Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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SARS-CoV-2 Testing, Prevalence, and Predictors of COVID-19 in Patients with Inflammatory Bowel Disease in Northern California

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Coronavirus disease 2019 (COVID-19), caused by the novel betacoronavirus severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is an unprecedented global pandemic.[1] Susceptibility to COVID-19 is a concern among patients with inflammatory bowel disease (IBD) who are at increased risk of infection due to immunosuppressive therapy. The receptor angiotensin-converting enzyme (ACE) 2, which mediates SARS-CoV-2 entry into cells, is upregulated in IBD[2] and may therefore increase host susceptibility. International cohorts have reported no increased risk of COVID-19 in patients with IBD[3,4]; however, these studies do not report the prevalence of SARS-CoV-2 testing and COVID-19 in patients with IBD. Our institution was among the first to initiate large-scale SARS-CoV-2 RNA testing in northern California. We characterized the prevalence and clinical predictors of COVID-19 in patients with IBD.

Methods

We performed a retrospective analysis of consecutive patients whose SARS-CoV-2 testing was performed at Stanford between March 04, 2020, and April 14, 2020. California counties tested, institutional testing eligibility, and performance are described in our Supplementary Methods. Our study was approved by the Stanford Institutional Review Board (Protocol 55975). We included all patients with a diagnosis of Crohn's disease (K50.xx), ulcerative colitis (K51.xx), and indeterminate colitis (K52.3) who underwent testing. We collected data including demographics, IBD characteristics (subtype, location, phenotype, disease activity), comorbid conditions, reasons for testing, symptoms, medications, and outcomes. We calculated prevalence of IBD among all patients tested and the prevalence of COVID-19 among patients with IBD. We performed univariate and multivariate logistic regression using the firthlogit method to determine predictors of COVID-19 in patients with IBD.[5] Our statistical analysis was performed with Statistics/Data Analysis (Stata/IC 15.1 for Windows; StataCorp, College Station, TX) and described in detail in our Supplementary Methods.

Results

Prevalence and Characteristics of Patients With IBD Undergoing SARS-CoV-2 Testing

From March 4, 2020, to April 14, 2020, 14,235 individuals were tested for SARS-CoV-2 at our institution with 8.2% (1160 of 14,235) testing positive. Among the tested patients, the prevalence of IBD was 1.2% (168 of 14,235). Table 1 summarizes the baseline characteristics of patients with IBD who underwent testing; 51.2% had ulcerative colitis, 39.3% had Crohn's disease, and 9.8% had indeterminate colitis. Of patients with IBD, 16.7% had active disease; 91.7% were symptomatic suggestive of COVID-19, 3.6% were asymptomatic but had a positive travel history, and 4.8% were asymptomatic but had direct exposure to a patient with COVID-19. Common presenting symptoms included cough (63.1%), sore throat (41.1%), dyspnea (37.5%), fever (35.7%), and body pain (32.1%). Gastrointestinal symptoms were present in 19.1% of patients with IBD; diarrhea (15.5%), abdominal pain (13.1%), and nausea and vomiting (8.9%) were most common.

Prevalence, Predictors, and Outcomes of COVID-19 in Patients With IBD

Among 168 patients with IBD tested, the prevalence of COVID-19 was 3.0% (5 of 168). Patients with IBD with COVID-19 were older (70.6 years vs 47 years, $P < .001$), more obese (60.0% vs 16.6%, $P = .011$), and more likely to have hypertension (80.0% vs 23.3%, $P < .001$) and diabetes mellitus (40.0% vs 9.8%, $P = .029$). Patients with IBD with COVID-19 were more likely to use ACE inhibitors (60.0% vs 6.1%, $P < .001$) and mesalamine (80.0% vs 33.1%, $P = .025$). In univariate analysis (Supplementary Table 1), age >66 years (odds ratio [OR] 31.37, $P = .003$), obesity (BMI ≥30) (OR 7.83, $P = .011$), hypertension (OR 13.58, $P = .021$), and ACE inhibitor use (OR 23.70, $P = .001$) were associated with increased risk of COVID-19 among patients with IBD. Our multivariate logistic regression model, which included age >66 years, obesity, hypertension, and ACE inhibitor use as covariates, showed that age >66 years was independently associated with increased risk (OR 21.30, $P = .022$) of COVID-19. Clinical outcomes of patients with IBD with COVID-19 are summarized in Supplementary Table 2. Four patients with IBD had a mild course, whereas 1 patient (Patient 3)

Abbreviations used in this paper: **ACE, angiotensin-converting enzyme; COVID-19, Coronavirus Disease 2019; IBD, inflammatory bowel disease; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.**

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Table 1. Baseline Clinical Characteristics of Patients With IBD Undergoing SARS-CoV-2 Testing

