



## A Supporting System for Management of Patients with Inflammatory Bowel Disease during COVID-19 Outbreak: Iranian Experience-Study Protocol

Amir Anushiravani<sup>1</sup>, Homayoon Vahedi<sup>1</sup>, Hafez Fakheri<sup>2</sup>, Fariborz Mansour-ghanaei<sup>3</sup>, Iradj Maleki<sup>2</sup>, Siavosh Nasser-Moghaddam<sup>1</sup>, Hasan Vosoghinia<sup>4</sup>, Mohammad Reza Ghadir<sup>5</sup>, Ahmad Hormati<sup>5,9</sup>, Nayyereh Aminisani<sup>6</sup>, Amir Reza Radmard<sup>7</sup>, Bardia Khosravi<sup>1</sup>, Bahar Saberzadeh-Ardestani<sup>1</sup>, Masoud Malekzadeh<sup>1</sup>, Sudabeh Alatab<sup>1</sup>, Anahita Sadeghi<sup>1</sup>, Sarvenaz Salahi<sup>8</sup>, Reza Malekzadeh<sup>1</sup>, Ali Reza Sima<sup>1,\*</sup>

1. Digestive Disease Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran
2. Gut and Liver Research Center, Mazandaran University of Medical Sciences, Sari, Iran
3. Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran
4. Gastroenterology and Hematology Department, Faculty of Medicine, Ghaem Hospital, Mashhad, Iran
5. Gastroenterology and Hepatology Diseases Research Center, Qom University of Medical Science, Iran
6. Department of Epidemiology and Statistics, Faculty of Health Sciences, Neyshabur University of Medical Sciences, Neyshabur, Iran
7. Department of Radiology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
8. Minimally Invasive Surgery Research Center, Iran University of Medical Sciences, Tehran, Iran
9. Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran

**\* Corresponding Author:**

Ali Reza Sima, MD  
Assistant Professor of Medicine,  
Digestive Diseases Research Institute,  
Tehran University of Medical Sciences,  
Shariati Hospital, Kargar Shomali Avenue,  
Tehran, Iran  
Tel: +98 21 82415104  
Fax: +98 21 82415400  
Email: simaalireza@gmail.com

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### ABSTRACT

#### BACKGROUND

The COVID-19 pandemic has affected the health care infrastructure dramatically, with abundant resources necessarily being redirected to COVID-19 patients and their care. Also, patients with chronic diseases like inflammatory bowel disease (IBD) may be affected in several ways during this pandemic.

#### METHODS

We used the Iranian registry of Crohn's and colitis (IRCC) infrastructure. We called and sent messages to follow-up and support the care of all registered patients. Besides, we prepared and distributed educational materials for these patients and physicians to reduce the risk of COVID-19 infection. We risk-stratified them and prepared outpatient clinics and hospitalization guidance for IBD patients.

#### RESULTS

Of 13165 Iranian patients with IBD, 51 have been diagnosed as having COVID-19. IBD patients made 1920 hotline calls. Among the patients with suspicious presentations, 14 COVID-19 infections were diagnosed. Additionally, 1782 patients with IBD from five provinces actively phone-called among whom 28 definite cases were diagnosed.

#### CONCLUSION

IBD patients' follow-up could help in diagnosing the affected IBD patients with COVID-19. Additionally, the performance of protective actions and preparing the patients and physicians for decisive proceedings are the principles of protection of IBD patients.

#### KEYWORDS:

Protocols, Care, Inflammatory bowel disease, COVID-19

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## INTRODUCTION

Concerns about the prevention of the novel coronavirus-2019 infection are increasing as the whole population is susceptible to the disease caused by this virus.<sup>1</sup> Individuals with elder age and underlying comorbidities, especially any type of cardiovascular dysfunctions, diabetes, and immunodeficiency, are at higher risk of COVID-19 related complications, including acute respiratory distress syndrome (ARDS), septic shock, sepsis, and multi-organ failure.<sup>2</sup> Therefore, healthcare systems should aim to design principles for patients with comorbidities to reduce the risk of COVID-19 infection for this population.

