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Responding to COVID-19: Perspectives From the Chinese Society of Gastroenterology



The pandemic of coronavirus disease 2019 (COVID-19) has been tremendously impacting the entire world since December 2019. COVID-19 was first reported to affect the respiratory tract and spread from person to person by respiratory droplets; therefore, pulmonologists as well as critical care physicians have been the leading force to counteract this public health crisis. The evidence of digestive system involvement in COVID-19 was first reported by a group in China.¹ There are increasing data showing that the gastrointestinal (GI) tract and liver might also represent target organs of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), and that infected patients could have corresponding organ damage and symptoms. More important, the evidence of SARS-CoV-2 detection in patient stool and the tentative fecal–oral route transmission have raised great concern and posed a challenge for control and prevention of COVID-19.² It is the indispensable duty of our gastroenterologists, as we did in the history of other epidemics, to be armed with knowledge, facts, and skills, and united in the battle against COVID-19. In this concise review, we aim to:

- Provide perspectives about how to respond to COVID-19 from the Chinese Society of Gastroenterology (CSG),
- Summarize disease manifestations or complications relevant to GI and liver involvement, and
- Propose recommendations for next steps regarding our future GI practice and care.

We expect that our response might be instructive for other GI communities to counteract the current unprecedented situation.

The CSG Response to the COVID-19 Outbreak

As the authorized academic association of gastroenterologists in China, we follow the guidance and recommendations of relevant government authorities. Several actions have been taken in response to the COVID-19 outbreak. According to a survey of 2216 GI doctors from all over China early in the outbreak of COVID-19, the awareness of digestive system damage and involvement in COVID-19 was low, ranging from 31% to 35%.³ To counteract this, the CSG rapidly organized a group of experts including gastroenterologists working in the forefront of COVID-19 patient care to discuss and reach a consensus on management of digestive disorders involved in COVID-19 (Table 1).⁴ This consensus includes recommendations regarding transmission route, clinical manifestation spectrum of digestive system involvement, practical guidelines on treatment based on the latest publications, and precautions regarding endoscopic procedure. In addition, precautions for GI outpatient clinic have been proposed.⁴ The CSG is composed of 25 subspecialty committees, depending on the disease spectrum. As a response to the increasing concern and inquiry about COVID-19 risk from the community of inflammatory bowel disease (IBD) in China, the Chinese IBD Committee affiliated with the CSG has issued timely recommendations for managing IBD patients in early February 2020, which is probably the first guideline regarding IBD and COVID-19 in the global community.⁵ The guideline includes practical recommendations regarding immunosuppressive agent and biologics use, diet, and intentional postponing of elective surgery and endoscopy, as well as personal protection provisions. The

guideline has recently become the most read article on the website of the *Chinese Journal of Digestion*, the official journal of the CSG.

The responses to an epidemic outbreak must be culturally appropriate. The measures implemented in China may be instructive for other countries now struggling to control COVID-19. More than 40,000 health care workers, including clinicians, nurses, laboratory technicians, and coordination staff members, have voluntarily been transferred to clinical care of COVID-19 patients in Hubei province from other parts of China. Gastroenterologists are an important part of the volunteer clinicians; they have provided practical consultant care opinions to patients with COVID-19, especially those with comorbidities or complications of the GI tract and liver. The CSG pays close attention to the situation of our gastroenterologists in Hubei province. To increase the awareness of COVID-19 in the GI community, we launched an online platform in the portal website of the CSG (available: www.csge.org.cn) for sharing clinical experiences from our gastroenterologists working in the front lines; they are typical examples of modern heroes in this unexpected war against a difficult enemy. Their professionalism and passion for the specialty, as well as their compassion for their patients, have greatly encouraged gastroenterologists nationwide.

Health care workers are especially at increased risk of exposure to COVID-19. Given that GI COVID-19 infection has been confirmed and fecal excretion of virus has been reported,^{1,6} much attention has been paid to the potential risk of infection during procedures such as endoscopy and colonoscopy. The CSG coordinated efforts by associations, including the Chinese Society of Digestive Endoscopy, in a comprehensive effort to propose recommendations and guidelines to prevent our gastroenterologists from infection in their clinical practice.

