The Impact of Inflammatory Bowel Diseases and Related Medications on COVID-19 Severity and Outcome: A Tertiary Referral Center Experience from Turkey

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ABSTRACT

Background: *Coronavirus disease-2019 has become a serious pandemic, and still remains a risk despite vaccines that have been developed. Among inflammatory bowel disease patients old age, inflammatory bowel disease activation, the existence of the comorbid disease, and using steroids are known risk factors for severe coronavirus disease-2019. But there are different data for drugs other than corticosteroids used. The aims of the study are to evaluate the prevalence and risk factors of severe coronavirus disease-2019 and the effect of inflammatory bowel disease drugs on severe coronavirus disease-2019.*

Methods: *In this study among 1195 inflammatory bowel disease patients, 130 patients who were found to be positive for severe acute respiratory syndrome coronavirus-2 between March 2020 and May 2021 were evaluated. Patients were divided into 3 groups as mild, moderate, and severe coronavirus disease-2019.*

Results: *Among 130 patients, 91 (70%) had mild, 16 (12.3%) had moderate, and 23 (17.7%) had severe coronavirus disease-2019. Being 60 years of age or older (P = .009), having at least 1 comorbid disease (P = .002), and having active inflammatory bowel disease (P = .001) were factors that increased the risk for severe coronavirus disease-2019. The use of mesalazine (P = .35), biologic agents (P = .23), and corticosteroids (P = .42) did not increase the risk of severe coronavirus disease-2019. The use of azathioprine seemed to decrease the risk of severe disease with univariate regression analysis however the significance disappeared with multivariate analysis.*

Conclusion: *Older age, active inflammatory bowel disease, and existence of at least 1 comorbid disease are risk factors for severe coronavirus disease-2019. However, drugs used in inflammatory bowel disease management do not increase the risk of severe coronavirus disease-2019. But due to the small number of patients, it is difficult to reach a definite conclusion about corticosteroids.*

Keywords: *Biological treatments, inflammatory bowel disease, inflammatory bowel disease treatments, SARS-CoV-2, severe COVID-19*

INTRODUCTION

Coronavirus disease-2019 (COVID-19) which is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first reported in Wuhan China in November 2019. The World Health Organization (WHO) enunciated that this viral infection constitutes a global public threat on January 30, 2020.[1] Following this statement, with the escalation in the speed of the spreading, they declared COVID-19 as a pandemic on March 11, 2020.[2] Subsequentially, COVID-19 became a pandemic disease that tremendously influenced the entire human race, and regardless of vaccinations being administered, due to the constantly developing new variants, it is still unknown when this pandemic will be taken under control.

Severe acute respiratory syndrome coronavirus-2 can cause pneumonia, respiratory failure, and even death. Although the substantial majority of those infected are either asymptomatic or have trivial symptoms, 14% of patients have severe COVID-19, and 5% are in need of intensive care.[3] According to WHO's statistics, as of July 7, 2021, more than 184 million people have been infected with SARS-CoV-2 and around 4 million people have died.[4] Research conducted until today shows that factors such as old age, smoking, existence of obesity, and comorbid diseases highly increase the risk of severe COVID-19.[5]

Immunomodulator and immunosuppressive treatments are largely used for the treatment of immune-related chronic inflammations such as ulcerative colitis (UC) and Crohn's disease (CD) which are both classified as inflammatory bowel disease (IBD). It is acknowledged that the use of immunomodulators/immunosuppressives and

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biological agents to achieve remission induction and maintenance can cause an increased risk of severe infections and pneumonia.[6,7] According to a study, the use of immun osuppressive/immunomodulator drugs and the combined use of biological treatments raises the risk of inducing opportunistic infections, furthermore, when used in addition to steroids, this risk is highly amplified.[7] Hence, many worries have risen among doctors and patients in regards to commencing new treatments and the continuation thereof. Due to this pandemic, many patients' treatments have been postponed or delayed and therefore activation rates have risen considerably.[5] However, while the number of SARS-CoV-2 cases has escalated, conducted studies have shown that the existence of IBD has not influenced the degree of risk of infection.[8,9] While there are studies done according to observational and reported cases to illustrate the effects of drugs used for the treatment of IBD on COVID-19 pneumonia and severe COVID-19, unfortunately, there are not any controlled studies. It has been reported that systemic steroid use increases the risk of infections while biological agents do not,[10-12] and there are conflicting data regarding the use of azathioprine (AZA).[10,13-15] Since the beginning of this pandemic, it has been agreed that disease activation and the existence of comorbid diseases represent a risk factor for COVID-19 in IBD patients, conversely, the use of immun omodulator/immunosuppressive agents do not increase the risk. However, it has been reported that a high dose (≥20 mg/day) of prednisolone can increase the risk of severe COVID-19.[16]

In this study, we retrospectively investigated the prevalence and the risk factors of severe COVID-19 disease in IBD patients who were followed up in our tertiary referral center.