On the other hand, COVID-19 has led the healthcare systems to use all the capacity of health centers to diagnose, treat, and care for the affected patients.<sup>3,4</sup> As a result, patients with chronic comorbidities such as inflammatory bowel disease (IBD), who have been under health centers' observation through the scheduled regular visits, can be exposed to the infection.<sup>5</sup> Decreasing the risk of infection by limiting these follow-up visits can also lead to lower disease flare-up and complications, especially for patients with IBD.<sup>6</sup> Therefore, programming for adjustment of routine cares, encouragement of health care providers to enter this modified program, the proper and timely reaction of the healthcare team to inform the patients and their families about the modality of performance of the program, as well as providing appropriate care at this time, are essentials to be considered for patients with chronic underlying comorbidities. These changes seem to be pivotal in maintaining the appropriate care of these patients and decreasing the chance of complications.<sup>7,8</sup>

Although conceptually, patients with IBD seem to be at higher risk of developing COVID-19 and affected by its complications, a report by the IBD Elite Union of China, which follow up patients with IBD at this time, stated that there were no proven COVID-19 cases among IBD patients as of March 17, 2020.<sup>6,9</sup>

In this report, we describe our experience and approach to patients with IBD during the SARS-COVID-19 pandemic in Iran to reduce the risk of COVID-19 infection, adjusting the routine care of these patients, detecting the IBD patients with COVID-19 infection, and planning for the possible complications during COVID-19 pandemic.

## MATERIALS AND METHODS

We designed a protocol for supporting patients with IBD during COVID-19 outbreak with three aspects, including reducing the risk of COVID-19 for such patients, adjustment of routine care to support the patients, as well as screening the patients for COVID-19 infection and management of COVID-19 for the infected patients with IBD, simultaneously (figure 1 and table 1).

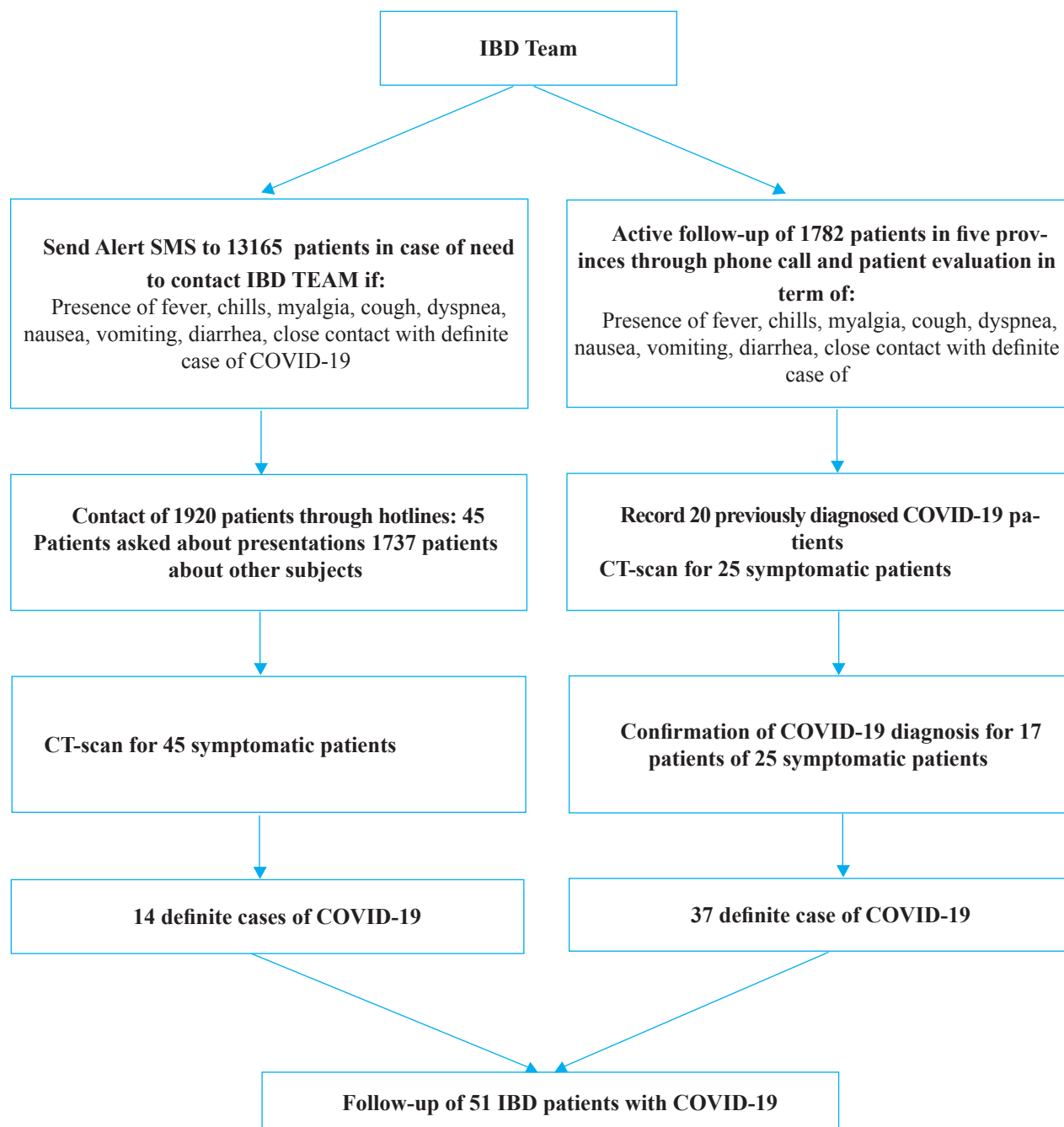
We used the Iranian registry of Crohn's and colitis (IRCC) infrastructure.<sup>10</sup> IRCC is a prospective multi-center registry with the cooperation of 449 gastroenterologists from all provinces of Iran, which has gathered the information of patients with IBD in 31 provinces since 2017.<sup>11</sup>

