From the American Epicenter: Coronavirus Disease 2019 in Patients with Inflammatory Bowel Disease in the New York City Metropolitan Area

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Background: We aimed to characterize patients with inflammatory bowel disease (IBD) and novel coronavirus disease 2019 (COVID-19).

Methods: We performed a case series of patients with IBD and confirmed or highly suspected COVID-19 to assess rates of severe outcomes.

Results: We identified 83 patients with IBD with confirmed (54%) or highly suspected (46%) COVID-19. The overall hospitalization rate was 6%, generally comprising patients with active Crohn's disease or older men with comorbidities, and 1 patient expired.

Discussion: In this series of patients with IBD, severe outcomes of COVID-19 were rare and comparable to similarly aged individuals in the general population.

Key Words: Coronavirus, SARS-CoV-2, COVID-19, inflammatory bowel disease

INTRODUCTION

In December of 2019, cases of pneumonia of unknown cause were reported in Wuhan, China, leading to the identification of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of coronavirus disease 2019 (COVID-19).[1] Since then, the COVID-19 pandemic has shifted geographically to Europe and North America, with the New York City (NYC) metropolitan area currently at the epicenter. Despite increasing data regarding the clinical characteristics of affected patients in the general population,[2] data are limited for populations at higher risk of infection, including patients with inflammatory bowel disease (IBD). Moreover, optimal management of immunosuppression in patients with IBD and COVID-19 is currently based on expert opinion.[3, 4] Preliminary evidence suggests that antirheumatic (ie, hydroxychloroquine [HCQ]) and anticytokine (ie, IL6 inhibitors) therapies may improve the outcomes of COVID-19 by mitigating the cytokine storm syndrome associated with severe COVID-19 and respiratory failure.[5] Therefore, patients receiving immunosuppression for IBD may have partial protection against severe outcomes of COVID-19 (ie, need for hospitalization, ventilation, or death). We aimed to characterize patients with IBD and COVID-19 and investigate the impact of IBD therapies on COVID-19 outcomes.

METHODS

We performed a case series of patients with IBD (Crohn's disease [CD], ulcerative colitis [UC]) at the IBD Center at NYU Langone Health, NYC, with confirmed or highly suspected COVID-19 from March 3 to May 10, 2020. High suspicion was defined as any patient residing in the NYC area presenting with new fever >99°F or a known contact positive for SARS-CoV-2 plus 1 or more respiratory symptoms (cough, pharyngitis, or shortness of breath) that could not be confirmed given restricted outpatient SARS-Cov-2 testing in NYC. We analyzed demographic, pharmacy, and IBD data with COVID-19 data and outcomes. Inflamatory bowel disease severity was estimated based on routinely measured clinical disease severity indices (eg, partial Mayo score for UC or Harvey-Bradshaw index for CD) documented in the most recent office visit note or routinely

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Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; Anti-TNF, antitumor necrosis factor

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measured endoscopic scoring (eg, Mayo endoscopic subscore for UC or simple endoscopic score for CD) documented in the most recent procedure note. Where these data were not available, IBD severity assessment was done by physician global assessment. Severe outcomes of COVID-19 were considered the requirement for an ER visit, hospitalization, ventilation, or death.

RESULTS

We identified 83 patients with IBD (CD [n = 56, 67%] or UC [n = 27, 33%]) with confirmed (n = 45, 54%) or highly suspected (n = 38, 46%) COVID-19 with a median follow-up of 52 days (range 11–72) from the onset of symptoms (Table 1). At COVID-19 symptom onset, the median age was 35 years (interquartile range [IQR], 27–45), 70% were white (n = 39), 89% were non-Hispanic (n = 74), and few had comorbidities. The majority had mild IBD activity (n = 26, 31%) or were in remission (n = 30, 36%). Few were on an oral corticosteroid (n = 10, 12%) or tofacitinib (n = 4, 7%), with the majority on a biologic (n = 58, 70%), largely an anti-TNF agent (n = 44, 53%). The most frequently reported symptoms were fever (n = 55, 66%) and cough (n = 46, 55%); fewer had new or worsening diarrhea (n = 26, 31%) or anosmia (n = 25, 30%). The overall hospitalization rate was 6% (n = 5; 1 intubation), with an additional

