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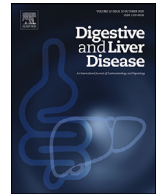
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# Digestive and Liver Disease

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## Correspondence

### Low frequency of COVID-19 in inflammatory bowel diseases



After its first description in December 2019, Covid-19, an infectious respiratory disease caused by the novel coronavirus SARS-CoV-2 (1), has spread throughout the world and on March 11, 2020 the World Health Organization declared it a pandemic. The SARS-CoV-2 infection is more frequent in elderly and in subjects with co-existing pathologies and weakened immune system. The risk of infection or death due to Covid-19 in patients with inflammatory bowel diseases (IBD) is unknown at this stage. However, it has been presumed that IBD patients who are on steroids, immunosuppressive drugs or biologics could be more susceptible to SARS-CoV-2 infection, as these therapies are associated with increased risk of viral infections (2).

To gain entry into the cells SARS-CoV-2 uses angiotensin-converting enzyme 2, a protein that is highly expressed in the human gut (3,4). An analysis of patients with SARS-CoV-2 infection showed that some patients experienced gastrointestinal symptoms/signs and the virus was identified in stool samples of infected patients. Viral RNA was present in the stool of over 50% of patients and, even after testing negative for SARS-CoV-2 in respiratory samples, nearly one fifth of the patients remained positive for the virus in stool samples (5,6). These findings suggest that the course of SARS-CoV-2 infection may involve cells of the gastrointestinal tract, a finding of importance for patients with IBD.

We here examined the frequency of symptoms/signs suggestive of Covid-19 in IBD patients and assessed the risk of SARS-CoV-2 infection in IBD.

This was an observational study including IBD patients regularly followed in our tertiary referral center at the “Tor Vergata University Hospital”, Rome, Italy. Like many countries worldwide, Italy has been placed under lockdown as Covid-19 cases surge in our country since February 2020. Consequently, the scheduled follow-up visits in the IBD centres were canceled or postponed and the patients have had the possibility to communicate with the IBD team through a dedicated phone number. During the calls, we recorded any symptom/sign suggestive of Covid-19 as well as information about direct contacts with subjects known to be affected by SARS-CoV-2 and data relative to the admission of the patients to the hospital for undergoing a nasopharyngeal swab to identify carriers of SARS-CoV-2. Clinical activity and management of the IBD patients were also monitored. All patients had provided their informed consent for the use of personal and clinical data for scientific purposes, and no patient refused to participate.

The study variables were summarized descriptively using numbers and percentages for discrete variables, while median and range were used for continuous variables. Cumulative incidence of SARS-CoV-2 infection in IBD was calculated dividing the positive cases by the overall population of IBD patients enrolled for the

study. Cumulative incidence of laboratory-confirmed SARS-CoV-2 infection in the Italian population was extracted from data of the Italian Health Minister ([www.salute.gov](http://www.salute.gov)). Incidence rate of SARS-CoV-2 in the IBD population was obtained with the direct method using the general Italian population as standard. Results were presented as odds ratios (OR) and their 95% confidence intervals (CI).

From March 24 to April 30, 2020, we collected information regarding 672 IBD patients who were scheduled to receive a visit at the Tor Vergata Hospital in the same period. Baseline demographic and clinical characteristics, as well as concomitant treatments for IBD are shown in the table. The median age of the patients was 46 years (range: 16–83), 46% of the patients were female, and 59% had a diagnosis of CD. No patient refused to provide information regarding his/her symptoms/signs. Most patients remain on stable therapy with conventional drugs or biologics, and 20 patients (3%) discontinued treatment during the Covid-19 outbreak (table 1). A flare-up occurred in 90 (13%) patients; adjustment of therapy led to disappearance of the symptoms in all the patients.

Ten out of 672 patients (1.5%) underwent rhino-pharyngeal swab: 3 patients because experienced respiratory symptoms, which were highly suggestive of Covid-19, and 7 patients because had a direct contact with SARS-CoV-2-infected individuals. Three out of these 10 patients resulted positive and two of them were hospitalized: one patient had a lung cancer and eventually died. Of the 672 patients, 38 (5.6%) had been travelling to high risk geographical areas and 64 (9.5%) had direct contacts with individuals living in high risk areas. All these patients experienced no suggestive symptoms of Covid-19.

On April 30, 2020 205,463 subjects were positive among an overall Italian population of 6031,7000. Cumulative incidence of laboratory-confirmed SARS-CoV-2 in Italy was 3.41 cases per 1000 inhabitants. In our IBD population, the crude incidence rate of SARS-CoV-2 infection was 4.46 cases per 1000 patients. Patients with IBD had a numerically, but non statistically higher standardized risk of SARS-CoV-2 infection compared with the general population (OR 1.31; 95% CI 0.26–3.85; p 0.50).

