Inflammatory Bowel Disease Management during the COVID-19 Pandemic: A Literature Review

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ABSTRACT

BACKGROUND:
Coronavirus disease 2019 (COVID-19) caused a global pandemic. Since its start, widespread safety measures have been adopted by nations worldwide. Crohn's disease (CD) and ulcerative colitis are two forms of inflammatory bowel disease (IBD). IBD is a common inflammatory illness with a high worldwide incidence. Its clinical symptoms include stomach discomfort, diarrhea, anorexia, and weight loss. Genetics, microbes, cigarette smoking, appendectomy, lack of personal hygiene, using anti-inflammatory agents, vitamin D deficiency, and stress are the main risk factors for IBD. COVID-19 pandemic raised concerns about the exacerbation of COVID clinical manifestations in patients with IBD and increasing the risk of mortality. During COVID-19 pandemic, intestinal inflammation, and promoting adherence need to be controlled using medications and vaccinations as a primary goal. In this review, we reviewed unique concerns about IBD risk in the population as well as management of the disease, and the effectiveness of vaccination during COVID-19 pandemic.

KEYWORDS: COVID-19, ARDS, Crohn's disease, IBD, Vaccination

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was firstly detected in December 2019, and rapidly spread all over the world, and eventually became a pandemic.[1] COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2] Main COVID-19 risk factors are aging, cardiovascular disease, diabetes, obesity, chronic obstructive pulmonary disease, and chronic kidney disease.[3] Due to over-inflammation and cytokine storms, some patients may present fatal consequences, including progressive pneumonia, acute respiratory distress syndrome (ARDS), and organ failure.[4] As of October 2021, over 235.5 million cases of COVID-19 and more than 4.5 million deaths had been reported globally, including 5 924 638 confirmed cases and 126,303 deaths in Iran. It is well documented that the angiotensin-converting enzyme 2 (ACE2), which is found not just in lung cells but also in the gastrointestinal system, mediates SARS-CoV-2 entrance into cells.[5] ACE2 is also crucial for regulating intestinal inflammation, which can

lead to a variety of illnesses.[6] ACE2 receptor exists in the distal ileum and to a lesser extent in the large intestine. It is mostly expressed in intestinal epithelial cells. Mucosal inflammation is frequently found in the same region in inflammatory bowel disease (IBD).[7,8] Various studies support that the average expression of ACE2 increased in people with IBD, mainly with Crohn's disease (CD).[9,10] IBD-related cytokines, such as IFN-gamma (*interferon gamma)* , may boost ACE2 expression through cytokine signaling that drives ACE2 promoter activity, supporting the idea that mucosal inflammation may enhance ACE2 expression.[9,11] CD and ulcerative colitis are two forms of IBD, which is a prevalent immune-mediated inflammatory illness with a high worldwide frequency.[12] Predisposing factors for IBD are genetics, microorganisms, cigarette smoking, appendectomy, lack of personal hygiene, overuse of anti-inflammatory drugs and antibiotics, vitamin D deficiency, diets, stress, and poor lifestyle.[13,14] Indirect evidence currently indicates that changes in the intestinal expression of ACE2 and TMPRSS2 (Transmembrane serine protease 2) directly influence viral entry into the host cells in patients with IBD.[15,16] Also, the expression levels of these proteins may be influenced by local inflammatory activity and epithelium damage. In addition to the full membrane ACE2 protein, proteolytic degradation can result in the formation of a soluble version of ACE2 at the surface of epithelial cells, which lacks a membrane anchor and circulates in tiny levels in the blood. The soluble version of ACE2 is thought to function as a competitive binding partner for SARS-CoV-2 virus, preventing the virus from attaching to the ACE2 receptor.[6] A disintegrin and metalloproteases 17 (ADAM17), a TNF-protease that was generated in patients with active IBD, regulates ACE2 membrane breakdown in the soluble form.[8] Typically, high expression levels of ACE2 in people with IBD elevate the level of soluble ACE2.[17,18] This expression can mediate the progression of the infection and susceptibility to infection, as well. In addition, in patients with IBD, the expression levels of ACE2 receptor may inhibit the anti-inflammatory immune response.

