Susceptibility of Patients with Inflammatory Bowel Disease to COVID-19 Compared with Their Households

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ABSTRACT

BACKGROUND:
Immunosuppressive agents used in the treatment of inflammatory bowel diseases (IBDs) could potentially increase the risk of coronavirus disease 2019 (COVID-19). We aimed to compare COVID-19 frequency in patients with IBD with their households and identify the related risk factors.

METHODS:
Firstly, a multi-centered, observational study on 2110 patients with IBD and 2110 age-matched household members was conducted to compare COVID-19 frequency. Secondly, the data of patients with IBD and COVID-19 who had called the COVID-19 hotline were added. Multivariable logistic regression was used to evaluate the effect of age, type and severity of IBD, the number of comorbidities, and medications on the frequency of COVID-19 among the patients with IBD.

RESULTS:
The prevalence of COVID-19 in patients with IBD and household groups was similar (34 [1.61%] versus 35 [1.65%]; $P = 0.995$). The prevalence of COVID-19 increased from 2.1% to 7.1% in those with three or more comorbidities ($P = 0.015$) and it was significantly higher in those with severe IBD ($P = 0.026$). The multivariable analysis only showed a significant association with anti-TNF monotherapy (OR: 2.5, CI: 0.97-6.71, $P = 0.05$), and other medications were not associated with COVID-19.

CONCLUSION:
The prevalence of COVID-19 in patients with IBD was similar to the household members. Only patients with IBD receiving anti-TNF monotherapy had a higher risk of COVID-19 susceptibility. This finding could be attributed to the higher exposure to the virus during administration in health care facilities.

KEYWORDS:
Inflammatory bowel disease, COVID-19, Medications, Frequency

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INTRODUCTION

As of April 18th, 2021, more than 140 million confirmed cases of coronavirus disease 2019 (COVID-19)around the globe have resulted in over 3 million deaths.[1] SARS-CoV-2 (severe acute respiratory

syndrome coronavirus 2) binds to their targets using angiotensin-converting enzyme 2 (ACE2), expressed by the epithelial cells of the lungs, liver, intestines, kidney, heart, and blood vessels.[2] It is present in high concentrations in the terminal ileum and colon[3] and its expression is increased when there is inflammation in the bowel, such as in patients with IBD.[4] Most studies have shown that COVID-19 does not occur more frequently in patients with inflammatory bowel diseases (IBDs) compared with the general population.[5-9]

The burden of IBD is rising globally, with about 6.8 million patients worldwide.[10] IBD is caused by an excess immune response to gut microbiota in genetically predisposed patients, usually resulting from an interaction between multiple environmental factors.[11] Corticosteroids, immunomodulators, and biologics are commonly used to treat IBD; however, there is an increased risk of viral and bacterial infections.[12] The prevalence of opportunistic infections varies and depends on the type and dose of immunosuppressant and the patient's age and comorbidities. Such a prevalence is higher in combination therapy.[12]

Studies from China and Italy have shown that severe COVID-19 has a lower incidence in patients with IBD than the normal population.[13] Also, immunosuppressive agents can blunt the cytokine storm, which is responsible for severe complications and mortality in patients with COVID-19.[14] These studies suggest that patients with IBD have a lower incidence of COVID-19 and lower mortality when infected. The cytokine profile in patients with severe COVID-19 experiencing cytokine storm is very similar to that seen in the inflamed bowel in the active phase of IBD, characterized by T cells hyperactivation and massive interleukin 2 and 6 (IL-2 and IL-6) production.[15,16] Most studies have reported outcomes and severity of COVID-19 in patients with IBD, while our study focuses on the frequency of COVID-19 in those who have IBD.

We hypothesized that the intestine could act as a secondary site for SARS-CoV2 virus tropism and infection, leading to greater susceptibility to COVID-19 in patients with IBD. Our goal was to determine the prevalence of COVID-19 among tested patients and identify risk factors in our large cohort of patients with IBD collected through the Registry of Crohn's and Colitis in order to guide preventive strategies and management of patients with IBD and their health care providers.

MATERIALS AND METHODS

This study had two phases. Firstly a prospective, multi-centered study was conducted, and data were gathered using the Registry of Crohn's and Colitis.[17] Patients were enrolled from March 11th, 2020, until May 31st.