Clinical variables	All patients with IBD (N = 168)	SARS-CoV-2 RNA Negative (n = 163)	SARS-CoV-RNA positive (n = 5)	*P*
Age, *y* (SD)	47.7 (±16.3)	47.0 (±16.0)	70.6 (± 4.2)	<.001
Age >66, n (%)	23 (13.7)	19 (11.7)	4 (80.0)	<.001
Gender, n (%)				
Male	80 (47.6)	78 (47.9)	2 (40.0)	.810
Female	88 (52.4)	85 (52.1)	3 (60.0)	
Ethnicity, n (%)				
White	103 (61.3)	99 (60.7)	4 (80.0)	.344
Hispanic	14 (8.3)	14 (8.3)	0 (0.0)	.501
Black	13 (7.7)	12 (7.4)	1 (20.0)	.283
Asian	29 (17.3)	29 (17.8)	0 (0.0)	.309
Pacific Islander	1 (0.6)	1 (0.6)	0 (0.0)	.863
Unknown	13 (7.7)	13 (8.0)	0 (0.0)	.518
Reason for SARS-CoV-2 testing, n (%)				
Symptomatic	154 (91.7)	149 (91.4)	5 (100)	.501
Asymptomatic, travel history	6 (3.6)	6 (3.7)	0 (0.0)	.667
Asymptomatic, exposure	8 (4.8)	8 (4.9)	0 (0.0)	.405
Clinical features, n (%)				
Fever	60 (35.7)	57 (35.0)	3 (60.0)	.230
Cough	106 (63.1)	102 (62.6)	4 (80.0)	.380
Nasal congestion	58 (34.5)	55 (33.7)	3 (60.0)	.200
Sore throat	69 (41.1)	67 (41.1)	2 (40.0)	.996
Dyspnea	63 (37.5)	61 (37.4)	2 (40.0)	.874
Fatigue	43 (25.6)	40 (24.5)	3 (60.0)	.067
Body pain	54 (32.1)	51 (31.3)	3 (60.0)	.159
Pneumonia	10 (6.0)	8 (4.9)	2 (40.0)	.131
Gastrointestinal symptoms, n (%)	32 (19.0)	31 (19.0)	1 (20.0)	.935
Abdominal pain	22 (13.1)	21 (12.9)	1 (20.0)	.589
Nausea/Vomiting	15 (8.9)	14 (8.6)	1 (20.0)	.364
Diarrhea	26 (15.5)	26 (16.0)	0 (0.0)	.338
Melena	1 (0.6)	1 (0.6)	0 (0.0)	.862
Hematochezia	2 (1.2)	2 (1.2)	0 (0.0)	.762
Hematemesis	1 (0.6)	1 (0.6)	0 (0.0)	.862
Weight loss	5 (3.0)	5 (3.0)	0 (0.0)	.695
Dysphagia	3 (1.8)	3 (0.9)	0 (0.0)	.762
COVID-19 testing setting, n (%)				
Outpatient	105 (62.5)	101 (62.0)	4 (80.0)	.352
Emergency department	43 (25.6)	40 (24.5)	3 (60.0)	.068
Inpatient	23 (13.7)	22 (13.5)	1 (20.0)	.893
Ulcerative colitis, n (%)				
Total	86 (51.2)	83 (50.1)	3 (60.0)	.641
E1	24 (27.9)	23 (27.7)	1 (33.3)	
E2	19 (22.1)	18 (21.7)	1 (33.3)	
E3	32 (47.1)	31 (37.3)	1 (33.3)	
Unknown	3 (1.8)	3 (3.6)	0 (0.0)	
Crohn's disease, n (%)				
Total	66 (39.3)	64 (39.3)	2 (40.0)	.931
L1	13 (19.7)	13 (20.3)	0 (0.0)	
L2	14 (21.2)	14 (21.9)	0 (0.0)	
L3	32 (48.5)	30 (46.9)	2 (100.0)	
L4	0 (0.0)	0 (0.0)	0 (0.0)	
Unknown	3 (4.7)	3 (4.7)	0 (0.0)	
Perianal disease, n (%)	12 (18.8)	12 (18.8)	0 (0.0)	
B1	43 (25.6)	42 (65.6)	1 (50.0)	
B2	10 (6.0)	9 (14.1)	1 (50.0)	
B3	8 (12.5)	8 (12.5)	0 (0.0)	
Unknown	1 (1.6)	1 (1.6)	0 (0.0)	
Indeterminate IBD, n (%)				