IBD management during the COVID-19 pandemic may be complicated for physicians and patients, especially when biological and immunosuppressive agents have been used.[19,20] Also, there is a concern about the impact of drugs on the risk of SARS-CoV-2 infection, and increasing the potential of virus replication and prolongation of the diseases, as well .[21,22] So far, immunosuppressive drugs such as high-dose corticosteroids, immunomodulators (thiopurines, methotrexate, and calcineurin inhibitors), anti-cytokine agents (including anti-TNF and anti-IL-12), anti-integrin drugs (vedolizumab), and small-molecule signaling inhibitors are used for the treatment of IBD.[23,24] Some risk factors exist for patients with IBD who are infected with SARS-CoV-2, such as; patients who receive immunosuppressive drugs, patients with active IBD and malnutrition, elderly patients, patients with intestinal inflammation with underlying diseases, pregnant patients with intestinal inflammation, and patients who receive CD and IBD drugs.[25-27] In this review, we aimed to understand the management of IBD patients during the COVID-19 pandemic. The research questions that guided this review article were as follows; what are the risks of COVID-19 infection in patients with IBD? Is there a link between IBD and COVID-19? And do IBD medications prevent patients from infection with SARS-CoV-2?

METHOD AND LITERATURE SEARCH

Up to May 28, 2021, we conducted searching PubMed, Google Scholar, and Web of Science databases among studies that include COVID-19 and IBD. The following medical topics heading words were joined using the Boolean operators "AND" or "OR": "COVID-19," “Crohn's disease,” “CD,” “ulcerative colitis,” “UC,” “inflammatory bowel disease,” and “IBD”. Only human studies were included in the review article. All authors independently reviewed the titles and abstracts to find eligible papers. Following that, full-text papers were reviewed for inclusion, and any discrepancies were resolved through collegial debate. All studies, which had the inclusion criteria, were included in the article as follows; adult and/or pediatric patients with a confirmed diagnosis of IBD, articles that had addressed at least one confirmed instance of COVID-19, and articles that had addressed the clinical treatment of patients with IBD and COVID-19. Reviews, systematic reviews, meta-analyses, guidelines, letters, and editorials that did not show original data were

excluded from our review article. The scheme of the search is shown in Figure 1.

ROLE OF ENDOSCOPY FOR IBD

Endoscopy is a valuable tool for the diagnosis of IBD.[28-30] Some endoscopic signs were reported in patients with IBD, including differentiating between different causes and between ulcerative colitis (UC) and CD as well as a thorough assessment of disease spread, activity, response to treatment, and even particular treatment approaches.[30] The most commonly used endoscopic methods are; ileocolonoscopic, flexible proctosigmoidoscopy, and esophagogastroduodenoscopy.[31,32] However, endoscopy and video capsule endoscopy are also involved in the care of IBD. Excessive involvement of the global health care system due to the COVID-19 epidemic as well as the need to limit the spread of the disease, requires a re-examination of primary care services and hospitals, including endoscopy units.[33,34] Patients with IBD are advised to follow the general WHO recommendations.[35] COVID-19 and its effects have been reported to represent a moderate to high risk in patients with IBD, particularly those treated with systemic corticosteroids, thiopurine, and biological therapies.[7,26,35,36] According to the British Digestive Association, the International Organization for the Study of Inflammatory Bowel Disease (IOIBD), the European Crohn's and Colitis Organization (ECCO), and the American Crohn's and Colitis Foundation (CCFA), all unnecessary endoscopic procedures including colorectal cancer screening and those done on patients with suspected gastrointestinal malignancies must be halted. Endoscopy is the only verified modality in life-threatening situations. In patients with IBD, before performing a diagnostic or therapeutic endoscopic examination, the risks and advantages of therapy must be considered.[29,30] It is of great importance to make sure that surgery is urgent or not. Patients who are candidates must be carefully chosen, and all related risks for patients and healthcare workers must be recognized. As upper endoscopy can cause cough and pharyngeal reflex or gag reflex, and a colonoscopy can cause bloating and defecation of pathogenic fluid, endoscopists are accidentally exposed to infectious particles during gastrointestinal care. Furthermore, SARS-CoV-2 may be detected in feces for several weeks after clinical recovery; however, it is unclear whether viral particles transmitted through feces may spread illness.[34] We reviewed four emergency scenarios to confirm the need for endoscopy in patients with IBD, as follows: (1) confirmation of a new diagnosis, particularly in a moderate to severe situation when biological medications have been used as a first-line treatment, (2) partial intestinal obstruction in patients with IBD, possibly due to neoplasia or ileocolonic anastomotic stenosis, (3) in patients with primary sclerosing cholangitis and (4) in dominant bile duct stenosis, cholangitis, and jaundice. In all other cases, the use of cross-sectional imaging such as ultrasonography or video capsule enteroscopy to support a clinical evaluation in patients with IBD during an epidemic must be postponed.[37,38]