After the announcement of the first case of COVID-19 in Iran, the preparations of educational materials for patients with IBD and updated recommendation for physicians have been started through the literature review. The purpose of providing the educational materials and recommendations was to inform physicians and patients with IBD about the modalities, which can reduce the risk of COVID-19 infection both for patients and healthcare providers.

The educational package was sent weekly through text messages and "WhatsApp" for all 13512 patients with IBD who have been registered in IRCC, since 2007. On the other hand, daily messages about the lack of higher risk of COVID for patients with IBD, the importance of continuing to take all medications, and the need to be in contact with the IBD team in case of the presence of COVID-19 manifestations, were sent through Instagram (Table 2).

Due to the need for easy access of patients to IBD team specialists, a hotline was designed for patients. It was advised for immediate hotline call in case of fever, cough, dyspnea, myalgia, sore throat, diarrhea, nausea, vomiting, or abdominal pain. This possibility was notified via text message to all registered patients with IBD. Additionally, active follow-up was performed through phone-call for assessing COVID-19 manifestation among patients with IBD in provinces with a higher frequency of IBD. During the calls with symptomatic patients, all known presentations of COVID-19 were checked, and the duration of symptoms was asked for each symptom.

Based on the risk factors, the British Society of Gastroenterology (BSG) designed a risk stratification system for patients with IBD, shown in Table 3.



**Fig.1:** The flowchart of the Iranian registry of Crohn’s and colitis for screening the patients with IBD for COVID-19

All patients with IBD have been categorized based on the BSG risk stratification system as high, moderate, and low risk.<sup>12</sup> All high-risk patients were recommended to be monitored closely by telephone. The other two groups should be educated and followed up based on the presence of the clinical characteristics of COVID-19.

Suspected patients were referred for clinical assessment

with a chest computed tomography (CT). The outcomes of CT scans were evaluated by two expert radiologists who were determined in each province. After the diagnosis of COVID-19, the affected patients were eventually treated according to national protocols. According to the national protocol, PCR testing was performed only for patients who needed hospital admission, and for others, decisions

