

# Exploring Gastrointestinal Manifestations Caused by COVID-19 in Brief

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## ABSTRACT

The outbreak of a novel coronavirus in Wuhan, China, in December 2019 led to a global crisis and a critical threat to the health of millions of people worldwide. Existing research indicates that besides typical respiratory symptoms and signs of COVID-19, gastrointestinal manifestations are also caused by coronavirus disease 2019 (COVID-19) and the main intention of this article is to compare the gastrointestinal disorders seen in patients infected by the virus as well as study the possible and logical mechanisms that may lead to these situations. The high rate of contagion of the virus and the number of current patients reveal the importance of this research and all other studies related to this subject.

**Keywords:** COVID-19; Gastrointestinal Symptoms; Diarrhea; Nausea, Liver Abnormalities

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## INTRODUCTION

The SARS-CoV-2 is an enveloped, non-segmented, positive-sense single-stranded RNA virus causes the 2019 coronavirus disease (COVID-19) pandemic(1,2). SARS-CoV-2 enters the lower respiratory tract cells via their angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in various human organs as well as the lungs(3). Research has confirmed that ACE2 is highly expressed in esophageal epithelial cells and absorptive enterocytes from the ileum and colon, which as a result, the digestive system is a potential route for infection, and the possibility of fecal

transmission should be considered to prevent further COVID-19 infections(4).

Fever, cough, fatigue, dyspnea, sore throat, headache, and myalgia or arthralgia are the most common symptoms seen in patients. In approximately 80 % of patients, mild symptoms are seen, and 20 % have severe diseases. Statistics also show critical disease symptoms such as septic shocks, respiratory arrests, or multiple organ failures occur in 5% of patients(5).

As SARS-CoV-2 was broadly concentrated as a respiratory tract virus, its degree of association in the body's gastrointestinal (GI) system is now considered, and several studies were done to indicate GI symptoms prevalence (table 1). A study that took place in the Zhejiang Province of China analyzed data of 651 patients and revealed that 11.4 % of the patients presented at least one GI symptom such as nausea, vomiting, or diarrhea. The average age of these patients was 46.1 years and 10.8 % of them had pre-existing liver disease. Of COVID-19 patients with GI side effects, a subset likewise experienced fundamentally higher paces of fever, fatigue, shortness of breath, and headache(6).

In another study, data of 204 COVID-19 patients

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**Table 1: Percentage of COVID-19 patients with GI manifestations in various studies**

Study	Number of Patients, N	GI symptoms, N (%)	No GI symptoms, N (%)
Jin et al (6)	651	74 (11.4 %)	577 (88.6 %)
Pan et al (7)	204	103 (50.5 %)	101 (49.5 %)
Zhang et al (8)	139	55 (39.6 %)	84 (60.4 %)
Lin et al (9)	95	58 (61.1 %)	37 (38.9 %)
Cheung et al (15)	59	15 (25.4 %)	44 (74.6 %)
Montazeri et al (17)	611	155 (25.4 %)	456 (74.6 %)

GI: Gastrointestinal, N- Number.

with an average age of 52.9 years from three hospitals in Hubei province, including Wuhan Hanan Hospital, Wuhan Union Hospital, and Huanggang Central Hospital, were analyzed, and the results demonstrated that 103 patients (50.5%) had a digestive symptom, including lack of appetite in 81 patients (78.6% cases), diarrhea in 35 patients (34%), vomiting in four patients (3.9%) and abdominal pain in two patients (1.9%)(7).

Additionally, by separating and examining electronic clinical records, including demographics, clinical manifestation, comorbidities, laboratory data, and radiological materials of 140 hospitalized patients with COVID-19 in Wuhan, China, about 1:1 ratio of male (50.7%) and female (49.3%) and an average age of 57.0 years were reported. Fever (91.7%), cough (75.0%), fatigue (75.0%), and GI symptoms (39.6%) were the most widely recognized clinical appearances(8).

In a study done by Lin L, and colleagues, 58 (61.1%) patients showed GI symptoms, 11 patients (11.6%) had GI symptoms on initial presentation before admission, and 47 patients developed GI symptoms during hospitalization(9).

The main aim of this article is to summarize the available data regarded to GI symptoms of COVID-19.

### The Gastrointestinal manifestations of COVID-19:

#### Diarrhea

In a meta-analysis done by AGA Institute, the pooled prevalence of diarrhea symptoms across 43 individual studies, including 10,676 RT-PCR tests confirmed COVID-19 patients was 7.7% (95% CI, 7.2–8.2%). And after separating the studies done in China from the studies of the other countries, the

pooled prevalence of diarrhea of other countries showed a considerable increase to 18.3% (95% CI, 16.6–20.1%) compared with the 5.8% (95% CI, 5.3–6.4%) prevalence in China(10).

Previously in the primary stages of the pandemic, it was thought that children were less susceptible to the infection(11). However, as time passed, the number of infected children had an upward trend, and critical pediatric cases were reported(12). Despite the difficulties of distinguishing of GI symptoms caused by pediatric COVID-19 or other viral illnesses, side effects of drugs, and disturbance of GI flora, a study by Baù M and others, shows that antibiotics are used by 20.4% of children that cause diarrhea, which is more severe in younger patients struggling with lower respiratory tract infections with intravenous antibiotics treatment(13).

