ORIGINAL RESEARCH

Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study

Cristina Bezzio ,[1] Simone Saibeni ,[1] Angela Variola,[2] Mariangela Allocca,[3,4] Alessandro Massari,[5] Viviana Gerardi,[6] Valentina Casini,[7] Chiara Ricci,[8] Fabiana Zingone,[9] Arnaldo Amato ,[10] Flavio Caprioli ,[11,12] Marco Vincenzo Lenti ,[13] Chiara Viganò,[14] Marta Ascolani,[15] Fabrizio Bossa,[16] Fabiana Castiglione,[17] Claudio Cortelezzi,[18] Laurino Grossi,[19] Monica Milla,[20] Daniela Morganti,[21] Luca Pastorelli,[22] Davide Giuseppe Ribaldone ,[23] Alessandro Sartini ,[24] Alessandra Soriano,[25] Gianpiero Manes,[26] Silvio Danese,[3,4] Massimo Fantini,[27] Alessandro Armuzzi,[28,29] Marco Daperno,[30] Gionata Fiorino ,[3,4] on behalf of Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD)

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/gutjnl-2020-321411).

For numbered affiliations see end of article.

Correspondence to
Dr Cristina Bezzio, Gastroenterology Unit, Rho Hospital, Rho (MI), ASST Rhodense, Garbagnate Milanese, Italy; cribezzio03@yahoo.it

Received 14 April 2020
Revised 18 April 2020
Accepted 20 April 2020
Published Online First 30 April 2020

To cite: Bezzio C, Saibeni S, Variola A, *et al*. *Gut* 2020;**69**:1213–1217.

ABSTRACT

Objectives COVID-19 has rapidly become a major health emergency worldwide. Patients with IBD are at increased risk of infection, especially when they have active disease and are taking immunosuppressive therapy. The characteristics and outcomes of COVID-19 in patients with IBD remain unclear.

Design This Italian prospective observational cohort study enrolled consecutive patients with an established IBD diagnosis and confirmed COVID-19. Data regarding age, sex, IBD (type, treatments and clinical activity), other comorbidities (Charlson Comorbidity Index (CCI)), signs and symptoms of COVID-19 and therapies were compared with COVID-19 outcomes (pneumonia, hospitalisation, respiratory therapy and death).

Results Between 11 and 29 March 2020, 79 patients with IBD with COVID-19 were enrolled at 24 IBD referral units. Thirty-six patients had COVID-19-related pneumonia (46%), 22 (28%) were hospitalised, 7 (9%) required non-mechanical ventilation, 9 (11%) required continuous positive airway pressure therapy, 2 (3%) had endotracheal intubation and 6 (8%) died. Four patients (6%) were diagnosed with COVID-19 while they were being hospitalised for a severe flare of IBD. Age over 65 years (p=0.03), UC diagnosis (p=0.03), IBD activity (p=0.003) and a CCI score >1 (p=0.04) were significantly associated with COVID-19 pneumonia, whereas concomitant IBD treatments were not. Age over 65 years (p=0.002), active IBD (p=0.02) and higher CCI score were significantly associated with COVID-19-related death.

Conclusions Active IBD, old age and comorbidities were associated with a negative COVID-19 outcome, whereas IBD treatments were not. Preventing acute IBD flares may avoid fatal COVID-19 in patients with IBD. Further research is needed.

Significance of this study

What is already known on this subject?

- COVID-19 has rapidly become a major health emergency worldwide, resulting in >1.7 million persons infected with 6% lethality.
- Patients with IBD are at increased risk of infection, especially when they have active disease and are taking immunosuppressive therapy.
- The characteristics and outcomes of COVID-19 in patients with IBD remain unclear.

What are the new findings?

- Active IBD, older age and presence of comorbidities have been found to be associated with a higher risk of COVID-19 pneumonia and death in patients with IBD.
- Concomitant therapy with biologics and immunosuppressants did not associate with worse COVID-19 prognosis in patients with IBD.

How might it impact on clinical practice in the foreseeable future?

- This is the first report on the characteristics and outcomes of COVID-19 in patients with IBD.
- Maintaining effective therapy to avoid disease flares in patients with IBD may reduce the risk of fatal COVID-19.