Up to April 30, 2020, more than 205,463 cases of SARS-CoV-2 infection have been diagnosed in Italy, accounting for 0,3% of the total population. Although, we need more robust epidemiological data to draw a conclusion regarding the incidence rate of Covid-19 in IBD, our findings suggest that IBD patients are not at increased risk of Covid-19 as compared with the general population. Indeed, after more than 2 months from the first Covid-19 patient diagnosed in Italy, only 3 out of our 672 patients (0,44%) were infected by SARS-CoV-2. Approximately one sixth of our patients, who had direct contacts with either infected patients or individuals living in high risk geographical areas or were themselves travelling to such regions, were negative for SARS-CoV-2 and/or remain asymptomatic.

**Table 1**  
Demographic and clinical characteristics of IBD patients.

Number of patients	672
Gender female n (%)	311 (46)
Median Age (range) years	46 (16–83)
Patients working during quarantine n (%)	125 (20)
Median co-habiting persons (range)	3 (1–8)
IBD diagnosis n (%)	
Crohn's disease	397 (59)
ulcerative colitis	269 (40)
IBD unclassified	6 (1)
Patients experiencing IBD flare n (%)	90 (13)
Current treatments n (%)	
No therapy	56 (9)
Mesalamine	367 (54)
Steroids	29 (4)
Immune suppressant	43 (6)
Anti-TNFa	183 (27)
Vedolizumab	27 (4)
Ustekinumab	31 (5)
Antibiotics	38 (6)
Experimental drug	6 (1)
Therapy discontinuation n (%)	20 (3)
Causes for therapy discontinuation n (%)	
Fear for covid-19	4 (0.6)
Adverse events	6 (0.9)
Physician's indication	1 (0.1)
Others	9 (1.3)

We are aware that the present study has some limitations. It is likely that the incidence of SARS-CoV-2 infection in our IBD population is underestimated as the majority of the patients did not undergo rhino-pharyngeal swab. However, in this context, it is noteworthy that such a diagnostic test was not provided to the general Italian population unless there were reasons to suspect SARS-CoV-2 infection. Thus, it is unlikely this limitation have had a major impact on the comparison of incidences. We restricted our analysis to the IBD patients scheduled to receive a visit during the study period and, therefore, this cohort could be not representative of our IBD population, which comprises more than 3000 patients. However, our data are in line with those published recently by Norsa and colleagues, who reported no case of SARS-CoV-2 infection in a cohort of IBD patients living in a high-risk area of Northern Italy (7). We did not attempt to assess risk factors for SARS-CoV-2 infection in IBD, as the only 3 cases documented in our study prevented the use of logistic regression models.

Notably, more than one third of our patients were receiving biologics and all of them experienced no Covid-19-related symptoms thus supporting the hypothesis that such drugs do not increase the risk of Covid-19 (8,9).

Based upon these data, we feel IBD patients should be encouraged to continue their treatment even during Covid-19 outbreak in order to prevent disease flares and IBD-associated complications. At the same time, IBD patients, particularly those with co-existing comorbidities (e.g. hypertension, diabetes, cardiovascular diseases) should strictly adhere to healthcare infection prevention and control measures.

### Declaration of CompetingInterest

Giovanni Monteleone served as an advisory board member for AbbVie. Emma Calabrese has received fees from ABBVIE, TAKEDA and JANSSEN. The other authors have no conflict of interest.

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Irene Marafini<sup>#</sup>, Silvia Salvatori<sup>#</sup>, Giorgia Sena<sup>#</sup>, Emma Calabrese<sup>#</sup>,  
Livia Biancone<sup>#</sup>, Giovanni Monteleone<sup>\*#</sup>  
Department of Systems Medicine, University of Rome "TOR  
VERGATA", Rome, Italy  
IBD group of Tor Vergata University Hospital, Rome, Italy

\*Correspondence.

E-mail address: [gi.monteleone@med.uniroma2.it](mailto:gi.monteleone@med.uniroma2.it) (G. Monteleone)

<sup>#</sup> Other collaborators of the IBD group of Tor Vergata  
University Hospital:

Edoardo Troncone, Patrizio Scarozza, Elena De Cristofaro,  
Ludovica Scucchi, Norma Alfieri, Benedetto Neri.

Affiliation: Department of Systems Medicine, University of Rome  
"TOR VERGATA", Rome, Italy