COVID-19 in Patients With Inflammatory Bowel Disease: A Single-center Observational Study in Northern Italy

Key Words: COVID-19, SARS-CoV-2, inflammatory bowel disease, Crohn's disease, ulcerative colitis

To the Editors,

Coronavirus disease 2019 (COVID-19), an infectious disease caused by coronavirus SARS-CoV-2, has rapidly spread to a global pandemic. For patients with inflammatory bowel disease (IBD), significant concern arises from the widespread use of immunosuppressive therapies, 1 yet preliminary data do not indicate a worse clinical course. 2,3 However, limited data are available concerning the risk of acquiring COVID-19.

We conducted a retrospective cohort study among adult IBD patients followed in our center in Lombardy, aimed at defining prevalence and risk factors for acquiring the infection.

All patients were individually contacted by phone between March and April 2020. Because during the study period virologic testing was available only for inpatients or health care workers besides laboratory confirmed diagnosis, we also included probable cases according to WHO reccomendations (ie, occurrence of an acute respiratory illness AND residence in a high-prevalence area or contact with a COVID-19 case). To ensure validity of the diagnosis of probable cases, one of the following additional criteria was also required: previous influenza vaccination or close contact with a COVID-19 case.

Patients provided verbal informed consent for the inclusion in the study.

Among 704 included patients (suppl Fig 1 and suppl Table 1), 53 (7.5%) were diagnosed with COVID-19,

© 2020 Crohn's & Colitis Foundation. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

> doi: 10.1093/ibd/izaa244 Published online 19 September 2020

and 9 (1.2%) had a laboratory-proven diagnosis. Demographic and clinical characteristics are listed in Table 1. At logistic regression, only severely active IBD (odds ratio [OR], 12.6; 95% CI, 1.7–92.4; P=0.01) was significantly associated with COVID-19 (suppl Table 2). Diarrhea was the presenting symptom in 26 (49%) patients, and significantly more cases reported diarrhea compared with non-COVID-19 patients (OR, 29; P < 0.0001), independently from disease activity at multiple regression analysis (suppl Table 2).

As of May 11, 2020, 81,507 laboratory-confirmed cases have been reported in Lombardy, with a cumulative incidence rate of 0.81%; in our cohort, this was roughly similar (1.2%). Yet given the inability to test outpatients with milder symptoms, a 10-fold higher period prevalence has been hypothesized based on mortality and assumptive case-fatality rate,⁴ again not dissimilar from our data.

Severely active IBD was associated with COVID-19, though this has to be considered with caution because severe flare leading to hospitalization was actually a reason for testing. No other association with any disease aspect, including immunosuppressive therapies, was found

Accordingly, maintaining effective treatment to avoid severe flares of IBD could reduce the risk of COVID-19.

Moreover, this diarrheapredominant picture of COVID-19 in IBD has to be taken into specific consideration to avoid erroneous attribution of newly developed symptoms and incorrect management.⁵ Chiara Viganò, MD,*,†o Sara Massironi, MD, PhD,*,† Lorena Pirola, MD,*,† Laura Cristoferi, MD,*,† Maria Fichera, MD,*,† Marianna Bravo, MD,*,†

Martina Mauri, MD,*,†
Alessandro Ettore Redaelli, MD,‡
Marco Emilio Dinelli, MD,‡ and
Pietro Invernizzi, MD, PhD*,†

From the *Division of Gastroenterology and Center for Autoimmune Liver Diseases; Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy; †European Reference Network on Hepatological Diseases (ERN RARE-LIVER), San Gerardo Hospital, Monza, Italy; †Interventional Endoscopy Unit, San Gerardo Hospital, University of Milano, Bicocca School of Medicine, Monza, Italy

Author Contribution: CV, SM, and MED planned and designed the study. LP, LC, MB, MM, and AER performed the data extraction and interviewing of patients. CV and SM analyzed the data. SM performed the statistical analyses. CV drafted the manuscript. SM, LC, MED, and LP provided critical review of the manuscript. PI provided major intellectual revision. The data underlying this article will be shared upon reasonable request to the corresponding author.