BACKGROUND

COVID-19 is an infectious respiratory syndrome with a wide spectrum of presentations and outcomes.[1 2] It is caused by a new virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first identified in Wuhan, China, but has now spread worldwide. COVID-19 has rapidly become a major health emergency that has evolved into a pandemic. On 30 January 2020, the WHO Director-General declared that the outbreak of this viral infection constitutes a Public Health Emergency of International Concern. SARS-CoV-2, and a few other highly pathogenic coronaviruses, pose a global threat to public health,[2 3] but the risk of severe disease and death is greater in elderly subjects and in those with comorbidities.[4 5]

Patients with IBD are generally at increased infectious risk, especially when being treated with steroids, immunosuppressants or biologics.[6] The nature and magnitude of this risk vary with the type of immunosuppressive drug and with the patient's sex and age. Immunosuppressant therapy increases the risk of opportunistic viral infections,[7] although one study found that the use of antitumour necrosis factor (TNF)-alpha appears to reduce the risk of opportunistic viral infections.[8] Preliminary data from China[9] and Italy[10] suggest that the incidence of severe forms of COVID-19 in patients with IBD could be lower than in the general population. The first reports of COVID-19 in patients with IBD with fatal outcomes are starting to emerge.[11]

So far, the risk, presentation and severity of coronavirus infection in patients with IBD have not been studied. This study aimed to describe how COVID-19 presents and evolves in patients with IBD, and to identify risk factors that predict the severity and outcomes of COVID-19 in patients with IBD.

METHODS

This was a prospective, observational cohort study initiated and supported by the Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD). All centres affiliated with IG-IBD were invited to participate in the study with an open call for participation sent in the first week of March 2020. Patient enrolment started on 11 March 2020.

Patients were eligible if they were adults who had an established diagnosis of Crohn's disease (CD) or UC for at least 6 months and who also had an either confirmed or likely diagnosis of COVID-19. A confirmed diagnosis of COVID-19 was defined as the PCR-confirmed presence of SARS-CoV-2 genome in a nasopharyngeal swab. A likely diagnosis was made in patients who did not undergo viral testing if they had a history of contact with an infected person, together with at least three of the following signs and symptoms: fever, cough, dyspnoea, dysosmia and dysgeusia, or CT findings of COVID-19 lung infection.[12 13] For all eligible patients, we collected the following data from medical charts: age, sex, IBD type, IBD treatments, IBD clinical activity (defined as a partial Mayo score ≥3 with a rectal bleeding subscore ≥1 for UC,[14 15] and a Harvey-Bradshaw Index for CD ≥5[16]), other comorbidities (expressed with Charlson Comorbidity Index (CCI)[17]), signs and symptoms of COVID-19 (fever, cough, dyspnoea, dysosmia/dysgeusia, pharyngitis, diarrhoea, arthralgia-myalgia/asthenia, rhinitis, dysphonia), therapies for COVID-19 and COVID-19 outcomes. These data were entered into an electronic database accessible to participating centres.

The primary objective was to describe the characteristics of COVID-19 in patients with IBD in terms of negative outcomes, such as the development of COVID-19-related pneumonia (demonstrated by chest CT or radiography), hospitalisation, respiratory therapy and death. The secondary objective was to investigate possible associations between baseline characteristics of patients with IBD and negative COVID-19 outcomes.

STATISTICAL ANALYSES

Because the incidence and prevalence of COVID-19 in the IBD population is not known, sample size was not calculated. Differences between subgroups of patients were tested for significance using Fisher's exact test. Associations among categorical variables were assessed for significance using the χ^2 test or Fisher's exact test, and logistic regression. A value of $p<0.05$ was considered to be statistically significant.

