SARS-CoV-2 infection as a potential trigger factor for de novo occurrence of inflammatory bowel disease

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The emergence of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which caused the coronavirus disease-2019 (COVID-19) pandemic, has raised concern among health care teams, especially those caring for patients with immune-mediated inflammatory diseases, such as inflammatory bowel disease (IBD) [1]. Since we know that acute viral gastroenteritis can trigger the onset of IBD [2], a literature search was conducted in PubMed, using the words [inflammatory bowel diseases], [SARS-CoV-2], [de novo], [onset], [COVID-19], [trigger], [Crohn's disease] and [Ulcerative colitis], selecting articles on the de novo occurrence of IBD after COVID-19.

Six cases of new-onset IBD, occurring after COVID-19 infection, were identified. There were four UC [3–6] cases and two CD [7,8] cases (Table 1). IBD following COVID-19 mainly occurred in women (four out of six). Half of the patients experienced gastrointestinal symptoms, particularly diarrhea, throughout the course of the COVID-19 infection. Three patients were hospitalized for COVID-19 symptoms, while none required mechanical ventilation or ICU admission. All patients presented with persistent or new-onset abdominal symptoms, along with positive inflammatory markers, including fecal calprotectin, despite having a negative nasopharyngeal swab for SARS-CoV-2. The time from the onset of digestive symptoms to the diagnosis of IBD ranged from less than one month to 4 months. The most frequently reported symptom was diarrhea, which started during or shortly after the diagnosis of COVID-19. The UC patients had bloody diarrhea, while the CD patients had watery or voluminous diarrhea. Half of the patients were treated with mesalamine as well as systemic or intestinal-releasing steroids for IBD.

The role of the SARS-CoV-2 as a trigger for IBD in the reported patients is plausible because all patients reported no gastrointestinal symptoms before the COVID-19 infection. The pathogenesis of IBD is multifactorial. It consists of a dysregulated immune response to components of the gut microbiota in genetically predisposed individuals. This self-sustaining inflammatory process is likely associated with environmental factors, including infections, directly involving the intestinal tract. Several studies have reported the connection between enteric infection-related dysbiosis and the subsequent development of IBD [2]. On the basis of this, we hypothesized that SARS-CoV-2 was a potential trigger. The intestinal epithelial cells are a major cellular target for SARS-CoV-2, which penetrates cells after binding to its functional receptor, angiotensin-converting enzyme 2 (ACE2). This results in the increased production of TNF-α [9]. The enhanced T-helper (Th)-17 lymphocyte response in COVID-19 induces one of the hallmarks of the immune dysregulation seen in IBD patients. Various autoimmune diseases, involving multiple organs, have reportedly occurred among patients infected with COVID-19. Molecular mimicry due to the immune cross-reaction between viral epitopes and host antigens may be implicated in some of these autoimmune diseases. The onset of IBD was notably caused by the loss of self-tolerance against commensal microbial antigens due to transient immunosuppression and abnormal immune reconstitution in genetically predisposed subjects infected with COVID-19 [10]. Following SARS-CoV-2 infection, the dysregulated interferon production and cytokine activation disrupt immune tolerance, triggering an abnormal immune response in the gut.

In conclusion, the current data highlighted the role of the SARS-CoV-2 virus as a possible trigger for the onset of IBD. However, further data from prospective studies that include large cohorts of patients with COVID-19 are needed to confirm this hypothesis and understand the extent of the event.

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AT, LRL, AG, and AP designed the study, recruited the patients and collected and analysed the data. AT wrote the first draft of the article.

Conflicts of interest

There are no conflicts of interest.

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Table 1. Characteristics of patients with inflammatory bowel disease (IBD) onset after SARS-CoV-2 infection

Author (Ref.)	Sex	Age (years)	COVID-19 symptoms	Therapy for COVID-19	Time from SARS-CoV-2 negativity to IBD diagnosis (months)	Type of IBD	Type of IBD treatment
Calabrese *et al*. [5]	F	19	Fever, nausea, vomiting, bloody diarrhea, loss of taste and smell, anemia	HCQ	1	UC	Oral BEC and MES
Taxonera *et al*. [6]	F	NA	Fever, sore throat, myalgia, bloodless watery diarrhea	HCQ, LOPRIT, AZI	4	UC	Oral and topic MES
Imperatore *et al*. [7]	M	55	Pneumonia	CS, AZI, HEP	4	UC	NA
Aydin *et al*. [8]	M	50	Fever, dyspnea and pneumonia	HCQ and AZI	1	UC	Oral and topic MES
Senthamizhselvan *et al*. [9]	F	33	Sore throat, fever, myalgia	ACE	<1	CD	CS and sulfasalazine
Tursi *et al*. [10]	F	47	Weakness, myalgia and diarrhea	ACE	3	CD	Oral BUD

ACE, acetaminophen; AZI, azithromycin; BEC, beclomethasone dipropionate; BUD, budesonide; CD, Crohn's disease; CS, systemic corticosteroids; HCQ, hydroxychloroquine; HEP, heparin; LOP–RIT, lopinavir–ritonavir; MES, mesalamine; UC, ulcerative colitis.

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