TABLE 1. Characteristics of the Patients with Confirmed or Highly Suspected COVID-19 and IBD

	Total (n = 83)	Ambulatory (n = 78)	Hospitalized (n = 5)
Demographics			
Age (median, IQR)	35 (27–45)	35 (27–44)	49 (25–76)
Sex			
Male	44 (53%)	40 (51%)	4 (80%)
Female	39 (47%)	38 (49%)	1 (20%)
Race			
White	58 (70%)	54 (70%)	4 (80%)
Black	5 (6%)	5 (6%)	0
Asian	3 (4%)	3 (4%)	0
Other	17 (20%)	16 (21%)	1 (20%)
Ethnicity			
Hispanic	9 (11%)	7 (9%)	2 (40%)
Non-Hispanic	74 (89%)	71 (91%)	3 (60%)
Comorbidities			
Organ transplantation	2 (2%)	2 (3%)	0
Kidney disease	1 (2%)	1 (1%)	0
Pregnancy	4 (5%)	3 (4%)	1 (20%)
Current malignancy	1 (2%)	0	1 (20%)
Hypertension	3 (4%)	3 (4%)	0
Diabetes mellitus	1 (2%)	1 (1%)	0
COPD	1 (2%)	1 (1%)	0
Asthma	9 (11%)	9 (12%)	0
ACE inhibitor/ARB use	6 (7%)	5 (6%)	1 (20%)
IBD Characteristics			
IBD subtype			
Crohn's disease	56 (67%)	52 (67%)	4 (80%)
Ulcerative colitis	27 (33%)	26 (33%)	1 (20%)
IBD disease status by physician assessment			
Remission	30 (36%)	30 (38%)	0
Mild	26 (31%)	24 (31%)	2 (40%)
Moderate	14 (17%)	13 (17%)	1 (20%)
Severe	6 (7%)	4 (5%)	2 (40%)
Unknown	7 (8%)	7 (9%)	0
IBD medication use			
None	4 (5%)	3 (4%)	1 (20%)

TABLE 1. Continued

	Total (n = 83)	Ambulatory (n = 78)	Hospitalized (n = 5)
5-ASA	13 (16%)	11 (14%)	1 (20%)
Immunomodulators	6 (7%)	5 (6%)	1 (20%)
Azathioprine/Mercaptopurine	2 (2%)	2 (3%)	0
Methotrexate	4 (5%)	3 (4%)	1 (20%)
Corticosteroids	10 (12%)	8 (10%)	1 (20%)
Prednisone	6 (6%)	4 (5%)	1 (20%)
>20 mg/daily	5 (4%)	3 (4%)	1 (20%)
Oral budesonide	4 (6%)	4 (5%)	0
Biologics	58 (70%)	56 (71%)	2 (40%)
Vedolizumab	5 (6%)	5 (6%)	0
Anti-TNF	44 (53%)	42 (53%)	2 (40%)
Infliximab	23 (28%)	23 (29%)	0
Adalimumab	21 (25%)	19 (24%)	2 (40%)
Ustekinumab	9 (11%)	9 (11%)	0
Tofacitinib	4 (5%)	4 (5%)	0
COVID-19 Characteristics			
COVID-19 symptoms			
Fever >99 F	55 (66%)	52 (66%)	3 (60%)
Cough	46 (55%)	44 (56%)	2 (20%)
Pharyngitis	21 (25%)	21 (27%)	0
Rhinorrhea	15 (18%)	15 (19%)	0
Diarrhea	26 (31%)	24 (30%)	2 (40%)
Ageusia	18 (22%)	18 (23%)	0
Anosmia	25 (30%)	25 (32%)	0
Shortness of breath	21 (25%)	17 (22%)	4 (80%)
Days of symptoms (median, IQR)	11 (5–15)	11 (6–15)	17 (9–32)
Positive SARS-CoV-2 testing	45 (54%)	40 (51%)	5 (100%)
Highly suspected COVID-19	38 (46%)	39 (49%)	0
Level of care			
Notified provider	28 (34%)	28 (36%)	-
Outpatient provider visit	48 (58%)	48 (61%)	-
Severe outcomes	7 (8%)	2 (3%)	5 (100%)
ER only	2 (2%)	2 (3%)	-
Hospitalized	5 (6%)	-	5 (100%)
ICU with intubation	1 (1%)	-	1 (20%)
IBD medication management			
Continued	58 (70%)	57 (72%)	1 (20%)
Held	13 (16%)	10 (13%)	3 (60%)
Reduced dose/frequency	7 (8%)	7 (9%)	0
After reduction, required holding	3 (4%)	3 (4%)	0
Medical therapies for COVID-19			
None	75 (90%)	74 (94%)	2 (40%)
Any COVID-19 therapy	8 (10%)	5 (6%)	3 (60%)
Hydroxycholorquine + Azithromycin	4 (5%)	2 (3%)	2 (40%)
Hydroxycholorquine	2 (2%)	2 (3%)	0
Azithromycin	1 (1%)	1 (1%)	0
Hydroxycholorquine + Azithromycin + Tocilizumab	1 (1%)	0	1 (20%)
Death	1 (2%)	0	1 (20%)
Days of follow-up (median, range)	52 (11–72)	52 (13–72)	47 (11–55)