Table 1 Baseline characteristics of patients with IBD with COVID-19

	Overall (n=79)	CD (n=32)	UC (n=47)
Age, years, median (range)	45 (18–80)	39 (18–73)	51 (23–80)
Female, n (%)	35 (44.3%)	15 (46%)	20 (43%)
Active disease, n (%)	22 (28%)	4 (12%)	18 (35%)
Concomitant therapy for IBD, n (%)			
None	5 (6%)	5 (16%)	0 (0%)
Aminosalicylates	24 (30%)	3 (9%)	21 (45%)
Thiopurines	6 (8%)	1 (3%)	5 (11%)
Systemic corticosteroids	9 (11%)	1 (3%)	8 (17%)
Calcineurin inhibitors	1 (1%)	1 (3%)	0 (0%)
Anti-TNF	29 (37%)	15 (47%)	14 (30%)
Vedolizumab	15 (20%)	5 (16%)	10 (21%)
Ustekinumab	3 (4%)	3 (9%)	0 (0%)
Investigational drugs (within a clinical trial)	2 (2%)	2 (6%)	1 (2%)
Pregnancy,n (%)	1 (1%)	0 (0%)	1 (2%)
Comorbidities,n (%)	30 (38%)	10 (31%)	20 (43%)
Charlson Comorbidity Index, n (%)			
0	43 (54%)	21 (66%)	22 (47%)
1	14 (18%)	7 (22%)	7 (15%)
2	12 (15%)	3 (9%)	9 (20%)
3	6 (8%)	1 (3%)	5 (11%)
4	3 (4%)	0 (0%)	3 (6%)
5	1 (1%)	0 (0%)	1 (2%)
Type of comorbidity, n (%)			
None	49 (62%)	22 (68%)	27 (57%)
Essential hypertension	9 (11%)	2 (6%)	7 (14%)
Coronary heart disease	5 (6%)	0 (0%)	5 (10%)
COPD	5 (6%)	0 (0%)	4 (8%)
CMV colitis	2 (3%)	0 (0%)	2 (4%)
Psoriasis	2 (3%)	2 (6%)	0 (0%)
Ankylosing spondylitis	2 (3%)	2 (6%)	0 (0%)
Rheumatoid arthritis	1 (1%)	1 (3%)	0 (0%)
Multiple sclerosis	1 (1%)	0 (0%)	1 (2%)
Undifferentiated connective tissue disease	1 (1%)	1 (3%)	0 (0%)
Hypothyroidism	1 (1%)	0 (0%)	1 (2%)
Kaposi's sarcoma	1 (1%)	0 (0%)	1 (2%)
COVID-19-related symptoms, n (%)			
None	2 (3%)	1 (3%)	1 (3%)
Fever	71 (90%)	28 (88%)	43 (91%)
Cough	52 (66%)	19 (59%)	33 (70%)
Dysosmia or dysgeusia	19 (24%)	10 (31%)	9 (19%)
Arthralgia or myalgia	18 (23%)	10 (31%)	8 (17%)
Dyspnoea	15 (19%)	8 (25%)	7 (15%)
Diarrhoea	12 (15%)	5 (16%)	7 (15%)
Rhino-pharyngitis	13 (16%)	8 (26%)	5 (10%)
Dysphonia	1 (1%)	1 (1%)	0 (0%)
Conjunctivitis	1 (1%)	1 (1%)	0 (0%)

CD, Crohn's disease; CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease.

RESULTS

Between 11 and 29 March 2020, we enrolled 79 consecutive patients with IBD with diagnosis of COVID-19. The patients were in treatment at one of 24 Italian IBD referral units for either CD (n=32) or UC (n=47). Overall, 49 patients had COVID-19 confirmed by a positive nasopharyngeal swab, while 30 cases were confirmed by clinical and radiological signs. Baseline characteristics of the patients are shown in table 1.

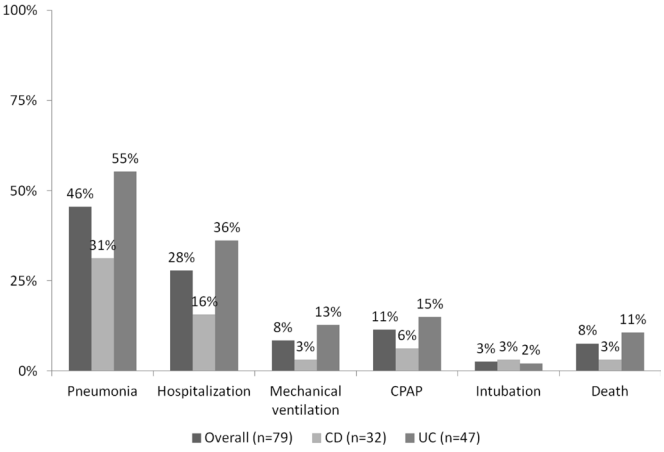

Figure 1 Negative outcomes of COVID-19 in the overall IBD cohort, and for patients with Crohn's disease (CD) and UC. CPAP, continuous positive airway pressure.

