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Original Article

COVID-19 Seroprevalence and Risk Factors in Inflammatory Bowel Disease Patients Receiving Immunosuppressive Treatment in the Pre-Vaccine Era

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Abstract

Objective: Inflammatory bowel diseases (IBD) are chronic conditions that often require immunosuppressive treatment. Although IBD patients may be more susceptible to COVID-19, studies have not shown an increased incidence in this group. This study aimed to assess the seroprevalence of COVID-19 in IBD patients and identify factors influencing infection rates and clinical outcomes, including disease activity and immunosuppressive treatment.
Methods: This study included IBD patients from the Istanbul University Gastroenterology Clinic between January 1 and June 1, 2021. Venous blood samples were collected, and antibodies against SARS-CoV-2 were detected using an enzyme-linked immunoassay. Results were reported as either positive or negative based on a cut-off index (COI ≥ 1.0).
Results: A total of 310 patients (110 with ulcerative colitis [UC] and 200 with Crohn's disease [CD]) were included. Antibody positivity was detected in 80 patients (25.8%), with 38.8% of them reporting a history of COVID-19, a significantly higher proportion than in the antibody-negative group (5.7%, $P < 0.001$). Among antibody-positive patients, 22.5% experienced symptomatic COVID-19, compared to 4.3% in the antibody-negative group ($P < 0.001$). No significant differences were observed in age, gender, comorbidities, or body mass index (BMI) between seropositive and seronegative patients.
Conclusion: Despite receiving immunosuppressive treatments, IBD patients did not experience an increased risk of severe COVID-19 outcomes. Serological screening proved useful in assessing the spread of COVID-19 in this population. Although IBD patients exhibited a higher seroprevalence, their prognosis remained generally mild, regardless of treatment type.
Keywords: COVID-19, Crohn's disease, ulcerative colitis

INTRODUCTION

Inflammatory bowel diseases (IBD) are chronic conditions characterized by alternating periods of remission and flare-ups, often requiring ongoing immunosuppressive therapy. Patients with IBD are known to have an increased risk of malnutrition due to inflammation and impaired nutrient absorption and are more susceptible to viral and bacterial infections as a result of immunosuppressive treatment.

At the onset of the COVID-19 pandemic, before vaccines became available, it was initially assumed that IBD patients would have a higher incidence of COVID-19 compared to the general population. However, reports from regions with high COVID-19 prevalence did not indicate an increased infection rate among IBD patients at that time.[1] One possible explanation is that these patients, aware of the risks associated with their chronic conditions and immunosuppressive therapies, had already been practicing partial social isolation. During the pandemic, they may have adhered more strictly to social distancing and isolation measures than the general population, potentially resulting in seropositivity rates that were lower or comparable to those seen in the broader community, contrary to initial expectations.

It has been suggested that immunosuppressive and immunomodulatory treatments may contribute to poorer outcomes in COVID-19 infections. In particular, asymptomatic COVID-19 carriers who initiate biological therapy could experience a worsened clinical course.[2] Conversely, some studies have indicated that immunomodulation may benefit patients with severe COVID-19 associated with hyperinflammatory syndrome.

This study, conducted during the pre-vaccine era, aimed to assess the seroprevalence of COVID-19 by analyzing antibodies in IBD patients with varied clinical profiles. Patients were categorized based on their clinical characteristics, the immunosuppressive medications they received, and their disease status (active or in remission). The study's objective was to investigate whether these factors influenced the frequency and clinical course of COVID-19 in this population.

MATERIALS AND METHODS

Patients

This prospective, observational study was designed to assess the seroprevalence of anti–SARS-CoV-2 antibodies in IBD patients followed at Gastroenterology Department of Cerrahpaşa Faculty of Medicine. All patients who visited the hospital between January 1 and June 1, 2021, were provided with information about the study, and informed consent was obtained from those who agreed to participate.

Demographic data were collected from the participants, and each patient was asked about a history of COVID-19 or any associated symptoms, including fever, cough, muscle pain, headache, shortness of breath, sore throat, diarrhea, and loss of smell or taste, occurring within the past 14 days. COVID-19-related hospitalizations, including ICU admissions, were reviewed using electronic health records. Additionally, a comprehensive evaluation of gastrointestinal symptoms was conducted, along with an assessment of IBD activity.

