# COVID-19 and Gastrointestinal Involvement

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## Introduction

Coronaviruses (CoV) are a large family of enveloped positive stranded RNA viruses in the order of *Nidovirales*, with a crown-like appearance at electron microscope. The subfamily *Orthocoronavirinae* of the family *Coronaviridae* is further classified into four coronavirus genera: Alpha-, Beta-, Delta- and *Gammacoronavirus*. *Betacoronavirus* genus is further separated in five subgenera (Embecovirus, Hibecovirus, Merbecovirus, Nobecovirus and *Sarbecovirus*).

Additional zoonotic coronaviruses have emerged and caused outbreaks in humans: SARS-CoV (2002, Betacoronavirus, subgenus Sarbecovirus), and MERS-CoV (2012, Betacoronavirus, subgenus Merbecovirus). In late 2019, a novel coronavirus related to a cluster of pneumonia cases in Wuhan, China (SARS-CoV-2) was identified. The SARS-CoV-2 is closely related to SARS-CoV and genetically clusters within Betacoronavirus subgenus Sarbecovirus.

Coronaviruses are zoonosis, meaning they are transmitted between animals and people. Whereas previous investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans, we do not know the exact source of the virus causes COVID-19 (1).

These viruses cause illness ranging from the common cold to more severe diseases such as Severe Acute Respiratory Syndrome (SARS-CoV) (2) and Middle East Respiratory Syndrome (MERS-CoV) (3). Coronavirus disease (COVID-19) is a new strain discovered in 2019 and has not been previously identified in humans (4).

The World Health Organization (WHO) has officially declared on March 11 the outbreak of COVID-19 as pandemic, after the disease caused by the new coronavirus spread to more than 100 countries and led to tens of thousands of cases within a few months.

## Epidemiological aspects

On December 31, 2019, China reported a cluster of cases of pneumonia in people associated with the Huanan Seafood Wholesale Market in Wuhan, Hubei Province (5). Although cases were originally reported to be associated with exposure to the seafood market in Wuhan, current epidemiologic data indicate that person-to-person transmission of COVID-19 is occurring. The actual epidemiological data of the plague is reported in Figure 1.
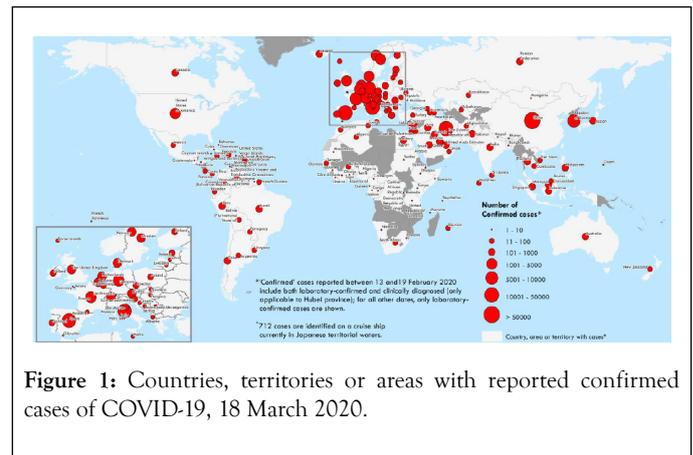


**Figure 1:** Countries, territories or areas with reported confirmed cases of COVID-19, 18 March 2020.

## Clinical aspects

The symptoms may appear 2-14 days after exposure and are commonly represented by fever, cough and shortness of breath. However, in the first case of 2019 coronavirus infection confirmed in the United States reported a 2-day history of nausea and vomiting on admission, and then passed a loose bowel movement. The authors reported positive tests of viral nucleic acid of loose stool and respiratory specimens (6). This first reported that COVID-19 might include also gastrointestinal involvement.

## Symptoms of GI involvement

Previous study has reported the viral detection in biopsy specimens and stool of patients with SARS and this may explain at least in part for the gastrointestinal symptoms (7). Also in COVID-19, gastrointestinal symptoms may be present in about 20% of the cases and are mainly represented by diarrhea, nausea, vomiting and abdominal pain (Figure 2) (8). Of particular interest is that only abdominal pain is statistically more frequent in clinically severe patients and admitted to intensive care unit (ICU) as compared to those that no require ICU (Figure 2) (8).
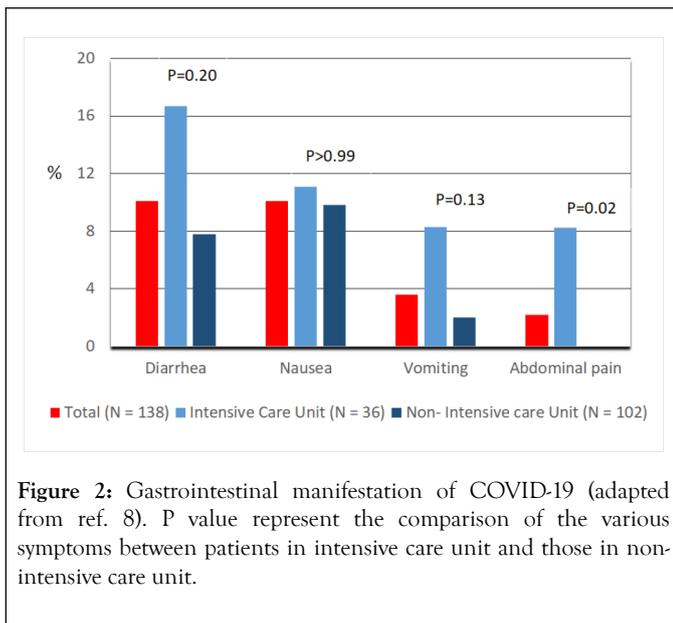
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**Citation:** Pezzilli R (2020) COVID-19 and Gastrointestinal Involvement. J Allergy Ther. 11: 291.

Of course, we need to take attention with fever in subjects who are suspected COVID-19.



**Figure 2:** Gastrointestinal manifestation of COVID-19 (adapted from ref. 8). P value represent the comparison of the various symptoms between patients in intensive care unit and those in non-intensive care unit.

**Pathogenesis of GI involvement**

While the 2019-nCoV is mainly distributed in lung, the infection also involves in the damages of heart, vessels, liver, kidney and other organs (9). 2019-nCov enters into host cells via cell receptor angiotensin converting enzyme II (ACE2) (10). ACE2 is highly expressed in the lung AT2 cells and also in esophagus upper and stratified epithelial cells and enterocytes from ileum and colon. The increased gastrointestinal wall permeability to foreign pathogens once virus infected, enteric symptoms will occur and this may suggest that GI system might be vulnerable to COVID-19 infection (11). Of course, we need to know the intestinal inflammatory pattern after coronavirus infection as happens after lung involvement (12). In fact, also in light of the possibility that drugs such *tocilizumab and* sarilumab, approved to treat rheumatoid arthritis, *have been proposed for* clinical trial in hospitalized patients with severe COVID-19 pneumonia because they are able to inhibit the receptor of proinflammatory cytokine such as interleukin 6 (13).

**Conclusions**

Even if lung involvement is the main complication of COVID-19 infection, it is possible that gastrointestinal involvement may be present and sometime may represents the onset of disease or occurs in the course of the illness. The inflammatory profile of intestine in COVID-19 affected patients need to be clarified also in view of new drugs proposed for treating these patients.

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