Table 1. Key Points of the Consensus on Diagnosis and Treatment of Digestive System Involvement in COVID-19 by the Chinese Society of Gastroenterology

Pathogen and route of transmission	Novel coronavirus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), respiratory droplets and contact transmission; fecal contamination is suspected.
Clinical manifestations in gastrointestinal symptoms	Most patients have respiratory symptoms, but some may present gastrointestinal symptoms first, including loss of appetite, diarrhea, nausea, vomiting, abdominal pain, GI bleeding in severe cases, and abnormal liver function.
Management recommendations	<p>Diarrhea: Mostly mild, differentiate causes, symptomatic treatment, prevention needed.</p> <p>Viral: May account for 22.2% of the patients with diarrhea.</p> <p>Drug-induced: Many antiviral agents cause diarrhea.</p> <p>Antibiotic-associated: Seen with elderly patients and comorbidity of chronic illness, particularly in patients with ventilation in the intensive care unit.</p> <p>Liver injury: Most COVID-19-associated liver injury is mild, with <2 times of abnormal liver function test and need no treatment.</p> <p>Diet and nutrition: Enteral nutrition by oral feeding is preferred. A nutritional risk assessment is recommended for severe patients. A nasogastric tube can be inserted for enteral nutrition for those who are unable to take food by mouth (such as those receiving mechanical ventilation).</p>
Precaution and limitation for GI examinations	<p>Endoscopy: Only emergency endoscopy is indicated during the outbreak, such as treatment of acute gastrointestinal hemorrhage, removal of foreign bodies in the digestive tract, suppurative obstructive cholangitis, and biliary pancreatitis. Screen for COVID-19 before the procedure and provide appropriate protection for the endoscopists in an isolated and preferably a negative-pressure room for the procedure.</p> <p>Suspend other examinations such as esophageal acid test, gastrointestinal motility test, hydrogen breath test, <i>Helicobacter pylori</i> test, and fecal antigen test.</p>

NOTE. Adapted from The Chinese Society of Gastroenterology. Consensus on diagnosis and treatment of digestive system involvement in COVID-19. Chinese Journal of Medicine 2020 <https://doi.org/10.3760/cma.j.cn112137-20200308-00645>.

Epidemics and public health crises pose great challenges to health care delivery. To minimize the risk of SARS-CoV-2 infection by avoiding close contact with infected patients in public areas such as hospitals, telemedicine has also been widely applied in our non-COVID-19 patient care, including virtual clinic visits, online clinic consultancy, and nurse-led care support based on interactive social care apps such as WeChat. These strategies have greatly facilitated care delivery to patients with chronic GI diseases such as IBD.

COVID-19 Disease Manifestations Relevant to GI and Liver Involvement

Although respiratory tract manifestations such as fever and cough are the most common reported symptoms in patients with COVID-19, symptoms within the GI tract have also been reported. A study of 138 confirmed patients with COVID-19 showed that the major symptoms included fever (98.6%), fatigue (69.6%), cough

(59.4%), myalgia (34.8%), and dyspnea (31.2%); GI symptoms included abdominal pain (3.6%), diarrhea (10.1%), and vomiting (3.6%). It is worth noting that 14 cases (10.1%) had initial symptoms of diarrhea and nausea, then fever and dyspnea.⁷ This finding is important for gastroenterologists for screening and identifying COVID-19 cases. However, the disease course and outcomes in these subgroups of patients requires further investigation. Another retrospective analysis of 1099 patients with COVID-19 showed that the main symptoms were fever (87.9%) and cough (67.7%); diarrhea (3.7%) and vomiting (5.0%) were less frequent. Among GI symptoms, the incidence of diarrhea and abdominal pain in patients with severe COVID-19 was higher than that in patients with mild COVID-19.⁸