Antibody Status

Venous blood samples were collected from all participants, and serum was stored at −70°C until analysis. SARS-CoV-2 antibody detection was performed using the electrochemiluminescence method on the Cobas e 601 platform (Roche Diagnostics, Switzerland). This test detected total antibodies, primarily IgG, targeting an epitope of the viral nucleocapsid protein. Results were interpreted using a cut-off index (COI) and categorized as negative (COI < 1.0) or positive (COI ≥ 1.0).

After serum samples were collected, seroprevalence was evaluated, and the results were analyzed retrospectively. Patients with positive IgG test results were subsequently re-interviewed to gather information on any symptoms suggestive of symptomatic COVID-19 that may have occurred in the past three months.

Statistical Analysis

Categorical data are presented as frequencies and percentages, while continuous variables are expressed as mean ± standard deviation. The Shapiro-Wilk test was used to assess the normality of continuous variable distributions. For normally distributed data, mean differences between two groups were analyzed using an independent sample *t*-test, whereas the Mann-Whitney *U* test was applied to non-normally distributed data. Categorical variable frequencies were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. A *p*-value of <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS for Windows, Version 26.0 (Armonk, NY: IBM Corp.).

Ethical Approval

This study was approved by the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Dean's Office Clinical Research Ethics Committee (Approval Number: 83045809-604.01.02, Date: 16.06.2020). All procedures adhered to the ethical standards of the institutional and/or national research committee, as well as the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical guidelines.

MAIN POINTS

- The seroprevalence of anti-SARS-CoV-2 antibodies was high among IBD patients during the pre-vaccine period; however, their prognosis remained favorable regardless of ongoing immunosuppressive or biological therapy.
- No significant differences were observed between SARS-CoV-2 antibody-positive and antibody-negative patients in terms of age, gender, comorbidities, or BMI.
- A history of COVID-19 infection was significantly more common in the antibody-positive group, yet no patients required hospitalization or ICU admission.
- Prolonged infliximab use was associated with higher antibody negativity, while high-dose mesalazine use was positively correlated with antibody positivity.
- Frequent hospital visits for biological therapy and increased social activity may have contributed to the higher seroprevalence observed in IBD patients.

RESULTS

Sociodemographic and Clinical Characteristics of the Study Patients

A total of 310 patients were included in the study, comprising 110 with ulcerative colitis (UC) and 200 with Crohn's disease (CD). Of these, 55.8% were male, with a mean age of 40.6 ± 12.7 years. The average follow-up period was 8.66 ± 6.25 years. Additional patient characteristics are presented in Table 1.

Table 1. Sociodemographic data and clinical characteristics of the patients

Variables	n=310
Age, years (mean ± SD)	40.6 ± 12.7
Sex, n (%)	
Male	173 (55.8)
Female	137 (44.2)
Diagnosis, n (%)	
Ulcerative colitis	110 (35.9)
Crohn's disease	196 (64.1)
Mean disease duration time ± SD, years	8.66 ± 6.25
Median (Range)	7.5 (1-38)
History of surgery, n (%)	67 (21.6)
Smoking history, n (%)	
Ex smoker	101 (32.6)
Active smoker	71 (22.9)
Patients using 5-ASA, n	174
Patients using azathioprine, n (%)	183
Patients using methotrexate, n (%)	12
Patients using infliximab, n (%)	152
Patients using adalimumab, n (%)	24
Patients using vedolizumab, n (%)	20
Patients using corticosteroids, n (%)	11
Patients using budesonide, n (%)	8
Endoscopic remission, n (%)	154 (49.8)
Clinical remission, n (%)	241 (77.7)
Extraintestinal manifestation, n (%)	12 (3.9)
Comorbidites, n (%)	76 (24.5)
BMI, kg/m^2 (mean± SD)	23.8 ± 4.54

SD, standart deviation; BMI, body massindex; 5-ASA, 5-aminosalicylic acid

Comparison of Patients with Positive and Negative SARS-CoV-2 IgG Results

A total of 80 patients tested positive for SARS-CoV-2 antibodies. Among them, 50% were male, with a mean age of 38.3 ± 12.3 years, comparable to the antibody-negative group. In the antibody-positive group, 67.5% had CD, a proportion similar to that of the antibody-negative group, in which 62.8% had CD.