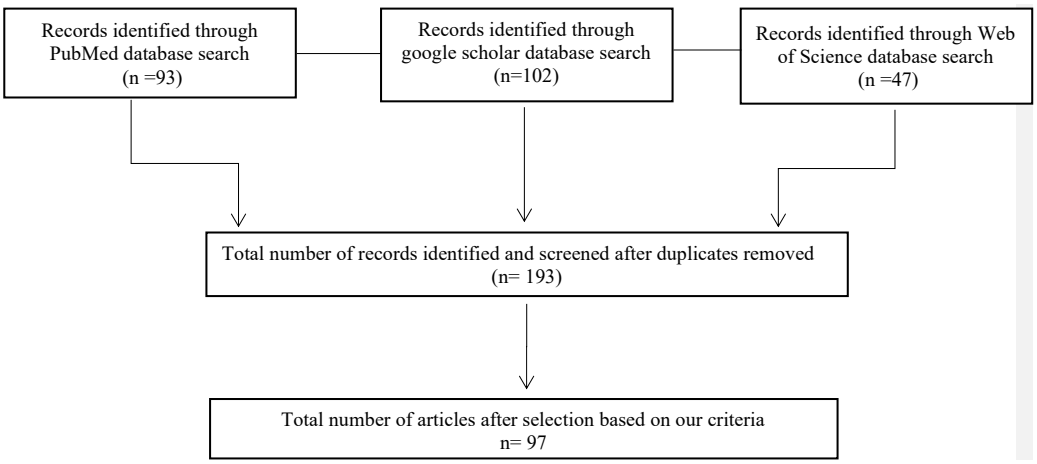

Fig. 1: The scheme of search using various databases. Totally, 97 articles were included in the study.

MANAGEMENT OF IBD DURING COVID-19

Managing of IBD during the COVID-19 outbreak has been complicated for physicians, particularly when it comes to determining whether or not to continue taking immunosuppressive medications. Although there is little knowledge about how this virus affects individuals with IBD, it is quickly developing.[39,40] Concerns about the impact of these medications on the risk of COVID-19 and interference with SARS-CoV-2 virus, and also the possibility of increased virulence and increased COVID-19 continuance are main concerns for physicians.[41,42] For patients with IBD, the main goal to remember is to treat active COVID-19 while maintaining the IBD recovery process in the patient.[43] We present current recommendations for the treatment of IBD during the COVID-19 outbreak. The summary of medications and related recommendations used for IBD treatment during COVID-19 are shown in Table 1.

