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Supplement Article

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# Management of Pregnant Inflammatory Bowel Disease Patients During the COVID-19 Pandemic

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## Abstract

The rapid emergence of the novel coronavirus [SARS-CoV2] and the coronavirus disease 2019 [COVID-19] has caused significant global morbidity and mortality. This is particularly concerning for vulnerable groups such as pregnant women with inflammatory bowel disease [IBD]. Care for pregnant IBD patients in itself is a complex issue because of the delicate balance between controlling maternal IBD as well as promoting the health of the unborn child. This often requires continued immunosuppressive maintenance medication or the introduction of new IBD medication during pregnancy. The current global COVID-19 pandemic creates an additional challenge in the management of pregnant IBD patients. In this paper we aimed to answer relevant questions that can be encountered in daily clinical practice when caring for pregnant women with IBD during the current COVID-19 pandemic.

**Podcast:** This article has an associated podcast which can be accessed at https://academic.oup.com/ecco-jcc/pages/podcast
**Key Words:** Pregnancy, inflammatory bowel disease, COVID-19, SARS-CoV2

## 1. Introduction

At the end of 2019 in Wuhan, China, a series of unexplained cases of atypical pneumonia led to the discovery of a novel coronavirus named severe acute respiratory syndrome – corona virus 2 [SARS-CoV2].[1–3] The virus has rapidly spread globally, and it was declared a pandemic on March 11, 2020. At the time of this writing, coronavirus disease 2019 [COVID-19] has affected more than 4 million people worldwide and accounted for nearly 300 000 deaths.[4] In the general population, patients with COVID-19 require hospitalization in about 23% of cases, although it is possible that this is an overestimation due to differences in testing capacity.

The SARS-CoV2 virus is transmitted by droplet infection as well as surface contact.[5] In the absence of a vaccine or effective treatment, many countries have adopted mitigation strategies to contain the virus as much as possible. Meticulous hand-hygiene and social distancing are widely accepted and effective public health measures in these mitigation strategies, whereas measures such as obligatory mouth-nose masks are under debate.

As with all communicable diseases, there are concerns about vulnerable subpopulations, including the specific subpopulation of pregnant inflammatory bowel disease [IBD] patients. Pregnant IBD patients are already challenged by the fact that they have to keep their IBD under control for the benefit of themselves and the health of their offspring.[6–13] In many cases this means continued immunosuppressive medication throughout the entire pregnancy to keep the disease in check. Intuitively, the use of immunosuppressive medication in times of a global pandemic raises serious concerns. Furthermore, questions about susceptibility to the virus, fear of vertical transmission and possible adverse effects on the pregnancy are common questions in current daily clinical practice.

Conclusive data on SARS-CoV2 in this specific subgroup of IBD patients are not yet available, but clinical guidelines in these exceptional times of a global pandemic are needed to guide everyday clinical practice.

## 1.1. Are pregnant IBD patients more susceptible to SARS-CoV2 infection/severe COVID-19 than non-pregnant IBD patients?

- ➢ Pregnant IBD patients should be considered at high risk for COVID-19.
- ➢ Adherence to general precautionary measures such as hand-hygiene and social distancing should be promoted for pregnant IBD patients as well as for their household partners.
- ➢ In the event of confirmed COVID-19 of a household member of a pregnant IBD patient, extensive hand-hygiene and social distancing measures should be taken immediately. The treating gastroenterologist should be notified. The pregnant IBD patient should monitor her body temperature twice daily and report to the treating gastroenterologist as soon as symptoms [fever, cough, dyspnoea, rhinitis, sore throat, anosmia, diarrhoea] occur.
- ➢ Once an effective and safe vaccine for SARS-CoV2 becomes available, all IBD patients should be vaccinated as soon as possible, preferably before conception. If the vaccine proves to be safe to administer during pregnancy, pregnant IBD patients should be vaccinated as well.

People at high risk for developing severe COVID-19 are still being identified. Currently identified risk groups for severe COVID-19 are the elderly and patients with multiple comorbidities, and there also appears to be a slight predominance in men.[14–16]

### 1.1.1. Pregnancy and COVID-19

Pregnant women are not immunocompromised in the classical sense of the word. However, immunological changes such as attenuation of cell-mediated immune responses take place during pregnancy,[17] rendering the pregnant woman more susceptible to infections from intracellular pathogens such as viruses.