MATERIALS AND METHODS

Between March 2020 and May 2021, from our IBD outpatient database, 1195 UC and CD patients were evaluated. Patients who came for a routine control were questioned whether they were diagnosed with SARS-CoV-2 infection or not, as for the patients who did not visit the clinic during the pandemic, either the hospital's or Public Health data system was used to check if they had undergone a polymerase chain reaction (PCR) test for SARS-CoV-2. Patients with a positive PCR test and/or who had typical findings in pulmonary computerized tomography (CT) scan were classified as SARS-CoV-2-positive patients. Information such as age, sex, diagnosis, medicines used for IBD, history of any other comorbid diseases such as diabetes mellitus, hypertension, hyperlipidemia, obesity, cardiovascular disease, cerebrovascular disease, chronic pulmonary disease, chronic liver and kidney disease, cancer, rheumatological disease, and organ transplantation were recorded. Patients' disease activation and remission state in the perspective of CD and UC were also recorded. Patients with UC with Partial Mayo Score <2 and patients with CD with a Harvey Bradshaw Index <5 were admitted as in clinical remission. Patients who had been infected with SARS-CoV-2 were further investigated. They were questioned about symptomatology, hospital admissions, the need for oxygen, and pulmonary imaging (including pulmonary CT scan) if applicable. Asymptomatic patients or patients with mild symptoms such as fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, and loss of taste and smell were defined as mild COVID-19. The patients who had evidence of pulmonary infiltration in pulmonary CT and/or chest x-ray and SpO_2 ≥94% were defined as moderate COVID-19. The patients who need oxygen therapy or high respiratory frequency (>30 breaths/min) and/or pulmonary infiltration in pulmonary CT are defined as severe COVID-19. Due to the fact that some COVID-19 patients were treated in other hospitals laboratory results could not be obtained. Variability of characteristics between patients with and without severe COVID-19 was assessed. And also, severe COVID-19 disease risk factors were evaluated.

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee (registry number: 2021000028 and approval number: 2021/28. Date: March 30, 2021).

Statistical Analysis

Statistical analyses were performed with Statistical Package for the Social Sciences 22 (IBM Corp.; Armonk, NY, USA). Mean and standard deviation were used for continuous values and percentages were used for categorical data. Differences between groups of patients for categorical value were tested with the χ^2 test and Fisher's exact test. Risk factors of severe COVID-19 were evaluated with logistic regression. A value of $P < .05$ was considered to be statistically significant.

RESULTS

One thousand one hundred ninety-five IBD patients were evaluated. Out of 1195 IBD patients, 130 patients had a COVID-19 disease diagnosis. In regard to these patients' demographic differences, 70 patients (53.8%) were male. The average age of patients was 44.3 ± 14.1 years and

most of them (58.5%) were follow-up patients with UC. Thirty-five patients (28.2%) had active IBD and 47 patients (36.2%) had at least 1 comorbid disease (Table 1). From the beginning of the pandemic to May 31, 2021, 130 (10.9%) patients were found to be infected by SARS-CoV-2. The diagnosis was confirmed in 129 of those patients with a positive PCR for SARS-CoV-2, and 1 patient was diagnosed by typical findings in pulmonary CT scan. Thirty-nine patients (30%) had COVID-19 pneumonia. Twenty-seven patients (20.8%) were hospitalized. The number of patients with mild, moderate, and severe COVID-19 was 91 (70%), 16 (12.3%), and 23 (17.7%), respectively (Table 1). One hundred nineteen patients were on IBD medications whereas the remaining 11 patients were receiving no medical treatment regarding IBD. Mesalazine was the most used drug in patients (n = 90, 69.2%). Forty-three patients (33.1%) were using AZA and the other 43 (33.1%) were using biological agents. As for biological agents, 30 patients (23.1%) were on anti-tumor necrosis factor (TNF) and 13 patients (9.9%) were on anti-integrin therapy. Patients receiving steroid therapy (n = 11) were as follows: 6 (8.5%) on budesonide, 5 on prednisolone or methylprednisolone (Table 2). Immunosuppressive and immunomodulatory drugs were stopped in all patients with SARS-CoV-2 positivity according to guidelines.[17-19] In patients using either systemic or topical mesalamine, the drug was continued.

