

SHORT COMMUNICATION

The digestive system and the COVID-19

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Abstract

The current pandemic coronavirus disease (COVID-19) is an ongoing healthcare crisis. While COVID-19 typically presents as fever and respiratory illness, almost 50% of the patients also have associated digestive symptoms which vary from abdominal pain to diarrhoea and indigestion. Literature review of association of COVID-19 with digestive symptoms was done using Google search and the results are presented herein.

Keywords: COVID-19, Coronavirus, Diarrhoea, Digestive symptoms.

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Introduction

The novel coronavirus disease (COVID-19) pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a member of the Betacoronavirus genus that also includes the SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Since the outbreak of COVID-19 in Wuhan, China, in December 2019, many publications on the signs, symptoms complications and treatment of the disease have been published. The disease mostly presents as a fever, fatigue and respiratory illness but many patients also have digestive or GI symptoms while few present with digestive symptoms as the first presentation.

A Google search was undertaken for articles, reviews or reports published in literature on COVID-19 from January to March 2020. Further search was done on the association of digestive symptoms with COVID-19. Case reports were excluded.

Gastrointestinal Symptoms

Huang et al were one of the few healthcare workers who reported the clinical features of COVID-19 in 41 patients admitted in January 2020.¹ These included 13 ICU and 28 non-ICU cases. Their initial symptoms were fever, cough, dyspnoea, myalgia or fatigue. Diarrhoea was seen in 3% cases. During the same time Chen et al reported 99 cases

suffering from SARS-CoV-2-infected pneumonia.² This group had older males and many had associated comorbidities. Apart from classical symptoms of fever, fatigue, cough, myalgia, and dyspnoea, 2% had diarrhoea and 1% had nausea and/or vomiting. GI symptoms appearing before the classic respiratory symptoms were reported by Wang and these included diarrhoea (10%), nausea (10%), and abdominal pain.³

The largest clinical study of COVID-19 patients who had associated digestive symptoms was undertaken in Hubei, China. The study included 204 hospitalised patients from three hospitals in Hubei, China and all were confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR).⁴ Digestive symptoms were seen in 48.5% of the patients, which included anorexia (84%), diarrhoea (29%), vomiting (0.8%), and abdominal pain (0.4%). Out of this cohort, 7 patients had digestive symptoms without any respiratory symptoms. The study further reported that the patients having only digestive symptoms or those that had with classical symptoms of COVID-19 along with GI symptoms had a prolonged disease and were less likely to be cured. The authors have cautioned that digestive symptoms are common in COVID-19 patients and as these digestive symptoms are non-specific, therefore it does not necessarily mean that the person has COVID-19; however, such patients without classic symptoms may continue to spread the disease.

Though most studies have been reported on patients having severe illness, the Union Hospital of Tongji Medical College in Wuhan was assigned for admitting patients with COVID-19 who had mild illness, and no difficulty in breathing or low blood oxygen levels.⁵ Out of 206 patients with low severity COVID-19, 48 patients had digestive symptoms only, 69 of them had both digestive and respiratory symptoms, while 89 patients had respiratory symptoms only. Overall, 117 patients had GI symptoms. Of these, 58% of the patients had diarrhoea, with 20% of these having diarrhoea as the first symptom, which lasted on an average for 5 days. Majority (73%) of these patients had a positive stool test for SARS-CoV-2 RNA. Almost one third patients never had any fever during this illness and therefore sought healthcare after a long time. These patients took a longer time to clear the virus, which was detected as a negative test for COVID-19.

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Table: Frequency of gastrointestinal symptoms in patients with COVID-19.

Author	Patients	Diarrhoea	Nausea	Vomiting	Abdominal Pain
Huang et al ¹	41	3%			
Chen et al ²	99	2%	1%		
Wang et al ³	138	10%	10%		
L Pan et al ⁴	204	29%		0.8%	0.4%
Han et al ⁵	206	58%			
Liu et al ⁸	30	30%			
Wong SH et al ⁹	Review	3.7%-35.6%	1%-17.3%	1%-6.4%	2.2%-5.8%

There is now a general agreement that the virus probably infects the gastrointestinal tract.^{5,6}

She et al reported that the symptoms of SARS-CoV infection were non-specific and apart from classic symptoms, some patients also presented with diarrhoea, which was previously reported in 10.6% cases of SARS and up to 30% in MERS. Medical or health-related workers probably have a higher frequency of GI symptoms and this was reported in a study of 30 medical workers suffering from coronavirus pneumonia in China.⁸ Out of 30 medical workers, 9 (30%) had GI symptoms, including diarrhoea and nausea. As digestive symptoms were more often recognised to be present in the COVID-19 patients, Wong undertook a comprehensive review on COVID-19 and the digestive system and showed that the frequency of diarrhoea ranged from 3.7%-35.6%, nausea 1%-17.3%, vomiting 1%-6.4% and abdominal pain 2.2%-5.8%.^{4,9} The frequency of GI symptoms in COVID-19 cases is shown in the table.

