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Uneventful Course in Patients With Inflammatory Bowel Disease During the Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak in Northern Italy

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See editorial on page 36.

Keywords: Coronavirus; COVID-19; Immunosuppression; Inflammatory Bowel Diseases.

Since December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for coronavirus disease 2019 (COVID-19) has caused a pandemic, with more than 350,000 cases and more than 15,000 fatalities reported worldwide so far (<https://www.healthmap.org/covid-19/>). The first case series from the Wuhan population, describing the clinical characteristics of the SARS-CoV-2 infection in China, were recently published.¹ However, further evidence is required to predict who is at higher risk of developing clinical symptoms.

After the outbreak in China, the Lombardy region in Italy has become one of the areas with the highest incidence of new cases, and the outbreak is estimated to have begun on February 18, 2020. In particular, the province of Bergamo has reported, to date, 6471 positive results on nasopharyngeal swab for SARS-CoV-2 in a population of 1,114,590 inhabitants and is, therefore, the province with the highest rate of infection per 100,000 inhabitants worldwide² (<http://www.salute.gov.it/portale/nuovocoronavirus/>). A recent publication by the IBD Elite Union, which incorporates the 7 largest inflammatory bowel disease (IBD) referral centers in China, with more than 20,000 patients with IBD, reported no cases of COVID-19. This report included the 3 largest tertiary IBD centers in Wuhan (Tongji Hospital, Union Hospital, and Zhongnan Hospital) and was dated March 8.³

However, there is still uncertainty as to whether patients with IBD are more susceptible to COVID-19. To date, several strategies have been introduced in China to better manage patients with IBD during the Chinese outbreak of SARS-CoV-2 (https://ecco-ibd.eu/images/6_Publication/6.8_Surveys/2nd_Interview_COVID-19_ECCO_Taskforce_published.pdf).

The aim of this communication is to report the experience of our IBD center during the epidemic of SARS-CoV-2 in an area of high prevalence of the infection in Italy.

Methods

This observational study included all patients with IBD (children and adults) regularly followed in our tertiary referral

center at “Papa Giovanni XXIII Hospital,” Bergamo, Italy, from February 19 to March 23, 2020. As per our follow-up policy, patients can communicate with our team through a dedicated e-mail address or a phone number to reach a case manager; thus, any complications, including signs of SARS-CoV-2 infection, are promptly reported to our team. Moreover, all patients admitted to the hospital undergo a nasopharyngeal swab to identify carriers of SARS-CoV-2.

Results

A total of 522 patients with IBD are currently followed in Bergamo, including 59 (11%) pediatric patients (7–18 years old). Patients' characteristics are described in Table 1. Over the period analyzed, all patients were advised not to modify their treatment regimen (see Table 1). In our IBD cohort, we did not report any case of COVID-19, and, in particular, no patient was admitted to the hospital with SARS-CoV-2-proven infection. More than half of our patients (59%) were receiving salicylate treatment exclusively. Patients receiving immunosuppressive treatments such as thiopurines or methotrexate, steroids, or other immunosuppressants (22% of our cohort) and patients receiving biologic treatment (infliximab, adalimumab, vedolizumab and ustekinumab, golimumab) (16%) continued their current dosage without noting any symptoms leading to a diagnosis of COVID-19. Over the same period, 479 patients without history of IBD were admitted to the hospital because of severe COVID-19 after presenting to our emergency department with respiratory failure.

Discussion

After more than 1 month from the SARS-CoV-2 outbreak in Bergamo and its surrounding area, no cases of COVID-19 have been reported in our IBD cohort. The recent onset of this pandemic outbreak, which is still ongoing, and the lack of epidemiologically robust data preclude us from drawing

Abbreviations used in this paper: COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; MERS, Middle East respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Most current article