**Table 1: The description of the steps in the protocol of the Iranian registry of Crohn's and colitis**

<p><b>First step: Education</b>  <b>Prepared the educational material for patients with IBD</b></p> <ul style="list-style-type: none"> <li>• Weekly reminders for general recommendations</li> <li>• Training package and reminders through text message, WhatsApp, and Telegram</li> <li>• Daily Instagram reminders for the patients</li> <li>• Educated the patients with text messages to be in contact through a hotline with the IBD specialist and to report the suspicious symptoms of COVID-19</li> </ul>
<p><b>Second step: Fast screening and COVID-19 diagnosis 1724 patients communicated with specialists to report the suspicious presentations</b>          Actively phone called the registered cases of IBD in five provinces with higher rates of IBD to evaluate the patients for COVID-19 presentations          Evaluated suspected patients with computed tomography (CT) and/or polymerase chain reaction (PCR)          (Performed CT only for outpatients)</p> <p style="text-align: center;"><b>51 patients were diagnosed as having COVID-19</b></p>
<p><b>Third step: Risk stratification</b></p> <ul style="list-style-type: none"> <li>• Risk stratification of IBD activity based on the system designed by the American Gastroenterology Association</li> <li>• Risk stratification of IBD patient for COVID-19 infection:             <ol style="list-style-type: none"> <li>i. Based on the risk factors of COVID-19 and severe outcomes based on the system designed by the British Gastroenterology Society (BGS)</li> <li>ii. Active follow-up of high-risk patients by phone call, especially in the five provinces: 1103 patients</li> <li>iii. Regular follow-up for low and moderate risk patients</li> </ol> </li> </ul>
<p><b>Fourth step: Outpatients clinic</b></p> <ul style="list-style-type: none"> <li>• Re-scheduling the visits with the telehealth system             <ol style="list-style-type: none"> <li>i. Screening and follow-up of the high-risk patients</li> <li>ii. Guidance of affected IBD patients' treatment and led them to the hospital or in-house treatment</li> <li>iii. Follow-up of both in-house and hospitalized patients' treatments</li> </ol> </li> <li>• Colonoscopy and infusion             <ol style="list-style-type: none"> <li>i. Assessment for personal protective equipment (PPE) usage</li> <li>ii. One physician and minimum number of healthcare personnel</li> </ol> </li> </ul>
<p><b>Fifth step: Recognizing hospitalized patients with IBD</b></p> <ul style="list-style-type: none"> <li>• Discharging all patients with IBD who got hospitalized for elective, screening, or non-urgent operations</li> <li>• Isolating hospitalized patients with IBD</li> </ul>
<p><b>Sixth step: weekly assessment of the protocol</b></p> <ul style="list-style-type: none"> <li>• Assessment of challenges</li> <li>• Solving the limitations</li> </ul>

**Table 2: The educational package and recommendations**

<p><b>Recommendations for the general population</b></p> <p>Staying at home, keeping proper social distancing, avoid touching face, washing hands, and disinfection with alcohol-based solutions</p>
<p><b>Recommendations for patients with IBD</b></p> <ul style="list-style-type: none"> <li>• Emphasis on compliance with health care guidelines</li> <li>• Emphasis on rapid contact with the IBD team of centralized specialists in case of having symptoms of COVID-19</li> <li>• Emphasis on continuing the use of IBD medications if asymptomatic</li> <li>• Emphasis on discontinuation of steroids, immunomodulatory, and anti-TNF drugs in case of presence of COVID-19 presentations</li> <li>• Emphasis on concise observation of programmed diet to prevent malnutrition</li> <li>• Recommendation for quitting smoking</li> <li>• Recommendation for sharing any stress and anxiety with IRCC specialist team</li> <li>• Checking the immunization program: the flu vaccination was performed for all patients previously.</li> </ul>

Updating information about educational package/recommendations have been sent through text messages and "WhatsApp" through weekly reminders

were made solely based on CT scans. We followed up the patients with IBD with confirmed COVID-19 infection at least up two weeks after the diagnosis.

On the other hand, the physicians who visited and followed-up the IBD patients had access to a web-based platform to report the cases of IBD with COVID-19 infection. The report form contained the following items: age, sex, weight, height, province, the activity of IBD, the therapeutic medications, year and month of COVID-19 diagnosis,

name of the center/physician, risk factors of COVID-19, the outcome of COVID-19 (alive, death), the treatment considered for COVID-19, hospital admission (name of the hospital, length of stay, need for ventilation, and intensive care unit [ICU] admission).

All elective screening procedures, which have been appointed pre- and post-operation, have been recommended to be canceled in hospitals. The wards of the hospitals' main building were allocated to patients with COVID-19.

