

Influence of Intestinal Inflammatory Diseases on Gastrointestinal Symptoms in Patients with Covid-19 †

Thiago Figueiredo Amaral, José Rodrigues Dos Santos Neto and Sávio Benvindo Ferreira*

Graduate Student, Center for Teacher Training (CFP), Federal University of Campina Grande (UFCG), Cajazeiras campus, Paraíba, Brazil; zztfazz@gmail.com (T.F.A.); jrs.neto15@hotmail.com (J.R.D.S.N.)

* Correspondence: savio.benvindo@professor.ufcg.edu.br.

† Presented at the 1st International Electronic Conference on Clinical Medicine, 15–30 September 2021; Available online: <https://eccm.sciforum.net/>.

Abstract: COVID-19 is characterized by pulmonary involvement, which has generated a large number of hospitalizations and studies worldwide, motivating researchers in search of a possible treatment and development of vaccines for the disease. However, other symptoms related to SARS-CoV-2 were less relevant in relation to studies published to date. Thus, there is a need to establish a relationship between patients with inflammatory bowel diseases and the symptoms of the gastrointestinal tract caused by COVID-19, since the involvement of the gastrointestinal tract affects up to 53% of patients who contract SARS-CoV-2. In this perspective, the present study is an integrative review carried out at the Virtual Health Library and PubMed based on the health descriptors: gastrointestinal diseases and COVID-19, applying the Boolean operator “AND” between them. The selection criteria used were the eligibility criteria: articles in Portuguese, English and Spanish, published between December 2019 and July 2020. Individuals with inflammatory bowel diseases, even with greater expression of ACE2, are not at increased risk of symptoms or worsening. Thus, based on the relationship between pre-existing symptoms and the symptoms of the new COVID-19, health professionals, based on their clinical experience, will be able to compose prophylactic measures and manage patients with COVID-19 and gastrointestinal symptoms more effectively.

Keywords: Covid-19; gastrointestinal symptoms; intestinal inflammatory diseases; gastrointestinal tract.

Citation: Amaral, T.F.; Neto, J.R.D.S.; Ferreira, S.B. Influence of Intestinal Inflammatory Diseases on Gastrointestinal Symptoms in Patients with Covid-19. *Proceedings* **2021**, *68*, x. <https://doi.org/10.3390/xxxxx>

Academic Editor(s):

Received: date

Accepted: date

Published: date

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2021 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Coronaviruses (CoVs) are viruses enveloped with a single positive strand RNA genome. Among those that infect humans, there is Sars-Cov-2, the agent responsible for COVID-19; a respiratory and infectious disease. It was found in bronchoalveolar lavage samples obtained from patients with pneumonia of unknown cause in the city of Wuhan, Hubei province, China, in December 2019 [1,2].

Covid-19 can cause respiratory failure, sepsis and septic shock, thromboembolism and/or multiple organ failure, including acute liver or heart damage. To date, the country has recorded more than 270,000 deaths and more than 11 million confirmed cases [3]. In this context, it is a severe respiratory syndrome in which its transmission occurs mainly via droplets or contact with contaminated objects and surfaces [4,5].

The mechanism of entry of the virus into the cell depends on the binding of the angiotensin-converting enzyme 2 (ACE2) receptor and its protein S. The ACE2 enzyme receptor, which is very present in the gastrointestinal tract, can cause direct or indirect damage to it, due to a generalized inflammatory response [6,7]. In this perspective, despite being a respiratory disease, the symptoms are varied, so the health team must be attentive, since the patient may present various symptoms, such as cough, fatigue, fever, muscle pain—common to the infection—as anorexia, diarrhea, abdominal pain, vomiting, nausea

[8,9]. Therefore, establishing relationships between patients' pre-existing diseases and their relationship with COVID-19 can reveal which individuals are prone to develop certain symptoms. Therefore, the study has the guiding question: "What is the possibility among individuals with inflammatory bowel diseases to develop gastrointestinal symptoms when contracting COVID-19?"

It is essential for medical practice and prevention programs to be aware of the likelihood that individuals will manifest any specific symptom during COVID-19 infection associated with the gastrointestinal tract. In addition, due to the lack of information on the topic, the present study aims to seek an intrinsic link between inflammatory bowel diseases and the appearance of gastrointestinal symptoms among those infected with SARS-CoV-2.

2. Methodology

A systematic search of the literature was carried out through the Virtual Health Library (VHL) and PubMed. For that, the descriptors in Health sciences (DeCS) were used: gastrointestinal diseases, COVID-19; as well as the Boolean operator "AND" between descriptors.

For the selection of articles, the following eligibility criteria were applied: articles in Portuguese, English and Spanish, published from December 2019 to July 2020, since in this period the first publications that reported gastrointestinal symptoms in patients with covid occurred -19, full text available in full. For exclusion: publications of the review genre and case reports, works that did not include in the title and abstract, the theme of the proposal and duplicate articles.

The search was carried out by two researchers on the same day, using the aforementioned descriptors on different computers and connections, in order to reduce the risk of bias in the selection of articles. In addition, in case of discrepancy between the results obtained by the researchers, a third researcher assisted in the elaboration of the search, thus minimizing the chance of errors.

3. Results and Discussion

Knowing that the ACE protein supports the infection, it is important to assess whether their expression in the GIT is directly related to the expression of symptoms. Thus, the proportions of cells that expressed ACE in the gastrointestinal tract were compared, it was observed that the upper GI tract (esophagus, stomach, duodenum) has an expression 13 times smaller than the lower gastrointestinal tract (ileum, colon, rectum) [10]. Thus, the correlation between ACE expression and TMPRSS may not be directly involved with the symptoms presented at the clinic of these patients, since the most commonly observed were in the upper gastrointestinal tract. However, the importance of proteins for the entry mechanism and pathophysiology is emphasized. Thus, more studies should be carried out in order to better understand this correlation.

