

The Impact of COVID-19 Virus on Inflammatory Bowel Disease Incidence

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Article's Information

Received: 11.02.2025
Accepted: 10.05.2025
Published: 16.05.2025

Keywords:

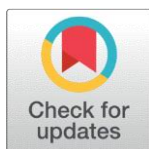
(COVID-19) Infected disease
2019, Coronavirus
Inflammatory Bowel Disease
Pandemic

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Abstract

The spread of the COVID-19 virus has resulted in unique challenges for individuals living with inflammatory bowel disease (IBD), a chronic condition affecting the gut. The virus behind the pandemic, SARS-CoV-2, uses ACE2 receptors—found in abundance in the gastrointestinal tract—to infect human cells, which explains why some COVID-19 patients experience digestive symptoms like diarrhea and abdominal pain. For individuals with IBD, who often rely on immune-suppressing medications to manage their condition, this has raised concerns about their vulnerability to the virus and the safety of continuing treatment. The good news is that research shows having IBD doesn't necessarily raise the probability of contracting COVID-19. However, certain treatment, like corticosteroids, may make severe outcomes more likely. Vaccination is especially important for IBD patients and has been shown to be safe, though its effectiveness might be slightly reduced depending on their medications. Despite the challenges, it's crucial for people with IBD to stay on top of their care during the pandemic, as skipping treatment can lead to flares and complications. This review highlights the need for thoughtful management of IBD during these unprecedented times and aims to reassure patients that balancing treatment and infection prevention is possible.



Pages:78-84

DOI:<https://doi.org/10.47419/bjbabs.v6i2.365>

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1. Introduction

Coronaviruses were recognized as the causative agents of common colds in humans until the early 2000s. However, MERS-CoV (Middle East Respiratory Syndrome) is a highly contagious respiratory virus that emerged in 2013, while SARS-CoV (severe acute respiratory syndrome) is a highly contagious respiratory virus that emerged in 2002. Both viruses resulted in severe respiratory syndrome and were greatly pathogenic to human beings, resulting in over 8000 individuals being diseased and 919 deaths initiated via SARS-CoV, and 2494 cases and 858 deaths caused via Middle East Respiratory Syndrome-CoV¹. In late 2019, the novel coronavirus, which is currently referred to as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), started spreading in the city of Wuhan, China, and then spread globally, resulting in a worldwide pandemic ².

The COVID-19 virus has quickly spread worldwide, causing a global pandemic, when SARS-CoV-2 is transmitted from person to person, it primarily does so by respiratory droplets and direct contact. Aerosol and fecal-oral transmissions are two other possible pathways. The virus has impacted populations in almost every part of the world, particularly affecting older persons and those with chronic health conditions, resulting in high rates of illness and death ^{1,14}.

To enter host cells, the RNA virus SARS-CoV-2 attaches itself to the angiotensin-converting enzyme-2 receptor using the receptor-binding domain of its spike protein. Receptors for angiotensin-converting enzyme-2 (ACE2) are abundant on the cells that line the intestines, although they are found all over the body ².

Coronavirus Disease 2019 (COVID-19) is a clinical manifestation of SARS-CoV-2 infection, which exhibits a wide range of symptoms. These symptoms can vary from no noticeable symptoms, to mild and temporary symptoms, to severe illness that requires hospitalization. In some cases, there can be an overactive immune response and cytokine storm, leading to shocks, failure of various organs, and ultimately death ³.

Several investigations indicated that 16% of cases had exclusively gastrointestinal (GI) symptoms, with a somewhat higher prevalence among men compared to women. The primary gastrointestinal symptoms included abdominal pain, diarrhea, decreased appetite, vomiting and nausea. Local inflammation, changed the barrier operation of the

intestinal wall, and SARS-CoV-2-associated intestinal dysbiosis are among the numerous physiopathological mechanisms that are implicated in these gastrointestinal manifestations. There are particular issues regarding people who have Inflammatory Bowel Diseases (IBD), a cluster of autoimmune disorders described via persistent gut inflammation. These patients often need immunosuppressive and biological therapy to manage their condition. Hence, it is crucial to have a deeper understanding of the development of gastrointestinal (GI) complications caused via COVID-19 in individuals with (IBD) ^{1,4,5}.