Previous data on related corona viruses SARS-CoV [SARS], Middle Eastern Respiratory Virus [MERS] and influenza virus suggest a more severe disease course in pregnant women.[18–22] Initial data regarding COVID-19 in pregnant women do not suggest increased rates or more severe disease as compared to the non-pregnant population.[23–26] However, the situation is evolving rapidly and recently several more worrisome publications have also appeared; a Swedish registry-based study reported an increased intensive care unit [ICU] admittance rate of pregnant or postpartum women with confirmed SARS-CoV2 infection when compared to non-pregnant women from the same age group.[27]

Furthermore, a case series from Iran reported the COVID-19 disease course in nine pregnant women of whom seven had died at the time of reporting.[28]

### 1.1.2. IBD and COVID-19

A frequently used strategy in IBD treatment is modulating or controlling an overactive immune system. It is possible that IBD treatments influence susceptibility to viral infections including SARS-CoV2. However, the immune suppression or modulation could have a beneficial effect on the course of COVID-19, as it has been hypothesized that severe COVID-19 with acute respiratory distress syndrome [ARDS] is related to a pro-inflammatory cytokine storm.[16,29,30] Independent of immunosuppressive therapy, IBD patients could also have an increased risk of COVID-19 because of higher expression of the intestinal ACE2 receptor,[31,32] the putative receptor for cell entry of SARS-CoV2.

Several studies on the incidence of SARS-CoV2 in IBD patients have been reported from endemic area's such as China, Italy, France, Spain and the USA.

In China, the Chinese Society of Gastroenterology recommended discontinuation of all IBD immunosuppressive agents, except for 5-aminosalicylic acid [5-ASA] formulations and thalidomide. In a prospectively observed cohort of 318 IBD patients, none of the patients became infected with SARS-CoV2 during study follow-up.[33]

In France and Italy, from the regions of Nancy and Milan the entire cohort of 6000 IBD patients were followed from the beginning of the pandemic. In total, 15 patients tested positive for SARS-CoV2, resulting in a cumulative incidence [CI] of 0.0025. The authors conclude that this CI does not differ significantly from the CI in the general population. None of the IBD patients with COVID-19 required ICU admittance and there was no mortality.[34]

A retrospective study from northern California, USA, identified all IBD patients from a cohort of 14 235 tested people for SARS-CoV2. IBD patients represented 168 cases of the 14 235 people tested. Only five of 168 IBD patients who were tested for SARS-CoV2 were positive. Four out of these five patients experienced a mild COVID-19 disease course, whereas one patient developed ARDS and died. The authors conclude that IBD patients are not being tested more than the general population and that the course of COVID-19 is not more severe in IBD patients.[35]

A Spanish study retrospectively collected IBD patients with confirmed SARS-CoV2 positivity in five different hospitals. They identified 40 IBD patients with confirmed SARS-CoV2 infection, of whom 50% were admitted to the hospital, but no ICU admissions occurred. There were two deaths [5%], both in elderly patients with several co-morbidities. Notably about one-third of the patients were treated with immunomodulators and 18% with a biological.[36]

A prospective case series from New York, USA, reported 86 cases of confirmed or suspected COVID-19 in patients with immune-mediated disease with or without immune-modulating or immunosuppressive therapy.[37] In this series, 37 of 86 COVID-19 patients [31%] had underlying IBD. Four of the IBD patients [11%] required hospitalization.

The overall incidence of hospitalization in all patients, not specifically IBD patients, who were treated with biologics or Janus kinase [JAK] inhibitors was 11%. However, in the hospitalized COVID-19 group there were more patients who were treated with corticosteroids, methotrexate and hydroxychloroquine. The authors of this case series conclude that COVID-19 disease course is comparable in this diverse group of immune-mediated diseases to the general population.

Furthermore, preliminary data from the SECURE-IBD database do not suggest an increased risk of COVID-19 in IBD patients, with a current 5% ICU admittance rate and a 4% mortality rate.[38]

Although these aforementioned studies from highly endemic areas do not suggest an increased susceptibility of [non-pregnant] IBD patients to SARS-CoV2 or severe COVID-19, this could reflect a very rigorous adherence to social distancing and extensive hygiene measures.

## 1.2. Does active inflammation from IBD during pregnancy increase susceptibility to SARS-CoV2 or severe COVID-19?

- ➢ In the non-pregnant population, active IBD has been associated with COVID-19 pneumonia and mortality risk, independent of corticosteroid use.