Overall population analysis

The most common COVID-19 symptoms were fever (90%), cough (66%), dysosmia/dysgeusia (24%), arthralgia/myalgia (23%), dyspnoea (19%), diarrhoea (15%) and rhino-pharyngitis (16%). Overall, 36 patients (46%) had COVID-19-related pneumonia, 22 (28%) were hospitalised, 7 (9%) required non-mechanical ventilation, 9 (11%) required continuous positive airway pressure (CPAP) therapy, 2 (3%) underwent endotracheal intubation and 6 (8%) died (figure 1). No significant differences between patients with CD and UC were found in terms of concomitant medications: steroids (p=0.13), thiopurines (p=0.52), anti-TNF (p=0.11) and vedolizumab (p=0.71). Three patients with CD were under treatment with ustekinumab, but no patient with UC was taking this drug because it is not reimbursed for patients with UC in Italy. The one patient taking both infliximab and azathioprine did not have pneumonia. One patient under triple immunosuppression (steroids+azathioprine+infliximab), who had a concomitant cytomegalovirus (CMV) infection and was hospitalised at the time of COVID-19 diagnosis, developed pneumonia but had full recovery.

Four patients (6%) were diagnosed with COVID-19 while they were being hospitalised for a severe flare of IBD. No significant differences were found between patients with UC and CD in terms of disease activity (p=0.13).

At least one comorbidity was present in 30 patients with IBD (38%). In the overall population, 9 (11%) had essential hypertension, 5 (6%) had coronary heart disease (CHD), and 5 (6%) had chronic obstructive pulmonary disease. Two patients with UC had CMV-related colitis (3%) treated with antiviral therapy. Eight patients (10%) had concomitant immune-mediated diseases (two psoriasis, two ankylosing spondylitis, one rheumatoid arthritis, one multiple sclerosis, one undifferentiated connective tissue disease and one hypothyroidism). The frequency of immune-mediated disease was significantly greater in patients with CD than UC (7 vs 1, p=0.02). One patient had concomitant Kaposi's sarcoma.

COVID-19 pneumonia

Among the 36 patients with pneumonia, 26 (72%) had UC and 10 had CD; altogether, 13 (36%) had active IBD. At the time of diagnosis, 18 (50%) were under treatment with 5-aminosalicylic acid, 7 (19%) were on steroids, 3 (8%) on thiopurines, 14 (39%) on anti-TNF, 5 (14%) on vedolizumab, 1 (3%) on ciclosporin and 1 on (3%) filgotinib as an experimental drug within a clinical trial. No patient was receiving ustekinumab. Fifteen patients had at least one comorbidity (19% systemic hypertension, 11% CHD and 5% immune-mediated diseases). All four patients who were hospitalised for an acute severe IBD flare developed COVID-19 pneumonia during the hospitalisation period.

Table 2 Association between potential risk factors and COVID-19-related pneumonia

Risk factor	OR	95% CI	P value
Age >65 years	5.87	1.15 to 29.66	**0.03**
CCI score >1	2.91	1.06 to 9.21	**0.04**
UC diagnosis	2.72	1.06 to 6.99	**0.03**
Active IBD	10.25	2.11 to 49.73	**0.003**
Corticosteroids	4.94	0.95 to 25.55	0.05
Thiopurines	1.21	0.22 to 6.40	0.82
Anti-TNF	1.18	0.47 to 2.97	0.71
Vedolizumab	0.53	0.16 to 1.73	0.29

Bold indicates p < 0.05.
CCI, Charlson Comorbidity Index; TNF, tumour necrosis factor.

A significant association was found between the risk of COVID-19 pneumonia and age over 65 years (p=0.03), UC diagnosis (p=0.03), moderate-to-severe disease activity (p=0.02), any disease activity (p=0.003) and a CCI score >1 (p=0.04) (online supplementary figure 1 and table 2). In contrast, concomitant IBD treatments were not associated with the risk of COVID-19 pneumonia. After adjustment for concomitant steroid use, active disease remained significantly associated with the risk of COVID-19 pneumonia (p=0.01).

COVID-19 pneumonia required hospitalisation in 22 patients (61%), 16 patients required subintensive respiratory assistance (non-mechanical ventilation or CPAP therapy, 44%), 2 patients (6%) required endotracheal intubation and 6 (16%) patients died. Hospitalisation and the need for respiratory assistance were significantly more frequent in patients with active IBD (both p<0.001). No association was found between concomitant IBD treatments and the need for hospitalisation or respiratory therapies for COVID-19 pneumonia.