A history of COVID-19 infection was reported in 38.8% of patients in the antibody-positive group, a significantly higher proportion than in the antibody-negative group (5.7%, $P < 0.001$). Additionally, symptomatic COVID-19 was observed in 22.5% of the antibody-positive group, compared to only 4.3% in the antibody-negative group ($P < 0.001$). A comparison of other parameters between the groups is provided in Table 2.

Comparison of Patients with Positive and Negative SARS-CoV-2 IgG Results in Terms of Ongoing Treatments

No significant differences were observed between the two groups regarding ongoing treatments, as shown in the parameter comparison in Table 3.

Comparison of Patients in the Antibody-Positive Group Based on Symptomatic vs. Asymptomatic Status

A comparison between the two groups revealed that the symptomatic group had a longer duration of IBD follow-up than the asymptomatic group (32.6 ± 15.6 vs. 21.0 ± 12.4 years, $p = 0.002$) and a shorter duration of 5-ASA use (3.73 ± 3.72 vs. 7.77 ± 5.84 years, $p = 0.026$). Other parameter comparisons between the two groups are presented in Table 4.

Table 2. Comparison of the groups in terms of antibody positivity

	Antibody Positive Group	Antibody Negative Group	*P* value
Number of patients, n (%)	80	230	
Mean age ± SD, years	38.3 ± 12.3	41.4 ± 12.8	0.057*
Sex			
Male, n (%)	40 (50)	133 (57.8)	0.225#
Female, n (%)	40 (50)	97 (42.2)	
IBD, n (%)			
Ulcerative colitis	26 (32.5)	84 (37.2)	0.455#
Crohn's disease	54 (67.5)	142 (62.8)	
Mean disease duration ± SD, years	7.48 ± 5.72	9.07 ± 6.38	0.050*
History of surgery, n (%)	14 (17.5)	53 (23.0)	0.299#
Comorbidities, n (%)	20 (25.0)	56 (24.3)	0.907#
Mean BMI ± SD, kg/m^2	23.4 ± 4.75	23.9 ± 4.47	0.466*
History of Covid 19 disease, n (%)	31 (38.8)	13 (5.7)	**<0.001#**
History of symptomatic Covid 19 disease, n (%)	18 (22.5)	10 (4.3)	**<0.001#**
History of surgery, n (%)	14 (17.5)	53 (23.0)	0.299#
Mean ASA dose ± SD, mg/day	3093 ± 872	2790 ± 811	**0.036***
Mean duration of ASA usage ± SD, years	6.63 ± 5.59	6.89 ± 4.89	0.759*
Mean AZA dose ± SD, mg	80.2 ± 32.2	82.0 ± 31.9	0.736*
Mean duration of AZA usage ± SD, years	3.82 ± 3.90	4.55 ± 3.67	0.238*
Mean duration of MTX usage ± SD	0.75 ± 0.35	1.92 ± 1.83	0.192*
Mean duration of IFX usage ± SD, years	2.22 ± 2.11	3.29 ± 2.55	**0.016***
Mean duration of ADA usage ± SD, years	1.70 ± 0.83	1.89 ± 1.38	0.768*
Mean duration of VEDO usage ± SD, years	1.30 ± 0.67	1.68 ± 1.00	0.445*
Mean corticosteroid dose ± SD, mg/kg/day	16.4 ± 5.72	21.1 ± 9.92	0.369*
Mean duration of corticosteroid usage ± SD, months	2.20 ± 0.83	2.16 ± 1.94	0.972*
Endoscopic remission, n (%)	44 (55.0)	110 (48.0)	0.283#
Clinical remission, n (%)	58 (72.5)	183 (79.6)	0.191#
Extraintestinal manifestation, n (%)	2 (2.5)	10 (4.4)	0.738&

SD, standart deviation; BMI, body massindex; IBD, inflamatuar bowel disease; ICR, iliocecal resection; 5-ASA, 5-aminosalicylic acid ; AZA, azathioprine; MTX, methotrexate; IFX, infliximab; ADA, adalimumab; VEDO, vedolizumab; CRP, c-reactive protein; WBX, white blood cell.
**Mann-Whitney U test, #Pearson Chi-Square test, &Fisher's Exact test.