➢ Active IBD during pregnancy may have a similar detrimental effect on the course of COVID-19, again underlining the importance of disease control during pregnancy.

Only anecdotal evidence of COVID-19 combined with active IBD during pregnancy exists. A single case report[39] described a pregnant patient with severe active ulcerative colitis in the early first trimester who was also concomitantly infected with SARS-CoV2. Disease activity was difficult to control as intravenous corticosteroids could not be switched to oral formulations. Because of the concomitant COVID-19, intravenous cyclosporine was preferred over infliximab as a rescue therapy. Unfortunately, the pregnancy ended with a spontaneous abortion. The patient was discharged after 11 days of hospital admission.

A prospective cohort study from Italy enrolled 78 non-pregnant IBD patients and one pregnant IBD patient with concomitant COVID-19.[40] Twenty-two patients were hospitalized [28.0%] and six patients died [8.0%]. The overall median age was 45 years, and 39 and 51 years for Crohn's disease [CD] and ulcerative colitis [UC], respectively. Active IBD was identified as one of the significant risk factors for developing COVID-19 pneumonia, even after adjustment for corticosteroid use. Concomitant IBD medication use was also not associated with pneumonia risk. Other risk factors for COVID-19 pneumonia were age above 65 years, at least one co-morbidity and UC diagnosis. Active IBD was also significantly associated with hospitalization and mechanical respiratory assistance. No details about the pregnant patient are provided in the paper.

Furthermore, active IBD was also significantly associated with mortality, again after adjustment for corticosteroid use. Age above 65 years and presence of at least one co-morbidity were also associated with mortality, and the authors also report that five out of six deaths were male.

### 1.3. Is there an increased venous thromboembolic risk in pregnant IBD patients with COVID-19?

➢ Independently, pregnant and postpartum women, IBD patients, as well as patients with severe COVID-19 have an increased venous thromboembolic [VTE] risk. No data are available on VTE risk in pregnant IBD patients who develop COVID-19.
➢ We recommend all hospitalized pregnant IBD patients should receive anti-coagulant prophylaxis, especially if hospitalized for active IBD, but also when admitted for COVID-19.
➢ Anti-coagulant prophylaxis should be considered in all pregnant IBD patients with active IBD with or without COVID-19 in an ambulatory setting and in all pregnant IBD patients without active IBD but with COVID-19 in an ambulatory setting.
➢ If a caesarean section has been performed, we recommend anti-coagulant prophylaxis during the time of hospitalization in all IBD patients. After discharge, continuation of anti-coagulant prophylaxis should be considered.

Pregnant and postpartum women in general have an increased VTE risk.[41] During pregnancy, due to hormonal changes there is an increase in factor VII, VII, X and fibrinogen, a decrease in protein S, while antithrombin III and protein C remain stable. Furthermore, the growing uterus and increased pelvic pressure can impede blood flow from the lower extremities, promoting deep vein thrombosis [DVT] risk. DVT risk is highest in the third trimester. After delivery, the uterus rapidly decreases in size, restoring blood flow from the lower extremities with possible dislodging of thrombi. Not surprisingly, the risk of pulmonary embolism is greatest in the early postpartum period.

It has also been established that IBD patients have an increased VTE risk. This risk is highest in IBD patients with active disease, IBD patients who have had recent surgery and in those who are hospitalized.[42–46] Anti-coagulant prophylaxis is recommended in all hospitalized IBD patients. Prophylaxis should be considered following discharge from the hospital, in IBD patients who have had recent surgery and in ambulatory IBD patients with active disease.[47]

An increasing body of evidence shows that patients with critical COVID-19 have an increased risk of thromboembolic events such as DVT and pulmonary embolism.[48–52] Whether patients with mild COVID-19 are also in a more pro-thrombotic state is unclear.

### 1.4. What are the risks of maternal COVID-19 on pregnancy outcomes?

➢ No data are available about potential teratogenic effects of COVID-19 in the first trimester.
➢ A significant rate of preterm births has been reported in pregnant women with COVID-19 as well as a very high caesarean section rate.
➢ Other less frequently reported adverse pregnancy outcomes include spontaneous abortion, preterm premature rupture of the membranes [PPROM], intrauterine fetal death, neonatal respiratory symptoms and neonatal death.

