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Covid19 Relation with Gastrointestinal Symptoms

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ABSTRACT

Since the end of December 2020, more than 78 million people worldwide had been infected with Coronavirus disease 2019 (COVID-19), a respiratory viral infection. Many Previous researches suggested that extreme acute respiratory syndrome coronavirus 1 and Middle East respiratory syndrome–related coronavirus infections could have an effect on the gastrointestinal (GI) system in this study; it will address the major GI manifestations of COVID-19, as well as the potential underlying pathophysiological mechanisms, as well as their diagnosis and management. GI manifestations have been identified in 11.4–61.1 percent of COVID-19 patients, with varying onset and severity. Anorexia, diarrhoea, nausea, vomiting, and abdominal pain/discomfort are the most common COVID-19-related GI symptoms. A small percentage of patients presented with an acute abdomen caused by an underlying condition such as acute pancreatitis, acute appendicitis, intestinal obstruction, bowel ischaemia, haemoperitoneum, or abdominal compartment syndrome. Coronavirus 2 RNA from severe acute respiratory syndrome has been detected in biopsies from all areas of the alimentary canal. The GI tract may be involved due to direct viral injury and/or an inflammatory immune system response, which can result in malabsorption, an imbalance in intestinal secretions and gut mucosal integrity, and enteric nervous system activation. The mainstay in counseling is supportive and symptomatic treatment. However, a small percentage of patients may need surgical or endoscopic care for acute abdominal and GI bleeding.

Introduction

Coronavirus disease 2019 (COVID-19) is affected by coronavirus 2 that causes serious acute respiratory syndrome (SARS-CoV-2). It is currently a pandemic, with over 79 million cases and over 1.7 million deaths worldwide as of December 26, 2020. To combat the pandemic, several vaccines have been produced. (2) The first record of coronavirus infections in animals was in the late 1920s, when acute respiratory infections occurred in North American domesticated chickens.(3) Human coronaviruses were reported in the 1960s4, and 7 strains currently affect humans. Human coronavirus OC43 (HCoV-OC43), human coronavirus HKU1 (HCoV-HKU1), human coronavirus 229E (HCoV-229E), and human coronavirus NL63 (HCoV-NL63) cause moderate disease, while human coronavirus NL63 (HCoV-NL63) causes extreme acute respiratory syndrome (SARS-CoV-1), Middle East respiratory syndrome–related coronavirus (MERS-CoV) and extreme acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are two viruses that have the ability to cause serious illnesses.(5–7) Infections with SARS-CoV-1 and MERS-CoV occurred in 2002

and 2012, respectively. 8 SARS-CoV-2 shares 70% and 40% genetic sequence similarities with SARS-CoV-1 and MERS-CoV, respectively. (9) While fever and respiratory symptoms predominate in coronavirus infections, gastrointestinal (GI) manifestations have been observed in patients infected with SARS-CoV-1, MERS-CoV, and SARS-CoV-2.

Most recent studies about Coronaviruses and the gastrointestinal system involvement

Human coronaviruses are classified into two groups: alpha (HCoV-229E and HCoV-NL63) and beta (HCoV-HKU1, HCoV-OC43, SARS-CoV-1, MERS-CoV and SARS-CoV-2). SARS-CoV-2 and SARS-CoV-1 are genetically identical and also use angiotensin-converting enzyme 2 (ACE2) as an entry receptor. (9) There is more research on the GI impact of SARS-CoV-1 and MERS-CoV than on the other coronaviruses. This may be because these coronaviruses have different degrees of GI involvement.

1) **HCoV-NL63 and HCoV-HKU1**

Initially, coronavirus-like molecules were discovered in intestinal infections and the stools of babies with necrotizing enterocolitis. Esper et al(25) discovered HCoV-HKU1 in stool specimens from children and adults with gastrointestinal disease. There were no positive HCoV-NL63, HCoV-229E, or HCoV-OC43 samples were collected. In a study conducted in France by Vabret et al.26, three HCoV-HKU1-infected persons were hospitalised for acute enteric disease, and HCoV-HKU1 was found in stool samples in two of them. While , Kanwar et al.(27) and Kumthip et al.(28) discovered that HCoV-HKU1 cause GI manifestations (diarrhoea, vomiting, nausea, and abdominal pain) in up to 57% and 38% of infected individuals, respectively. According to Bouvier et al(29), HCoV-HKU1-related GI symptoms typically appear on the fourth day of infection in otherwise healthy adolescents and adults.

2) **SARS-CoV-1**

GI involvement was present in 30–70% of SARS-CoV-1 patients during the epidemic. 17 Srikantiah et al.30 discovered vomiting and diarrhoea in 63 percent and 75 percent, respectively, of SARS-CoV-1-infected patients in a small sample. According to Hui et al.13, the most common GI symptoms are nausea/vomiting (20–35%) and diarrhoea (20–25%). SARS-CoV-1 positivity rates in urine, nasopharyngeal aspirate, and feces were 42 percent, 68 percent, and 97 percent, respectively, until day 14 of

disease.Other tests discovered diarrhoea in up to 25% of patients. (33–31) According to Chan et al(34), 5.8 percent of their patients presented with fever and diarrhoea (mostly watery with no blood or mucus).

