

## PEDIATRIC COVID 19 AND THE GUT

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### Gastrointestinal symptoms of Covid-19 in children

Though children with Covid-19 patients typically present with a respiratory illness, some children have reported gastrointestinal symptoms including poor appetite, nausea, vomiting, diarrhoea and abdominal pain during the course of the disease. Covid-19 related diarrhoea most often occurred 1 to 8 days after the onset, with a median time of 3.3 days. Some patients had diarrhoea as the first symptom, and the diarrhea lasted for 1-14 days with diarrhoea appearing watery in one third<sup>1,2</sup>. Hao et al have reported that in cohort of 74 adult patients with COVID-19 and GI symptoms had increased family clustering and tendency for severe/critical illness<sup>3</sup>.

Lu et al have reported that diarrhoea and vomiting were observed in 15 (8.8%) and 11 (6.4%) in a cohort of 171 children with Covid-19<sup>4</sup>.

In another study by Yi et al that investigated viral shedding in pediatric Covid-19 patients, diarrhoea was observed in three out of the ten infected children. They have observed positive real-time RT-PCR results in rectal swabs in eight out of ten children which remained detectable well after nasopharyngeal swabs turned negative, suggesting that the gastrointestinal tract may shed virus and fecal-oral transmission may be possible<sup>5</sup>.

### Mechanisms of gastrointestinal tract involvement

There are many reasons why SARS- CoV- 2 appears to cause digestive symptoms.

1. Angiotensin converting enzyme 2 (ACE-2) receptor and transmembrane serine protease 2 (TMPRSS2) are key proteins of SARS-CoV- 2 cell entry process. Coexpression of these two proteins in the same cell is critical for viral entry. Alveolar type II cells are the main cell type coexpressing ACE2 and TMPRSS2 in lung tissue. In addition, ACE2 and TMPRSS2 are also coexpressed in both upper epithelial and gland cells from oesophagus and absorptive enterocytes from ileum and colon<sup>6</sup>. After viral entry, virus-specific RNA and proteins are synthesized in the cytoplasm to assembly new

virions, which can be released to gastrointestinal tract. The continuous positive detection of the viral RNA from feces suggests that the infectious virions are secreted from the virus-infected gastrointestinal cells. This gastrointestinal tropism of SARS- CoV- 2 can explain the digestive symptoms including diarrhoea and fecal-oral transmission could be an additional route for viral spread<sup>7</sup>.

2. SARS-CoV-2 indirectly or directly (due to a possible enteropathic effect) damages the digestive system through an inflammatory response and cause digestive symptoms.

3. The virus itself may cause disorders of the intestinal flora, which could result in digestive symptoms.

4. Changes in the composition and function of the digestive tract flora affect the respiratory tract through the common mucosal immune system, and respiratory tract flora disorders also affect the digestive tract through immune regulation. The effect is called the “gut-lung axis”, which may further explain why patients with COVID-19 pneumonia often have digestive symptoms<sup>8</sup>.

### Pediatric Covid-19 in patients with chronic luminal disorders

Covid-19 has implications for the management of children with chronic luminal diseases. Indeed, the presence and number of comorbidities is associated with poorer clinical outcome in patients with COVID-19 from the adult clinical experience. There is increasing concern regarding the risk that IBD patients being infected with SARS-CoV-2<sup>9</sup>. The overall available evidence suggests that IBD patients do not have an increased risk of developing Covid-19 and should stay on IBD medications. Patients receiving immune suppressors should be carefully monitored for the occurrence of symptoms and/or signs suggesting Covid-19<sup>10</sup>.

## Key recommendations for managing Pediatric IBD during the COVID-19 epidemic

(Adapted from references 11 & 12)

### General

IBD *per-se* does not currently seem to be a risk factor for acquiring SARS CoV- 2, nor for a more severe infection

For decreasing the risk of contracting SARS-CoV2 in children with IBD, adhere to the same measures as in the local population during the pandemic (e.g. good hand hygiene, avoiding contact with anyone with respiratory symptoms and social distancing).

When possible by local situation and resources, children should continue follow-up visits to ensure appropriate monitoring of the disease. However, remote telemedicine consultations, along with the use of surrogate markers of inflammation (ESR, CRP, patient-reported outcomes) may be an alternative to face-to-face office visits during the epidemic, especially for those in remission. The option of delaying visits should be considered on an individual basis.

Active IBD disease should be treated according to the standard guidance PIBD protocols as before the epidemics, since the risk of IBD complications in active IBD outweighs any risk of COVID-19 complications, especially in children.

There is currently no concrete evidence that any of the IBD treatments increases the risk for acquiring SARS-CoV-2 or for a more severe infection once infected. Therefore, uninfected children should generally continue their medical treatment, including immunomodulators and biologic therapies, as the risk of a disease flare outweighs any estimated risk of SARS-CoV2 infection

### Medications

Continue current treatment if disease is stable, and contact your doctor for suitable medicine if disease has flared

Corticosteroids can be used to treat disease relapses, but as always recommended in children, the drug should be weaned as soon as possible.

In Crohn's disease exclusive enteral nutrition should be preferred.

Use of mesalamine should be continued and should not increase the risk of infection

The use of anti-TNFs should be continued at the

regular intervals and doses. Infusion centres should minimize crowding and implement screening procedures for suspected COVID-19.

Switching from infliximab to adalimumab in a stable child should be discouraged unless impossible to provide intravenous infusions, since the risk of disease exacerbation after such a switch has been documented in the clinical trial setting.

### Surgery and endoscopy

Postpone elective surgery and non-urgent endoscopy  
Screening for COVID-19 before emergency surgery

### Patients with IBD and fever

Contact your IBD doctor about potential option to visit fever outpatient clinic with personal protection provisions if temperature continues over 38°C

Suspend immunosuppressive treatment during an acute febrile illness until fever subsides and the child returns to normal health, irrespective of the SARS-CoV2 testing status.

Mesalamine should never be suspended.

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