Data on pregnancy outcomes in pregnant women with COVID-19 are rapidly expanding, but mostly with case reports and case series. A summary of maternal and neonatal outcomes in COVID-19-confirmed pregnancies is presented in Table 1. We acknowledge a lack of accuracy in these numbers because of heterogeneous reporting across the included case reports and probable publication bias.

Strikingly, the rate of preterm birth [26.0%] is higher when compared to the worldwide general population [11.0%].[53] The explanation is likely to be iatrogenic as reflected by the very high rate of caesarean sections [70.0%] and a much lower rate of PPROM [2.9%].

### 1.5. Is there a risk of vertical transmission of SARS-CoV2?

➢ There is a possibility of vertical transmission of SARS-CoV2, but there is currently insufficient evidence to support this hypothesis.

Theoretically, intrauterine transmission of SARS-CoV2 to the child before birth is possible due to placental ACE2 expression. None of the case reports included in Table 1 demonstrated clinical suspicion of vertical transmission, but there was no uniformity in the method of reaching these conclusions.

Amniotic fluid has been tested for SARS-CoV2 in two pregnant patients who had COVID-19 in the first trimester of pregnancy. The amniotic fluid was obtained in the second trimester after both women recovered from the virus. Both amniotic fluid samples were negative for SARS-CoV2 in real time reverse transcriptase polymerase chain reaction [RT-PCR] and no IgG or IgM antibodies against SARS-CoV2 could be detected.[68] Another report tested the amniotic fluid from ten pregnancies with COVID-19 in the third trimester. All RT-PCR tests for SARS-CoV2 were negative.[55]

Several reports have demonstrated positive RT-PCR results for SARS-CoV2 nucleic acid on nasopharyngeal or throat swabs in neonates at different time intervals after birth.[69–71] The major issue in these reports remains whether the neonate contracted the virus through intrauterine infection or contact with the mother or other caregivers after birth. This problem could be avoided by serological testing for antibodies to SARS-CoV2 in the neonate directly after birth.

**Table 1.** Clinical maternal and neonatal outcomes of confirmed COVID-19 cases during pregnancy

| Clinical pregnancy outcome | Number of cases [%] |
|---|---|
| | Pregnant women *n* = 455, neonates *n* = 366[a] |
| Maternal ICU admittance | 51/455 [11%] |
| Maternal mechanical ventilation | 45/455 [9.9%] |
| Maternal mortality | 7/455 [1.5%] |
| Spontaneous abortion | 4/455 [0.9%] |
| Preterm premature rupture of membranes [PPROM] | 13/455 [2.9%] |
| Preterm birth [<37 weeks] | 95/366 [26.0%] |
| Extreme preterm birth [<34 weeks] | 18/366 [4.9%] |
| Intrauterine fetal death | 5/366 [1.4%] |
| Neonatal vertical transmission | 0/366 [0.0%] |
| Neonatal respiratory symptoms | 3/366 [0.8%] |
| Caesarean section | 255/366 [70.0%] |
| Neonatal death | 6/366 [1.6%] |

[a]Discrepancy between mothers and neonates because of spontaneous abortions in the first trimester, but mostly because not all included references reported completed pregnancies.

[b]Based on published data.[24,25,28,54–67]

A case report of a neonate with positive IgM and IgG levels 2 h after birth has raised suspicion of possible vertical transmission.[72] Unlike IgG, IgM cannot pass freely across the placenta, because it is too large. It is therefore believed that the elevated IgM levels in the neonate reflect the immune response of the child instead of maternal antibodies against SARS-CoV2. The neonate did not develop symptoms of COVID-19 and repeatedly tested negative for SARS-CoV2 in the RT-PCR on the nasopharyngeal swabs.

Another case series reported six mothers with confirmed COVID-19 and their six neonates. Although all RT-PCRs for SARS-CoV2 on throat swabs and serum were negative, five out of six neonates had positive IgG antibodies and two out of six had positive IgM antibodies against SARS-CoV2.[73]

The two studies did not test the amniotic fluid or the placenta. Although these positive IgM tests suggest vertical transmission, they are not conclusive given that IgM testing comes with several challenges including false-positives, false-negatives and cross-reactivity.