Immunosuppressive Drugs

The principle of effective management of IBD is the suppression of the immune system through targeted small molecules or biologics. Finally, in patients with IBD, immune system suppression is a clinically significant issue during COVID-19.[44-46] To date, the infectious rate of SARS-CoV-2 in patients with IBD who receive immunosuppressive therapy appears to be similar to the overall population.[40,47] Theoretically, beneficial effects may be seen in some immunosuppressive drugs used for IBD. It is well known that COVID-19 is associated with a cytokine storm that leads to ARDS and death. In patients with severe disease, most inflammatory cytokines, such as IL-6, are significantly elevated.[46,48] In addition to antiviral therapy, targeted immunosuppression, such as IL-6 antagonists (tocilizumab), is one of the methods used for the treatment of COVID-19. In this way, TNF antagonists or steroids may be able to alleviate COVID-19 symptoms. Surprisingly, individuals who had any immunosuppressive therapy had a lower rate of severe COVID-19 infection.[46]

5-Aminosalicylates and Sulfasalazine

5-Aminosalicylates (5-ASAs) and sulfasalazine drugs have been used as a first-line for the maintenance and stability of UC treatment.[49] It seems to be no evidence of a higher infection risk due to the use of these drugs, as in a large cohort study, 5-ASAs', showed no elevated risk of major or opportunistic infections. Without fear of increasing or exacerbating the risk of COVID-19, 5-ASA treatment should be maintained. If the patient comes into touch with someone who has COVID-19, 5-ASA treatment should be continued.[50,51]

Corticosteroids

The impact of corticosteroids is considered to be divergent on viral infections, including the SARS-COV-2 virus. On the one hand, these agents suppress the immune response mediated by chemokine synthesis and leukocyte migration, which leads to viral clearance and long-term virulence. On the other side, they inhibit cytokine storms by reducing the production of inflammatory cytokines such as IL-1, IL-2, IL-6, TNF-α, and IFN-γ.[52,53] According to a recent study, methylprednisolone decreases the risk of death in individuals with ARDS. Various studies showed no link between corticosteroids and a high risk of COVID-19. The use of steroids in COVID-19 treatment is still debatable, and the provided evidence should be taken with caution. We do know that taking corticosteroids (particularly prednisolone ≥ 20 mg) raises the risk of opportunistic infections and respiratory infections, such as influenza and pneumonia, as well as severe infection, hospitalization, and death. It should be noted that topical steroids like budesonide and beclomethasone offer potential advantages over systemic steroids with fewer adverse effects.[54,55] Finally, if possible, avoid corticosteroids and consider rapid dose reduction with a change to budesonide.[56,57] In this case, the risk of IBD flare should be considered. If the patient requires corticosteroids to manage flare-ups, beclomethasone or budesonide should be considered. In CD, exclusive intestinal nutrition should be considered as a treatment option .[58-62]

Immunomodulator Drugs

Immunomodulatory drugs are widely used as monotherapy or in combination therapy in the treatment of IBD to keep the healing process continues and also improve the pharmacological performance of biological drugs.[63] Extensive immunosuppression

Table 1. The summary of medications and related recommendations used for IBD treatment during COVID-19