Table 3. Comparison of antibody positive and negative groups in terms of medical treatment

Variables	Positive	Negative	*P* value
Number of patients (n)	80	230	
Immunosuppressive, n (%)	2 (2.5)	16 (7)	0.174&
Immunomodulator, n (%)	5 (6.3)	6 (2.6)	0.159&
Immunosuppressive and immunomodulator, n (%)	111 (48.3)	43 (53.8)	0.398#
Corticosteroid, n (%)	6 (7.5)	13 (5.7)	0.590&
5-ASA, n (%)	10 (12.5)	35 (15.2)	0.552#
5-ASA and immunomodulator, n (%)	28 (35)	71 (30.9)	0.495#
5-ASA and immunosuppressive, n (%)	26 (32.9)	68 (29.6)	0.577#

5-ASA,5-aminosalicylic acid.
#Pearson Chi-Square test, &Fisher's Exact test.

Due to the presence of only one patient using methotrexate and vedolizumab in the symptomatic group, a comparison could not be conducted. Similarly, in the asymptomatic group, only one patient was using budesonide and corticosteroids, preventing a meaningful comparison.

Comparison of Patients with Positive SARS-CoV-2 IgG Results Based on COVID-19 Infection History

Among patients with positive SARS-CoV-2 IgG results, 31 had a history of COVID-19 infection. In this group, 51.6% were female, whereas in the group without a history of infection, a significantly higher proportion of female patients was observed (84.6%, $p = 0.04$). A comparison of other parameters between the groups is provided in Table 5.

Table 4. Comparison of symptomatic and asymptomatic patients within the antibody-positive group

Variables	Asymptomatic	Symptomatic	*P* value
Number of patients (n)	62	18	
Mean age ± SD, years	37.4 ± 12.3	41.3 ± 12.2	0.246*
Sex, n (%)			
Male	32 (48.4)	8 (44.4)	0.592#
Female	30 (51.6)	10 (55.6)	
IBD, n (%)			
Ulcerative colitis	18 (29.0)	8 (44.4)	0.219#
Crohn's disease	44 (71.0)	10 (55.6)	
Smoking history, n(%)			
Ex smoker	16 (25.8)	3 (16.7)	0.724#
Active smoker	18 (29.0)	6 (33.3)	
Mean smoking pack year ± SD, years	5.46 ± 8.15	6.55 ± 9.45	0.632*
Comorbidity, n (%)	16 (25.8)	4 (22.2)	1.000&
Mean BMI ± SD, kg/m^2	23.0 ± 4.21	25.1 ± 6.15	0.322**
History of resection, n (%)	11 (17.7)	3 (16.7)	1.000&
Mean disease duration ± SD, years	21.0 ± 12.4	32.6 ± 15.6	**0.002***
Mean Covid 19 IgG antibody levels ± SD, AU/ml	46.3 ± 64.7	46.0 ± 52.8	0.982*
Mean 5-ASA dose ± SD, mg	3006 ± 899	3333 ± 778	0.271*
Mean duration of 5-ASA usage ± SD, years	7.77 ± 5.84	3.73 ± 3.72	**0.026***
Mean AZA dose ± SD, mg	82.3 ± 31.7	72.7 ± 34.3	0.386*
Mean duration of AZA usage ± SD, years	4.00 ± 4.09	3.18 ± 3.18	0.543*
Mean duration of IFX usage ± SD, years	2.36 ± 2.17	1.62 ± 1.82	0.378*
Mean duration of ADA usage ± SD, years	2.0 ± 1.0	1.25 ± 0.35	0.401*
Colonoscopic remission, n (%)	34 (54.8)	10 (55.6)	0.957#
Clinic remission, n (%)	44 (71.0)	14 (77.8)	0.569#
Extraintestinal manifestation, n (%)	2 (3.2)	0 (0)	1.000&

SD, standart deviation; BMI, body massindex; IBD, inflamatuar bowel disease; ICR, iliocecal resection; 5-ASA, 5-aminosalicylic acid; AZA, azathioprine; IFX, infliximab; ADA, adalimumab
**Mann-Whitney U test, #Pearson Chi-Square test, &Fisher's Exact test