### 1.6. How to test a pregnant IBD patient for SARS-CoV2?

- ➢ The preferred SARS-CoV2 test is by nasopharyngeal/throat swab and RT-PCR for SARS-CoV2 nucleic acid.
- ➢ With a high clinical suspicion of COVID-19, but an initial negative test, we recommend keeping the patient in strict isolation and repeat the test after 24 h.
- ➢ To limit radiation as well as contrast enhancement exposure to the mother and fetus, computed tomography [CT] of the chest should not be routinely performed to diagnose COVID-19 in pregnant IBD patients.

### 1.7. When to test a pregnant IBD patient for SARS-CoV2?

- ➢ All pregnant IBD patients with symptoms [fever, cough, dyspnoea, lymphopaenia] should be tested for SARS-CoV2.
- ➢ Pregnant IBD patients presenting with new-onset diarrhoea should be tested for SARS-CoV2 in addition to standard faecal bacterial cultures and *Clostridium difficile* cultures.
- ➢ In times of an epidemic/pandemic, all pregnant IBD patients who are admitted to the hospital [for delivery or other reasons] should be tested for SARS-CoV2, irrespective of symptoms.

The most common symptoms of COVID-19 are fever, cough and shortness of breath; gastrointestinal symptoms such as nausea and diarrhoea are the presenting symptoms in 10% of cases.[15,29] As serological tests are currently being developed, the standard test to detect SARS-CoV2 is a nasopharyngeal swab with RT-PCR for SARS-CoV2 nucleic acid. The specificity of this test is nearly 100%, but the sensitivity, mainly because of sampling error, is between 66 and 80%.[74] Therefore, if a patient tests negative by RT-PCR but clinical suspicion for COVID-19 remains high, the patient should be kept in isolation and tested again 24 h later.

In non-pregnant patients, chest CT has been suggested as a routine diagnostic test for COVID-19 pneumonia alongside the RT-PCR.[74–76]. The disadvantages of chest CT include the risk of allergic reaction to the administrated contrast enhancement, contrast-related nephropathy, and the risk of maternal and fetal radiation exposure. In our view, chest CT should therefore not be routinely performed to diagnose COVID-19 in pregnant IBD patients. The decision to perform chest CT should be carefully weighed on an individual basis and should only be performed if it alters the therapeutic strategy significantly, for example to diagnose pulmonary embolism.

Two studies from New York, one of the epicentres of the SARS-CoV2 outbreak, suggest the importance of universal screening for SARS-CoV2 in all pregnant patients who require hospitalization.[77,78] In the first study, 215 pregnant women admitted for delivery were tested by RT-PCR; the largest group tested negative [84.6%], 13.5% were asymptomatic but tested positive, and the remaining 1.9% were both symptomatic and tested positive for SARS-CoV2. All four symptomatic women presented with fever. Of the 29 asymptomatic women who tested positive for SARS-CoV2, three developed a fever before postpartum discharge.

In the latter study, 161 pregnant women were tested upon admittance for any indication to the hospital. Thirty-two women [19.9%] tested positive for SARS-CoV2 of whom 11 [34.0%] were symptomatic and 21 [66.0%] were asymptomatic.

The findings from these studies underline the importance of universal screening for all pregnant women who are admitted to the hospital, as this has consequences for in-hospital isolation measures, allocation of personal protective equipment [PPE] and monitoring of the newborn for symptoms of COVID-19.

## 2. Management of IBD during pregnancy in times of the COVID-19 pandemic

A summary of recommended management options during pregnancy is given Table 2. Note: Advice on medication might change in the near future.

### 2.1. IBD medication in pregnant women with quiescent IBD during the COVID-19 pandemic

- ➢ We recommend treatment as usual according to European Crohn's and Colitis Organisation [ECCO] guidelines.
- ➢ We do not recommend prophylactic discontinuation of maintenance medication to limit infection risk.

### 2.2. IBD medication in pregnant women with quiescent IBD and COVID-19

- ➢ We recommend temporary withholding IBD drugs in pregnant IBD patients with concomitant COVID-19, irrespective of the severity of infectious symptoms.