Drugs used for IBD treatment	Recommendations
Sulfasalazine and 5-aminosalicylates (5-ASAs) (mesalazine)	• Without fear of increasing or exacerbating the risk of COVID-19, 5-ASA treatment should be maintained. • If the patient comes into touch with someone who has COVID-19, the 5-ASA treatment should be continued.
Corticosteroids	• If possible, avoid corticosteroids and consider rapid dose reduction with a change to budesonide. In this case, the risk of IBD flare should also be considered. • If the patient requires corticosteroids to manage flare-ups, beclomethasone or budesonide should be considered. • In CD, exclusive intestinal nutrition (EEN) should be considered as a treatment option.
Immunomodulators (azathioprine, mercaptopurine, methotrexate)	• Avoid starting treatment with thiopurine or raising the dosage: As a result, patients are able to prevent possible harmful effects as well as multiple pathological monitoring. • Recommend withholding JAK inhibitors for 14 days if the patient has come into touch with someone who has COVID19. • If the patient tests positive for SARS-CoV-2, temporarily withhold JAK inhibitors until the patient's infection has resolved.
Biologics (anti-TNF agents, ustekinumab, vedolizumab, infliximab, adalimumab)	• If a patient is on infliximab and has to be injected in a healthcare setting like a hospital, the medication can be changed to adalimumab, which the patient can use at home. In General, the unnecessary change from infliximab to the following anti-TNF skin formulations is not recommended since that might raise the risk of recurrence. • If the patient is recovering or is elderly, discontinue immunomodulatory therapy altogether or temporarily to reduce the risk of infection. • If the patient comes into touch with someone who has COVID19, anti-TNF therapy should be discontinued for 14 days. Continuing therapy with the other biologic drugs would be no problem. • Do not prescribe biologic medicines until the patient's infection has resolved if the patient tests positive for SARS-CoV-2 or if the patient's COVID-19 is exacerbated.
JAK inhibitors (tofacitinib, baricitinib)	• Use the lowest effective dose to maintain the recovery process: If possible, preferably 5 mg twice daily for patients. • During the pandemic, tofacitinib should not be started unless it is the only option. As a result, patients are able to prevent possible harmful effects as well as multiple pathological monitoring. • Recommend withholding JAK inhibitors for 14 days if the patient has come into touch with someone who has COVID19. • If a patient tests positive for SARS-CoV-2 or has a COVID-19 exacerbation, wait until the virus has cleared before prescribing tofacitinib.

by these drugs has the potential to increase patients' vulnerability to viral infections as well as their persistence and reactivation.[64] However, there is low evidence to support that these drugs are linked to a higher risk of respiratory infections. Tofacitinib is related to a higher risk of severe and opportunistic infections. Recent studies confirmed that methotrexate did not increase the risk of infection in patients with non-inflammatory rheumatoid arthritis as well as with respiratory infections. Treatment with thiopurine or increasing the dose must be avoided. It would be better if thiopurines withhold for 14 days if the patient has come into touch with someone who has COVID-19. If the patient's tests were reported positive, temporarily withhold thiopurines until the patient's infection is resolved .[58,65-67]

Biologics

During COVID-19 period, biologic therapies (anti-TNF agents, ustekinumab, and vedolizumab) appear to be safe and secure. SARS-CoV-2 enters into the host cells via attaching to the ACE-2.[16,68] It is well known that ACE2 expression is lower in patients who receive anti-tumor necrosis factor drugs (anti-TNFs), including

vedolizumab, ustekinumab, and steroids compared with patients without immunosuppression, suggesting that these drugs may limit viral entrance and disease progression.[69] New findings revealed that anti-TNF monotherapy or combination therapy slightly increased the chance of pneumonia in individuals who receive TNF antagonists.[70] If a patient is on infliximab and has to be injected in a healthcare setting like a hospital, the medication can be changed to adalimumab, which the patient can use at home. In general, the unnecessary change from infliximab to the following anti-TNF skin formulations is not recommended because it may raise the risk of recurrence.[71] If the patient is recovering or is elderly, discontinue immunomodulatory medication temporarily to reduce the risk of infection. If the patient comes into touch with someone who has COVID19, anti-TNF medication should be discontinued for 14 days. Continuing therapy with other biologic drugs has no problem. Do not prescribe biologic medicines until the patient's tests are reported positive for SARS-CoV-2.[59]

JAK Inhibitors

Tofacitinib is indeed an oral Janus kinase (JAK) inhibitor, which is used to treat UC in individuals who have become resistant to biologics. JAK inhibitors (tofacitinib, baricitinib) may impair viral immunity. Tofacitinib, for example, has been found in long-term trials to increase the incidence of herpes zoster infection.[72-74] During COVID-19 period, the use of the lowest effective dose to maintain the recovery is recommended, preferably 5 mg twice daily for patients, if possible. However, tofacitinib should not be started unless it is the only option. As a result, patients are able to prevent possible harmful effects as well as multiple pathological monitoring. It would be better for thiopurines to be withheld for 14 days if the patient has come into touch with someone who has COVID-19. If the patient's test is positive for SARS-CoV-2, or has a COVID-19 exacerbation, wait until the virus be cleared before prescribing tofacitinib.[58]