Table 1. Continued

Clinical variables	All patients with IBD (N = 168)	SARS-CoV-2 RNA Negative (n = 163)	SARS-CoV-RNA positive (n = 5)	*P*
Total	16 (9.8)	16 (9.8)	0 (0.0)	.634
BMI, kg/m^2, n (%)				
<25.0 (normal or underweight)	90 (53.6)	89 (54.6)	1 (20.0)	.146
25.0–29.9 (overweight)	50 (29.8)	49 (30.0)	1 (20.0)	.656
≥30.0 (obese)	30 (17.9)	27 (16.6)	3 (60.0)	.011
Smoking, n (%)				
Current	10 (6.0)	10 (6.1)	0 (0.0)	.988
Former	26 (15.5)	26 (16.0)	1 (20.0)	
Never	131 (80.0)	127 (77.9)	4 (80.0)	
Alcohol use, n (%)				
Yes	72 (42.9)	69 (42.3)	3 (60.0)	.701
No	100 (57.1)	98 (60.1)	2 (40.0)	
Hypertension, n (%)				
Yes	42 (25.0)	38 (23.3)	4 (80.0)	<.001
No	126 (75.0)	125 (76.7)	1 (20.0)	
Diabetes mellitus, n (%)				
Yes	18 (10.7)	16 (9.8)	2 (40.0)	.029
No	150 (89.3)	147 (90.2)	3 (60.0)	
Medications, n (%)				
ACE inhibitor	13 (7.7)	10 (6.1)	3 (60.0)	<.001
ARB	10 (6.0)	10 (6.1)	0 (0.0)	.574
PPI	33 (19.6)	33 (20.2)	0 (0.0)	.271
H2 Blocker	19 (11.3)	18 (11.0)	1 (20.0)	.513
Steroids	34 (20.2)	33 (20.2)	1 (20.0)	.984
5-ASA	58 (34.5)	54 (33.1)	4 (80.0)	.025
6MP/Azathioprine	9 (5.4)	8 (4.9)	1 (20.0)	.131
Methotrexate	6 (3.6)	6 (3.7)	0 (0.0)	.667
Anti-TNF agent, no. (%)	34 (20.2)	33 (20.2)	1 (20.0)	.984
Vedolizumab	10 (6.0)	10 (6.1)	0 (0.0)	.574
Ustekinumab	4 (2.4)	4 (2.5)	0 (0.0)	.727
Tofacitinib, no (%)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Antiplatelets	11 (6.5)	10 (6.1)	1 (20.0)	.205
Anticoagulant	11 (6.5)	10 (6.1)	1 (20.0)	.205
NSAIDs	20 (11.9)	20 (12.2)	0 (0.0)	.412

5-ASA, mesalamine; ARB, angiotensin receptor blocker; B1, nonstricturing, nonpenetrating CD; B2, stricturing CD; B3, penetrating CD; BMI, body mass index; CD, Crohn's disease; E1, distal UC; E2, left-sided UC; E3, extensive UC; L1, ileal CD, L2, colonic CD, L3, ileocolonic CD; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; TNF, tumor necrosis factor; UC, ulcerative colitis.

developed pneumonia and acute respiratory distress syndrome and died despite aggressive interventions.

Discussion

To our knowledge, this is the first study to evaluate the prevalence of SARS-CoV-2 testing and COVID-19 in patients with IBD in a US cohort. The prevalence of IBD among patients undergoing SARS-CoV-2 testing is 1.2%, which is comparable to the prevalence of IBD (1.3%) in the US adult population.[6] Our COVID-19 positivity rate of 3% in patients with IBD is comparable to the population-weighted prevalence of SARS-CoV-2–positive serology in Santa Clara county at 2.8%.[7] Our data suggest that patients with IBD are not disproportionately being tested more, nor do they have a higher rate of SARS-CoV-2 positivity compared with the background population in northern California. One explanation is that increased ACE 2 expression may not mediate SARS-CoV-2 susceptibility in patients with IBD. Another possibility is that immunosuppressive medications in patients with IBD may attenuate viral-induced respiratory inflammation leading to an asymptomatic or mild COVID-19 course in patients with IBD who subsequently do not seek testing. Our study also demonstrates that patients older than 66 years are at increased risk of COVID-19. Our results are consistent with a prior retrospective study from China that demonstrated that older age is an independent predictor of COVID-19.[8] The exact mechanisms underlying susceptibility to COVID-19 in elderly patients are unclear and warrant further investigation.

Our study has several strengths. First, our study provides novel epidemiological data that can inform patients with IBD and clinicians. Currently, there are no published reports estimating the prevalence of COVID-19 among patients with IBD in the United States. Second, we identified predictors of COVID-19 among patients with IBD, highlighting the

increased susceptibility of COVID-19 with older age. Third, our study included patients from a large geographic area encompassing a diverse patient population. Our study has several limitations. First, our study was observational and cannot establish causation or account for unmeasured confounders. Second, we were unable to assess the predictors of COVID-19 morbidity and mortality with our small sample size and low event rate. A significantly larger sample size is needed to further clarify predictors of COVID-19 outcomes. Third, our study reflects testing performed by a single center and may not be generalizable to other institutions.

