The position statement of the Polish Society of Gastroenterology and the Polish National Consultant in Gastroenterology regarding the management of patients with inflammatory bowel disease during the COVID-19 pandemic

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Introduction

The pandemic of coronavirus disease 2019 (COVID-19), caused by the intercontinental spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has brought dramatic changes to the functioning of the modern world within the timespan of just a few months.

Patients with chronic diseases, including inflammatory bowel diseases (IBD), are among those particularly affected by the current situation. The widespread use of immunosuppressive medicines in the treatment of this group of diseases raises serious concerns among patients as well as physicians. This document was designed to facilitate diagnostic and therapeutic decision-making during the pandemic.

One should keep in mind that the short time since the pandemic onset has been insufficient to obtain good quality data with high evidence levels. This position of the Polish Gastroenterology Society is based on the Chinese experience as well as on documents developed to date by the British Society of Gastroenterology (BSG) and European Crohn's and Colitis Organisation (ECCO) [1–5].

Intestinal manifestations of COVID-19

The most common symptoms of COVID-19 are fever, dry cough, shortness of breath, and fatigue. Some patients may also experience gastrointestinal symptoms such as nausea, vomiting, abdominal pain, or diarrhoea. Virus particles are found mainly in respiratory secretions; a smaller percentage is also detected in stool. No faecal-oral transmission has been confirmed for SARS-CoV-19. Also, no reports are available regarding the potential impact of the infection on IBD exacerbations [1–5].

Risk of SARS-CoV-2 infection in IBD patients

The spread of SARS-CoV-2 occurs in human communities. The greater the number of people and the longer the contact times, the greater the risk of infection. Thus, as demonstrated by observations made to date in areas with the highest COVID-19 morbidity, a significant percentage of infections is associated with visits to hospitals or clinics. This is the most important factor responsible for increasing the risk of infection among IBD patients. Pharmacotherapeutic agents, particularly

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steroids, may also be considered potential risk factors in cases of IBD exacerbations. No independent increase in the likelihood of infection was demonstrated for IBD, particularly during remission [1, 6, 7].

General principles to reduce the risk of SARS-CoV-2 infection in IBD patients

Patients should limit their contact with healthcare professionals, while not interrupting the treatment that has led to IBD remission. This also applies to in-hospital administration of biological medicines, because the maintenance of IBD remission is of utmost importance. Furthermore, in order to reduce the risk of transmission, it is necessary to follow common guidelines regarding limited contact with other people (especially direct person-to-person contact, particularly with individuals showing any signs of infection, as well as those who have recently travelled), frequent hand hygiene, and caution not to touch one's eyes, mouth, or nose (in Poland, all relevant information can be found at www.pzh.gov.pl). It is also recommended not to use public transport, especially during peak hours. A great deal of evidence suggests that viral replication is particularly intense during the prodromal period; this results in a high risk of infection being spread by individuals not yet presenting with any obvious signs of the disease. The estimated R_0 factor for SARS-CoV-2 (i.e. the number of consecutive individuals who may acquire the infection from a single infected person) is 2.5 [2–4].

COVID-19 severe course risk factors in IBD patients

According to the BSG position paper, IBD patients can be classified into groups of high, medium, and low risk of severe COVID-19, although the data supporting such a classification are of poor quality. Classification into one of the groups determines epidemiological recommendations to be followed in cases of particular patients [1].

High risk – absolute isolation indicated

1. IBD patients with concomitant diseases (cardiovascular, respiratory, diabetes) and/or patients aged ≥ 70 years receiving treatment as indicated for the medium risk group.
2. IBD patients of any age and concomitant disease status meeting at least one of the following criteria:

- intravenous or oral steroids received at a dose of ≥ 20 mg of prednisolone (or equivalent);
- ongoing combination therapy (biological and immunosuppressive agents – within the first 6 weeks);
- moderate to severe disease despite immunosuppressive/biological therapy;
- short bowel syndrome;
- parenteral nutrition requirement.

Medium risk – rigid restriction of social contact indicated

Patients receiving the following medications:

- anti-TNF monotherapy;
- vedolizumab;
- ustekinumab;
- methotrexate;
- thiopurine;
- calcineurin inhibitors;
- Janus kinase inhibitors;
- combination treatment (after the first 6 weeks).

Low risk – restriction of social contact indicated

Patients receiving the following medications:

- 5-ASA preparations;
- topical drugs;
- locally acting steroids (budesonide);
- antibiotics;
- anti-diarrhoeal drugs.

Concomitant diseases and age are the main factors responsible for increased risk of severe COVID-19 course. Data on the effects of pharmacotherapeutic agents are limited, and there is no unambiguous evidence for immunosuppressive/immunomodulatory drugs increasing the risk of severe COVID-19 course. Furthermore, because cytokine storm has been highlighted as the main factor responsible for the development of lesions in severe COVID-19, anticytokine medications have been used in experimental treatment of COVID-19 [1, 2].

Recommendations regarding organisation of work at IBD treatment facilities

The COVID-19 epidemic has resulted in a major change in the organisation of health care systems. Reducing the risk of infection for both patients and staff as well as timely identification, isolation, and treatment of patients suspected of having COVID-19 have become priorities. Operation of facilities where IBD patients are treated should be adapted to these changed conditions; this pertains to both inpatient and outpatient care as well as to biological therapy administration settings [1–5].