3) **MERS-CoV**

MERS-CoV patients had extensive GI involvement. (35) Zumla et al(36) recorded nausea (21%), vomiting (21–33%), and diarrhoea (26–33%) in MERS-CoV patients. Abdullah et al.37 discovered GI symptoms in 35% of the patients they analyzed in eastern Saudi Arabia.

Gastrointestinal manifestations in COVID-19

GI presentations have been identified in 11.4–61.1 percent of COVID-19 patients. Anorexia, diarrhoea, nausea, vomiting, and abdominal pain/discomfort are among the most common COVID-19-related GI symptoms. (15–16, 21–22, 38) Anorexia and diarrhoea were the most common GI manifestations in some reports, although nausea and vomiting were more common in others. While Han et al.
(15) Discovered that COVID-19-associated GI symptoms are more frequent in women (65.7 percent vs 51.1 percent), no other researchers have discovered this trend.

Clinical characteristics of patients with COVID-19 and GI manifestations

					GI symptoms, n (%)				
First author, year (country)	Article type	Total no of patients	Average age (years)	Patients with GI symptoms, n (%)	Anorexia	Diarrhoea	Nausea or vomiting	Abdominal pain/discomfort	GI/rectal bleeding
Chen N, 2020[38] (China)	RA	99	55.5	3 (3)	NA	2 (2)	1 (1)	NA	NA
Chen Y, 2020[39] (China)	RA	42	52	8 (19)	NA	7 (16.67)	Nausea: 4 (9.52)Vomiting: 3 (7.14)	5 (11.9)	NA
Guan, 2020[40] (China)	RA	1099	47	97 (8.8)	NA	42 (3.8)	Nausea or vomiting: 55 (5)	NA	NA
Han, 2020[15] (China)	RA	206	62.5	117 (56.8)	102 (49.5)	67 (32.5)	Vomiting: 24 (11.7)	9 (4.4)	NA

Huang, 2020[41] (China)	RA	38	49	NA	NA	1 (3)	NA	NA	NA
Jin, 2020[42] (China)	RA	651	46.14	74 (11.4)	NA	53 (8.1)	Nausea: 10 (1.5)	NA	NA
							Vomiting: 11 (1.6)		
Lin, 2020[43] (China)	RA	95	NA	58	17 (17.9)	23 (24.2)	Nausea: 17 (17.9)	2 (2.1)	NA
							Vomiting: 4 (4.2)		

					GI symptoms, n (%)				
First author, year (country)	**Article type**	**Total no of patients**	**Average age (years)**	**Patients with GI symptoms, n (%)**	**Anorexia**	**Diarrhoea**	**Nausea or vomiting**	**Abdominal pain/discomfort**	**GI/rectal bleeding**
Luo S, 2020[44] (China)	RA	1141	53.8	183 (16)	180 (98)	68 (37)	Nausea: 134 (73)	45 (25)	NA
							Vomiting: 119 (65)		
Martin, 2020[45] (USA)	RA	41	70.4	41	NA	NA	NA	NA	41 (33.4)
Mauro, 2020[46] (Italy)	RA	4871	75	23	NA	NA	NA	NA	23 (0.5)

➢ Diarrhoea

Diarrhoea has been identified in 2–50% of cases and is more frequent in serious disease (moderate 69.2 percent, severe 100 percent). (16) Han ET al.(15) discovered that diarrhoea appeared as a first symptom in 20% of their patients, while the remainder experienced it up to 10 days after the onset of respiratory symptoms. The majority of patients were confirmed to have had non-severe, non-dehydrating, low-volume diarrhoea that lasted on total 5.4 days and improved by day 13.

➢ Nausea and vomiting

Luo et al. discovered increased rates of nausea and vomiting after COVID-19, while many other research find a lower occurrence. More extreme illness was associated with a higher rate of nausea. Patients who present with nausea, vomiting, or

diarrhoea are more likely to have fever than those who only have one of the symptoms. (15) Vomiting and milk avoidance were observed in COVID-19 neonates, as well as respiratory symptoms.

- **Abdominal pain**

While abdominal pain is reported at a lower rate than other Clinical signs, it is normal in patients receiving intensive care. Many symptoms including acute pancreatitis, acute appendicitis, intestinal obstruction, small bowel ischaemia, sigmoid ischaemia, haemoperitoneum, haemopneumoperitoneum, or abdominal compartment syndrome were among the causes of abdominal discomfort in a small number of patients. Seelinger et al (21) identified seven COVID-19 patients who needed emergency surgery caused by acute abdomen.

