrhea Weight loss | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Fever Anorexia | Cough Fever Anorexia | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Dyspnea Cough Anorexia Fever Muscle pain Diarrhea | Dyspnea Cough Anorexia Fever | Dyspnea Cough Anorexia Fever |
| Lung involvement | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | |
| Oropharyngeal and nasopharyngeal swabs for SARS-CoV-2-PCR | + | + | - | + | - | - | + | + | - | + | - | - | |
| Hospital stay for COVID-19 (days) | 17 | No | 18 | 5 | 5 | 7 | No | 7 | 17 | 6 | 15 | 3 | |
| Treatments for COVID-19 | Azithromycin HCQ Favipiravir Enoxaparin Meronem Anakinra | Azithromycin HCQ | Enoxaparin HCQ, Favi, | Azithromycin HCQ | Azithromycin HCQ | Azithromycin HCQ IL-1 receptor antagonist | Azithromycin HCQ | Azithromycin HCQ | Azithromycin HCQ | Azithromycin HCQ | Azithromycin HCQ IL-1 receptor antagonist | Azithromycin HCQ | |
| Bowel activity in COVID-19 | Moderate | Moderate | Mild | Severe | Moderate | Severe | Mild | Mild | Moderate | Mild | Mild | Mild | |
| Drug changes and management in COVID-19 pandemic | AZA stopped IFX and 5-ASA continued | IFX was switched to VEDO | AZA stopped IFX dose skipped | No change | No change | IFX changed to VEDO and after COVID treatment total colectomy | ADA dose skipped AZA stopped | No change | ADA dose skipped | No change | Anti-IL17A dose skipped | ADA dose skipped | |
| Stay in ICU | No | No | No | No | No | No | No | No | No | No | No | No | |
| Death | No | No | No | No | No | No | No | No | No | No | No | No | |

AZA, azathioprine; BMI, body mass index; M, male; F, female; IBD, inflammatory bowel disease; ICU, intensive care unit; COVID-19, coronavirus disease 19; SARS-CoV2; PCR, polymerase chain reaction; UC, ulcerative colitis; CD, Crohn's disease; IFX, infliximab; ADA, adalimumab; VEDO, vedolizumab; 5-ASA, 5-Acetylsalicylic Acid; CRD, Chronic renal disease; HT, Hypertension; DM, Diabetes Mellitus; ITP, Idiopathic thrombocytopenic purpura; CMV, Cytomegalovirus; CHB, Chronic hepatitis B.

Table 2. Comparison of Characteristics of IBD Patients Who Diagnosed with and Not Diagnosed with COVID-19

| | Diagnosed with COVID-19 | | | | P |
|-----------------------------|-------------------------|------|--------------|------|-------------|
| | Yes (n = 12) | | No (n = 195) | | |
| | n | % | n | % | |
| Gender | | | | | |
| Male | 7 | 58.3 | 126 | 64.9 | .642 |
| Female | 5 | 41.7 | 68 | 35.1 | |
| Smoking | | | | | |
| Non-smoker | 6 | 50.0 | 108 | 58.4 | .728 |
| Ex-smoker | 2 | 16.7 | 34 | 18.4 | |
| Smoker | 4 | 33.3 | 43 | 23.2 | |
| Employment status | | | | | |
| Yes | 2 | 18.2 | 14 | 12.4 | .584 |
| No | 9 | 81.8 | 99 | 87.6 | |
| IBD diagnosis | | | | | |
| UC | 6 | 50.0 | 55 | 28.4 | .111 |
| Crohn's | 6 | 50.0 | 139 | 71.6 | |
| Biological agent | | | | | |
| Yes | 9 | 75.0 | 139 | 71.6 | .802 |
| No | 3 | 25.0 | 55 | 28.4 | |
| Extraintestinal involvement | | | | | |
| Yes | 5 | 41.7 | 56 | 29.0 | .346 |
| No | 7 | 58.3 | 137 | 71.0 | |
| Eye involvement | | | | | |
| Yes | 2 | 16.7 | 5 | 2.6 | .009 |
| No | 10 | 83.3 | 189 | 97.4 | |
| Joint involvement | | | | | |
| Yes | 3 | 25.0 | 30 | 15.5 | .413 |
| No | 9 | 75.0 | 164 | 84.5 | |
| Perianal disease | | | | | |
| Yes | 1 | 8.3 | 39 | 20.1 | .468 |
| No | 11 | 91.7 | 155 | 79.9 | |
| Mesalazine | | | | | |
| Yes | 7 | 58.3 | 119 | 61.3 | .836 |
| No | 5 | 41.7 | 75 | 38.7 | |
| Anti-TNF | | | | | |
| Yes | 6 | 50.0 | 123 | 63.4 | .352 |
| No | 6 | 50.0 | 71 | 36.6 | |
| VEDO | | | | | |
| Yes | 3 | 25.0 | 16 | 8.2 | .086 |
| No | 9 | 75.0 | 178 | 91.8 | |

(Continued)