TABLE 2. COVID-19 Patients Requiring Evaluation in Emergency Room or Hospitalization

Patient, Level of Care	Age, Sex	IBD Subtype, Current Severity	IBD Medications and Management	Relevant Co-Morbidities	COVID-19 Symptoms	Imaging	Hospital Course and Outcomes
1 ER	34 Male	UC, Remission	Infliximab (held)	None	Fever > 101 Cough Runny Nose	CXR: Coarsened markings	Regular room; room air Not treated for COVID-19 Discharged within 24 hours Plan to continue regular infliximab infusions
2 ER	26 Female	UC, Remission	5-ASA (continued)	None	Fever > 99 Cough Shortness of breath	None	Regular room; room air Not treated for COVID-19 Discharged within 24 hours Continued 5-ASA
3 Hospital	25 Male	CD, Moderate	Adalimumab (held)	None	Fever > 102 Cough Shortness of breath	None	COVID Unit; room air Not treated for COVID-19 Discharged at day 2 Plan to continue regular adalimumab injections
4 Hospital	26 Female	UC, Severe	Prednisone (continued)	First trimester pregnancy	Shortness of breath	CXR: Coarsened markings	COVID unit/admitted for UC flare and COVID-19; supplemental oxygen via nasal canula COVID-19 treated with hydroxychloroquine + azithromycin UC treated with cyclosporine and tapering prednisone Experienced spontaneous abortion on hospital day 11 Discharged on hospital day 12 on cyclosporine, prednisone, and plan for outpatient infliximab
5 Hospital	72 Male	CD, Mild	5-ASA (held)	Prostate cancer	Fever > 101 Cough Diarrhea Shortness of breath	CT chest: multifocal patchy consolidation concerning for multifocal pneumonia	COVID unit, transferred to ICU; supplemental oxygen via nasal canula then intubated on hospital day 9 COVID-19 treated with hydroxychloroquine + azithromycin + tocilizumab Remains intubated with grim prognosis
6 Hospital	80 Male	CD, Mild	Adalimumab, Methotrexate (held)	Parkinson's disease	Shortness of breath	CXR: Coarsened markings with patchy appearance; scattered airway inflammation and/or consolidation	COVID Unit; Supplemental oxygen via nasal canula then non-rebreather (DNR/DNI) IBD therapies held COVID-19 treated with hydroxychloroquine + azithromycin Died on hospital day 11
7 Hospital	25, Male	CD, Severe	None, noncompliant	None	Fever >101 Diarrhea	CXR: Clear lungs	COVID unit/admitted for CD pelvic abscess, ileocolitis, and COVID-19; transient supplemental oxygen via nasal canula Not treated for COVID-19 CD treated with abscess drainage and antibiotics Discharged on hospital day 7 on antibiotics and plan for outpatient anti-TNF

2 patients requiring an ER visit (2%; Table 2). Inflammatory bowel disease therapies were held in 13 (16%), and the dose/frequency of administration was reduced in 3 (4%). Treatment with HCQ or azithromycin was offered for 8 patients (10%). Median duration of symptoms was 11 days (IQR, 5–15). Of 5 patients who required hospitalization, the majority were patients with active CD or older men with comorbidities, and 1 (1%) expired.