Key recommendations

1. Patient visits at the facilities sites should be restricted to essential minimum.
2. In-person visits should be replaced by virtual visits, particularly for patients in clinical remission.

3. Patients should be allowed to contact the site at any time by telephone or email.
4. Prior to each visit, patients should be interviewed for potential signs of respiratory infection and a body temperature reading should be taken.
5. Diagnostic tests should be kept to essential minimum, and endoscopic screening tests should be deferred.
6. Consideration should be given to replacing invasive (endoscopic) examinations with non-invasive methods (determination of calprotectin levels, abdominal ultrasound, CT).
7. Biological treatment administration facilities should be located in the clean area of the hospital, away from areas where patients with COVID-19 might be present. The facilities should also be reorganised to avoid excessive crowding of patients (appropriate distances between patients – usually about 2 m, reduced number of staff members in contact with patients).
8. Prior to a visit involving administration of a biological drug, it is recommended that patients be interviewed by telephone for potential infection symptoms.

Treatment of IBD patients during the COVID-19 pandemic [1–8]

- Patients in clinical remission should continue their previous treatment.
- The risk of SARS-CoV-2 infection during hospitalisation due to IBD exacerbation exceeds that related to the use of immunomodulatory drugs.
- Subcutaneous biological drugs may be advantageous compared to intravenous drugs (home administration, shorter facility staying times); this should be taken into account when starting new treatment.
- However, IV preparations should not be switched to other subcutaneous formulations, because this might increase the risk of exacerbation.

Principles regarding the use of individual groups of medications

1. Steroids:
- use should be restricted, particularly at doses of ≥ 20 mg of prednisolone (or equivalent);
- patients receiving steroids (especially at high doses) should remain in self-isolation;
- accelerated dose-reduction paths should be considered (equivalent to prednisolone dose reduction rate of 10 mg/week);
- if possible, locally acting steroids (budesonide – Entocort, Cortiment MMX) should be preferred.

2. Immunosuppressive therapy:
- no evidence on the potential to increase the risk of SARS-CoV-2 infection;
- initiation of immunosuppressive monotherapy is not recommended during the COVID-19 pandemic because the therapeutic effect is delayed and early complications may develop;
- combination therapy with biological medicines may be initiated only in cases of particularly severe IBD following careful consideration of the risk-to-benefit ratio;
- withdrawal should be considered in patients above 65 years of age or in patients with chronic diseases who remain in long-term clinical remission.

3. Anti-TNF therapy (adalimumab, infliximab):
- no evidence on the potential to increase the risk of SARS-CoV-2 infection;
- monotherapy should be considered; adalimumab is the drug of choice when starting new treatment due to a lower risk of antibody formation as compared to infliximab; in addition, subcutaneous administration route reduces the need for visits at the treatment site;
- it is not recommended that the switch be made from intravenous to subcutaneous administration only to reduce the number of required visits.

4. Anti-$\alpha 4\beta 7$ integrin therapy (vedolizumab):
- no evidence on the potential to increase the risk of SARS-CoV-2 infection;
- it is the drug of choice, particularly in the treatment of elderly patients because (according to the data collected to date) it has the lowest effect on the increased risk of concomitant infections.

5. Anti-IL12/23 therapy (ustekinumab):
- no evidence on the potential to increase the risk of SARS-CoV-2 infection;
- subcutaneous administration in maintenance therapy is an advantage of this drug.

6. Janus kinase inhibitors (tofacitinib):
- no evidence on the potential to increase the risk of SARS-CoV-2 infection.

7. 5-Aminosalicylic acid (5-ASA) preparations:
- no evidence on the potential to increase the risk of SARS-CoV-2 infection;
- in cases of mild exacerbation symptoms, oral dosages should be optimised first; topical treatment should also be considered.

Managing IBD patients with suspicion or diagnosis of COVID-19

At present, no clear evidence is available regarding a potential increase in the risk of severe course of COVID-19 or death in patients receiving immunosuppressive/immunomodulatory medicines. However, withdrawal of thiopurine and tofacitinib should be considered in patients suspected of COVID-19, due to the mechanism

of action of both drugs. Thiopurine and tofacitinib reduce the number of circulating CD4+ lymphocytes, which may result in longer duration of infection and a more severe course of COVID-19. Methotrexate should not interfere with the course of the SARS-CoV-2 infection, but consideration should also be given to deferring the upcoming dose of the medicine. Administration of biological drugs should also be deferred until SARS-CoV-2 is excluded. High doses of steroids (≥ 20 mg of prednisolone) should be avoided and accelerated dose reduction should be considered for this group of drugs. Risk associated with IBD exacerbation should always be taken into account when making decisions to switch treatments [7–9].

If COVID-19 is confirmed in an IBD patient in remission, discontinuation of all medications (except 5-ASA and symptomatic medications, if applicable) should be considered. Because the average duration of COVID-19 is typically 3–4 weeks, the length of the discontinuation period should not adversely affect the course of IBD. If COVID-19 is confirmed in a patient with an active IBD, therapeutic decisions should be made by interdisciplinary teams and with particular caution; high-dose steroids should be avoided [1, 5].

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