**Table 2.** Summary of IBD management during pregnancy in times of the COVID-19 pandemic

| Management of pregnant women | With quiescent IBD | With active IBD, depending on severity |
|---|---|---|
| Without COVID-19 | - Treatment as usual[a]<br>- Continue maintenance medication | - Induction of remission as usual,[a] but avoid corticosteroids<br>- Consider exclusive enteral nutrition as remission induction |
| With COVID-19 | - Discontinue all IBD medication, except 5-ASA<br>- Close monitoring of patient after drug cessation<br>- Consider anticoagulant prophylaxis | - Consider anticoagulant prophylaxis<br>- Hospital admission<br>- Start anticoagulant prophylaxis<br>- Discontinue/taper/avoid corticosteroids and thiopurines<br>- Continue/optimize 5-ASA<br>- Consider budesonide<br>- Consider exclusive enteral nutrition<br>- Consider cyclosporine<br>- Consider anti-TNF initiation/optimization<br>- Consider delivery |

[a]According to ECCO guidelines.[79]

➢ 5-ASA preparations could be continued depending on future outcome of the SECURE data.
➢ Close monitoring for relapse of IBD activity after drug cessation should be considered.

Since the last ECCO reproduction guidelines, vedolizumab, ustekinumab and tofacitinib have been introduced in the treatment of IBD.[79] Although there are still uncertainties with regard to the safety of these latter drugs during conception and pregnancy,[80–82] it is advised to continue drugs if a patient is pregnant to prevent IBD relapse. The risk of relapse is low after stopping anti-tumour necrosis factor [anti-TNF][83], but it is recommended to continue anti-TNF during all trimesters during the SARS-CoV2 pandemic to prevent disease relapse, as relapse is associated with a negative COVID-19 outcome.[40]. If a pregnant patient is on combination therapy with thiopurines and anti-TNF alpha and in long-term remission before conception, it should be considered to stop thiopurines if anti-TNF levels are adequate.[84] Corticosteroids should be avoided in pregnant IBD patients who are in stable remission.[85,86]

### 2.3. IBD medication in pregnant women with a relapse of IBD during the COVID-19 pandemic

➢ In general it is advised to timely treat pregnant IBD women with a relapse also during the SARS-CoV2 pandemic according to current ECCO guidelines.
➢ Treatment includes optimization of current drugs or switch to another class of drugs that are used as induction and maintenance IBD therapy.
➢ Corticosteroids should be avoided if possible.
➢ Avoid initiating thiopurines for the treatment of relapse during pregnancy.
➢ Induction of remission with enteral nutrition might be a safe alternative in patients with mild to moderate IBD relapse.

### 2.4. IBD medication in pregnant women with a new onset of IBD during the COVID-19 pandemic

➢ In general it is advised to timely treat pregnant women with a new diagnosis as usual also during the SARS-CoV2 pandemic according to current ECCO guidelines.
➢ Treatment with drugs used as both induction and maintenance therapy is preferable.
➢ Corticosteroids should be avoided if possible.
➢ Avoid initiating thiopurines during pregnancy.
➢ Induction of remission with enteral nutrition might be a safe alternative in patients with mild to moderate IBD.

Depending on IBD severity, initiation or optimization of exclusive enteral nutrition, 5-ASA, budesonide and biologics could be used to induce remission in pregnant patients.[79,87] Corticosteroids during pregnancy as remission induction for active inflammation should preferably be withheld to prevent infection with SARS-CoV2.[85–88] If corticosteroids cannot be avoided, tapering should be done as soon as clinically possible. Corticosteroids have been linked to increased COVID-19 risk in an observational study,[38,89] and during pregnancy SARS-CoV2 increases the risk of several adverse pregnancy outcomes [see above]. While thiopurines have shown anti-viral properties *in vitro*,[68] this remains to be studied *in vivo*. Cessation will not lead to immediate elimination of active metabolites as the median thiopurine elimination half-life has been measured at 6.8 days whereas total immune reconstitution is expected to take even longer.[69]

### 2.5. IBD medication in pregnant women with an IBD relapse and COVID-19

➢ We recommend hospital admission for all pregnant IBD patients with active IBD and confirmed SARS-CoV2 infection, irrespective of the severity of respiratory symptoms or the severity of IBD disease activity.
➢ Corticosteroids should be avoided.
➢ Thiopurine maintenance therapy should be discontinued.
➢ Induction of remission with exclusive enteral nutrition might be a safe alternative in patients with mild to moderate IBD relapse and COVID-19.
➢ 5-ASA drugs could be continued and optimized.
➢ Depending on disease location and severity, consider budesonide as remission induction.
➢ Depending on disease location and severity, consider cyclosporine as an alternative treatment option.
➢ Consider optimizing anti-TNF drugs.
➢ In confirmed COVID-19 and active IBD in the third trimester, delivery should be considered.