2. Overview on IBD

Inflammatory Bowel Diseases is an illness defined via chronic, non-infectious inflammation of the gastrointestinal tract. It comprises mainly of Crohn's disease (which be able to impact any part of the gastrointestinal tract), ulcerative colitis (which is restricted to the colonic mucosa), and indeterminate colitis ⁶. Symptoms of diarrhea and abdominal discomfort are common in ulcerative colitis and Crohn's illness. Ulcerative colitis is more common than Crohn's illness when it comes to rectal bleeding symptoms, yet people who have Crohn's disease commonly experience perianal illness and weight loss⁷. About 10% of cases present with disease onset in children, characterized via severe and chronic inflammatory progression that necessitates lifetime treatment, results in a significant financial strain, and demands ongoing support from the healthcare system⁸. The resultant inflammation of the bowel appears to be caused via immune system dysregulation as a result to alterations in normal gut bacteria. Studies on genetics have indicated that interactions of the host and microbe, play an important role in UC and CD pathogenesis, and they include genetic areas that order the microbial defense and inflammation of the intestinal area⁶. Environmental variables' roles as causes or triggers of the overreaction to pathogens is still in the area of an ongoing debate⁷. IBD treatments have grown in recent years. Medications such as amino salicylates, corticosteroids (CSs), immunomodulators, and biologics, together with other general therapies and surgical resection (if necessary), regulate symptoms⁹.

3. Overview on Covid-19 illness

The SARS-CoV-2 was first known in the last month of 2019, in Wuhan, China, and it is this virus that causes the infection of COVID-19¹⁰. Consistent with discoveries regarding SARS-CoV^{11,12}, and MERS-CoV¹³, SARS-CoV-2 is thought to traverse species to commence initial human infections; it is currently disseminated predominantly through human-to-human transmission¹⁴.

The recognized marks of COVID-19 infected persons include fever and respiratory manifestations. Nevertheless, gastrointestinal symptoms including diarrhea, vomiting, and abdominal discomfort usually appear as signs of the condition. The first verified case of COVID-19 in the US was documented in the first month of 2020 and it was related to a 35-year-old male who had recently returned from China. He had been sick with a dry cough for two days and had been vomiting when admitted. He began to have diarrhea and stomach pain on his second day in the hospital¹⁵.

4. Effect of Covid19 on IBD Patients

Even though the root reason that causes the IBD is still mysterious, the majority of researchers come to an agreement that the IBD-related tissue damage is the outcome of an intense immune reaction to luminal bacteria in genetically susceptible individuals brought on via a multitude of environmental factors¹⁶.

COVID-19 infection correlates with elevated levels of interleukin-1B and tumor necrosis factor- α (TNF- α), which are involved in IBD pathophysiology. IBD is marked via phases of relapse and remission, with primary clinical manifestations including ache in the abdomen, fever, and diarrhea. The disease involves a compound interplay between inflammatory and remodeling routes mediated via various number of cytokines¹⁷.

Although there is yet no proof indicating that SARS-CoV-2 exacerbates underlying IBD, it is now widely acknowledged that numerous people with the COVID-19 disease may have signs and symptoms in the digestive tract [16]. Research has revealed the existence of SARS-CoV-2 in stool, with continued viral shedding in stool long after the resolution of respiratory symptoms¹⁸. Research recommends continual IBD medication therapy and care during the epidemic of COVID-19, such as standard medical checkups, endoscopic examinations, and laboratory testing¹⁹. Covid 19 virus penetrates cells in humans through

interactions with angiotensin-converting enzyme 2 (ACE2)¹⁸. The ACE2 is a monocarboxypeptidase primarily recognized for its role in cleaving multiple peptides in the system of renin-angiotensin and additional substrates¹⁶. The ACE2 is consistently shown via the epithelial cells of the lungs, intestine, the kidneys, and blood vessels, with particularly high quantities found in the terminal ileum and the colon²⁰.