Table 5. Comparison of groups in terms of of antibody positivity in the patient groups those have positive COVID-19 history

Variables	Positive	Negative	*P* value
Number of patients	31	13	
Mean age ± SD, years	40.8 ± 12.8	36.5 ± 13.9	0.333*
Sex, n (%)			
Male	16 (48.4)	2 (15.4)	0.040#
Female	15 (51.6)	11 (84.6)	
IBD, n (%)			
Ulcerative colitis	3 (23.1)	13 (41.9)	0.314&
Crohn's disease	10 (76.9)	18 (58.1)	
Mean BMI ± SD, kg/m^2	24.7 ± 5.67	22.1 ± 4.32	0.146*
Mean disease duration ± SD, years	30.2 ± 14.4	22.7 ± 15.3	0.132*
Comorbidities, n (%)	8 (25.8)	2 (15.4)	0.697&
Smoking history, n (%)			
Ex smoker	8 (25.8)	6 (46.2)	0.413&
Active smoker	9 (29.0)	3 (23.1)	
History of resection, n (%)	3 (9.7)	3 (23.1)	0.339&
Mean duration of 5-ASA usage ± SD, years	4.78 ± 5.41	3.08 ± 2.33	0.466*
Mean duration of AZA usage ± SD, years	3.39 ± 4.60	3.30 ± 3.66	0.956*
Mean duration of IFX usage ± SD, years	1.13 ± 1.30	01.96 ± 2.38	0.401*
Colonoscopic remission, n (%)	17 (54.8)	9 (69.2)	0.376#
Clinic remission, n (%)	24 (77.4)	9 (69.2)	0.706&
Extraintestinal manifestation, n (%)	0 (0)	2 (15.4)	0.082&

SD, standart deviation; BMI, body massindex; IBD, inflamatuar bowel disease; 5-ASA, 5-aminosalicylic acid; AZA, azathioprine; IFX, infliximab.
**Mann-Whitney U test, #Pearson Chi-Square test, &Fisher's Exact test.

Due to only one patient using methotrexate in the group with a known history of COVID-19 infection, a meaningful comparison for this treatment could not be performed. Similarly, as there were no patients using budesonide in this group, a comparison was not possible. Regarding vedolizumab and adalimumab, two patients in the positive history group and one in the negative history group were on these treatments, making statistical comparison unfeasible.

DISCUSSION

Immune response dysregulation plays a key role in the pathogenesis of IBD. Since most IBD treatments have immunosuppressive effects, it has been hypothesized that IBD patients may be at higher risk for both SARS-CoV-2 infection and severe disease progression.[3] However, current data do not support this hypothesis. Considering that hyperinflammation is a major contributor to COVID-19 mortality, it has been suggested that immunosuppressive therapies may help mitigate excessive inflammatory responses, potentially reducing disease severity.[4,5]

Diagnosing SARS-CoV-2 infection is challenging. Although PCR-based nasopharyngeal swabs are the gold standard, they have limitations, including sampling errors, the need for specialized equipment, and variability in viral replication.[6,7] Most data on IBD and COVID-19 come from symptomatic cases confirmed by positive swabs.[1,8,9] However, many infections are asymptomatic.[10,11] Serological tests measuring seroprevalence provide a more accurate means of tracking infection rates and transmission among IBD patients.

However, serological methods have drawbacks, including delayed antibody detection, cross-reactivity, and weakened responses in immunosuppressed patients. ELISA tests targeting viral spike (S) and nucleocapsid (N) antigens are considered reliable, with the test used in our study reporting 85% sensitivity and 98% specificity.

In COVID-19, factors associated with increased mortality and morbidity include advanced age, male gender, comorbidities, obesity, and active smoking.[12-15] In our study, no significant differences were observed between SARS-CoV-2 antibody-positive and antibody-negative patients regarding age, gender, comorbidities, or BMI. Notably, none of the patients who contracted COVID-19 required hospitalization or ICU admission.