In the meantime, it is also necessary to evaluate patients with pre-existing intestinal diseases that predispose greater expression of the protein. Thus, the study by Monteleone et al. [11] pointed out that patients with Crohn's disease (CD) and patients with ulcerative colitis (UC), the main inflammatory bowel diseases (IBDs) in humans, are possibly associated with an increased risk of complications, such as infections, due to immunosuppressive drug therapy and/or the chronicity of intestinal inflammation that increases the expression of ACE2. In the same study, patients with Crohn's showed ACE2 expression 1.3 times greater than that of the control, in addition to increased expression of TMPRSS2 (1.25 times greater), in contrast to ulcerative colitis with ACE expression (1.27 times less) and TMPRSS (1.5 times less) than in the control samples. However, the study by Cao et al. [8] did not show any interference in the history of gastrointestinal comorbidities in the appearance of symptoms and infection.

Thus, although patients with Crohn's present more expression of ACE2, this does not support an increased risk of infection in patients with previous inflammatory bowel diseases, since, according to Guerra et al. [12], only 82 of the 805 patients (10.2%) with inflammatory bowel disease, were diagnosed with covid-19, with 51.2% having Crohn's; the prevalence of gastrointestinal symptoms was the same found in patients without previous diseases 41 (50%). Thus, as demonstrated by Lee et al. [10], a greater expression of these proteins does not directly reflect a greater involvement in these tissues.

4. Conclusions

The evidence points out that the increased expression of ACE does not corroborate an increased risk in patients with inflammatory bowel diseases, therefore it does not fit the risk profile. However, the importance of further research is highlighted in order to elucidate the association between the ACE protein and the manifestation of symptoms.

Funding:

Institutional Review Board Statement:

Informed Consent Statement:

Data Availability Statement:

Conflicts of Interest:

References

1. Ren, L.L.; Wang, Y.M.; Wu, Z.Q.; Xiang, Z.C.; Guo, L.; Xu, T.; Jiang, Y.Z.; Xiong, Y.; Li, Y.J.; Li, X.W.; et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chin. Med J.* **2020**, *133*, 1015.
2. Zhang, S.Y.; Lian, J.S.; Hu, J.H.; Zhang, X.L.; Lu, Y.F.; Cai, H.; Gu, J.Q.; Ye, C.Y.; Jin, C.L.; Yu, G.D.; et al. Clinical characteristics of different subtype and risk factors for the severity of illness in patients with COVID-19 in Zhejiang, China. *Infect. Dis. Poverty* **2020**, *9*, 85.
3. Brasil. Ministério da Saúde Coronavirus Brasil. Brasília. 2021. Available online: <https://covid.saude.gov.br> (accessed on 12 October 2020).
4. Xie, Y.; Wang, Z.; Liao, H.; Marley, G.; Wu, D.; Tang, W. Epidemiologic, clinical, and laboratory findings of the COVID-19 in the current pandemic: Systematic review and meta-analysis. *BMC Infect. Dis.* **2020**, *20*, 640.
5. Brasil. Ministério da Saúde. Guia de vigilância epidemiológica. Brasília. 2020. Available online: <https://coronavirus.saude.gov.br/manejo-clinico-e-tratamento> (accessed on 12 October 2020).
6. Pan, L.; Mu, M.; Yang, P.; Sun, Y.; Wang, R.; Yan, J.; Li, P.; Hu, B.; Wang, J.; Hu, C.; et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am. J. Gastroenterol.* **2020**, *2020*, 115.
7. Luo, S.; Zhang, X.; Xu, H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). *Clin. Gastroenterol. Hepatol.* **2020**, *18*, 1636.
8. Cao, C.; Chen, M.; He, L.; Xie, J.; Chen, X. Clinical features and outcomes of COVID-19 patients with gastrointestinal symptoms. *Crit. Care* **2020**, *24*, 340.
9. Kaafarani, H.M.A.; el Moheb, M.; Hwabejire, J.O.; Naar, L.; Christensen, M.A.; Breen, K.; Gaitanidis, A.; Alser, O.; Mashbari, H.; Bankhead-Kendall, B.; et al. Gastrointestinal complications in critically ill patients with COVID-19. *Ann. Surg.* **2020**, *272*, e61–e62.
10. Lee, J.J.; Kopetz, S.; Vilar, E.; Shen, J.P.; Chen, K.; Maitra, A. Relative Abundance of SARS-CoV-2 Entry Genes in the Enterocytes of the Lower Gastrointestinal Tract. *Genes* **2020**, *11*, 645.
11. Monteleone, G.; Franzè, E.; Laudisi, F. Expression of Receptors for SARS-CoV-2 in the Gut of Patients with Inflammatory Bowel Disease. *Gut Liver* **2020**, *14*, 530–531.
12. Guerra, I.; Algaba, A.; Jiménez, L.; Mar Allier, M.; Garza, D.; Bonillo, D.; Esteban, L.M.M.; Bermejo, F. Incidence, Clinical Characteristics, and Evolution of SARS-CoV-2 Infection in Patients With Inflammatory Bowel Disease: A Single-Center Study in Madrid, Spain. *Inflamm. Bowel Dis.* **2020**, *27*, 25–33.