COVID-19-related deaths

COVID-19 led to death in six patients (five men). The patients' median age was 73 years (range 53–80 years; four were over 65 years of age). Half of the patients had active IBD, two were being hospitalised for a severe IBD flare at the time of COVID-19 diagnosis, and five had UC. Three cases had concomitant hypertension, and three had CHD; all had a CCI score >0 and four had a score >2 (online supplementary figure 1). Regarding concomitant IBD treatments, three patients were taking 5-aminosalicylic acid, two systemic steroids and one anti-TNF therapy. All these patients received respiratory therapy: five had subintensive treatment (mechanical ventilation or CPAP), and two had endotracheal intubation before death.

Age over 65 years (p=0.002), active IBD (p=0.02), moderate-to-severe active disease (p=0.005) and higher CCI score were significantly associated with COVID-19-related death in our IBD cohort (table 3). When adjusted for steroid use, moderate-to-severe disease remained significantly associated with COVID-19-related death (p=0.02).

DISCUSSION

The COVID-19 pandemic is a challenge for healthcare systems worldwide. Italy has been the first European country affected by the pandemic since 20 February 2020. Since then, as of 10 April 2020, according to preliminary data released by the Italian

Table 3 Association between potential risk factors and COVID-19-related death

Risk factor	OR	95% CI	P value
Age >65 years	19.6	2.95 to 130.6	0.002
CCI score >1	16.66	1.80 to 153.9	0.01
Active IBD	8.45	1.26 to 56.56	0.02
UC diagnosis	2.95	0.31 to 27.73	0.34
Corticosteroids	6.28	0.89 to 44.24	0.064
Anti-TNF	0.40	0.04 to 3.78	0.42

CCI, Charlson Comorbidity Index; TNF, tumour necrosis factor.

Ministry of Health and the Italian Civil Protection, >140 000 cases have been confirmed, and >18 000 people have died; 30% of cases were reported in Lombardy region, and 69% in northern Italy.

The impact of COVID-19 on immune-mediated disease remains unknown, as does the risk of COVID-19-related complications and death. This is particularly true in patients with IBD who are frequently treated with immunosuppressive agents and who are at risk of serious opportunistic infections.[6]

We identified 79 patients with IBD who developed COVID-19 since the beginning of the pandemic. This number is relatively small compared with the general population infected by SARS-COV-2 in Italy. The geographic distribution of our IBD population was in line with the general distribution of the confirmed cases in Italy, since 85% of our study population lives in northern Italy. These numbers suggest that patients with IBD are not at higher risk of being infected by the SARS-COV-2 than the general population.

Active IBD was found to associate with a negative COVID-19 outcome (pneumonia, respiratory support, hospitalisation and death). All these patients had active disease before their COVID-19 diagnosis and were under treatment for a disease flare. The majority of them had active UC with at least mild rectal bleeding. Therefore, although we cannot exclude that in some cases, diarrhoea was due to COVID-19,[18] gastrointestinal symptoms were related mainly to IBD. A diagnosis of UC significantly associated with COVID-19 pneumonia, but not with death. Other factors significantly associated with worse outcomes were older age and higher CCI score, whereas numerically more men died in our cohort. Old age, comorbidities and male sex have also been found to be risk factors for lethality in the general Italian population.[5] These findings suggest that COVID-19 complications and lethality in patients with IBD reflect the natural history of COVID-19, and are apparently unrelated to the use of immunosuppressive therapy.

About 50% of patients with IBD who developed pneumonia, and 50% of patients who died, were not under any immunosuppressive therapy (such as systemic corticosteroids, thiopurines, small molecules and monoclonal antibodies). Whether to stop or continue immunosuppressive therapy in IBD is debated. The International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) suggests to continue maintenance therapy, paying attention only to high doses of systemic corticosteroids (>20 mg/day prednisone or equivalent).[19] Ping *et al* reported no case of COVID-19 among 318 patients with IBD in Wuhan, China, but they nonetheless stopped immunosuppressive therapy preventively.[9] Our data show there was no increased risk of negative COVID-19 outcome related to the use of immunosuppressive drugs, while a trend towards statistical significance was observed for concomitant corticosteroid therapy. This find is concordant with IOIBD recommendations,[19] but there is a significant risk of COVID-19 pneumonia and death in patients with active disease. Moreover, four patients with IBD who were hospitalised for a severe IBD flare developed COVID-19, which was fatal in two cases. Severe active disease requiring the use of steroids, especially in elderly patients, could be associated with worse outcomes, as recently reported.[11] This finding highlights the need to continue effective maintenance therapy in order to avoid severe IBD flares, which would require hospital visits for testing or admission. Since hospitals may be the place with the highest risk of infection as long as the pandemic lasts, there is a consequent need to restructure IBD care and to replace hospital visits with virtual clinics and remote monitoring,[20–22] whenever possible.