A multicenter study by the Italian Inflammatory Bowel Disease Group reported six deaths among 71 IBD patients with SARS-CoV-2 infection. However, no IBD-specific factors, such as medications, disease location, or disease duration, were found to be associated with mortality or morbidity.[16]

There is no evidence suggesting that immunosuppressive or biological therapies increase the risk of COVID-19 infection or worsen its clinical course. Consequently, scientific communities have recommended continuing these treatments.[3,17] In our study, antibody positivity was higher in patients with a known history of COVID-19 compared to those without, despite the widespread use of immunosuppressive and immunomodulatory therapies in this group (48.7%).

Two studies have investigated SARS-CoV-2 prevalence in IBD patients.[18,19] In the first study, among 90 patients receiving biological therapy, IgG and IgM antibody positivity rates were each 21%, suggesting that many patients experienced asymptomatic infections.[18] Similarly, our study observed a seropositivity rate of 22.5%. Only half of these patients had a known history of COVID-19, yet none had asymptomatic disease. This finding indicates that asymptomatic infections in IBD patients may be quite common.

In a study investigating seroprevalence, male gender was found to be protective against COVID-19 infection, while advanced age correlated with an increased frequency of antibody positivity.[20] In our study, no gender differences were observed; however, antibody positivity was found to increase with longer disease duration. Regardless of the dosage, patients with prolonged infliximab use exhibited a higher rate of antibody negativity. Additionally, despite having had COVID-19, female patients demonstrated a lower rate of antibody formation.

A study by Berteer et al.[21] included 354 patients receiving biological agents from three centers, utilizing an ELISA test to detect anti-SARS-CoV-2 IgG and IgA. Antibody positivity rates in IBD patients were found to be comparable to those in the control group. Similarly, our study detected comparable antibody levels between patients using immunosuppressive agents and those not receiving such treatments.

Another retrospective study screening 1,912 IBD patients reported no increased infection frequency compared to the general population.[22] Conversely, a study conducted in Poland found that the proportion of IBD patients with SARS-CoV-2 infection, determined by IgG antibodies, was significantly higher than in non-IBD individuals. Notably, no symptomatic infection cases were observed in this group. Similar to our study, this research also had a high prevalence of biological agent use among the patient population.[20]

A possible explanation for the higher seropositivity rates in IBD patients could be their younger age and increased social activity. Additionally, the frequent need for hospital visits due to biological therapy may elevate the risk of infection transmission.[18,23]

Another potential factor contributing to higher SARS-CoV-2 seropositivity in IBD patients may be the treatments they receive. Although patients on biological therapy were initially considered at greater risk for SARS-CoV-2 infection, it has been proposed that these treatments might exert a protective effect by mitigating hyperinflammatory responses.

Some studies have identified a strong correlation between mesalazine use and elevated antibody levels.[20] Similarly, in our study, high-dose mesalazine use was positively associated with antibody positivity. However, the complex and not fully understood mechanisms underlying mesalazine's effects complicate the interpretation of these findings in the context of COVID-19 infection risk. The high prevalence of mesalazine use in our cohort may have influenced the observed results.

Our study has several limitations. The exact timing of viral exposure in patients with positive IgG antibodies could not be determined, as serum samples were collected only at their initial study visits. Additionally, comparisons based on the most recent intake of immunosuppressants were not feasible. Another limitation was the absence of antibody titer follow-up in seropositive patients.

CONCLUSION

This study evaluated the seroprevalence of anti-SARS-CoV-2 antibodies in IBD patients during the pre-vaccine period. Our findings indicate that while IBD patients had an increased risk of COVID-19 infection with high seroprevalence rates, their prognosis remained favorable regardless of the treatment received.

Ethics Committee Approval: Ethics committee approval was obtained from Istanbul University-Cerrahpaşa Faculty of Medicine Dean's Office Clinical Research Ethics Committee (Approval Number: 83045809-604.01.02, Date: 16.06.2020).