Table 2. Comparison of Characteristics of IBD Patients Who Diagnosed with and Not Diagnosed with COVID-19 (Continued)

| | Diagnosed with COVID-19 | | | | P |
|---|-------------------------|------|----------------|------|-------------|
| | Yes (n = 12) | | No (n = 195) | | |
| | n | % | n | % | |
| Biological agent | | | | | |
| IFX | 3 | 37.5 | 100 | 71.9 | .070 |
| ADA | 3 | 37.5 | 23 | 16.5 | |
| VEDO | 2 | 25.0 | 16 | 11.5 | |
| AZA | | | | | |
| Yes | 5 | 41.6 | 105 | 54.1 | .401 |
| No | 7 | 58.4 | 89 | 45.9 | |
| SZP | | | | | |
| Yes | 2 | 16.7 | 7 | 3.6 | .032 |
| No | 10 | 83.3 | 187 | 96.4 | |
| Diarrhea | | | | | |
| Yes | 4 | 33.3 | 39 | 20.1 | .274 |
| No | 8 | 66.7 | 155 | 79.9 | |
| Abdominal pain | | | | | |
| Yes | 4 | 33.3 | 38 | 19.6 | .251 |
| No | 8 | 66.7 | 156 | 80.4 | |
| Fever | | | | | |
| Yes | 8 | 66.7 | 12 | 6.2 | .001 |
| No | 4 | 33.3 | 181 | 93.8 | |
| Nausea | | | | | |
| Yes | 7 | 58.3 | 15 | 7.7 | .001 |
| No | 5 | 41.7 | 179 | 92.3 | |
| Vomiting | | | | | |
| Yes | 7 | 58.3 | 11 | 5.7 | .001 |
| No | 5 | 41.7 | 183 | 94.3 | |
| Loss of appetite | | | | | |
| Yes | 8 | 66.7 | 20 | 10.3 | .001 |
| No | 4 | 33.3 | 174 | 89.7 | |
| Weight loss | | | | | |
| Yes | 8 | 66.7 | 24 | 12.4 | .001 |
| No | 4 | 33.3 | 170 | 87.6 | |
| Comorbidities | | | | | |
| Yes | 3 | 25.0 | 30 | 15.5 | .382 |
| No | 9 | 75.0 | 164 | 84.5 | |
| Age (years) (mean ± SD) | 49.5 ± 10.95 | | 41.21 ± 13.61 | | .040 |
| BMI (kg/m ²) (mean ± SD) | 23.78 ± 4.27 | | 25.24 ± 4.67 | | .292 |
| Disease duration (months) (mean ± SD) | 119.75 ± 111.89 | | 117.98 ± 81.31 | | .943 |
| Duration of biological agent use (months) (mean ± SD) | 47.22 ± 47.75 | | 45.15 ± 37.8 | | .876 |

BMI, body mass index; COVID-19, coronavirus disease 19; IBD, inflammatory bowel disease; IFX, infliximab; ADA, adalimumab; VEDO, vedolizumab; UC, ulcerative colitis. sd, standard deviation. P-value for categorical variables was obtained from Chi-square test. For quantitative variables, P-value was obtained from Student's t-test. A P value < .05 was considered statistically significant and these are indicated in bold in the table.

the incidence of COVID-19 infection compared to the general population. In our study, the incidence of COVID-19 in the patients with IBD was 5.79%, whereas the rate of COVID-19 infection in our country during the same period, namely between March 13, 2020 and June 30, 2020, was determined as 5.91% ($P = .944$). The fact that patients with IBD do not have an increased risk in terms of the incidence of COVID-19 infection compared to the normal population may be related to our patient group consisting of younger individuals. In our study group, the mean age of the patients with IBD was 41.75 ± 13.58 years.¹⁰ In addition, it has been emphasized in many studies that an important factor in the pathogenesis of SARS-CoV-2 virus causing COVID-19 infection is the cytokine storm triggered by the virus, and that anti-TNF drugs used for the treatment of IBD reduce the risk of COVID-19 infection by affecting through this pathogenesis.¹¹⁻¹³ In our study group, the rate of patients with IBD using biological agents was as high as 71.5%. In our study, 87% of the patients with IBD were not employed because of their isolation at home, and the incidence of COVID-19 infection among these was not different from the general population.

It has been reported in various studies from the very beginning of the pandemic that age is one of the most important risk factor for COVID-19 infection.^{14,15} In our study, the mean age of the patients diagnosed with COVID-19 infection in the group of patients with IBD was higher than those who were not diagnosed with COVID-19.

Although the levels of ACE2 used by SARS-CoV-2 as receptors in tissues were found to be higher in the intestines of individuals with Crohn's disease, no difference was reported between Crohn's disease and UC in terms of the risk of SARS-CoV-2 infection.¹⁶⁻¹⁸ In our study, regarding the diagnosis of IBD, there was no difference between Crohn's disease and UC in terms of the incidence of COVID-19 infection.