This study has several limitations. First, not all IBD cases were included because there is no national registry for patients with IBD in Italy. The identified patients were recruited mainly because they reported their COVID-19 diagnosis to their referral centre, they were hospitalised or they were in contact with their physician during a virtual visit. The relatively few patients, however, is in line with a report from Bergamo Hospital, where there were no cases of COVID-19 among patients with IBD, and no hospitalisations, in one of the most affected areas of northern Italy.[10] Second, the diagnosis and tallying of COVID-19 cases in Italy differ from region to region, and may be underestimated or overestimated depending on the geographical provenience. We identified our patients with COVID-19 based on criteria of the Italian Ministry of Health,[23] but some patients may remain undiagnosed. Third, the study was limited to investigate risk factors related to IBD that might be less frequent. In this context, data from large, multicentre registries, such as the SECURE-IBD registry, may be helpful to confirm our findings.

CONCLUSION

This is the largest report on the characteristics and outcomes of COVID-19 in patients with IBD. Active disease, especially in elderly patients with comorbidities, was associated with negative COVID-19 outcomes, whereas IBD treatments were not. Preventing patients with IBD from being hospitalised for acute flares may be the best way to avoid fatal COVID-19 in this patient population. Larger studies with longer follow-up periods are needed to confirm these findings.

Author affiliations
[1]Gastroenterology Unit, Rho Hospital, Rho (MI), ASST Rhodense, Garbagnate Milanese, Italy
[2]IBD Unit, Don Calabria Sacred Heart Hospital, Negrar, Veneto, Italy
[3]IBD Center, Gastroenterology, Humanitas Clinical and Research Center - IRCCS, Rozzano, Milan, Italy
[4]Department of Biomedical Sciences, Humanitas University, Milan, Italy
[5]Gastroenterology Unit, ASST Fatebenefratelli Sacco, Milano, Lombardia, Italy
[6]Medicine, Gastroenterology and Digestive Endoscopy Department, Poliambulanza Brescia Hospital, Brescia, Lombardia, Italy
[7]UOC Gastroenterology and Digestive Endoscopy, ASST Bergamo Est, Seriate, Lombardia, Italy
[8]Gastroenterology Unit, ASST Spedali Civili di Brescia, Brescia, Lombardia, Italy
[9]Department of Surgical, Oncological and Gastroenterological Sciences, University of Padua, Padova, Veneto, Italy
[10]Division of Digestive Endoscopy and Gastroenterology, Valduce Hospital, Como, Italy
[11]Gastroenterology and Endoscopy Unit, La Fondazione IRCCS Ca' Granda Ospedale Maggiore di Milano Policlinico, Milano, Lombardia, Italy
[12]Department of Pathophysiology and Transplantation, University of Milan, Milano, Lombardia, Italy
[13]First Department of Internal Medicine, Università degli Studi di Pavia, Pavia, Lombardia, Italy
[14]Gastroenterology Unit, Azienda Ospedaliera San Gerardo, Monza, Lombardia, Italy
[15]Gastroenterology Unit, Ospedale Santa Maria di Ca Foncello, Treviso, Veneto, Italy
[16]Division of Gastroenterology, IRCCS Ospedale Casa Sollievo della Sofferenza, San Giovanni Rotondo, Puglia, Italy
[17]Gastroenterology, Federico II University Hospital, Napoli, Campania, Italy
[18]Gastroenterology Uniit, ASST dei Sette Laghi, Varese, Lombardia, Italy
[19]Department of Medicine and Aging Science, University Gabriele d'Annunzio of Chieti and Pescara, Chieti, Abruzzo, Italy