DISCUSSION

In this case series of patients with IBD and symptomatic COVID-19 in the NYC area, the epicenter of the pandemic in the United States, severe outcomes of COVID-19 were uncommon, with a hospitalization rate of 6% and mortality rate of 1%. With over 2 months of total follow-up, baseline immunosuppression did not appear to modify the risk of severe outcomes. Compared with reports in the general population, patients with IBD may present with a higher burden of gastrointestinal symptoms due to COVID-19, in particular diarrhea and ageusia, although more data are required.[2, 6]

According to the NYC Health Department, as of May 15, 2020, there were 187,848 confirmed cases of SARS-CoV-2 and 49,580 COVID-19 hospitalizations in NYC, suggesting a case-hospitalization rate of 26%.[7] This high rate of hospitalization is likely due to restricted outpatient testing in NYC and the relatively older general population with COVID-19, where hospitalization rates are substantially increased. Thus, limiting our population to those with laboratory-confirmed SARS-Cov-2 testing, the hospitalization rate was 11% in patients with IBD. Although limited in sample size, our data reveal a hospitalization rate on par with similarly aged subjects in NYC.[7] Additionally, consistent with reports in the general population, factors such as age, male sex, and comorbidities were associated with COVID-19-related hospitalization in patients with IBD.[8] Hospitalization for COVID-19 was more common in patients with active CD, suggesting uncontrolled CD may be an additional risk factor for severe outcomes. In the ongoing SECURE-IBD registry, COVID-19 is also more common in patients with CD than UC, although the overall hospitalization rate is 33%.[9] This large difference in hospitalization in the SECURE-IBD registry may be due to selection bias toward more severe cases, underreporting of mild cases that may not present to medical care or testing, and perhaps even misclassification of IBD or attribution of a hospitalization to COVID-19 rather than a complication of IBD by referring providers.

A better understanding of the implications of COVID-19 in patients with IBD and the effects of immunosuppressive therapies is urgently needed to guide gastroenterologists in caring for patients with IBD during this pandemic. In our sample, few patients required delay, reduction, or cessation of IBD therapies due to COVID-19 symptoms. For 3 patients on tofacitinib with active IBD, COVID-19 symptoms persisted with dose reduction and required temporary therapy cessation. Although further data are required, similar to recommendations from the CDC for health care providers returning to work, we resumed immunosuppression 72 hours after being afebrile, with near resolution or minimal respiratory symptoms at least 7 days from symptom onset. In those who required an interruption in therapy, all were restarted without adverse outcome. Patient 6 (Table 2), an 80-year-old male previously maintained on adalimumab with methotrexate, was not restarted on IBD therapies and expired on hospital day 11. Patient 4 was hospitalized for acute severe UC complicated by COVID-19 in her first trimester of pregnancy. Cyclosporine was given rather than infliximab for its shorter half-life in the event of COVID-19 progression. Though the patient experienced a spontaneous abortion, her colitis and COVID-19 improved, and she was recently initiated on outpatient ustekinumab. In sum, treatment for moderately to severely active IBD and COVID-19 was chosen on a case-by-case basis.

In conclusion, patients with IBD seem to be similarly at risk for COVID-19 and related outcomes to correspondingly aged individuals in the general population. Severe outcomes of COVID-19 were rare and generally limited to older men with comorbidities and/or patients with active CD. All patients who continued or restarted IBD therapies did so without clinical consequence. Although we did not find evidence of an effect of IBD therapies on COVID-19 outcomes, further data are required. The optimal management of IBD and COVID-19 remains undefined but likely requires a multidisciplinary team and a careful, individualized approach.

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