There are 13 165 registered patients with IBD in 31 provinces in the Crohn's and Colitis cohort. Due to resource limitations, we only approached patients with IBD in six provinces with the highest number of patients. All patients with IBD in six provinces were called. A questionnaire was filled including data regarding age, sex, ethnicity, place of residence, COVID-19 status, and date of diagnosis, weight, height, IBD type, and activity (classified as remission, mild, moderate, severe) based on the patients' reports,[18] IBD medications used, and clinical manifestations of COVID-19 (cough, chills, dyspnea, fever, sore throat, abdominal pain, diarrhea, nausea, vomiting, myalgia, headache, and anorexia). We also collected the same data from household members of the patients. If the person was under 9 years old, the guardian answered the questions. We performed propensity score matching (PSM) using a 1:1 ratio to remove the effect of age difference between patients with IBD and household controls. Both groups were compared considering COVID-19 (Figure 1). The age-matched IBD and household groups were compared regarding the frequency and risk factors for COVID-19.

In the second phase, we sought the risk factors of COVID-19 by comparing those who had and did not have this disease in the IBD group. In addition to IBD patients with COVID-19 from the first phase, the data of COVID-19 patients with IBD who had called the COVID-19 hotline were added. They were guided as to what to do and, if necessary, referred to a local physician. These patients were followed up to assess COVID-19 confirmation. Data regarding age, sex, ethnicity, place of residence, weight, height, IBD type and activity (classified as remission, mild, moderate, severe) based on the patients' reports, IBD medications used, and clinical manifestations of COVID-19 were gathered from patients with IBD patients and COVID-19.