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0016-5085/\$36.00

<https://doi.org/10.1053/j.gastro.2020.03.062>

Table 1. Characteristics of the IBD Population of Bergamo

Characteristics	Value
Number of patients, n	522
Female, n (%)	219 (42)
Age, y, median (range)	46 (7–86)
Disease phenotype, n (%)	
Crohn's disease	186 (36)
Ulcerative colitis	336 (64)
Previous IBD-related surgery, n (%)	69 (13)
Treatments, n (%); age, y, median (range)	
Anti-inflammatory (salicylates)	304 (58); 49 (9–86)
Thiopurines or methotrexate	89 (17); 44 (7–78)
Biologics (infliximab, adalimumab, ustekinumab and vedolizumab, golimumab)	82 (16); 37 (13–72)
Steroids	16 (3); 45 (13–80)
Other immunosuppressants (tacrolimus, cyclosporin, mycophenolate mofetil)	11 (2); 41 (21–65)
Not receiving therapy	20 (4); 59 (19–79)

certain conclusions regarding its incidence and its effects in specific populations of patients. However, if we base our calculation on a mathematical model applied to the Wuhan region, which estimated that 86% of cases were undocumented, we could speculate that in Bergamo province, 46,220 patients were infected by SARS-CoV-2, accounting for 4% of the total population.⁴ From this model, we could estimate that 21 patients among our IBD cohort should have been infected. Furthermore, biologic treatments, administered either in hospital setting (infliximab, vedolizumab) or at home (adalimumab, golimumab, and ustekinumab), were regularly continued without complications.

There is lack of evidence regarding Coronaviridae infection in patients with IBD, especially those receiving immunosuppressive treatment. An extensive nationwide population-based study performed in France, including nearly 191,000 adult patients with IBD, showed 262 opportunistic infections, with an apparent decreased risk in patients receiving anti-tumor necrosis factor monotherapy compared with those receiving thiopurine monotherapy (hazard ratio, 0.57; 95% confidence interval, 0.38–0.87).⁵

If we look back to recent history, we can find 2 outbreaks of coronaviruses with high lethality, sharing with SARS-CoV-2 the same family of viruses and the characteristics of zoonoses: the severe acute respiratory syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) coronavirus infections. Immunosuppression was not found to be a risk factor for either SARS or MERS, and no patient with IBD as the only risk factor

was reported to develop severe SARS- or MERS-related disease.

Systemic inflammation is a crucial target for the treatment of COVID-19 pneumonia,⁶ even though salicylates have not been tested as a modifying agent. However, a recent report seems to suggest an important role of a cytokine cascade in the development of COVID-19 acute respiratory distress.⁷ This speculation supports the theory that patients receiving immunosuppressive treatments could be at lower risk of developing complicated SARS-CoV-2 complications.⁸

Our data cannot definitely ascertain the rate of SARS-CoV-2-infected patients in our cohort of patients with IBD. In fact, only patients with severe symptoms and/or with established contact with infected patients received a nasopharyngeal swab, leaving the asymptomatic individuals out of the count. However, we believe that our estimated rate of infection should be reliable, because it has been calculated according to well-established criteria (<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/index.html>).

Based on our evaluation, as of March 23, we conclude that none of our patients with IBD was affected by a complicated SARS-CoV-2-related pneumonia. All our patients were advised to continue their current immunosuppressive regimens.

These findings warrant further investigation to confirm our preliminary findings and to allow the implementation of guidelines for the treatment of these patients during the SARS-CoV-2 global pandemic.

References

1. Guan W-J, et al. *N Engl J Med* 2020;382:1708–1720.
2. Nacoti M, et al. *NEJM Catalyst Innovations in Care Delivery*. Available at: <https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0080>. Accessed March 2020.
3. Mao R, et al. *Lancet Gastroenterol Hepatol* 2020;5:425–427.
4. Li R, et al. *Science* 2020;368:489–493.
5. Kirchesner J, et al. *Gastroenterology* 2018;155:337–346.
6. Stebbing J, et al. *Lancet Infect Dis* 2020;20:400–402.
7. Mehta P, et al. *Lancet* 2020;395:1033–1034.
8. D'Antiga L. *Liver Transpl* 2020;26:832–834.

Received March 23, 2020. Accepted March 26, 2020.

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Conflicts of interest

The authors disclose no conflicts.