The patients with severe (54.5 ± 15.2) and moderate (45.5 ± 15.4) COVID-19 were older than with mild disease (41.5 ± 12.5) (mild vs moderate/mild vs severe, *P* = .26/.001, respectively). Thirty-five patients (28.2%) had active IBD at the time of detection of SARS-CoV-2. The percentage of active IBD patients in mild, moderate, and severe COVID-19 groups were 20.9%, 31.3%, and 47.8%, respectively (mild vs moderate, *P* = .36, and mild vs severe *P* = .009). Also the existence of at least 1 comorbid disease rates were 25.3% in mild, 50% in moderate, and 69.6% in severe COVID-19 patients' groups (mild vs moderate *P* = .04, mild vs severe *P* = .001) (Table 1).

With respect to administered drugs, patients using AZA were younger than patients not receiving (users/non-users: 38 ± 12.2/47.4 ± 14, *P* = .001). Also the patients' age differences between mesalazine (users/non-users: 45.1 ± 14/42.4 ± 14.4, *P* = .32), steroids (users/non-users: 47.2 ± 18.2/44 ± 13.8: *P* = .48), biological agents (users/non-users: 42 ± 13.5/45.5 ± 14.4, *P* = .19) users and non-users were not significant (Table 3). Between mild, moderate, and severe COVID-19 patients, there was no difference in the number of patients using mesalazine (68.1%/62.5%/78.3%, *P* = .53), biologic agents (35.2%/37.5%/21.7%, *P* = .44), and steroids (9.9%/6.3%/4.3%, *P* = .66). But in severe COVID-19 group the patients using AZA were less than in mild (mild/severe: 37.3%/8.7%, *P* = .02) (Table 2).

Out of 130 patients with COVID-19, 6 patients died. Two (1.5%) patients' deaths were related to COVID-19, 2 patients had a history of coronary heart disease leading to acute coronary syndrome, 1 patient who had a history of ischemic cerebrovascular disease died as a result of ischemic stroke, and 1 patient died due to complications related to postoperative sepsis. Three patients who died as a result of coronary heart disease and ischemic cerebrovascular disease were in remission for IBD. One of the

Table 1. Clinical and Demographic Characteristics of the Patients

	All Patients, n = 130 (100%)	Mild, n = 91 (70%)	Moderate, n = 16 (12.3%)	Severe, n = 23 (17.7%)	*P*, Mild-Moderate	*P*, Mild-Severe
Gender						
Male	70 (53.8)	50 (54.9)	8 (50)	12 (52.2)	.71	.81
Female	60 (46.2)	41 (45.1)	8 (50)	11 (47.8)		
Age						
mean ± SD	44.3 ± 14.1	41.5 ± 12.5	45.5 ± 15.4	54.5 ± 15.2	.26	**.001**
Age ≥60	21 (16.2)	8 (8.8)	3 (18.8)	10 (43.5)	.23	**.001**
UC	76 (58.5)	52 (57.1)	12 (75)	12 (52.2)	.18	.67
CD	54 (41.5)	39 (42.9)	4 (25)	11 (47.8)		
Active IBD	35 (28.2)	19 (20.9)	5 (31.3)	11 (47.8)	.36	**.009**
At least 1 comorbid disease	47 (36.2)	23 (25.3)	8 (50)	16 (69.6)	**.04**	**.001**
Smoker	22 (16.9)	16 (17.6)	3 (18.8)	3 (13)	.92	.83

IBD, inflammatory bowel disease.
The bold numbers are statistically significant values.