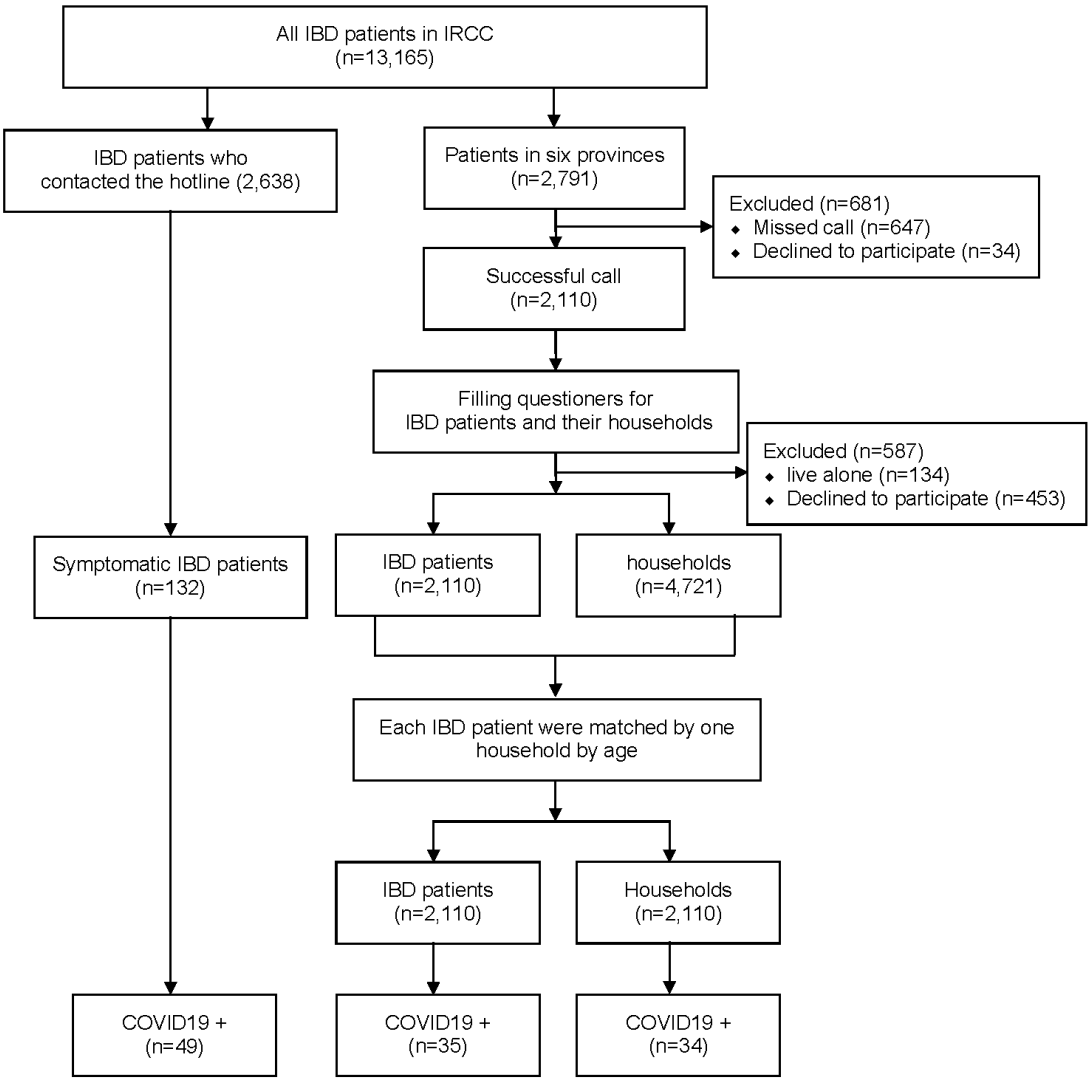

Fig. 1. Patient enrollment flowchart.

In this study, patients who had previous contact with a patient with COVID-19 and three or more of the following were considered likely to have this disease: cough, fever, dyspnea, dysosmia, dysgeusia, or computed tomographic (CT) findings suggestive of the disease. These data were reviewed by an expert team, a gastroenterologist, and a radiologist, and the diagnosis was made based on the team's decision. Patients with polymerase chain reaction (PCR)-confirmed nasopharyngeal swab tests were considered to have the disease. Duplicates and erroneous reports were removed.

Statistical Analysis

In the first phase, descriptive analysis was used to show demographic data and clinical manifestations. To compare COVID-19 in those with and without IBD, we performed PSM using a 1:1 ratio to remove the effect of the age difference and then measured and compared the prevalence of COVID-19 between them.

In the second phase, we assessed the effect of age, type and severity of IBD, the number of comorbidities, and medications used (anti-tumor necrosis factor [TNF], immunomodulators [azathioprine, 6-mercaptopurine, methotrexate], 5-ASA compounds, corticosteroids, Janus kinase (JAK) inhibitors, and combo therapy [anti-TNF with immunomodulator]) on the susceptibility to COVID-19 among patients with IBD. After performing univariable logistic regression for selecting covariates based on a *P* value less than or

Table 1. Demographics and clinical characteristics of patients with IBD and households

Variable [a,b]	Total (N= 4220)	Households (n=2110)	Patients with IBD (n=2110)	*P* value
Age (y), n (%)				
0-9	90 (2.1)	45 (2.1)	45 (2.1)	1.000
10-19	624 (14.7)	312 (14.7)	312 (14.7)	
20-29	1376 (32.6)	688 (32.6)	688 (32.6)	
30-39	914 (21.6)	457 (21.6)	457 (21.6)	
40-49	662 (15.6)	331 (15.6)	331 (15.6)	
50-59	392 (9.2)	196 (9.2)	196 (9.2)	
60-69	124 (2.9)	61 (2.8)	63 (2.9)	
≥70	38 (0.9)	20 (0.9)	18 (0.8)	
Gender, n (%)				
Male	2083 (49.3)	1,097 (51.9)	986 (46.8)	0.001
Female	2135 (50.6)	1,016 (48.8)	1,119 (53.1)	
Comorbidity, n (%)				
Hypertension	288 (6.8)	132 (6.2)	156 (7.3)	0.160
Coronary heart disease	164 (3.8)	82 (3.8)	82 (3.8)	1.000
Diabetes	207 (4.9)	108 (5.1)	99 (4.6)	0.569
COPD	3 (0.1)	3 (0.1)	0 (0.0)	0.250
Asthma	61 (1.4)	18 (0.8)	43 (2.0)	0.002
Cancer	20 (0.4)	9 (0.4)	11 (0.5)	0.823
History of stroke	5 (0.1)	5 (0.2)	0 (0.0)	0.062
Chronic renal disease	72 (1.7)	20 (0.9)	52 (2.4)	0.000
Chronic liver disease	161 (3.8)	36 (1.7)	125 (5.9)	0.000
Current smoker	181 (4.2)	88 (4.1)	93 (4.4)	0.761
Tabaco	87 (2.0)	36 (1.7)	51 (2.4)	0.129
Other	165 (3.9)	64 (3.0)	101 (4.7)	0.003
Number of comorbidities, n (%)				
0	3146 (74.4)	1652 (78.1)	1494 (70.7)	0.000
1	805 (19.0)	340 (16.0)	465 (22.0)	
2	200 (4.7)	94 (4.4)	106 (5.0)	
≥3	75 (1.7)	27 (1.2)	48 (2.2)	
COVID-19 related symptoms, n (%)				
Cough	215 (5.0)	85 (4.0)	130 (6.1)	0.002
Chills	197 (4.6)	80 (3.7)	117 (5.5)	0.008
Dyspnea	0.12 (5.2)	76 (3.6)	145 (6.8)	0.000
Fever	280 (6.6)	113 (5.3)	167 (7.9)	0.001
Sore throat	134 (3.1)	41 (1.9)	93 (4.4)	0.000
Abdominal pain	1 (0.0)	1 (0.1)	0 (0.0)	1.000
Diarrhea	5 (0.1)	1 (0.1)	4 (0.1)	0.375
Nausea	9 (0.2)	0 (0.0)	9 (0.4)	0.004
Vomiting	4 (0.0)	2 (0.1)	2 (0.1)	1.000
Myalgia	140 (3.3)	50 (2.3)	90 (4.2)	0.001
Headache	56 (1.3)	18 (0.85)	38 (1.80)	0.010
Anorexia	10 (0.2)	3 (0.14)	7 (0.33)	0.343