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REFERENCES

1. Norsa L, Indriolo A, Sansotta N, Cosimo P, Greco S, D'Antiga L. Uneventful Course in Patients With Inflammatory Bowel Disease During the Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak in Northern Italy. *Gastroenterology*. 2020;159(1):371-372. [CrossRef]
2. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034. [CrossRef]
3. Brenner EJ, Ungaro RC, Gearry RB, et al. Corticosteroids, But Not TNF Antagonists, Are Associated With Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results From an International Registry. *Gastroenterology*. 2020;159(2):481-491.e3. [CrossRef]
4. Monteleone G, Ardizzone S. Are Patients with Inflammatory Bowel Disease at Increased Risk for Covid-19 Infection? *J Crohns Colitis*. 2020;14(9):1334-1336. [CrossRef]
5. Neurath MF. COVID-19 and immunomodulation in IBD. *Gut*. 2020;69(7):1335-1342.
6. Zhu N, Zhang D, Wang W, et al.; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733. [CrossRef]
7. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581(7809):465-469. Erratum in: *Nature*. 2020;588(7839):E35. [CrossRef]
8. Luo S, Zhang X, Xu H. Don't Overlook Digestive Symptoms in Patients With 2019 Novel Coronavirus Disease (COVID-19). *Clin Gastroenterol Hepatol*. 2020;18(7):1636-1637. [CrossRef]
9. Monteleone G, Ardizzone S. Are Patients with Inflammatory Bowel Disease at Increased Risk for Covid-19 Infection? *J Crohns Colitis*. 2020;14(9):1334-1336. [CrossRef]
10. Gao Z, Xu Y, Sun C, et al. A systematic review of asymptomatic infections with COVID-19. *J Microbiol Immunol Infect*. 2021;54(1):12-16. [CrossRef]
11. Meo SA, Alhowikan AM, Al-Khlaiwi T, et al. Novel coronavirus 2019-nCoV: prevalence, biological and clinical characteristics comparison with SARS-CoV and MERS-CoV. *Eur Rev Med Pharmacol Sci*. 2020;24(4):2012-2019.
12. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clin Microbiol Infect*. 2020;26(6):767-772. [CrossRef]
13. Simonnet A, Chetboun M, Poissy J, et al.; LICORN and the Lille COVID-19 and Obesity study group. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. *Obesity (Silver Spring)*. 2020;28(7):1195-1199. Erratum in: *Obesity (Silver Spring)*. 2020;28(10):1994. [CrossRef]
14. Zheng Y, Xu H, Yang M, et al. Epidemiological characteristics and clinical features of 32 critical and 67 noncritical cases of COVID-19 in Chengdu. *J Clin Virol*. 2020;127:104366. [CrossRef]
15. Zhao Q, Meng M, Kumar R, et al. The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. *J Med Virol*. 2020;92(10):1915-1921. [CrossRef]
16. Bezzio C, Saibeni S, Variola A, et al.; Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD). Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. *Gut*. 2020;69(7):1213-1217. [CrossRef]
17. Bonovas S, Fiorino G, Allocca M, et al. Biologic Therapies and Risk of Infection and Malignancy in Patients With Inflammatory Bowel Disease: A Systematic Review and Network Meta-analysis. *Clin Gastroenterol Hepatol*. 2016;14(10):1385-1397.e10. [CrossRef]
18. European Crohn's and Colitis Organisation. Ferreira de Abreu CM;1st Interview COVID19 ECCO Taskforce. Accessed August 3, 2020. https://ecco-ibd.eu/images/6_Publication/6_8_Surveys/1st_interview_COVID-19%20ECCOTaskforce_published.pdf
19. European Crohn's and Colitis Organisation. Zhu LR, Mao R, Fiorino G, Schneider T;2nd Interview COVID19 ECCO Taskforce. Accessed August 3, 2020. https://ecco-ibd.eu/images/6_Publication/6_8_Surveys/2nd_Interview_COVID-19_ECCO_Taskforce_published.pdf
20. Łodyga M, Maciejewska K, Eder P, et al. Inflammatory bowel disease is associated with higher seroprevalence rates of antibodies against SARS-CoV-2. *Pol Arch Intern Med*. 2021;131(3):226-232. [CrossRef]
21. Berte' R, Mazza S, Stefanucci MR, et al. Seroprevalence of SARS-CoV2 in IBD Patients Treated with Biologic Therapy. *J Crohns Colitis*. 2021;15(5):864-868. [CrossRef]
22. Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. *Aliment Pharmacol Ther*. 2020;52(2):276-283. [CrossRef]
23. Kennedy NA, Jones GR, Lamb CA, et al. British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic. *Gut*. 2020;69(6):984-990. [CrossRef]