Table 2. Drugs Comparison of Mild, Moderate, and Severe COVID-19 Groups

	All Patients, n = 130 (100%)	Mild, n = 91 (70%)	Moderate, n = 16 (12.3%)	Severe n = 23 (17.7%)	*P*, Mild-Moderate	*P*, Mild-Severe
Receiving any treatment	119 (91.5)	84 (92.3)	14 (87.5)	21 (91.3)	.52	.87
Mesalazine	90 (69.2)	62 (68.1)	10 (62.5)	18 (78.3)	.66	.34
Mesalazine monotherapy/ combined	50 (55.6) 40 (44.4)	31 (50) 31 (50)	6 (60) 4 (40)	13 (72.2) 5 (27.8)	.56	.10
AZA	43 (33.1)	34 (37.4)	7 (43.8)	2 (8,7)	.63	**.008**
AZA monotherapy/combined	8 (18.6) 35 (81.3)	7 (20.6) 27 (79.4)	1 (14.3) 6 (85.7)	0 (0) 2 (100)	.70	1
Biologic agent	43 (33.1)	32 (35.2)	6 (37.5)	5 (21.7)	.86	.22
Biologic agent monotherapy/ combined	12 (27.9) 31 (72.1)	8 (25) 24 (75)	1 (16.7) 5 (83.3)	3 (60) 2 (40)	1	.14
Anti-TNF	30 (23.1)	24 (26.4)	4 (25)	2 (8.7)	.91	.07
Anti-TNF monotherapy/ combined	9 (30) 21 (70)	6 (25) 18 (75)	1 (25) 3 (75)	2 (100) 0 (0)	1	.09
Corticosteroid	11 (8.5)	9 (9.9)	1 (6.3)	1 (4.3)	.65	.40
Anti-integrin	13 (9.9)	8 (8.8)	2 (12.5)	3 (13)	.64	.54

IBD, inflammatory bowel disease; TNF, tumor necrosis factor.
The bold numbers are statistically significant values.

2 patients whose deaths was associated with COVID-19, was a 37-year-old woman with active UC who had undergone a liver transplant due to primary sclerosing cholangitis and was using mesalazine and anti-integrin. The other patient was a 59-year-old woman with quiescent CD under mesalazine treatment. She had hypertension as a comorbidity.

In univariate regression analysis, being 60 years or older (odds ratio [OR]: 8; 95% CI: 2.7-23.9, *P* = .001), having at least 1 comorbid disease (OR: 6.8; 95% CI: 2.5-18.5, *P* = .001), and the presence of active IBD (OR: 3.5; 95% CI: 1.3-9.1, *P* = .01) increased the risk of COVID-19, while the use of AZA (OR: 0.2; 95% CI: 0.1-0.7, *P* = .02) reduced the risk. There is no significant increase in risk when the use of steroid, mesalazine and biological agents are taken into account (*P* = .42, .35, and .23, respectively). Multivariate regression analysis was evaluated according to age, comorbidities, the disease activation and using AZA; the risk of severe COVID-19 was increased in the patients who was >60 years old (OR: 6.5; 95% CI: 1.6-26.5, *P* = .009), who had at least 1 comorbid disease (OR: 6.9; 95% CI: 2-24.2, *P* = .002), and active IBD (OR 10.7; 95% CI: 2.8-41.6, *P* = .001) but AZA did not affect the risk (OR: 0.2 ; 95% CI: 0.1-1.1, *P* = .07) (Table 4).

Table 3. The Differences in Mean Age Between Drug Users and Non-users

	Users	Non-users	*P*
Mesalazine	45.1 ± 14	42.4 ± 14.4	.32
AZA	38 ± 12.2	47.4 ± 14.1	**.001**
Corticosteroids	47.2 ± 18.2	44 ± 13.8	.48
Biological agent	42 ± 13.5	45.5 ± 14.4	.19
Anti-TNF	41.4 ± 14	45.2 ± 14.2	.20
Anti-integrin	43.4 ± 12.9	44.4 ± 14.3	.81

TNF, tumor necrosis factor; AZA, azathioprine.
The bold numbers are statistically significant values.

DISCUSSION

In this study, 1195 patients were evaluated, amongst which 130 patients (14.5%) had SARS-CoV-2 infection. In IBD patients, COVID-19 pneumonia was 30%, hospitalization was 20.8%, and deaths directly connected to COVID-19 were 1.5%. According to the official data at the time of the completion of our study, the COVID-19 mortality rate in the general population in Turkey was 0.9%. The mortality rate in our patient group was slightly higher than in the general population. However, since we do not have the detailed data on other risk factors in patients who died due to COVID-19 in the general population and there was no control group in our study, it is difficult to state how statistically significant this difference is.[20] Since the

Table 4. Univariate and Multivariate Regression Analysis for Risk of Severe COVID-19