Address correspondence to: Chiara Viganò, MD, Division of Gastroenterology and Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, University of Milano-Bicocca, San Gerardo Hospital, Via Pergolesi 33, Monza, Italy. E-mail: chiara.vigano@hotmail.it.

Conflicts of Interest: PI, CV, SM, LP, LC, MF, MB, and MM are members of the European Reference Network on Hepatological Rare Diseases (ERN RARE LIVER).

REFERENCES

- D'amico F, Danese S, Peyrin-Biroulet L; ECCO COVID taskforce. Inflammatory bowel disease management during the COVID-19 outbreak: a survey from the European Crohn's and Colitis Organization (ECCO). Gastroenterology. 2020;S0016-5085(20)30578-3. doi: 10.1053/j. gastro.2020.04.059.
- 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. 2020:69:1213–1217.
- 3. Brenner EJ, Ungaro RC, Gearry RB, et al. Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19

TABLE 1. Demographic and Clinical Characteristics of COVID-19 IBD Patients Compared with Non COVID-19 IBD Patients

	IBD Patients With COVID-19 (n=53)	IBD Patients Without COVID-19 (n=651)	P
Age(years)	50 (42–62)	53 (41–65)	P = ns
Females	26 (49)	275 (42.2)	P = ns
Type of IBD			
Crohn's disease	20 (37.7)	275 (42.2)	P = ns
Ulcerative colitis	33 (62.3)	376 (57.7)	
CD extension			
Ileal	10 (50)	95 (34.5)	P = 0.02
Colonic	2 (10)	69 (25)	
Ileocolonic	8 (40)	111 (40.4)	
Upper disease	5 (25)	21 (7.6)	
Perianal disease	0 (0)	33 (12)	
UC extension			
Proctitis	11 (33)	72 (19.1	P = 0.004
Left-sided colitis	15 (46)	106 (28.2)	
Extensive colitis	7 (21)	198 (52.7)	
Flu vaccination	23 (43.4)	320 (49.1)	P = ns
Active cigarette smoking	8 (15.1)	110 (16.9)	P = ns
Therapy for IBD			
None	4 (7.5)	59 (9)	P = ns
Aminosalicylates	30 (56.6)	365 (56.1)	
Immunosuppressants (thiopurines /methotrexate)	8 (15.1)	97 (14.9)	
High dose systemic corticosteroids	2 (3.7)	9 (1.4)	
Anti-TNF	8 (15.1)	87 (13.4)	
Vedolizumab	1 (1.9)	25 (3.8)	
Ustekinumab	1 (1.9)	15 (2.3)	
Investigational drugs (within a clinical trial)	0 (0)	1 (0.1)	
Disease Activity			
Inactive	44 (83)	554 (85)	P = 0.01
Mild	5 (9.5)	72 (11)	
Moderate	2 (3.8)	23 (3.5)	
Severe	2 (3.8)	2 (0.3)	
Comorbidities			
Systemic hypertension	9 (16.9)	148 (22.7)	P = ns
Cardiac disease	5 (9.4)	31 (4.8)	
COPD	2 (3.8)	25 (3.8)	
Diabetes mellitus	0 (0)	31 (4.8)	
Chronic kidney disease	3 (5.7)	14 (2.1)	
Any comorbidity	18 (33.9)	277 (42.5)	P = ns
BMI	23.5 (21–27)	24.1 (21.6–26.6)	P = ns

Data are reported as absolute frequencies (%) and medians (IQR). Abbreviations: CD, Crohn's disease; UC, ulcerative colitis; COPD, chronic obstructive pulmonary disease; BMI, body mass index.

outcomes in patients with inflammatory bowel diseases: results from an international registry. *Gastroenterology.* 2020. doi: 10.1053/j.gastro. 2020.05.032.

^{4.} Signorelli C, Scognamiglio T, Odone A. COVID-19 in Italy: impact of containment measures and prevalence estimates of infection in the general population. *Acta Biomed.* 2020;91: 175–179.

Parigi TL, Bonifacio C, Danese S. Is it Crohn's disease? Gastroenterology. 2020;S0016-5085(20)30587-4. doi: 10.1053/j.gastro.2020. 04.066.