Overall in a systematic review done by Kumar A and co-workers, among the GI symptoms, which were studied, diarrhea was the most common symptom, seen in 9%, followed by nausea/vomiting and abdominal pain, which were presented in 5% and 4%(14).

Also, in a meta-analysis in which the pooled prevalence of GI symptoms (including loss of appetite, nausea/vomiting, diarrhea, or abdominal pain) was 17.6%, after the loss of appetite (26.8%), diarrhea was the most reported GI symptom (12.5%) followed by nausea/vomiting (10.2%), and abdominal pain/discomfort (9.2%)(15). On the other hand, in Iran, diarrhea was the second most common symptom reported in 31.8% of the patients after nausea, which was present in 42.8% of the patients being the most reported symptom. Vomiting with 26.8% and abdominal pain with 12% were the other GI symptoms in addition to the elevation of albumin, alkaline phosphatase, aspartate aminotransferase,

**Table 2: Gastrointestinal symptoms in patients with COVID-19**

Ref.	Number of patients with available data	Anorexia / Loss of appetite (n, %)	Diarrhea (n, %)	Nausea (n, %)	Vomiting (n, %)	Abdominal pain/ discomfort (n, %)	GI bleeding (n, %)
Pan et al (7)	204	81 (39.7%)	35 (17.15%)	NA	4 (2%)	2 (1%)	NA
Zhang et al (8)	139	17 (12.2)	18 (12.9)	24 (17.3)	NA	8 (5.8)	NA
Lin et al (9)	95	17 (17.9%)	23 (24.2%)	17 (17.9%)	4 (4.2%)	NA	6 (6.3%)
Mokarram et al (16)	91	40 (43.9%)	29 (31.8%)	39 (42.8%)	24 (26.3%)	11 (12%)	5 (5.4%)
Montazeri et al (17)	451	NA	42 (9.3%)	92 (20.4%) for both nausea and vomiting		22 (4.9%)	2 (0.3%)

and alanine aminotransferase in 26.3%(16).

### Nausea/vomiting

Results of reviewing 26 studies, which included 5955 COVID-19 patients (confirmed by laboratory real-time reverse transcription-polymerase chain reaction[RT-PCR] testing), showed that the overall pooled prevalence of nausea/vomiting was 7.8% (95% CI, 7.1%–8.5%) but after dividing the patients into subgroups the results varied. 1901 patients from seven studies (including patients from Germany, Singapore, United States, Australia, and The Netherlands) demonstrated a significantly higher pooled prevalence of 14.9% (95% CI, 13.3–16.6%) in comparison with the overall average prevalence and the prevalence of the studies from China, which was 5.2% (95% CI, 4.4%–5.9%)(10). In a study including 155 patients with GI symptoms out of a total of 611 SARS-CoV-2 inpatients referred to Sina Hospital, a hospital affiliated to Tehran University of Medical Sciences, 115 (18.8%) patients reported nausea/vomiting, which was the most common GI symptom and also 20 patients (3.2%) did not show any respiratory symptoms and only had GI symptoms. In this study, the ratio of men to women was 1.61 (377 men compared with 234 women), and the average age of patients was  $56.19 \pm 16.15$  years(17). The overall results of the prevalence of GI symptoms in different studies are variable (table 2).

### Liver abnormalities

The liver, located in the abdominal cavity, beneath the diaphragm, and on top of the stomach, is the second largest organ and the largest gland in the

human body, which is constantly exposed to dietary antigens, viruses, and bacteria. Medical records of hospitalized patients with SARS-CoV-2 between March and September 2020 in four different cities of Iran, including Ali Asghar Hospital of Shiraz, Bahman Hospital of Mashhad, Ganjavian Hospital of Dezful, and Razi Hospital of Rasht demonstrated that 24 patients (26.3%) had abnormal levels of either albumin, ALP, aminotransferase (AST) or alanine aminotransferase (ALT) and 10 patients (10.9%) had a previous history of liver disease.(16) In a meta-analysis that searched PubMed for studies published between January 1, 2020, and March 25, 2020, 23 studies had data on liver function tests, and their results showed that AST was elevated by 25% (559/2226) of the patients and ALT was elevated in 23% (477/2107) of the patients. Also, serum bilirubin and prothrombin time (PT), had a significant increase in 9% (130/1471) and 7% (55/750) of the patients. However, fewer studies had information about serum albumin, and it was under the normal range in 60% (491/817) of the patients(14).

57 studies were reviewed by AGA Institute and 34 had data on liver abnormalities in which 15.0% (95% CI, 13.6–16.5) of patients across 16 studies, which included 2514 patients with confirmed COVID-19 by laboratory RT-PCR testing, above the upper limit of normal AST was reported.

Abnormal ALT and abnormal bilirubin, defined as any value above the ULN, were reported in 15.0% (95% CI, 13.6–16.4%) and 16.7% (95% CI, 15.0–18.5%) of the patients across 17 and 10 studies(10).

### CONCLUSION

In patients with COVID-19, GI symptoms such as

anorexia, diarrhea, nausea, vomiting, bleeding, and abdominal pain are common, and even some patients have shown GI symptoms despite the absence of any respiratory symptoms. Many studies have shown that COVID-19 patients with GI symptoms have more severe conditions and a greater risk of mortality in comparison with patients without GI symptoms. GI symptoms should not be underestimated and sufficient attention should be paid to early or mild GI symptoms in patients, which indicates the probability of being infected and transmitting the virus. Liver injuries and elevation in enzymes may also occur in patients with COVID-19.

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