Table 1. Continued

Variable [a,b]	Total (N= 4220)	Households (n=2110)	Patients with IBD (n=2110)	*P* value
Asymptomatic	3528 (83.4)	1813 (85.80)	1715 (81.16)	0.000
COVID-19 diagnosis, n (%)				
COVID-19 positive (PCR)	72 (1.7)	34 (1.6)	35 (1.6)	0.995
Disease type, n (%)				
Crohn's disease	528 (24.9)	N/R	528 (24.9)	N/A
Ulcerative colitis	1562 (73.9)	N/R	1562 (73.9)	
IC, n (n)	23 (1.1)	N/R	23 (1.1)	
IBD activity, n (%)		**N/R**		
Remission	1368 (64.8)	N/R	1368 (64.8)	N/A
Mild	413 (19.5)	N/R	413 (19.5)	
Moderate	220 (10.4)	N/R	220 (10.4)	
Severe	108 (5.1)	N/R	108 (5.1)	
Concomitant therapy for IBD, n (%)		**N/R**		
5-ASA	1527 (36.1)	N/R	1527 (36.1)	N/A
Corticosteroids	119 (2.8)	N/R	119 (2.8)	N/A
Thiopurines, 6 MP, MTX, monotherapy	680 (16.09)	N/R	680 (16.09)	N/A
Anti-TNF without Thiopurines, 6 MP, MTX	291 (6.89)	N/R	291 (6.89)	N/A
Anti-TNF with Thiopurines, 6 MP, MTX	184 (4.35)	N/R	184 (4.35)	N/A
JAK inhibitor	27 (0.64)	N/R	27 (0.64)	N/A

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; 5-ASA, 5-Aminosalicylic Acid; AZA, Azathioprine; MTX, Methotrexate; JAK, Janus kinase; N/S: not significant; N/R: not relevant

[a] Percentages do not include missing values.

[b] Percentages from each subcategory may not add up to the exact number of total reported cases due to missing values and/or non-mutually exclusive variables.

equal to 0.2, multivariable logistic regression was used to assess the association and susceptibility of these variables to COVID-19 among patients with IBD.

Data were analyzed using STATA software version 11, and *P* values <0.05 were considered statistically significant.

RESULTS

A total of 2791 patients with IBD were registered in six provinces in the Registry of Crohn's and Colitis. 2110 patients answered our call and co-operated (response rate: 75.6%) between March 11th and May 31st, 2020. 134 patients with IBD lived alone and 453 did not co-operate to share their household members' information; totally 4721 households were enrolled. In the first phase, to compare the frequency of COVID-19 between patients with IBD and households, we enrolled 2110 age-matched patients with IBD and 2110 persons without IBD.

