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Gastrointestinal symptoms in patients with COVID-19: Is there a relationship with mortality and new variations of SARS-CoV-2?

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Abstract

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although, respiratory symptoms are typical the digestive system is also a susceptible target with gastrointestinal symptoms present even in the absence of respiratory symptoms. The gastrointestinal symptoms of COVID-19 include diarrhea, abdominal pain, anorexia, and nausea among other symptoms. Some questions that remain to be answered include: Do patients with gastrointestinal symptoms have a higher mortality? SARS-CoV-2 variants are already a global reality: Do these variants present with a greater prevalence of gastrointestinal symptoms? Do patients with these symptoms warrant more intensive care unit care?

Key Words: COVID-19; SARS-CoV-2; Gastrointestinal symptoms; Intensive care unit; Variant

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Core Tip: With the emergence of new variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its clinical manifestations, the following questions have arisen: are gastrointestinal symptoms and complications the same as the other variants or are they different? And are these related to severity of the disease? In this letter to the editor, we discuss the relationship between the new SARS-CoV-2 variants with gastrointestinal manifestations and the severity of disease with the new variants.

Citation: Ribeiro IB, de Moura DTH, de Moura EGH. Gastrointestinal symptoms in patients

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TO THE EDITOR

We read with interest the article by Cao *et al*[1] titled "Coronavirus disease 2019 (COVID-19) and its effects on the digestive system."

In 2020, our team conducted a cohort study[2] evaluating 400 patients diagnosed with COVID-19 that, even though it is the largest study in Latin America, unfortunately, was not included in the author's review. In our study, 33.25% of patients reported one or more gastrointestinal symptoms, with diarrhea being the most common, representing approximately 17% of the total. This data corroborates the author's review. It was also found that when these patients had gastrointestinal symptoms, they had a greater tendency to have other concomitant symptoms, especially myalgia and fatigue ($P < 0.05$).

It was also observed that patients with chronic kidney disease ($P < 0.05$), using chronic immunosuppressants, or chronic use of angiotensin receptor blockers or angiotensin-converting enzyme inhibitors had a higher prevalence of gastrointestinal symptoms. Admission to the intensive care unit (ICU), need for mechanical ventilation, length of stay in the ICU, length of hospital stay, need for vasopressor support, laboratory results, and hospital mortality did not differ based on the presence of gastrointestinal symptoms ($P > 0.05$). Regression analyzes showed that immunosuppression [odds ratio (OR): 2.60 (95% confidence interval (CI): 1.20-5.63)], male sex [OR: 1.94 (95%CI: 1.12-3.36)], and older age [OR: 1.04 (95%CI: 1.02-1.06)] were associated with increased mortality.

As described above, our study[2] demonstrated, before the emergence of the new variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[3,4], that gastrointestinal symptoms were not associated with a greater need for ICU admission or the severity of the disease in patients in Latin America.

This is a very controversial topic; some studies suggest a less severe clinical evolution in patients with gastrointestinal symptoms[5,6], whereas in the study by Redd *et al*[7], there was no statistical difference.

The study by Leal *et al*[8], evaluating 234 European patients with digestive symptoms, also had a more favorable and non-severe prognosis.

In a review carried out by Wang *et al*[9], it was observed that pancreatic damage or mesenteric ischemia/thrombosis could increase mortality.

In the pediatric population, in the study by de Paula *et al*[10], logistic regression analysis identified that laboratory-confirmed COVID-19 pediatric patients with gastrointestinal symptoms had an increased risk of cardiac abnormalities confirmed by echocardiogram (OR: 6316; 95%CI: 1.717-79043; $P = 0.012$).

We emphasize that in all these studies there was no distinction regarding the variety of SARS-CoV-2 studied.

It is currently known that the high expression of angiotensin-converting enzyme 2 in the lung and the intestinal tract makes the small bowel and colon highly susceptible to SARS-CoV-2 infection, which offers a potential explanation for diarrhea observed in many COVID-19 patients. Since tryptophan absorption requires angiotensin-converting enzyme 2, its deficiency can alter the intestinal microbiota and cause intestinal inflammation[11].

Given the above, we believe a more realistic discussion to be made, and we ask the authors the following: (1) Do patients with gastrointestinal symptoms have more severe disease outcomes or not? (2) Do SARS-CoV-2 variants have a greater gastrointestinal involvement? (3) Do SARS-CoV-2 variants have a relationship between gastrointestinal symptoms and/or disease severity? and (4) Do these patients have a greater need for admission to ICUs?

Finally, we would like to congratulate and thank the authors on the level of shared evidence.

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