TREATMENT OF COVID-19 IN PATIENTS WITH IBD

Due to the rapid progression of COVID-19 worldwide, new therapeutic options resulting from clinical trials can provide guidelines to physicians for the treatment of patients with IBD. Some data support that the incidence of COVID-19 infection appears to be lower in patients with IBD. In some studies, it was reported that IBD as an underlying disease does not increase the risk of COVID-19. It should be highlighted that there is no proven treatment for COVID-19 in patients with IBD; however, protection and reducing the risk of COVID-19 is recommended as the best option for patients with IBD.[75] Healthcare systems of various countries proposed some recommendations for patients with IBD including; postponing the elective surgeries, admission of urgent patients to the hospital, and re-scheduling the patients' visits. Based on the experiences achieved during the COVID-19 pandemic, supportive care and treatment of subsequent problems are the mainstays of COVID-19 treatment in patients with IBD. In this regard, and according to the published data, some medications have been reported for the treatment of COVID-19 in patients with IBD that might be helpful. According to published clinical trials in China, lopinavir/ritonavir does not offer any improvement in terms of discharge or remission of patients. Chloroquine with antiviral effects against SARS-CoV-2 has been used in patients with IBD. It was proposed that its effects be mediated by some mechanisms such as: interfering with viral attachment to the cell membrane, raising the endosomal pH need for virus/cell fusion, and interacting with glycosylation of surface receptors of ACE-2 during the pre-entry phase of the SARS-CoV-2. There is no proof that existing IBD therapies increase the risk of COVID-19 severity. When comparing patients who had different therapies for systemic or localized intestinal immunosuppression for IBD to all who did not receive immunosuppression, the probability of COVID-19 infection did not increase. Immune suppression has also been found to have no impact on the severity of COVID-19, including the requirement for hospital admission and death. Although it has not been proven, several treatments, including anti-TNF, anti-IL-6, and JAK inhibitors, could inversely have a result in recovering from COVID-19. According to newly published data, new therapeutic ways may provide safety benefits over existing therapies. In this regard, during the COVID-19 period, to obtain high ability for IBD management and maintain clinical response

and remission in a safer manner, new methods are proposed such as; anti-trafficking therapies, Janus kinase and tyrosine kinase inhibitors, and microbiota-based therapy.[72]