From the beginning of the SARS-CoV-2 pandemic, how biological agents and immunomodulators may affect the course of the disease and how drug management should be for IBD appeared to be important issues. Norsa et al¹⁹ reported that none of the patients with IBD followed up in Italy had COVID-19 infection until the end of March, while 22% were on biological agent and 22% were on immunomodulator therapy. Also, in the data published by Tursi et al²⁰ based on the Surveillance Epidemiology of Coronavirus Under Research Exclusion-IBD database,

it was stated that anti-TNF treatment did not increase the risk of COVID-19, and that only 15% of individuals diagnosed with COVID-19 were on anti-TNF therapy. In our patient group, the use of a biological agent or AZA did not increase the risk of COVID-19 infection. Since our patient group pertained to a university hospital, which is a tertiary center, and our patient profile was associated with more complicated diseases, the rate of the patients using biological agents was higher. While 75% of the IBD patients diagnosed with COVID-19 infection were using biological agents, 72% of the patients not diagnosed with COVID-19 infection were using biological agents. When the treatment of our patients was evaluated in our study, it was determined that the IBD patients who were diagnosed with COVID-19 infection used higher rate of sulfasalazine than those who were not diagnosed with COVID-19. It is known that sulfasalazine has proapoptosis-inducing effect, especially on T lymphocytes.²¹ In the literature, it has been reported that the use of sulfasalazine does not pose an increased risk in patients in studies evaluating the Disease-Modifying Anti-Rheumatic Drugs treatment for rheumatological diseases, rather than studies evaluating sulfasalazine use in IBD and COVID-19 infection.^{22,23} In our patient group, extraintestinal findings were prominent in the patients diagnosed with COVID-19 who were using sulfasalazine. These patients also had a history of biological agent use. Therefore, it would not be right to conclude that sulfasalazine alone increases the risk of COVID-19 infection. The evaluation of the data from multi-center studies in milder periods of the pandemic process may enable us to obtain clearer results. In the clinical practice update based on expert comments by American Gastroenterological Association in the COVID-19 outbreak, they made recommendations for the management of patients with IBD by classifying the patients as follows: (1) patients not infected with SARS-Cov-2, (2) patients infected with SARS-Cov-2 but asymptomatic, and (3) patients with intestinal disease with COVID-19 infection as active or inactive patients. According to this, the patients in the first group were recommended to continue their treatment in the same way. For those in the second group, it was recommended that thiopurine, methotrexate, and tofacitinib be discontinued, and biological agents delayed for 2 weeks to monitor the patient's symptoms for COVID-19 infection. In the third group of patients, that is, for patients with COVID-19 infection, it was recommended to discontinue thiopurine, methotrexate, tofacitinib, and biological therapies during the viral infection process and to restart after symptom recovery and, if possible, negative by viral test.²⁴

In our study, it was found that nausea, vomiting, loss of appetite, and weight loss were significantly more frequent in our IBD patient group diagnosed with COVID-19 infection than those who were not diagnosed with COVID-19 infection when the gastrointestinal symptoms of the patients diagnosed with COVID-19 were evaluated. However, there was no difference between the 2 groups in terms of diarrhea complaint. It was stated in the early stages of the pandemic that 3.8% of 1099 patients in China had diarrhea complaints; however, various studies reported that this rate may vary between 2% and 50%.^{25,26}

In our study, the management of drug treatment in patients was also evaluated during the pandemic period. It was determined that 31.9% of the patients changed their medications and 58.8% of them changed their medications upon recommendation of a physician. As a change in medication, anti-TNF dose was observed to be omitted most frequently. The management of the medical treatment for IBD has remained a confusing issue in the pandemic period because of the presence of drugs affecting the immune system. On the one hand, the requirement of parenteral administration of some biological agents for hospital conditions, which are high-risk areas for SARS-CoV-2 virus infection, on the other hand, the uncertainties about the effects of biological agents on the SARS-CoV-2 virus may have caused our approach to be anti-TNF omission mainly. Guideline of the British Gastroenterology Association recommended that anti-TNFs in the guideline they issued for the management of IBD in the first period of the COVID-19 outbreak do not increase the risk of COVID 19 infection, and if possible, it should be continued as monotherapy. In addition, it was stated that in order for patients to be less exposed to the risk of COVID 19 infection, it was stated that if possible, anti-TNF drugs could be converted into forms in which they could apply subcutaneously themselves.²⁷

In conclusion, the fact that both IBD and SARS-Cov-2 virus have a pathogenesis associated with differentiated immune response has caused IBD to attract more interest during the COVID-19 pandemic period. According to our observations during the pandemic period and studies on this specific patient group in addition to the theoretical information, we have come closer to reach consensus in the management of the disease. In these days when the world is still undergoing the pandemic, we intended to contribute to the literature by sharing the data of our IBD patients that we followed up in our university hospital, which is one of the

pandemic centers of İstanbul, an important city of the world with a population of 16 million. The incidence of COVID-19 infection among the patients with IBD evaluated in our study was not different from that of the general population, and the rates of biological agent use were similar between IBD patients diagnosed with and not diagnosed with COVID-19 infection.

Ethics Committee Approval: The study was approved by the medical ethics committee of İstanbul University (No: T16_22_16.).

Informed Consent: Written/verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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