Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

are not the best comparison population. We greatly appreciate the potential mechanistic explanations for this association presented by Magro et al. However, we agree that the current data do not warrant any major changes in mesalamine prescription patterns but call for further studies. In the interim, we propose limiting mesalamine to indicated and high-value clinical situations.

We hope the IBD community will stay tuned as we explore risk associations with other IBD medications and will visit our website www.covidibd.org for current data and updates. This registry would not be possible without the help of the international IBD community, to which we are incredibly grateful.

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References

1. Stallmach A, et al. Crit Care 2020;24:444.
2. Rodríguez-Lago I, et al. Gastroenterology 2020;159:781–783.
3. Brenner EJ, et al. SECURE-IBD [Internet]. 2020 [cited 2020 Jan 6]. Available from: www.covidibd.org.
4. Ungaro RC, et al. Gut 2020 Oct 20 [Epub ahead of print].
5. Agrawal M, et al. Inflamm Bowel Dis 2020 Dec 16 [Epub ahead of print].
6. Fedak KM, et al. Emerg Themes Epidemiol 2015;12:14.

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Gastrointestinal Involvements in Children With COVID-related Multisystem Inflammatory Syndrome

Dear Editors:

We read with interest the article by Miller et al[1] reporting the gastrointestinal involvement in COVID-related multisystem inflammatory syndrome in children (MIS-C). Indeed, gastrointestinal symptoms are not uncommon in patients with Coronavirus Disease 2019 (COVID-19) (severe acute respiratory syndrome coronavirus 2 [SARS-Cov-2]) infection and may occur in the absence of any respiratory symptoms. As SARS-Cov-2 can also infect enterocytes through an angiotensin system by binding the angiotensin-converting enzyme 2 receptors, digestive symptoms might present in 50.5% of adult patients. Compared with adults, 13% of COVID-19–infected children are reported to have diarrhea, followed by nausea/vomiting (11%) and abdominal pain (6%).[2] Besides the report of Miller et al,[1] we have reviewed recent studies that describe pediatric patients diagnosed with Kawasaki-like MIS-C, who also presented with a variety of gastrointestinal symptoms and signs.[3–8] Strikingly, we found that 90% of 72 children with MIS-C, which was higher than the report of Miller et al.,[1] had gastrointestinal manifestations, most of which consisted of abdominal pain, vomiting, and diarrhea (Table 1). Besides, 10% of MIS-C cases had some rare presentations mimicking appendicitis and peritonitis, of which 3 cases were surgically explored. In contrast, only 2.3% to 4.6% of children with classic Kawasaki disease have been reported complicated with gastrointestinal involvement.

The high incidence of gastrointestinal involvement in MIS-C cases is unclear. The most plausible pathomechanism might be attributed to the overwhelming multiorgan inflammation, including the digestive system. This hypothesis might be further substantialized by the significantly high inflammatory markers and positive SARS-Cov-2 antibodies in the serum of most children, but negative viral reverse transcriptase polymerase chain reaction (RT-PCR) in nasopharyngeal swab or feces. Furthermore, the gastrointestinal investigations also showed mesenteric lymphadenitis and serous effusions (ascites) in severe cases, which implied that an active inflammatory reaction occurred in the digestive systems. However, a recent study on COVID-related gastrointestinal involvement showed that up to 41% of children without MIS-C had positive SARS-Cov-2 RT-PCR in feces.[9] This finding may also reflect that the high incidence of gastrointestinal symptoms in MIS-C cases is likely due to the heightened inflammatory response.

Conclusively, our summary suggests that the gastrointestinal manifestations should not be overlooked in children with COVID-related MIS-C, and meticulous evaluation of the inflammatory response of the digestive

Table 1. Demographics and Clinical Characteristics of MIS-C Patients with Gastrointestinal Involvement

Case series	MIS-C cases, n	Age (median)/ Gender, n	Incomplete KD, n (%)	GI involvements, n (%)	GI symptoms/ signs, n (%)	Findings of GI system examination
Riphagen et al (2020)	8	8 y; male: 5	8 (100)	7 (88)	Diarrhea: 7 (88); vomiting: 4 (50); abdominal pain: 6 (75)	Not described in detail
Toubiana et al (2020)	21	7.9 y; male: 9	10 (48)	21 (100)	Abdominal pain with vomiting and diarrhea: 20 (95); acute surgical abdomen: 2 (10)	Abdominal ultrasound: peritoneal effusions in 4, 1 had abdominal surgery for suspected appendicitis with a final diagnosis of aseptic peritonitis
Belhadjer et al (2020)	35	10 y; male: 18	35 (100)	29 (83)	Abdominal pain, vomiting, or diarrhea present in 80	Exploratory laparoscopy in 2 cases due to suspected appendicitis, with a confirmed diagnosis of mesenteric lymphadenitis
Licciardi et al (2020)	2	9.5 y, male: 2	0	2 (100)	Abdominal pain and diarrhea: 2 (100), vomiting: 1 (50)	Abdominal ultrasound: both showed mesentery lymphadenitis or enlarged mesenteric lymph nodes
Waltuch et al (2020)	4	10 y, male: 3	3 (75)	4 (100)	Abdominal pain: 4 (100), diarrhea:	Abdominal ultrasound: mild ascites and inflammatory gallbladder in 1; abdominal CT: suspected appendicitis in 1
Dallan et al (2020)	2	10 y, male: 2	2 (100)	2 (100)	Abdominal pain: 2 (100); peritoneal signs: 2 (100); vomiting: 1 (50)	Abdominal CT: mesenteric lymphadenitis in 1

CT, computed tomography; GI, gastrointestinal; KD, Kawasaki disease; MIS-C, multisystem inflammation syndrome in children.

system is essential to prevent unnecessary exploratory surgical intervention.

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References

1. Miller J, et al. Gastroenterology 2020;159:1571–1574.
2. Parri N, et al. N Engl J Med 2020;383:187–190.
3. Belhadjer Z, et al. Circulation 2020;142:429–436.
4. Toubiana J, et al. BMJ 2020;369:m2094.
5. Waltuch T, et al. Am J Emerg Med 2020;38:2246.e3–2246.e6.
6. Licciardi F, et al. Pediatrics 2020;146:e20201711.
7. Riphagen S, et al. Lancet 2020;395:1607–1608.
8. Dallan C, et al. Lancet Child Adolesc Health 2020. [Epub ahead of print]. https://doi.org/10.1016/S2352-4642(20)30164-4.
9. Xiong X, et al. medRxiv 2020: 2020.04.29.20084244.

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Reply. We thank the authors of "Gastrointestinal involvement in children with COVID-related multisystem inflammatory syndrome" for responding to our article reporting the high prevalence of gastrointestinal