[20]Gastroenterology Unit, Azienda Ospedaliero Universitaria Careggi, Firenze, Toscana, Italy
[21]Gastreonterology Unit, ASST Rhodense, Garbagnate Milanese, Lombardia, Italy
[22]Gastroenterology Unit, IRCCS Policlinico San Danato, San Donato Milanese, Lombardia, Italy
[23]Division of Gastroenterology, Department of Medical Sciences, University of Turin, Torino, Piemonte, Italy
[24]Internal Medicine, Gastroenterology Unit, Bufalini Hospital, AUSL della Romagna, Cesena, Italy
[25]Gastroenterology Division, Arcispedale S Maria Nuova, Reggio Emilia, Emilia-Romagna, Italy
[26]Gastroenterology Unit, ASST Rhodense, Garbagnate Milanese, Lombardia, Italy
[27]Unit of Gastroenterology, Department of Medical Science and Public Health, University of Cagliari, Cagliari, Sardegna, Italy
[28]IBD Unit, Policlinico Universitario Agostino Gemelli, Roma, Lazio, Italy
[29]Università Cattolica del Sacro Cuore Facoltà di Medicina e Chirurgia, Roma, Lazio, Italy
[30]Gastroenterology Unit, Azienda Ospedaliera Ordine Mauriziano di Torino, Torino, Piemonte, Italy

Correction notice This article has been corrected since it published Online First. Affiliation 3 has been updated.

Twitter Angela Variola @angela.variola, Laurino Grossi @rinogrossi62 and Massimo Fantini @Max_Fantini

Acknowledgements The authors would like to thank Daniela Gilardi, Simona Radice and Dr Federica Furfaro (Humanitas, Rozzano, Milan, Italy) and Maria Teresa Grassi and Natalia Di Pasquale (ASST Rhodense, Rho, Milan, Italy) for their contribution to the data collection. Valerie Matarese provided scientific editing.

Contributors CB, SS planning the study, drafting the article, analysis and interpretation of data. GF drafting article, analysis and interpretation of data. All other authors: data collections, critical revision of article for important intellectual content. All authors approved the final version of the manuscript including authorship list.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests CB received lecture fees from Takeda, AbbVie and Janssen. SS received lecture fees from Takeda Pharmaceuticals and Janssen Pharmaceuticals and served as a consultant and a member of Advisory Boards for AbbVie and Janssen Pharmaceuticals. AV received lecture fees from Takeda and AbbVie and served as consultant for MSD, Pfizer and Janssen. MA received consulting fees from Nikkiso Europe and lecture fees from Janssen, Abbvie and Pfizer. CR reports personal fee from Abbvie, Janssen Cilag, MSD, Recordati, Takeda and Vifor. FC served as consultant and a member of advisory board for Mundipharma, AbbVie, MS&D, Takeda, Janssen, Roche, Celgene and received lecture fees from AbbVie, Amgen, Ferring, Takeda, Allergy Therapeutics and unrestricted research grants from Giuliani, Sofar, MSD, Takeda, AbbVie. FB served as a member of advisory board for Biogen and Janssen, Takeda, Celgene, Mundipharma, AbbVie and MSD. FC served as consultant and a member of advisory board for Mundipharma, AbbVie, MS&D, Takeda, Janssen, Roche, Celgene and received lecture fees from AbbVie, Amgen, Ferring, Takeda, Allergy Therapeutics. DGR served as consultant and received lecture fees from Janssen, Ferring, Errekappa. SD served as a speaker, consultant and advisory board member for Schering-Plough, Abbott (AbbVie) Laboratories, Merck, UCB Pharma, Ferring, Cellerix, Millenium Takeda, Nycomed, Pharmacosmos, Actelion, Alfa Wasserman, Genentech, Grunenthal, Pfizer, AstraZeneca, Novo Nordisk, Cosmo Pharmaceuticals, Vifor and Johnson and Johnson. MCF received fees as member of advisory boards and participation to sponsored symposia from AbbVie, Takeda, Jannsen-Cilag, Pfizer, Sandoz. AA served as a consultant for AbbVie, Allergan, Amgen, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Ferring, Gilead, Janssen, Lilly, MSD, Mylan, Pfizer, Roche, Samsung Bioepis, Sandoz and Takeda; MD served as a speaker, consultant and advisory board member for AbbVie, Takeda, Janssen, Norgine, Pfizer, MSD, Celltrion, Roche, Gilead, Bioclinica, Ferring, SOFAR, Chiesi, Zambon. GF received consultancy fees from Ferring, MSD, AbbVie, Takeda, Janssen, Amgen, Sandoz, Samsung Bioepis, Celltrion.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study protocol was approved by the IG-IBD Scientific Committee and by the Coordinating Ethical Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