Recent studies of single cell RNA sequencing of human tissues demonstrated that the cell receptor angiotensin covering enzyme II is expressed in epithelial cells of the digestive system as well as liver cells.⁹ Liver abnormalities in COVID-19 patients may be due to liver cell dysfunction or other causes, such as drug toxicity and

systemic inflammation. In a cohort of 1099 patients with COVID-19, abnormal liver function tests including elevated aspartate aminotransferase, alanine aminotransferase, and total bilirubin were found in 168 (168/757, 22.2%), 158 (158/741, 21.3%), and 76 (76/722, 10.5%) of patients, respectively.⁸ Data regarding alkaline phosphatase and gamma-glutamyl transpeptidase were not provided in this study.⁸ Another study that included 333 COVID-19 cases with liver function tests was recently reported in a Wuhan medical center. The incidence of liver injury was 39.6% (132/333) with the majority (71.2%, 94/132) being mild elevation in liver enzyme tests. Total bilirubin was elevated in only 13 patients (13/333, 3.9%). Regarding underlying liver conditions, 12 patients had a history of chronic hepatitis B and 2 patients had a history of chronic hepatitis C, but the detection of viral nucleic acid showed no active hepatitis.¹⁰ There was no significant difference in the ratio of liver injury between patients in an intensive care unit (45.6%, 26/57) or the general ward (38.4%, 106/276) ($P > .05$). However, in another study

including 305 confirmed COVID-19 cases, the incidence of liver injury in patients in intensive care (67.4%, 31/46) was significantly higher than that on general wards (34.1%, 88/258) ($P < .05$).¹¹

Data regarding the macroscopic changes of the GI tract in patients with COVID-19 are scarce. In the only case who underwent endoscopy because of upper GI bleeding from a cohort of 73 patients with COVID-19, no abnormalities were observed in the stomach, duodenum, colon, or rectum, with the exception of multiple bleeding ulcers (4–6 mm in diameter) in the esophagus by endoscopy. Histology showed numerous infiltrating plasma cells and lymphocytes as well as interstitial edema in the lamina propria of the stomach, duodenum, and rectum.¹ Autopsy studies are important to help investigate the histopathologic changes in the GI tract in COVID-19. Currently, there is only 1 published autopsy report of an 85-year-old man with COVID-19, which showed segmental dilatation and stenosis in the small intestine.¹² Further studies are needed to clarify whether this finding is secondary to COVID-19 or a preexisting GI comorbidity.

Future Outlook for GI Practice and Care during COVID-19

Our response is evolving as our knowledge about COVID-19 evolves. To fight against this public health crisis with numerous uncertainties, it is imperative for the entire health care community to respond in a collaborative fashion, and even establish a response mechanism for enabling rapid actions for the next crisis. Several action items about GI practice, care, and research should be implemented.

Gastroenterologists serve patients who are potentially more vulnerable to COVID-19 because of underlying digestive disorders. The presence and number of comorbidities was reported to be

associated with poorer clinical outcome in patients with COVID-19.⁸ In China, we have a large population of patients with digestive disorders, including chronic liver disease and GI cancer, and an increasing number of patients with IBD. However, whether these underlying conditions could increase the risk of COVID-19, and their impact on prognosis of COVID-19 remain unknown.¹³ For this reason, several national registry studies including COVID-19 risk in IBD, which is similar to the model of Surveillance Epidemiology of Coronavirus Under Research Exclusion in the United States, are ongoing to evaluate these questions. This will greatly facilitate our GI practice and care for our patients.

Importantly, SARS-CoV-2 virus RNA was detected in the stool specimen from patients with COVID-19 and could persist throughout the course of illness resolution.^{1,14,15} Although virus detection in the stool does not necessarily equate to virus infectivity and direct evidence of fecal transmission of COVID-19 has yet to be identified, the implementation of high-level disinfection for surfaces potentially contaminated by feces is strongly recommended. Emerging evidence shows persistence of SARS-CoV-2 virus RNA in stool samples or rectal swabs even after respiratory specimens tested negative.^{6,16} In a recent landmark clinical investigation of 10 pediatric COVID-19 cases in China, 8 persistently tested positive on rectal swabs even after nasopharyngeal testing was negative, suggesting that the GI tract may continue to shed the virus.⁶ The updated criteria for hospital discharge of COVID-19 patients includes resolution of fever and respiratory symptoms, improvement in acute exudative lesions on chest computed tomography scans, as well as 2 consecutively negative reverse transcriptase polymerase chain reaction test results of respiratory samples with interval of ≥ 24 hours.¹⁵ Whether fecal or rectal swab reverse transcriptase polymerase chain reaction results

should also be included in future discharge criteria needs to be further investigated.

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Conflicts of interest

The authors disclose no conflicts.



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