- **Anorexia**

Anorexia was the most prevalent symptom in a meta-analysis of 60 studies, accounting for problems with enteral feeding and maintaining sufficient nutritional status. (30) Additionally, individuals who subsequently experienced recurrent pneumonia had a higher rate of anorexia on admission. (29)

The beginning of GI symptoms may occur at any time. They appear at the beginning of the disease in some people (before another clinical manifestations), but they appear later in other people. Just 11.6 percent of COVID-19 cases with Clinical signs identified by Lin et al. had symptoms on admission to hospital, while the majority developed symptoms late. Those with dominant GI symptoms were admitted to the hospital relatively late than those who have respiratory symptoms. There was a corresponding pause in diagnosis and care. (16) The number of patients with mostly GI symptoms presented to the hospital with a substantial gap, as did the diagnosis. When compared to their non-GI counterpart, their clinical path was challenging, and there was a high prevalence of deterioration to serious disease (requiring mechanical ventilation and ICU care). (15, 16, 40, 32,) Individuals had quite a longer stay in hospital since their discharge was postponed until the virulence was cleared. This observation may be due to a combination of factors. Though treatment lag may have played a role, studies have also revealed higher viral replication and viral loads in patients with GI manifestations.

How COVID-19 involved the gastrointestinal tract?

SARS-CoV-2 infiltrates host cells through ACE2 receptors. (38) Increased cell penetration potency is achieved in three ways: high binding sensitivity of the trigger protein's receptor-binding domain (RBD), avoidance of the human immune response by reduced exposure of the RBD from the outside, and stimulation of the virus's Furin protease before entry into host cells, decreasing its reliance on target cell proteases.

A. ACE2 receptor expression

The ACE2 receptor is found with both the solid and hollow intestines. ACE2 messenger RNA (mRNA) is expressed primarily in the GI tract and is maintained by the intestinal epithelial neutral amino acid transporter B0AT1 (SLC6A19). (22)
A single-cell transcriptomics research discovered increased ACE2 transcription in the upper esophagus. In a separate case–control study, moreover, immunohistochemistry revealed reduced expression of ACE2 and nucleocapsid proteins in the esophagus.

B. Saliva

SARS-CoV-2 RNA is present in saliva and can play an essential part in virus infection from person to person. The viral load in saliva decreases as the disease progresses. Saliva can be used to identify viruses during the acute process and has some benefits over nasopharyngeal swabs, such as flexibility of detection, lower risk to healthcare staff, and lower expense**.**

C. Oesophagus, stomach and small and large intestines

SARS-CoV-2 RNA was discovered in biopsy samples taken from the oesophagus, liver, duodenum, and rectum. Interference of the GI tract during COVID-19 may be due to potential viral injury and/or an aggressive immune response, which could result in malabsorption, an imbalance of intestinal secretions, and enteric nervous system activation. The introduction of SARS-CoV-2 into host organism can result in an immune response. This results in T-helper cell recruitment, a cytokine storm, and organ damage. Diabetes patients are more vulnerable to the cytokine storm effects of COVID-19. Virus-induced diarrhoea could be caused by a change in intestinal permeability, resulting in enterocyte malabsorption.

D. Stool viral RNA in COVID-19

SARS-CoV-2 viral shedding by feces is possible. Chen et al discovered no connection between stool viral RNA positivity and GI manifestations. Sixty-seven percent of the COVID-19 patients had SARS-CoV-2 RNA in their feces, but only 19 percent had GI symptoms. People who are diagnosed with digestive symptoms, on the other hand, are more liable to be faecal viral RNA positive than those who present with respiratory symptoms (73.3 percent vs 14.3 percent). Patients that have intestinal problems take longer time to remove the infection from their stools as well. (15) Zhang et al discovered that the virus was more prevalent in feces than in respiratory samples (83 percent vs 67 percent). The capacity for faecal–oral spread is increased by viral replication in the digestive tract. The existence of viral RNA in stools, nonetheless, does not correspond with transmissibility because nucleic acid recognition does not distinguish between infective and non-infective (dead or antibody-neutralized) viruses. The diagnosis of faecal viral RNA by RT-PCR testing in COVID-19 patients at various time points can aid in management (especially so in patients with GI symptoms). It should aid in deciding the efficacy of treatment and when quarantine should be lifted.

Conclusion

Multiple COVID-19 patients have significant GI manifestations. Up to this point, the results have provided us with new and significant knowledge into the GI effects of SARS-CoV-2 and their fundamental pathophysiology. Additional research should be facilitated in further clearly understanding the many unknown aspects of COVID-19 and the GI tract. The review article have summarized the major GI manifestations of COVID-19 in this analysis and addressed the potential mechanisms and aspects related to their diagnosis and management. During the current disease outbreak, checking for SARS-CoV-2 should be observed in patients with GI symptoms, even though they do not have any usual COVID-19 symptoms. As more research using GI imaging and histological findings become accessible, the long-term effects of the various GI manifestations should become better established.

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