The process via which the coronavirus and the cell membranes of host cells fuse, in conjunction with binding to ACE2, is essential for the establishment of a positive infection. This procedure is mediated via a "spike" protein or particular fusion, which is stimulated through proteolytic cleavage prompted via host cell trypsin-like proteases, whose activity has been testified to be up-regulated in the IBD¹⁶. Also, the administration of immunosuppressive medications for IBD has been correlated with a heightened danger of infections. The previous data indicate that people with IBD may serve as the perfect host for SARS-CoV-2 virus infection¹. Still, compared to grownups, kids with IBD have a shorter duration of coronavirus illness and need less hospitalization or intensive care⁸. On another hand, Bezzio et al. found no significant difference in disease flare rates between SARS-CoV-2-infected IBD patients, children, and adults in remission ($n = 28$ of 118, 23.7%) and individuals without the infection ($n = 25$ of 137, 18.3%), ($p = 0.35$)²¹. A study involving young females who had never smoked and presented to the emergency section with a seven-day episode of 38°C fever, sore throat, dyspnea, myalgia, and watery diarrhea (6–7 stools/day) resulted in simultaneous diagnoses of COVID-19 and ulcerative colitis (UC). This dual diagnosis complicated the assessment of whether the endoscopic and histologic changes were attributable to UC or to the virus alone. It is unlikely that the patient had ulcerative colitis at the time of the COVID19 infection diagnosis, given the absence of prior symptoms in the digestive tract and the rapid onset of the non-bloody, watery diarrhea as a presenting indicator of COVID-19²².

Patients expressed concerns regarding the potential threat of COVID-19 infection associated with the consumption of immunosuppressive treatments for IBD, in addition to their fears of contracting the virus itself. The findings of a study indicated that systemic corticosteroids were significantly linked to higher odds of severe COVID-19 and mortality, while Interleukin-12/23 antagonists along with TNF α antagonists did not

show such associations. Furthermore, the mixture treatment involving TNF α antagonists and thiopurine was linked to heightened dangers of hospitalization and mortality, while monotherapy with TNF α antagonists, interleukin-12/23, and integrin antagonists was linked to reduced threat of hospitalization and mortality. In a comparable way, additional studies have reported protective effects associated with the use of biologics [19]. Experts advise that consistent treatment for IBD is essential for effective disease management and to prevent recurrence or exacerbation^{23,24}.

5. Physiological effects of Covid on IBD

Based on a study that was done in Asia/South Korea, more than 50% of IBD patients canceled or postponed their medical appointments because of the panic they felt from the pandemic of COVID-19, and very few people with IBD who had worsening symptoms actually sought medical help¹⁹.

During the last three weeks since 21 February 2020, 42.9% (36) of the (84) planned outpatient's appointments were cancelled. The majority (88.8%), (n = 32) of the cancelled appointments were so because of government indications to avoid any potentially avoidable interaction of patients with hospitals, and therefore, the nonurgent appointments were cancelled and rearranged via hospital personnel, while in 11.2% of cases (n = 4), the appointments were cancelled via the patients due to panic they felt from the pandemic of COVID-19¹⁷.

Ever since its first characterization in December 2019, the COVID-19 has engendered a universal atmosphere of apprehension, referred to as "coronaphobia," which has significantly heightened the prevalence of diverse psychiatric manifestations¹.

Individuals identified with ulcerative colitis and Crohn's disease appear to exhibit analogous responses to the COVID-19 pandemic, demonstrating comparable stages of depressive indicators, anxiety, apprehension regarding the contraction of COVID-19, concerns about transmitting the virus to others, adherence to prescribed medication regimens, and perceptions of IBD symptoms. There was no surprise in this finding, as patients with CD and UC typically exhibit comparable mental health profiles in non-pandemic conditions, characterized via heightened stages of depression, as well as anxiety, relative to control groups, yet without significant differentiation between both forms of IBD²⁵.

The initial apprehension regarding the infection of COVID-19 among individuals within the inflammatory bowel disease (IBD) population, which was predicated on the information presented at the time, now appears to be unwarranted. Cumulative evidence indicates that inflammatory bowel disease (IBD) does not constitute a comorbidity that significantly elevates the threat of acquiring COVID-19, with the exception of individuals undergoing treatment through 5-aminosalicylic acid (5-ASA). Moreover, while the prognosis of infected patients is significantly influenced via the therapeutic approach employed, it appears that individuals with IBD exhibit COVID-19 results comparable to those of the general community. On the other hand, individuals receiving corticosteroids appear to exhibit a less favorable prognosis at present²⁰.