In summary, our results provide much needed epidemiological data and reassurance that COVID-19 rates in patients with IBD may be comparable to the general population. Age older than 66 years was a strong independent predictor of COVID-19 among patients with IBD.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.05.009.

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Conflict of interest
The authors disclose no conflicts.

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Supplementary Methods

Patients resided in several northern California counties, including Santa Clara, San Mateo, Santa Cruz, San Francisco, and Alameda. Patients were offered SARS-CoV-2 RNA testing at our institution if they had symptoms or findings suggestive of COVID-19 (fevers, cough, dyspnea, pneumonia), had a recent travel history with high COVID-19 cases, or had direct exposure to a patient with COVID-19. All SARS-CoV-2 RNA testing was performed using samples from a nasopharyngeal swab. The clinical sensitivity of the COVID-19 test at our institution is 96% (using repeat testing within 48 hours as a surrogate gold standard and assuming all negatives are false negatives) and clinical specificity approaches 100%.

The rate of SARS-CoV-2–positive tests, predictive value of clinical variables on the primary outcome, OR with its 95% confidence interval, and *P* values were assessed using Statistics/Data Analysis (Stata/IC 15.1 for Windows, StataCorp, College Station, TX). We calculated the prevalence of IBD among patients undergoing SARS-CoV-2 testing by dividing the number of patients with IBD tested by total number of patients tested in our population. The prevalence of SARS-CoV-2 positivity was calculated by dividing the number of patients with IBD with positive SARS-CoV-2 tests over the number of total patients with IBD tested. Dichotomous variables were analyzed for outcomes using the χ^2 test or the Fisher exact test where appropriate, and continuous variables were analyzed using *t* tests if normally distributed, or the Wilcoxon test for non-normal data. Correction for multiple testing was included. All variables were analyzed initially in a univariate fashion to determine their association with COVID-19. *P* values of factors that showed evidence of an association on COVID-19 ($P < .05$) then were analyzed on multivariate regression analysis. Rare events may lead to complete separation and problems with convergence in conventional logistic regression models. The Firth method is a general approach to reducing rare event and small-sample bias in maximum likelihood estimation. Because of the small sample size and low event rate for outcome of patients with COVID-19 with IBD, we used the firthlogit penalized maximum likelihood logistic regression in our analysis.

Supplementary Table 1. Univariate and Multivariate Predictors of COVID-19 Among Patients With IBD

	Univariate predictors			Multivariate predictors		
Clinical variables	OR	95% CI	*P*	OR	95% CI	*P*
Age >66 y	31.37	3.33–295.46	.003	21.30	1.56–291.00	.022
Obesity (BMI ≥30)	7.83	1.25–49.12	.011	1.35	0.09–21.54	.830
Hypertension	13.58	1.47–125.15	.021	3.65	0.30–45.11	.313
Diabetes mellitus	6.29	0.98–40.49	.053			
ACE inhibitor use	23.70	3.55–158.44	.001	10.61	0.67–168.09	.094
Mesalamine (5-ASA)	8.44	0.92–77.37	.059			

BMI, body mass index; CI, confidence interval.

Supplementary Table 2. Clinical Characteristics and Outcomes in Patients With IBD With COVID-19

Patient number	Demographics ethnicity	Montreal classification	Disease activity	IBD medications	COVID-19 symptoms	Mild COVID-19		Severe COVID-19			
						Outpt[a]	ED[b]	Hosp[c]	ICU[d]	MV[e]	Death
1	68 F White	CD L3, B2	A	Prednisone IFX	Fever, Cough Fatigue	Yes	Yes	No	No	No	No
2	74 M White	CD L3, B1	R	5-ASA	Cough	Yes	Yes	No	No	No	No
3	76 M Black	UC	R	5-ASA	Fever Dyspnea	No	No	Yes	Yes	Yes	Yes[a]
4	69 F White	UC E3	R	5-ASA	Fever, Cough Fatigue	Yes	No	No	No	No	No
5	66 F White	UC E2	R	5-ASA AZA	Cough Dyspnea	Yes	No	No	No	No	No

5-ASA, mesalamine; A, active; AZA, Azathioprine; B1, nonstricturing, nonpenetrating CD; B2, stricturing CD; B3, penetrating CD; CD, Crohn's disease; E1, distal UC; E2, left-sided UC; E3, extensive UC; ED, emergency department; F, female; Hosp, hospitalization; IFX, Infliximab; ICU, intensive care unit; L1, ileal CD, L2, colonic CD, L3, ileocolonic CD; M, male; MV, mechanical ventilation; Outpt, outpatient; R, remission; UC, ulcerative colitis.

[a]Patient died of acute respiratory distress syndrome.

[b]ED = Emergency Department.

[c]Hosp = Inpatient Hospitalization.

[d]ICU = Intensive Care Unit Admission.

[e]MV = Mechanical Ventilation.