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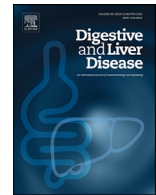
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Correspondence

Challenges in paediatric inflammatory bowel diseases in the COVID-19 time

Dear Editor,

The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in China in December 2019, now involves the whole world [1,2]. As of March 15, 2020, more than 160000 cases and more than 6000 deaths in over 150 countries have been reported (<https://www.worldometers.info/coronavirus/>). Few cases of COVID-19 in children and adolescents have also been described [3–5], with a null death rate in the group 0–10 years, and 0.2% in the group 10–19 years. The majority of the most severe clinical courses and deaths have occurred among the elderly and those with chronic comorbidities, often receiving immunosuppressive and/or immunomodulatory treatment [1,2].

It is well known that patients with inflammatory bowel disease (IBD) have an increased risk of infections, particularly opportunistic infections, due to a multifactorial immunological impairment [6,7]. The novel coronavirus seems to dysregulate immune response in infected individuals, mainly by acting on lymphocytes, especially T-cells [8]. Whether patients with IBD may be more susceptible to COVID-19 is a reasonable concern. Currently no cases of IBD patients infected by SARS-CoV-2 have been reported. International IBD non-profit organisations issued online advices and preliminary recommendations regarding COVID-19 management in adults with IBD [9,10]. We would like to emphasize the importance of addressing main concerns from IBD paediatric patients during the COVID-19 epidemic, taking into consideration their peculiar disease characteristics and comorbidity spectrum.

Beyond immunological dysregulations commonly underlying IBD, risk factors for infections in children with IBD are represented by rare monogenic disorders, including primary immunodeficiencies, poor nutritional status and, above all, in comparison to adults, the more frequent need for early and/or combined immunosuppressive and biologic therapies [6,7]. Currently no evidence supports treatment suspension in mild or moderate cases of COVID-19, neither in children living in an endemic area, also due to the washout period of most immunomodulators (such as azathioprine, methotrexate) and biologics. An exception could be raised by steroid treatment. In paediatric IBD, different studies have shown steroids carrying higher risk of infections compared with anti-tumor necrosis factor (TNF)- α , while the risk of immunomodulators and anti-TNF- α agents, given alone, seems to be comparable [6,7]. In addition, steroids are not effective for the treatment of lung injury or shock in adults' SARS-CoV-2 infection [11]. In line with these observations, discontinuation (or at least tapering) of steroid treatment during COVID-19 epidemic may be a reasonable option.

As the risk of infections is generally higher in case of combination therapy (biologics plus immunomodulators) in adult and paediatric patients with IBD [6,7], caution should be used with this therapeutic strategy during the COVID-19 epidemic. In a population-based study of IBD paediatric patients treated with infliximab, infections arose in those patients under combination therapy with immunomodulators [12].

Whether this is the most appropriate time to start an immunomodulatory treatment is also on discussion. The immunosuppressive effect of these drugs should not be overlooked, since it may eventually increase the risk of infectious complications and promote the spreading of COVID-19; however, active IBD itself has been thought to be a potential risk factor for SARS-CoV-2 infection. Overall, it seems wise to apply an individual risk assessment, avoiding the postponement of new treatment (or increasing in dose an ongoing treatment) in case of severe disease flares. For patients on biologics, switching to subcutaneous self-injection medication (i.e. adalimumab) at home could be encouraged, aiming to limit hospital appointments, or if intravenous medication (i.e. infliximab) is not available.

Several reports suggest the possible involvement of the gastrointestinal system in SARS-CoV-2 infection [1–5,13]. Indeed, although the most common clinical presentation of COVID-19 is a moderate-to-severe respiratory illness, abdominal pain, diarrhoea (3.8%), nausea, and vomiting (5%) can also occur [2]. In the retrospective analysis of hospitalized children carried out from January 7 to January 15, 2020 in Wuhan, China, COVID-19 was detected in 6 previously healthy children, 4 presenting with vomiting [5]. A 22-year old male presented with diarrhoea at the onset of COVID-19 [13]. However, current clinical evidence does not support COVID-19 as a cause of IBD flares, and therefore a systematic exclusion of COVID-19 in the setting of an IBD flare is not recommended. In cases with suspected symptoms of COVID-19, prompt medical evaluation and careful follow-up are crucial. Only where exposure to confirmed COVID-19 occurs (viral RNA detection from nasal and pharyngeal swab specimens, according to the World Health Organization), discontinuation of all immunosuppressive and biological treatment could be taken into consideration, as recommended during any severe infection [6,7].

In conclusion, while waiting for more specific data concerning the risk of COVID-19 in children with IBD and, more generally, in paediatric patients on immunosuppressive therapy, it seems reasonable to carefully weigh the risks/benefits ratio of treatment with immunomodulators and biologics, especially in areas of high infection rate or outbreaks. In addition, all IBD children and their household contacts should be encouraged to practice good hygiene and to fulfil all the other preventive measures in order to reduce the risk of SARS-CoV-2 exposure.

Conflict of interest

None declared.

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None.

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