**Table 3: Risk stratification of the British Society of Gastroenterology (BSG)**

Highest risk	Moderate risk	Lowest risk
<b>Advise SHIELDING (compulsive self- isolation)</b>	<b>Recommended enhanced social-distancing</b>	<b>Recommendation for general populations</b>
<p>-IBD patients with comorbidities and/or age<math>\geq</math>70 years and are on treatment for IBD except for 5ASA, budesonide, beclometasone, or rectal therapies</p> <p>-IBD patients, regardless of comorbidity and age, meet at least one of the following criteria:</p> <ul style="list-style-type: none"> <li>• Oral or intravenous prednisolone more than 20 mg daily</li> <li>• New induction with combo therapy (starting biologics within previous 6 weeks)</li> <li>• Moderately to severely active disease despite the immunosuppressive/ immunomodulator/ biologics</li> <li>• Short gut syndrome requiring nutritional support</li> <li>• Requiring parenteral nutrition</li> </ul>	<p>Patients with the following medications:</p> <ul style="list-style-type: none"> <li>• Immunosuppressive/biologic treatment</li> <li>• Anti-TNF therapy (infliximab, adalimumab, golimumab)</li> <li>• Janus kinase inhibitors (tofacitinib)</li> <li>• Thiopurine (azathioprine, mercaptopurine, thioguanine)</li> <li>• A calcineurin inhibitor( tacrolimus, cyclosporine)</li> </ul>	<p>Patients on the following medications:</p> <ul style="list-style-type: none"> <li>• 5ASA</li> <li>• Orally administered and topical use of steroid (budesonide and beclometasone)</li> <li>• Therapies for bile-acid diarrhea (colestyramine, colestevlam, colestipol)</li> <li>• Anti-diarrheal agents such as loperamide</li> <li>• Antibiotics for bacterial overgrowth or perianal disease</li> </ul>

Most of the patients with IBD who had admitted to hospitals for non-urgent reasons were recognized and discharged from the hospital, and their care was continued on an outpatient basis. On the other hand, hospitalized patients with IBD were isolated to decrease contact with the virus.

Supporting the regular visits of IBD patients were advised to be performed based on the type of needed care. The first step to discover the type of care for IBD patients was the assessment of the basal status of IBD in each patient and stratification based on the risk factors of IBD progression. American Gastroenterology Association risk stratification.<sup>13,14</sup> was used for describing the basal status of the patients and the risk of disease progression for all registered patients. After categorizing the patients based on the status of IBD, the risk factors of COVID-19 infection among these patients were assessed.

Telehealth was recommended to be used for visiting the patients with IBD for providing high-quality care without the risk of COVID-19 transmission<sup>15</sup> as much as possible (table 4). However, the following outpatient care has been recommended to be performed by safe outpatient clinics. These clinics have been determined for performing laboratory assessment, imaging, and wound/stoma care.

We advised patients and physicians to cancel elective colonoscopic examinations. Colonoscopic examinations were performed only for new IBD patients with severe active disease who were candidates for biological therapy or patients with a severe flare-up. In other cases, colonoscopic examinations were replaced by fecal calprotectin.<sup>16</sup>

With this purpose, the British Society of Gastroenterology has grouped the patients based on the presence of COVID-19 symptoms, previous contact with a susceptible case of COVID-19, and history of traveling to high-risk areas to provide the safety of both personnel of clinics and patients during any procedure. Patients with a history of traveling to high-risk areas or previous contact with a susceptible case of COVID-19 was considered as an intermediate-risk group. However, patients who had at least one symptom other than the history of traveling and contact have been considered as high-risk groups.<sup>12</sup> Others who had no history of contact and travel without any presentations have been considered as a low-risk group. The personal protective equipment (PPE) was determined based on this grouping system, shown in Table 5.<sup>17</sup>

We recommended that all patients were informed through a phone call for referring to clinics and recommended to wear masks and gloves. They got to triage at the entrance based on the clinical presentation (measuring body temperature, asking about the presence of symptoms), and histories of contact and traveling. No relatives were allowed to enter the clinic. The seating arrangement for awaiting patients was conducted by highlighting the chairs, which had a distance of approximately 1.8 meters. It was recommended to use the minimum furniture and equipment. The rooms had negative pressure. The procedural room, including colonoscopy and infusion, was a dedicated room. The minimum number of personnel, including nurses and physicians, were present in clinics. During the procedure, social distancing was