	Univariate Analysis		Multivariate Analysis	
Characteristics	OR (95% CI)	*P*	OR (95% CI)	*P*
Gender	0.9 (0.4-2.2)	.81	-	-
Age ≥60	8 (2.7-23.9)	**.001**	6.53 (1.6-26.5)	**.009**
Diagnosis (UC/CD)	1.2 (0.5-3.1)	.67	-	-
Active IBD	3.5 (1.3-9.1)	**.01**	10.7 (2.8-41.6)	**.001**
At least 1 co-morbid disease	6.8 (2.5-18.5)	**.001**	6.9 (2-24.2)	**.002**
Smoking	1.7 (0.9-3.2)	.10	-	-
Mesalazine	1.7 (0.6-5)	.35	-	-
AZA	0.2 (0.1-0.7)	**.02**	0.2 (0.1-1.1)	.07
Biological agent	0.5 (0.2-1.5)	.23	-	-
Anti-TNF	0.3 (0.1-1.2)	.09	-	-
Anti-integrin	1.6 (0.4-6.4)	.54	-	-
Corticosteroid	0.4 (0.1-3.4)	.42	-	-

IBD, inflammatory bowel disease; TNF, tumor necrosis factor; AZA, azathioprine; UC, ulcerative colitis; CD, Crohn's disease.
The bold numbers are statistically significant values.

beginning of the pandemic, various numbers of hospitalization and mortality have been reported in IBD patients who contracted SARS-CoV-2 infection. A study conducted on the Italian population showed that hospitalization in IBD COVID-19 patients was 28%, and mortality was 7.6%. In a review involving 1028 COVID-19-positive IBD patients, the hospitalization rate was relatively similar (30.6%) compared to the previous study, but the mortality was lower (3.8%).[10,21] According to SECURE-IBD database, the hospitalization rate of IBD COVID-19 patients was 15%, and mortality was 4%.[22] While the hospitalization rate in our patients was similar, the mortality rate was lower than that published in the literature. It is acknowledged that there is a history of chronic vascular disease in our patients who died due to ischemic cerebrovascular disease and ischemic heart disease; however, it is unknown whether COVID-19 is a direct trigger factor. That is why we did not evaluate these patients as deaths due to COVID-19.

Age, the consumption of systemic steroids, presence of comorbidity, and active disease have been shown to be risk factors for COVID-19 pneumonia and severe COVID-19. According to previous studies, advanced age, and the presence of comorbid diseases increase the risk for severe COVID-19 in IBD patients, as in the normal population.[10,13,23-26] But it is not clear whether the type of IBD or activation of IBD increases the risk for severe COVID-19. While there are studies showing that there is no difference between UC and CD, there are also studies showing that UC increases the risk.[10,13,24,25] Similarly, there are different studies that show that IBD activation also increases the risk of severe COVID-19 or does not.[10,13,24] In our study, almost half of patients aged 60 and over (43.5%) had severe COVID-19, and 69.6% of all patients with severe COVID-19 had at least 1 comorbid disease. On the other hand, about half of 35 active IBD patients (n = 16) had moderate and severe COVID-19 and active IBD patients constituted 47.8% of the severe group. We observed the results that as COVID-19 disease became more serious, the proportion of patients with active IBD, that were ≥60 years old and who had the presence of at least 1 comorbid disease was increasing. Between mild to moderate COVID-19 patients, these increases were not significant for age and active IBD but were significant for patients with at least 1 comorbid disease. In the severe COVID-19 group, percentage of patients who were ≥60 years old, with active IBD, and with at least 1 comorbid disease was significantly higher than in the mild group. In addition, we did not determine any difference in the severity of COVID-19 between UC and CD.

Aside from these factors, the use of immunosuppressi ves/immunomodulators and/or biological drugs have not been shown to have any significant effects on the increase of severe COVID-19. Reports of the effect of these drugs on severe COVID-19 or COVID-19 pneumonia have been notified since the beginning of this pandemic. Nevertheless, because studies are only conducted through observation and case reports, and there are not any randomized studies, various results of the effect of these drugs on COVID-19 have been observed. It is recognized that the use of steroids in IBD patients increases the risk of severe COVID-19.[12,24,27] In our study, 11 SARS-CoV-2 infected patients were using steroids during infection. Among these 11 patients, only 1 patient developed severe COVID-19 and it was perceived that steroids did not increase the risk of severe disease. However, due to the inadequate number of patients using systemic steroids, it is inappropriate to achieve a definite conclusion.