### 2.6. IBD medication in pregnant women with a new onset of IBD and COVID-19

➢ We recommend hospital admission for all pregnant IBD patients with active IBD and confirmed SARS-CoV2 infection, irrespective of the severity of respiratory symptoms or the severity of IBD, for close maternal and fetal monitoring.

- ➢ Depending on IBD severity, initiation of 5-ASA orally or locally, exclusive enteral nutrition and budesonide could be used to induce remission.
- ➢ Depending on location and severity, cyclosporine or anti-TNF could be initiated.
- ➢ Corticosteroids should be avoided if possible.
- ➢ Avoid initiating thiopurines during pregnancy.
- ➢ In confirmed COVID and active IBD in the third trimester, delivery should be considered.

Treating a pregnant woman with COVID-19 and with a new onset of IBD or relapse is a delicate balance because of the negative effects of disease activity on the pregnancy outcome,[79] the negative effect of disease activity on the outcome of COVID-19[40] and the largely unknown effects of IBD drugs on the outcome of COVID-19.[38] To avoid deterioration due to COVID-19, corticosteroids should be avoided. Depending on IBD severity, initiation or optimization of 5-ASA, exclusive enteral nutrition and budesonide could be used to induce remission.[79] Cyclosporine for severe colitis could be used as a rescue therapy to induce remission and could be preferred over anti-TNF alpha because of a shorter half-life and elimination time.[39] The risk of opportunistic infections in patients treated with cyclosporine is perceived to be low.[90] In addition, cyclosporine has demonstrated antiviral properties by reducing viral replication in the related coronaviruses SARS-CoV and MERS-CoV *in vitro*.[91] Although the effects on the course of the SARS-CoV2 infection are unknown, alternatively anti-TNF could be initiated to effectively treat IBD activity and to minimize the negative effects of IBD activity on the course of COVID-19.[92]

### 2.7. When can IBD treatments be resumed after cessation because of COVID-19?

- ➢ IBD medication discontinued because of COVID-19 can be resumed after two negative RT-PCRs on SARS-CoV2 nucleic acid on nasopharyngeal swabs.

### 2.8. Breastfeeding and COVID-19

- ➢ There is no absolute contraindication for breastfeeding in IBD patients in general.
- ➢ If maternal clinical condition allows, in maternal COVID-19 and confirmed SARS-CoV2 positivity in the neonate breastfeeding can be given as usual.
- ➢ In maternal COVID-19 and SARS-CoV2 negativity in the neonate breastfeeding can be given, with extensive hygiene measures. An alternative in this situation is expressing the breastmilk and bottle-feeding this to the neonate by a non-infected person.

The potential benefits of breastfeeding for mother and child have been well demonstrated.[93] In general, there is no contraindication for breastfeeding in IBD patients and patients should be advised based on the current ECCO guideline.[79] Limited studies have investigated the presence of SARS-CoV2 in breastmilk, but to date no SARS-CoV2 has been detected.[25,66] However, mothers with COVID-19 could infect the neonate through close contact and droplet infection. The WHO currently recommends women with COVID-19 to be encouraged to breastfeed, because the benefits of skin-to-skin contact and breastfeeding outweigh the risk of infection. However, adherence to strict hygiene measures is recommended, i.e. handwashing before and after touching or feeding the neonate, wearing a medical mask during any contact with the neonate, sneeze or cough into a tissue and immediate disposal of the tissue afterwards, and routine cleaning and disinfecting surfaces the mother has touched.[94] Alternatively, if the mother is very fearful of infecting the neonate but also has a desire to breastfeed, she could be advised to express the breastmilk and have a non-infected person bottle-feed the neonate.

## 3. Summary

Management of pregnant women with IBD during the COVID-19 pandemic is challenging. In general, IBD relapse must be prevented both for the outcome of the pregnancy and to minimize the negative outcomes of COVID-19. Specific challenges include the risk for thromboembolic events and the negative outcomes of the pregnancy in cases of maternal COVID-19. Therefore, a multidisciplinary approach is warranted during pregnancy together with close monitoring of both the mother and the child *in utero*.

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## Podcast

This article has an associated podcast which can be accessed at https://academic.oup.com/ecco-jcc/pages/podcast

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