In the second phase, 2638 patients with IBD had contacted our hotline, from March 11th, 2020, until May 31st, with questions regarding COVID-19 and their IBD. 132 patients reported suspicious symptoms for COVID-19, of whom COVID-19 was confirmed in 49 patients; thus, the total number of patients with IBD and with COVID-19 in the second phase summed up to 84.

Demographic and clinical data are presented in Table 1. The mean age was 42.1 (±13.8) years. 51.9% of patients with IBD and 46.8% of households were men. Most of the patients with IBD had ulcerative colitis (73.9%) and most of them were in clinical remission (64.8%). The most commonly used medication for IBD was 5-ASA (36.1%). Hypertension was the most frequent comorbidity in both IBD and household groups (6.2 and 7.3%, respectively). Overall, 19.0% had one comorbidity, 4.7% had two, and 1.7% had three or more comorbidities. The prevalence of COVID-19 in IBD and household groups did not differ (34 [1.61%] versus 35 [1.65%] *P*=0.995).

Table 2. COVID-19 status by demographic, clinical, and treatment characteristics of patients with IBD

Variable	Overall 2159 (100%)	Without COVID 2075 (96.11%)	With COVID 84 (3.89%)	*P* value
Disease type, n (%)				
Crohn's disease	546 (25.2)	522 (25.1)	24 (28.57)	0.630
IC	23 (1.1)	23 (1.1)	0 (0.00)	
Ulcerative colitis	1590 (73.6)	1530 (73.7)	60 (71.43)	
Age (y), n (%)				
0-9	46 (2.1)	45 (2.1)	1 (1.1)	0.304
10-19	318 (14.7)	307 (14.8)	11 (13.1)	
20-29	702 (32.5)	678 (32.7)	24 (28.5)	
30-39	474 (21.9)	448 (21.6)	26 (30.9)	
40-49	337 (15.6)	327 (15.7)	10 (11.9)	
50-59	198 (9.1)	189 (9.1)	9 (10.7)	
60-69	63 (2.9)	62 (2.9)	1 (1.1)	
≥70	18 (0.8)	16(0.77)	2 (2.38)	
Sex, n (%)				
Male	1004 (46.6)	969 (46.8)	35 (41.6)	0.373
Female	1147 (53.3)	1098 (53.1)	49 (58.3)	
Comorbidity, n (%)				
Hypertension	162 (7.5)	151 (7.2)	11 (13.1)	0.056
Coronary heart disease	85 (3.9)	80 (3.8)	5 (5.9)	0.380
Diabetes	103 (4.7)	96 (4.6)	7 (8.3)	0.117
Asthma	45 (2.0)	43 (2.0)	2 (2.3)	0.694
Cancer	11 (0.5)	11 (0.5)	0 (0.0)	1.000
History of stroke	0 (0)	0 (0)	0 (0)	-
COPD	0 (0)	0 (0)	0 (0)	-
Chronic renal disease	52 (2.4)	48 (2.3)	4 (4.7)	0.141
Chronic liver disease	130 (6.0)	122 (5.8)	8 (9.5)	0.161
Current smoker	96 (4.4)	91 (4.3)	5 (5.9)	0.420
Tobacco	51 (2.3)	50 (2.4)	1 (1.1)	0.721
Other	102 (4.7)	96 (4.6)	6 (7.1)	0.287
Number of comorbidities, n (%)				
0	1523 (70.5)	1473 (70.9)	50 (59.5)	0.015*
1	475 (22.0)	453 (21.8)	22 (26.1)	
2	110 (5.0)	104 (5.0)	6 (7.1)	
≥3	51 (2.3)	45 (2.1)	6 (7.1)	
IBD disease activity, n (%)				
Remission	1386 (64.3)	1341 (64.7)	45 (53.5)	0.026*
Mild	426 (19.7)	410 (19.8)	16 (19.0)	
Moderate	230 (10.6)	216 (10.4)	14 (16.6)	
Severe	113 (5.2)	104 (5.0)	9 (10.7)	
Concomitant therapy for IBD, n (%)				
5-ASA	1556 (72.1)	1497 (72.1)	59 (70.2)	0.710
Corticosteroids	128 (5.9)	115 (5.5)	13 (15.4)	0.001*
Thiopurines, 6 MP, MTX	695 (32.1)	667 (32.1)	28 (33.3)	0.813
Anti-TNF without Thiopurines, 6 MP, MTX	306 (14.1)	286 (13.7)	20 (23.8)	0.016*
Anti-TNF with Thiopurines, 6 MP, MTX	191 (8.8)	180 (8.6)	11 (13.1)	0.168
JAK inhibitor	27 (1.2)	27 (1.3)	0 (0.0)	0.623