Biological agents such as anti-TNF and anti-integrin do not increase the risk of severe COVID-19; in fact, some published studies indicate that such biological medicines reduce the risks of severe COVID-19.[10-12,14,27-29] During an infection of SARS-CoV-2, B and T lymphocytes' count

decrease. Meanwhile, in severe COVID-19, regulator T lymphocytes which produce anti-inflammatory cytokines such as IL-10 and TGF-beta which suppress immune response with cell–cell interaction decrease while the production of proinflammatory cytokines is increased by neutrophils. These conditions induce an increase in different cytokines along with TNF which causes a cytokine storm that eventually leads to triggering multi-organ failure.[28] For this reason, it is thought that anti-TNF and the other biological agents have a positive contribution to cytokine storm due to the fact that increase in the level of cytokines causes severe COVID-19. In accordance with previous studies, our study also confirms the suggestion that biological agents do not increase the risk of severe COVID-19.

The case is different for AZA. There are various results of thiopurines' effect on the risks for severe COVID-19 and related pneumonia. According to recent data obtained from SECURE IBD, it has been revealed in 1 study which has the highest number of IBD patients suffering from COVID-19, the treatment of thiopurine (monotherapy or in combination) when compared with anti-TNF monotherapy shows an increase in severe COVID-19 risk.[12] However, there are also many studies from several countries like Italy, Danish, USA, and Japan which show that thiopurine does not increase the risk of severe COVID-19.[10,13-15,30] In an in vitro study[31] previously done on the Middle East Respiratory Syndrome Coronavirus, it was observed that mercaptopurine suppresses viral protease, and there was a debate whether this effect can be achieved against viruses in antiviral treatments. Since there are not any studies performed on SARS-CoV-2, it would be speculative to assume that mercaptopurine would show the same outcome. In our study, we have ascertained that thiopurine treatment does not carry any risks for severe COVID-19. However, such a good prognosis might be attributed to the fact that patients treated with thiopurine are relatively younger than those not receiving this treatment. The recommended guidelines for thiopurine treatment during COVID-19 require that administration of this drug should be ceased after the diagnosis of COVID-19. Treatments should be resumed in patients in remission and those who are negative for SARS-Cov2 infection.[17-19,32] It should be emphasized that since these entire results are attributed to observational studies, thiopurine should be used with caution.

In our study, the most used drug for IBD patients was mesalazine, which has been used safely for years, and there are not any data showing that it increases the risk of infection in IBD patients. We observed that the use of this drug does not increase the risk of severe COVID-19. However, according to the most recent publication in SECURE IBD database, it has been indicated that the risk of severe COVID-19 increases in patients treated with mesalazine/sulfasalazine in comparison to patients treated without mesalazine/sulfasalazine. Also, compared to anti-TNF monotherapy with mesalazine/sulfasalazine monotherapy, the risk of COVID-19 was again higher in the mesalazine/sulfasalazine group. In the same study, no considerable difference was noticed between patients who received mesalazine and those who did not receive any treatment for IBD, and according to the results, mesalazine, which is important in the treatment of mild to moderate UC, was not recommended to be discontinued during the COVID-19 pandemic. But it has been said that it is possible to reduce or not use mesalazine in patients with a limited contribution of mesalazine to treatment, such as CD, or in patients with a high risk of severe COVID-19 (such as advanced age) who have been added to biological therapy.[12] In contrast to this study, there are several publications suggesting that mesalazine does not increase the risk of severe COVID-19 and COVID-19 pneumonia.[10,13,33] Someone can argue that increased risk of COVID-19 in patients using mesalamine might be due to the cease of other immunosuppressive drugs in high-risk patients. Due to the differences in outcomes, it is still not possible to confirm that mesalazine is a risk factor for severe COVID-19.

This study is important in that it includes a large number of single-center IBD patients and is the first study to evaluate the severity of COVID-19 in IBD patients in Turkey. One of the limitations of our study was that it was retrospective. Some of our patients were hospitalized and treated in other centers due to COVID-19. Therefore, we did not use laboratory parameters for COVID-19 severity. This was the other limitation of our study. However, we used parameters that could learn from medical reports and from questioning the patients like pulmonary CT reports, oxygen requirement, need for a mechanical ventilator, severe shortness of breath, and history of intensive care to determine COVID-19 severity.

CONCLUSION

In summary, we have confirmed that drugs used in IBD management do not increase the risk of severe COVID-19. Nevertheless, it would be speculative to state the same thing for steroid treatment. Older age, active IBD, and the presence of comorbid diseases are more significant

factors when assessing the risk for developing severe disease in COVID-19 patients.

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