ORCID iDs
Cristina Bezzio http://orcid.org/0000-0003-0076-8549
Simone Saibeni http://orcid.org/0000-0001-5677-2534
Arnaldo Amato http://orcid.org/0000-0002-4397-4142
Flavio Caprioli http://orcid.org/0000-0002-8077-8175
Marco Vincenzo Lenti http://orcid.org/0000-0002-6654-4911
Davide Giuseppe Ribaldone http://orcid.org/0000-0002-9421-3087
Alessandro Sartini http://orcid.org/0000-0003-1573-6451
Gionata Fiorino http://orcid.org/0000-0001-5623-2968

REFERENCES

1 Zhou P, Yang X-L, Wang X-G, *et al*. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579:270–3.
2 World Health Organization. Novel coronavirus (COVID-19) situation. Secondary novel coronavirus (COVID-19) situation, 2020. Available: https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd
3 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;24:2012–9.
4 Guan W-jie, Ni Z-yi, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020.
5 Onder G, Rezza G, Brusaferro S. Case-Fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020. doi:10.1001/jama.2020.4683. [Epub ahead of print: 23 Mar 2020].
6 Rahier JF, Magro F, Abreu C, *et al*. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014;8:443–68.
7 Beaugerie L, Kirchgesner J. Balancing benefit vs risk of immunosuppressive therapy for individual patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol* 2019;17:370–9.
8 Kirchgesner J, Lemaitre M, Carrat F, *et al*. Risk of serious and opportunistic infections associated with treatment of inflammatory bowel diseases. *Gastroenterology* 2018;155:e10:337–46.
9 Ping A, Mengyao J, Haixia R, *et al*. Protection of 318 inflammatory bowel disease patients from the outbreak and rapid spread of COVID-19 infection in Wuhan, China. *Lancet* 2020.
10 Norsa L, Indriolo A, Sansotta N, *et al*. Uneventful course in IBD patients during SARS-CoV-2 outbreak in northern Italy. *Gastroenterology* 2020. doi:10.1053/j.gastro.2020.03.062. [Epub ahead of print: 02 Apr 2020].
11 Mazza S, Sorce A, Peyvandi F, *et al*. A fatal case of COVID-19 pneumonia occurring in a patient with severe acute ulcerative colitis. *Gut* 2020;69:1148–9.
12 Salehi S, Abedi A, Balakrishnan S, *et al*. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol* 2020:1–7.
13 World Health Organization. Coronavirus. Secondary coronavirus, 2020. Available: https://www.who.int/health-topics/coronavirus
14 Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med* 1987;317:1625–9.
15 D'Haens G, Sandborn WJ, Feagan BG, *et al*. A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. *Gastroenterology* 2007;132:763–86.
16 Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980;1:514.
17 Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
18 Xiao F, Tang M, Zheng X, *et al*. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020.
19 International Organization for the study of Inflammatory Bowel Disease (IOIBD). IOIBD Update on COVID19 for Patients with Crohn's Disease and Ulcerative Colitis. Secondary IOIBD Update on COVID19 for Patients with Crohn's Disease and Ulcerative Colitis, 2020. Available: https://www.ioibd.org/ioibd-update-on-covid19-for-patients-with-crohns-disease-and-ulcerative-colitis/
20 Danese S, Cecconi M, Spinelli A. Management of IBD during the COVID-19 outbreak: resetting clinical priorities. *Nat Rev Gastroenterol Hepatol* 2020. doi:10.1038/s41575-020-0294-8. [Epub ahead of print: 25 Mar 2020].
21 Fiorino G, Allocca M, Furfaro F, *et al*. Inflammatory bowel disease care in the COVID-19 pandemic era: the Humanitas, Milan experience. *J Crohns Colitis* 2020. doi:10.1093/ecco-jcc/jjaa058. [Epub ahead of print: 24 Mar 2020].
22 Ungaro RC, Sullivan T, Colombel J-F, *et al*. What should Gastroenterologists and patients know about COVID-19? *Clin Gastroenterol Hepatol* 2020. doi:10.1016/j.cgh.2020.03.020. [Epub ahead of print: 18 Mar 2020].
23 Ministero della Salute. COVID-19. Aggiornamento della definizione di caso. Secondary COVID-19. Aggiornamento della definizione di caso, 2020. Available: http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2020&codLeg=73669&parte=1%20&serie=null