Abbreviations: IC, Indeterminate colitis; COPD, Chronic Obstructive Pulmonary Disease; 5-ASA, 5-Aminosalicylic Acid; AZA, Azathioprine; MTX, Methotrexate; JAK, Janus Kinase.
*Statistically significant

Table 3. Univariate and multivariate regression for potential risk factors of COVID-19 in patients with IBD

Covariates (Ref)	Univariable analysis			Multivariable analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Ulcerative colitis (Crohn's disease)	0.85	(0.52-1.38)	0.519	-	-	-
Gender, (Male)	1.23	(0.79-1.92)	0.349	-	-	-
Age, (0-9)	**Ref.**			**Ref.**	**-**	**-**
10-19 years	1.61	(0.20-12.78)	0.651	1.55	(0.11-20.17)	0.736
20-29 years	1.59	(0.21-12.04)	0.652	1.09	(0.09-13.29)	0.943
30-39 years	2.61	(0.34-19.70)	0.352	1.85	(0.15-22.72)	0.631
40-49 years	1.37	(0.17-11.01)	0.763	1.19	(0.09-15.60)	0.894
50-59 years	2.14	(0.26-17.34)	0.475	2.54	(0.18-35.50)	0.488
60-69 years	0.72	(0.04-11.91)	0.822	2.25	(0.05-89.86)	0.665
≥70 years	5.62	(0.47-66.32)	0.170[a]	3.33	(0.13-82.38)	0.461
Number of comorbidities, (0)						
1	1.43	(0.85-2.38)	0.171[a]	1.28	(0.59-2.78)	0.520
2	1.69	(0.71-4.05)	0.232	.83	(0.20-3.45)	0.803
≥3	3.92	(1.60-9.63)	0.003[a]	1.01	(0.09-10.30)	0.992
IBD disease activity (Remission)						
Mild	1.66	(0.79-3.46)	0.177[a]	.86	(0.34-2.15)	0.749
Moderate	.85	(0.48-1.53)	0.611	.91	(0.43-1.91)	0.812
Severe	2.21	(0.95-5.15)	0.065[a]	1.12	(0.36-3.44)	0.844
Concomitant therapy for IBD (None)						
5-ASA	.91	(0.56-1.46)	0.703	-	-	-
Corticosteroids	3.12	(1.67-5.80)	0.000[#]	1.87	(0.80-4.36)	0.147
Thiopurines, 6 MP, MTX	1.05	(0.66-1.67)	0.819	-	-	-
Anti-TNF without Thiopurines, 6 MP, MTX	1.95	(1.16-3.27)	0.011[a]	2.56	(0.97-6.71)	**0.055***
Anti-TNF with Thiopurines, 6 MP, MTX	1.58	(0.82 -3.045)	0.165[a]	.51	(0.15-1.67)	0.268

Abbreviations: IBD, Inflammatory bowel diseases; 5-ASA, 5-Aminosalicylic acid; AZA, Azathioprine; MTX, Methotrexate
[a] Variables with *P* value less than 0.2 in univariable analysis were entered into the multivariable analysis.
*Statistically significant.

Table 2 shows the demographic and clinical characteristics of patients with IBD with and without COVID-19. It illustrates that COVID-19 susceptibility was not related to the type of IBD (ulcerative colitis or Crohn's disease), age group, or sex. The prevalence of COVID-19 increased from 2.1% to 7.1% in those with three or more comorbidities ($P = 0.015$). The prevalence of COVID-19 was significantly higher in those with severe IBD compared with those in remission ($P = 0.026$). Patients with COVID-19 were more likely to use corticosteroids (15.4% versus 5.5%, $P = .001$). Likewise, those receiving anti-TNFs without immunomodulators had a higher COVID-19 susceptibility (23.81% versus 5.54%, $P = 0.016$). There was no significant association between the use of 5-ASA, immunomodulators, and combo therapy with COVID-19 susceptibility.

