

BACKGROUND AND INTRODUCTION

Following the first reports of cases of acute respiratory syndrome in the Chinese Wuhan municipality at the end of December 2019, Chinese authorities have identified a novel coronavirus as the main causative agent. The outbreak has rapidly evolved affecting other parts of China and outside the country. Cases have been detected in several countries in Asia, but also in Australia, Europe, Africa, North as well as South America. On February 12th 2020, the novel coronavirus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) while the disease associated with it is now referred to as COVID-19. Human-to-human transmission has been confirmed but more information is needed to evaluate the full extent of this mode of transmission. The evidence from analyses of cases to date is that COVID-19 infection causes mild disease (i.e. non-pneumonia or mild pneumonia) in about 80% of cases and most cases recover, 14% have more severe disease and 6% experience critical illness. The great majority of the most severe illnesses and deaths have occurred among the elderly and those with other chronic underlying conditions (<https://www.ecdc.europa.eu/en/current-risk-assessment-novel-coronavirus-situation>).

The aim of the current document is to provide to health care professionals some understanding and knowledge on the best care we can offer to our patients in general and particularly those under immunosuppressive/ immunomodulatory treatment in the current situation of the COVID-19 epidemic.

Due to the urgency, ECCO has suggested gathering together a group of gastroenterologists with special interest in Opportunistic Infections and infectious disease experts, in order to provide on a regular basis guidance to the physicians of the ECCO community.

This guidance shall not replace any national recommendations from health care authorities but must be understood as an additional piece of information that will be updated when necessary based on our better understanding of this novel disease. Similarly, the following guidance is not accompanied by any ECCO recommendations.

The format below is based on an interview by gastroenterologists and experts in infectious disease from various places in Europe and reviewed by the COVID-19 ECCO Taskforce.

The COVID-19 ECCO taskforce is composed of members of the Opportunistic Infection Guidelines Consensus, members of the ECCO Governing Board and infectious disease experts.

QUESTIONS & ANSWERS

- **Can coronavirus COVID-19 mimic or induce an IBD flare?**

According to clinical and scientific evidence, the most common symptoms of COVID-19 are fever, fatigue, dry cough, myalgia and dyspnoea. Still, abdominal pain, diarrhoea, nausea, and vomiting can also appear, but with less frequency.¹ The coronavirus family cause both gastrointestinal and respiratory diseases. SARS-CoV-2 is present in substantial amounts in the stool of COVID-19 patients' cases. A recent case report evidenced that diarrhoea was the onset symptom of COVID-19, in a young male patient.² This case highlighted the possible involvement of the gastrointestinal system in the transmission of SARS-CoV-2.² Current evidence does not support COVID-19 infection as a cause of IBD flares. However, this situation would not be unexpected, as even without causing gastrointestinal infection, H1N1v was associated with mild flares during the first week of viral infection, mostly in ulcerative colitis patients.³

- **Shall we discourage IBD patients with stable disease to come to IBD clinics in hospital?**

Yes, if COVID-19 is disseminated in the community. The available statistics are elucidative: in the beginning of the epidemic in Wuhan, China, from 138 infected patients, 57 (41.3%) were presumed to be infected at the hospital. From these, 40 were health care professionals and 17 were patients hospitalized for other reasons.^{1,4}

Thus, IBD patients shall be advised to: **i)** have a stock of medication at home; **ii)** change to subcutaneous self-injection medication to avoid hospital appointments; **iii)** limit home exits; **iv)** avoid crowds, as much as possible (CDC recommendations).

In areas with multiple imported cases or limited local transmission, where surveillance has been activated and the testing capacity is effective, the risk is currently considered low to moderate (ECDC). In the case of critical hospital appointments/treatments, patients should be advised to practice preventive measures for COVID-19: wash hands frequently, cover the cough or sneeze into a tissue and throw the tissue in the bin, then clean hands, and avoid close contact with other persons. The means of transport of the patients to the hospital is also important; patients should avoid buses and trains, especially in peak hours. As age may be a key factor, hospital visits shall be discouraged for the elderly.

- **Are IBD patients under immunosuppressive/immunomodulatory treatment at increased risk of catching COVID-19? Or at risk of a more severe disease course?**

IBD patients are not at increased risk of catching COVID-19 and data concerning immunomodulated or immunosuppressed patients and SARS-CoV-2 infection are very scarce. The elderly and those with comorbidities (cardiovascular disease, diabetes, chronic respiratory disease, hypertension and cancers) are at risk of more severe infection and have higher case fatality rates (10.5%, 7.3%, 6.5%, 6.0%, 5.6%, respectively) than those without comorbidities (0.9%).¹

As the risk of severe infections (such as respiratory infections) is slightly higher in patients under immunosuppression and/or biological therapies, it is expected that the same might occur in SARS-CoV-2 infections.

Even though the numbers are still limited, it seems that groups with relative immunosuppression, such as very young children, pregnant women, and HIV patients, do not appear to be at higher risk of complications (British HIV Association, BHIVA).

Particular attention should be devoted to smokers, in whom there is evidence of high susceptibility to COVID-19.⁵ This is probably related to the fact that tobacco increases the gene expression of the angiotensin converting enzyme, the binding receptor for this virus.

- **How can we reduce the risk for our IBD patients to catch COVID-19 infection?**

Because SARS-CoV-2 replicates efficiently in the upper respiratory tract, infected individuals produce a large quantity of virus in this region during the prodrome period. In this stage, due to the absence of symptoms, individuals keep their usual activities, contributing to the spread of the infection.⁶

As a safe vaccine is not available yet, reduction of SARS-CoV-2 exposition is the key to decrease the risk of infection. General preventive recommendations are:

- avoid contact with infected people;
- avoid touching your eyes, nose, or mouth with unwashed hands;
- clean hands often by washing them with soap and water, for at least 20 seconds, and/or using an alcohol-based hand sanitizer that contains 60%–95% alcohol. This procedure is particularly important after going to the bathroom, before eating, and after coughing, sneezing or blowing your nose. Soap and water should be used if hands are visibly dirty.