**Table 4: The outline of telehealth visits for patients with IBD**

Telehealth visits with two simultaneous lines	
Regular IBD management	COVID management
<ul style="list-style-type: none"> <li>• Discovering the active status of the disease or reassessing the patients' response</li> <li>• Adjusting the proper dose of medication or changing the medications</li> <li>• Co-operating for re-prescription of the medications</li> <li>• Insisting on continuing medications</li> <li>• Discontinuation of steroids, immunomodulators/biologics, and anti-TNF drugs in case of presence of COVID-19 presentations: starting IBD drugs after 14 days.<sup>16</sup></li> <li>• Wound/stoma care</li> <li>• Coordinating for teleworking (as far as possible)</li> </ul>	<ul style="list-style-type: none"> <li>• Screening the patients based on the clinical characteristic of COVID-19</li> <li>• Introducing the suspected patients to safe clinics for laboratory assessments and CT</li> <li>• Following up the patients with suspected presentations based on the imaging/ laboratory outcomes</li> <li>• Following up the affected patients' in-house treatments or hospital admission</li> </ul>

In the case of hospital admission, IBD patients were isolated in a separate room.

**Table 5: The BSG risk stratification for the usage of Personal Protective Equipment**

Personal Protective Equipment (PPE)		
Low-risk	Intermediate	High-risk
Surgical mask Hairnet Goggles Single-use gown Gloves	For colonoscopy, it is the same as low-risk.	N95 or FFP2 masks Hairnet Goggles Water-resistant long sleeve gown Minimum two pairs of gloves

considered between the personnel and the patients. The steps of disinfection were performed for scopes of colonoscopy and infusion after doing the procedure. Especially more observation was conducted if the patients were categorized in the high-risk group.

This study was approved by the ethics committee of Tehran University of Medical Sciences. Informed consent was obtained from the study participants.

## RESULTS

Based on the recommended protocol of IRCC, patients with IBD made 1920 hotline calls from February until April. Among the patients with suspicious presentations, 14 patients were diagnosed as having COVID-19 based on the findings of CT scans. Additionally, 1782 patients of five provinces with a higher rate of IBD actively phone-called and were evaluated in terms of COVID-19 presentations. By this active follow-up, 37 definite cases were diagnosed. Therefore, 51 patients with underlying IBD were diagnosed as having COVID-19.

## DISCUSSION

In this descriptive study, we described the study protocol of the supporting system for patients with IBD in Iran,

which aimed to reduce COVID-19 infection among such patients, adjust the routine care of the patients, and detect the IBD patients with COVID-19 infection.

There are several disagreements about whether underlying IBD increases the risk of COVID-19 infection. However, the best opinion for IBD patients is the use of qualified hygiene for washing hands, nose/mouth covering with a tissue, and limiting close contact with upper/lower respiratory tract symptomatic persons.<sup>6,8</sup> Nevertheless, healthcare systems of various countries are planning for IBD patients to limit their risk of COVID-19 infection.

The general recommendations for the prevention of COVID-19 were announced for IBD patients in Milan and China. Elective surgeries were postponed, and urgent patients were admitted to the hospital and assessed in gastroenterology and surgical units. Multidisciplinary team meetings were held virtually. A checklist was designed to investigate the signs and symptoms of COVID-19, and PPE principles were implemented in outpatient clinics and hospitals. To avoid crowding, the patients' visits were re-scheduled.<sup>18,19</sup>

Many patients with IBD have simultaneous other diseases, including systematic lupus erythematosus,<sup>20</sup> celiac,<sup>21</sup> and malignancies.<sup>22</sup> With the expansion of the



database, and due to the novelty of SARS-CoV-2, it is crucial to observe the effects and outcomes of COVID-19 on patients with IBD or patients with IBD and its concurrence diseases.

Based on the experiences achieved during the COVID-19 pandemic, it is crucial to conduct alternative strategic plans for IBD patients to prevent the optimal care interferences that can occur during a disease epidemic for such patients. Designing strategic plans with simultaneous education of IBD patients and physicians can decrease the severe outcomes and severe complications.

The data is now being completed for Iranian IBD cases through IRCC IBD protocol. The structure of the protocol is dynamic and is based on the ongoing education of both IBD patients and physicians, which is one of the duties of IRCC.

This study will allow analyses of information about Iranian IBD patients with Covid-19 infection. These data will provide: 1) Patients' demographics and clinical characteristics; 2) Patients' outcomes; 3) Treatment strategies and their potential efficacy and safety.

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#### ETHICAL APPROVAL

There is nothing to be declared.

#### CONFLICT OF INTEREST

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

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