Despite finding a significant association in univariable analysis between COVID-19 susceptibility and at least three comorbidities, moderate and severe to mild IBD activity, corticosteroid use, and anti-TNF monotherapy (Table 3), multivariable analysis only showed a significant association between COVID-19 susceptibility and anti-TNF monotherapy (OR: 2.5, CI: 0.97-6.71, $P = 0.05$), and using other medications were not associated with COVID-19 susceptibility (Table 3).

DISCUSSION

We have reported the results of a national prospective cohort from a national registry. The prevalence of COVID-19 in patients with IBD was similar to the household members in our cohort. Only those receiving

anti-TNF monotherapy showed a higher COVID-19 susceptibility. We identified 34 (1.61%) patients with COVID-19 in the IBD group and 35 (1.65%) patients with COVID-19 in the household groups. This shows that our patients with IBD did not have a higher chance of getting this disease compared with the household members.

Healthcare systems have collapsed during the COVID-19 pandemic worldwide.[13] Since the start of COVID-19 pandemic in Iran, as of April 18th, 2021more than 2.2 million cases have been confirmed, and 66327 people have died.[1] We have presented a national reporting system studying the frequency of COVID-19 in adult patients with IBD, based on data recorded in the Registry of Crohn's and Colitis.

There were no cases of COVID-19, reported by An and colleagues among 318 patients with IBD in Wuhan, China, even though they had discontinued the use of immunosuppressives.[19] Burke and co-workers studied the effect of immunosuppression on the risk of COVID-19 in a cohort of 5302 patients with IBD. They found that systemic immunosuppression was not associated with an increased risk of COVID-19.[20] Our data showed that there was no increased risk of COVID-19 due to immunosuppressive drugs other than monotherapy with anti-TNF. Our results support the findings of the meta-analysis done by Singh and colleagues.[21]

In our study, monotherapy with anti-TNF was associated with COVID-19 susceptibility among patients with IBD. Several studies have investigated the role of anti-TNF therapy on COVID-19 outcomes such as ICU admission, intubation, and death among patients with IBD, and they did not find a significant association.[22-24] This could be due to the different effect of anti-TNF therapy on disease susceptibility and severity. However, this result should be interpreted cautiously since this finding could be attributed to more exposure to infectious sources in patients with IBD who used anti-TNF therapy compared with patients with IBD using other medications.

A large French population-based study from 2009 until 2014, which included almost 210001 adult patients with IBD, showed a decreased risk of opportunistic viral infections in patients using only anti-TNF therapy compared with those on thiopurines (HR, 0.57; 95% CI, 0.38–0.87).[25] Our study showed the exact opposite results regarding SARS-CoV-2. We have to keep in mind that their study was conducted before the COVID-19 pandemic, and further studies should investigate the effect of different anti-TNF subtypes.

In the past two decades, there were two outbreaks of the coronavirus; the severe acute respiratory syndrome (SARS) and the Middle Eastern respiratory syndrome coronavirus (MERS-CoV) infection, sharing the same family of viruses and characteristics with SARS-CoV-2. There was no association between immunosuppression and the development of severe SARS or MERS.[26]

The International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) recommends continuing maintenance therapy and only highlights an increased risk of infection in those on corticosteroid doses above 20 mg/d prednisone or its equivalent.[27]

In our opinion, the best advice for patients with IBD in the COVID-19 pandemic is to follow the generally accepted advice of frequently washing the hands, covering the mouth and nose with a tissue or sleeve when coughing or sneezing, using a surgical mask in crowded areas, and avoiding close contact with anyone with flu-like symptoms. Patients should avoid using public toilets since reports state that the virus can be spread in fecal samples and aerosols.[5]

This study's major strength was its multicenter large sample size with geographically diverse samples, using data from the Registry of Crohn's and Colitis database. Our limitations were that we could not contact every patient with IBD, and we included only those with a positive PCR. Another limitation was the selection bias caused by patients who called our hotline, as they were probably more likely to have had symptoms. Also, reporting bias could influence the results because the patients with IBD answered the questions about themselves and their household members.

We conclude that only patients with IBD receiving monotherapy with anti-TNF have a higher COVID-19 susceptibility and should take the precautions more seriously. Other patients with IBD have the same risk as the household members.

ETHICAL APPROVAL

This study was approved by the Digestive Diseases Research Institute's Ethics Committee of Tehran University of Medical

Sciences (IR.TUMS.MEDICINE.REC.1399.197).

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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