Whenever possible steroids should be tapered as they can increase the risk of severe infection.

- **Should IBD patients stop taking immunosuppressive/immunomodulatory treatment during COVID-19 infection?**

Due to the washout period of most immunosuppressants (as such as azathioprine, methotrexate) and biologicals, suspension of immunosuppressive/immunomodulatory treatments would not be useful in mild or moderate cases of COVID-19 disease. An exception is corticosteroids therapy; the available data suggest an increased mortality and secondary infection rates in influenza infections and impaired clearance of SARS-CoV and MERS-CoV, along with complications of corticosteroids therapy in survivors. Concerning SARS-CoV-2 infection, steroids were not effective for the treatment of lung injury or shock.⁷ In this context, suspension of steroids therapy will be recommended.⁷

In severe and critical patients, the risk of more side effects and more drug interactions in patients on immunosuppressive/immunomodulatory treatment should be considered and evaluated. Suspension of these drugs would probably be advisable.

- **Should IBD patients stop taking immunosuppressive/immunomodulatory treatment if they live in an endemic area?**

Current evidence does not support treatment suspension, in patients living in an endemic area, nor it has been recommended before in similar situations, namely during SARS-CoV infection or pandemic H1N1v. However, mitigation strategies to reduce the risk during infusion therapies, in day care clinics, should be implemented.

The decision might be different in the case of starting immunosuppressive / immunomodulatory treatment. Whenever possible, during the COVID-19 epidemic, treatment should be postponed based on an individual risk assessment.

- **Should IBD patients stop taking immunosuppressive/immunomodulatory treatment or take any further measures if they had close contact with someone with proven COVID-19 infection?**

In the case of a close contact with a proven COVID-19 infected person, IBD patients should be followed **according to national recommendations**, as any other person. Social isolation is a key factor and careful follow-up and prompt medical evaluation in case of symptoms development are crucial. The R_0 for COVID-19 (number of persons a COVID-19 patient can infect) is estimated to be 2.5 and clusters of cases are

common. Unlike SARS-CoV, transmission of SARS-CoV-2 may occur during the prodromal period when those infected are mildly ill, and carry on usual activities, which contributes to the spread of infection.⁶ However, data on the effects of treatment suspension are scarce and it does not seem reasonable to stop medication.

- **What shall I advise IBD patients who want to travel into endemic areas?**

IBD patients shall be discouraged from traveling to endemic areas, in which community transmission is evident.

On 8 March 2020, the CDC advised travellers, especially those with underlying medical conditions, to "defer all cruise ship travel worldwide" given the increased risk of person-to-person transmission of SARS-CoV-2. The elderly and those with health issues should avoid crowded places, long flights, and other potentially high-risk situations.

Interview realized with Prof Dr Cândida Abreu on behalf of the COVID-19 ECCO Taskforce

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Note

Since the infection is dynamic and knowledge and evidence are growing rapidly, some of this guidance will be regularly updated based on tailored recommendations for each region according to the best evidence.

Two independent projects are being set up very recently to increase our knowledge on this novel disease in our IBD patients. We encourage you to participate.

The first project is an ECCO survey to better appreciate your view and understanding of the current situation. The coronavirus pandemic is a difficult time for everyone, including physicians and IBD patients. None of us have experienced a similar emergency, which requires dealing with complex situations, of which we know little or nothing, and which evolve day by day.

For this reason, we invite you to participate in a short survey on your current management, your fears and the difficulties you are facing every day in the context of this serious global pandemic.

The survey compilation takes only a few minutes and we ask you to respond before 20 March due to the emergency setting. This project is accessible following the link:

<https://survey.ecco-ibd.eu/index.php/433996?lang=en>

The second project is a global initiative from the International Organization for the study of IBD (IOIBD) to record timely proven cases of COVID-19 infection in our IBD patient. We encourage IBD clinicians worldwide to report ALL cases of COVID-19 in their IBD patients, regardless of severity (including asymptomatic patients detected through public health screening). Reporting a case to this Surveillance Epidemiology of Coronavirus) Under Research Exclusion (SECURE)-IBD registry should take approximately 5 minutes. With the collaboration of our entire IBD community, we will rapidly be able to define the impact of COVID-19 on patients with IBD and how factors such as age, comorbidities, and IBD treatments impact COVID outcomes. This project will be accessible following the link: <https://covidibd.web.unc.edu/>

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England)*. 2020;395(10223):497-506.
2. Song Y, Liu P, Shi XL, et al. SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. *Gut*. 2020:gutjnl-2020-320891.
3. Rahier JF, Papay P, Salleron J, et al. Influenza A (H1N1)v infection in patients with inflammatory bowel disease: a case series. *Aliment Pharmacol Ther*. 2011;33(4):499-500.
4. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020:e201585.
5. Cai G. Bulk and single-cell transcriptomics identify tobacco-use disparity in lung gene expression of ACE2, the receptor of 2019-nCov. *medRxiv*. 2020:2020.2002.2005.20020107.
6. Heymann DL, Shindo N, Scientific WHO, Technical Advisory Group for Infectious H. COVID-19: what is next for public health? *Lancet (London, England)*. 2020;395(10224):542-545.
7. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet (London, England)*. 2020;395(10223):473-475.