Isolation of SARS-CoV-2 RNA from other sites

Cipriano et al in his review paper reported that the virus was found in the stool, oropharynx, nasopharynx and the respiratory tract.¹⁰ In 24% of the cases, the virus persisted in the stool even after the respiratory virus had cleared. Another review also showed that SARS-Cov-2 RNA was seen in 36-53% of the stool samples,¹¹ while one study reported the presence of virus in stool in 55% cases.¹² The faecal samples became positive 2-5 days after the sputum sample but remained positive for 1-11 days longer than the respiratory samples.¹¹ The virus has also been detected from the rectal swabs.¹³

The persistence of the virus in the stool after its clearance from the respiratory samples puts a question mark at the definition of disease transmission and risk of infection. The Centers for Disease Control and Prevention (CDC) recommends that the possibility of disease transmission and infection risk for COVID-19 should be dismissed after two negative respiratory tests done \geq 24 hours apart.¹⁴

Persistence of the virus in stool many days after the respiratory clearance of the virus raises the possibility of faecal-oral disease transmission of COVID-19 and that is why it is recommended to undertake RT-PCR from stool samples.³ The presence of the virus in the saliva of patients suffering from COVID-19 has also led to concerns and precautions from the dental community.¹⁵

Angiotensin converting enzyme 2 as possible site of entry of virus

To determine the site of entry of the virus into the GI tract, researchers have reported that angiotensin converting enzyme 2 (ACE2), a trans-membrane protein, serves as the main entry point into cells for some coronaviruses including SARS-CoV-2.¹⁶ Another researcher argued that the rate of GI symptoms might be higher in patients with COVID-19 because the virus uses the ACE2 pathway.¹⁷ It is possible that the virus enters the GI tract using the "trachea-oesophagus-ileum-colon" pathway because ACE2, the entry receptor for SARS-CoV-2, is highly expressed in lung alveolar type 2 (AT2) cells, in the upper and stratified epithelial cells of the oesophagus, and in enterocytes of the ileum and colon.¹⁸ This implies that SARS-CoV-2 can infect and replicate in the GI tract and therefore there is a need to look for its implications on the disease management, transmission, and control of infection.

Precautions

The editorial by Abbas et al also highlights the association of GI symptoms in COVID-19 patients and also reminds the gastroenterologists of observing extreme caution and their own protection while undertaking endoscopic procedures in the time of pandemic and especially in patients suffering from COVID-19.¹⁹ The possible impact of COVID-19 on GI care as summarised by the American College of Gastroenterology, and endorsed by American Association for the Study of Liver Diseases (AASLD), American Society for Gastrointestinal Endoscopy (ASGE) and American Gastroenterological Association (AGA)

includes following recommendations:²⁰

1. All elective procedures should be delayed
2. Perform only urgent procedures like endoscopy for symptomatic GI bleeding, dysphagia, pancreatitis (ERCP), pancreatitis (EUS), GI obstruction and few others.
3. All endoscopic procedures should be considered aerosol-generating procedures (AGP) due to possible coughing, retching and passing flatus during the procedure
4. All endoscopes are at risk of generating aerosol and micro-droplets due to their design and suction/inflation.
5. Reduce the number of members of the endoscopy team. All members should wear a full set of personal protective equipment (PPE) and observe following precautions:
 - a. Hand hygiene
 - b. Wear an N95 mask. This mask often needs fitting by an expert and can be reused. If contaminated, it can be disinfected with hydrogen peroxide vapour.
 - c. Wear a full set of PPE (gown, gloves, hair cover, eye protection (goggles or face shield)). Wear a plastic gown if possible.

Conclusion

Diarrhoea, nausea and abdominal pain are common GI symptoms which occur in 3-55% cases suffering from COVID-19. These symptoms may appear with or without respiratory symptoms. Cases with GI symptoms tend to have a longer and more severe disease and continue to shed the virus in the stool for many days after the virus has cleared from the respiratory system. ACE2 receptor is thought to be the potential entry point in the GI tract. During the pandemic, perform only emergency lifesaving procedures and all members of the endoscopy team should wear full set of PPE.

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