VACCINATION

Vaccination against COVID-19 has raised concerns about the safety and efficacy of the vaccine in patients with IBD. To date, IBD organizations have confirmed that the risks of SARS-CoV-2 immunization are expected to be very low in patients with IBD. Like other vaccines that have been used for years, such as the flu and pneumonia vaccines, there are no signs that the symptoms of IBD be worsened or peaked after vaccination.[76,77] It is recommended that all patients with IBD, regardless of immunomodulatory methods, be vaccinated as soon as they can receive the vaccine. SARS-CoV-2 vaccines, including messenger RNA vaccines, replication-incompetent vector vaccines, inactivated vaccines, and recombinant vaccines, can be safely used for patients with IBD.[78-81] Vaccination resulted in a protective antibody level after two doses of vaccination in patients with IBD regardless of the type of vaccine.[79-82] Patients with IBD can produce an immune response to different vaccines, although high-dose systemic corticosteroids, especially when combined with other immunosuppressive drugs, may reduce the immunogenicity of the vaccine.[80] Patients with IBD receiving immune system modulators produce a lower response to vaccination than optimal antibody response, especially after a single dose of vaccine. Two doses of the vaccine cause a change in seroconversion in most patients; however, the next dose of vaccine should be avoided, especially in patients who receive infliximab. Although vaccination is less effective in immunocompromised individuals, it still offers better protection against COVID-19. Patients should not stop their vaccination as it may put them at a greater risk for the catastrophic consequences of COVID-19. The effect of vaccination has been measured in cases of COVID-19 after immunization (usually one or two weeks after the second dose). Immunogenicity is measured as an ability for neutralizing antibody and/or T cell response to spike protein. Treatment with corticosteroids, an immune regulator, and/or anti-TNF is associated with optimal vaccine response. Patients with IBD on infliximab or adalimumab show lower antibody titers and serum conversion rates than controls in response to inactivated influenza virus, subunit pneumococcal pneumonia, and HBV vaccine. This reaction may be exacerbated by thiopurines and methotrexate alone or in combination with anti-TNF therapy. Patients with rheumatoid arthritis on tofacitinib showed a normal antibody response to the flu vaccine and a reduced response to the pneumococcal vaccine, which did not improve the temporary discontinuation of the drug. Although in patients with IBD, treatment with vedolizumab did not alter their immune responses to the flu, treatment with vedolizumab may reduce the effect of the vaccine. Several prominent COVID-19 vaccines are based on mRNA technology (Pfizer, Moderna) or non-repetitive adenoviral vectors that express spike protein (AstraZeneca/Oxford, J&J, Sinovac, and Sputnik V). These vaccines have been reported to stimulate strong protein-specific antibody responses as well as T4+ and CD8+ cell responses. Evidence suggests that both B and T cell-mediated immunity are required to produce optimal protection against COVID-19. Inactivated (Sinopharm, Sinovac) and vector-based vaccines show the lowest immunogenicity, while mRNA vaccines have higher antibody titers. There is a concern that replication-competent vaccines may cause disease in immunocompromised hosts.[78,82] Vaccination against COVID-19 is necessary for patients with IBD aged >16 years, regardless of the severity of the disease. Suppression of the immune system is not contraindicated. The ChAdOx1 nCoV-19 vaccine (Oxford/AstraZeneca) is approved for people under 18 years old. However, the UK Joint Committee on Vaccination and Immunisation (JCVI), states that it may be used between the ages of 16-17 when there is no access to or availability of an approved alternative to COVID-19.[81] Although the following antibody response is optimal in patients with IBD who receive one dose of vaccine; however, protective antibody levels are obtained with two doses of vaccine in most patients, even in those taking anti-TNF and anti-integrin drugs.[79,81] In some studies, it was shown that patients with IBD who received infliximab and vedolizumab had lower optimal antibody responses to COVID19 vaccines, including SARS-CoV-2 mRNA

BNT162b2 (Pfizer-BioNTech) mRNA, ChAdOx1 nCoV-Ast (Oxca), and m3are (NIH-Moderna). Infliximab is associated with immunogenic attenuation of BNT162b2 and ChAdOx1 nCoV-19 vaccines in patients with CD, and smoking is associated with lower remittance rates.[80] Influenza and SARS-CoV-2 vaccines should not be given at the same time. Other vaccinations such as influenza and pneumococcus should be given at least 7 days after SARS-CoV-2 immunization.

CONCLUSION

According to the current study, in comparison to the general population, the risk of COVID-19 appears to be lower in patients with IBD in terms of hospital admissions, admission to critical care unit, and death. It is recommended that endoscopy be postponed in IBD patients during the COVID-19 pandemic, except in case of emergency conditions. Current IBD therapies do not appear to enhance the risk or the severity of COVID-19. When comparing those who received various IBD therapies for systemic and local intestinal immunosuppression to those who did not, the risk of COVID-19 infection did not increase. Anti-TNF, anti-IL-6, and JAK inhibitors, for example, may be beneficial in recovering from COVID-19; however, this fact has not been proven. In patients with IBD, COVID-19 immunization is likewise safe, and it is advised that the patients receive only one dose of the vaccine. In IBD patients, immune response produced by different vaccines may reduce the immunogenicity of the vaccine when they receive high-dose systemic corticosteroids, especially in combination with the other immunosuppressive drugs. In patients who receive corticosteroids, reduction of vaccine efficacy must be considered. However, although COVID-19 vaccination is less effective in immunocompromised individuals, it still offers better protection against the disease, and it should not stop as it may put them at greater risk of COVID-19.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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