Anxiety and depressive disorders are commonly observed among individuals diagnosed with IBD, with prevalence rates of (forty-one %) for anxiety and 34.7% for depression in individuals experiencing active infection. These psychological conditions are considered potential predictors of illness activity and relapses. It is considered that depression is regarded as proinflammatory and is believed to affect the clinical manifestation of IBD. Consequently, inflammation procedures and their associated symptomatology appear to contribute to elevated ranks of depressive state, thereby ensnaring the individual in a self-reinforcing cycle of inflammation and depression²⁵.

During the initial stages of the sickness, an online investigation conducted with the support of the European Federation of CD and UC associations distinctly revealed a link gap between healthcare professionals and patients. Notably, the patients that reported alleviation of their concerns following medical consultations represent only 11 %¹.

6. Covid19 vaccination and IBD

Multiple vaccines of Covid-19 virus are in advanced points of clinical development, with a limited number currently approved or pending approval. At the last month of 2020, the Pfizer-COVID-19 vaccine got approval in the Great Britain, then America., and subsequently the EU countries. Subsequently, several countries approved the Moderna vaccine, a second mRNA vaccine, and the AstraZeneca inoculation, an inactivated vaccine. The British Society of Gastroenterology issued guidelines regarding COVID-19 vaccination for individuals with IBD.

The International Organization for the Study of Inflammatory Bowel Disease (IOIBD) advises that individuals with inflammatory bowel disease (IBD) receive vaccination against COVID-19, emphasizing that vaccination should not be postponed due to the administration of immune-modifying therapies²⁶.

The IOIBD has recently issued commendations primarily derived from the extrapolation of safety and efficacy data from other inoculations. Non-live inoculations are deemed not dangerous for individuals with IBD, regardless of the use of “immune-modifying” therapies; however, it is recognized that the immune response may be somewhat diminished in these cases. Previous studies indicate a diminished response to influenza and pneumococcal vaccinations in individuals with IBD who are cured with immunosuppressant and anti-TNF agents¹.

It is advisable for all patients with IBD to receive inoculation against COVID-19 at the earliest opportunity, in accordance with local policies, regardless of their medication status. The IOIBD expert panel indicates that the COVID-19 inoculations currently available are not dangerous for individuals with IBD. However, it is essential for patients to be conscious that the efficacy of the vaccine may be reduced if administered during corticosteroid therapy²⁷.

7. Conclusions

The COVID-19 pandemic has been especially tough for people living with Inflammatory Bowel Disease (IBD), a condition that's often treated with medications that affect the immune system. Early on, there were real concerns that having IBD might make someone more likely to catch the virus or suffer worse outcomes. But as research has progressed, the good news is that simply having IBD doesn't seem to increase the risk of getting COVID-19 or lead to more severe illness—unless someone is on systemic corticosteroids, which are linked to more serious complications and higher mortality rates. Interestingly, COVID-19 can cause symptoms like diarrhea and stomach pain because the virus binds to ACE2 receptors found in the gut. That overlap in symptoms has made it tricky at times to tell the difference between a COVID-19 infection and an IBD flare-up.

Throughout the pandemic, many people with IBD ended up missing medical appointments—either due to concerns about catching the virus or because of changes in hospital policies. Unfortunately, this

sometimes led to lapses in care and worsening of symptoms. On top of that, mental health challenges like anxiety and depression have become more common among IBD patients, adding another layer of difficulty.

On a more positive note, COVID-19 vaccines have proven to be both safe and important for people with IBD. While those on immune-suppressing medications might not get as strong of a response, vaccination is still strongly recommended by experts, including the International Organization for the Study of Inflammatory Bowel Disease (IOIBD).

In short, while the pandemic has posed real challenges, people with IBD can still maintain good health with the right care. Staying on top of treatment, looking after mental health, and getting vaccinated are all key to staying well in this new era.

Conflicts of Interest: The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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