

January, 25<sup>th</sup> 2021

**Professor Lian-Sheng Ma**

**Editor-in-Chief of World Journal of Gastroenterology**

Dear Professor Lian-Sheng Ma,

Thank you for the opportunity to revise our manuscript for further consideration for publication at the World Journal of Gastroenterology. Below we provide a point-by-point response to the questions and suggestions raised by the reviewers. We think the new version of our manuscript incorporating the reviewers' feedback may clarify the aims and findings of the study and we hope you will find it suitable for publication at the World Journal of Gastroenterology.

Sincerely,

Natalia Sousa Freitas Queiroz

Paulo Gustavo Kotze

**REVIEWER COMMENTS:**

The IBD societies and experts have strongly recommended that patients should not discontinue their IBD medications. 1. Did patients with IBD infected COVID-19 continued their IBD medications? 2. Is there any known difference between CD and UC in terms of COVID-19 infection risk and outcome? 3. What were the common manifestation of COVID-19 in patients with IBD?

Thank you very much for these important considerations. Even though we recognize the lack of literature addressing these important questions, this study aimed to assess geographical distribution of IBD patients at highest risk of COVID-19 and correlate these data with COVID-19 mortality rates in different states of Brazil. We did not evaluate outcomes of COVID-19 in IBD patients in Brazil, due to the methodology of the study. We added a text acknowledging this limitation in the discussion session as follows:

“Important additional limitations of our study include the absence of follow-up to patients who replied the survey. By not having this information, we could not describe in detail if patients who had COVID-19 infection continued their medications, possible differences between UC and CD or common manifestations of SARS-CoV-2 among included patients, due to methodological issues.”

Noteworthy, a recent study from our group described the characteristics of patients with IBD with a positive test for SARS-CoV-2 and evaluated the association between clinical characteristics, IBD therapies and COVID-19 symptoms with the need of hospitalization in Brazil <sup>[1]</sup>. Among 74 IBD (72,6% CD) patients, it was showed that the proportion of IBD patients who stopped therapy during COVID-19 was 64.0% for biologics, 53,6% for immunomodulators and 9.5% for corticosteroids. Gastrointestinal symptoms attributable to COVID-19 were reported in 52.7% of patients and the most common symptom was diarrhea (92.3%). Clinical complications from COVID-19, defined as thromboembolic events, gastrointestinal bleeding, renal or cardiac disfunction and/or other unspecified complications, were reported in 21.6% of patients.

In addition, we do not believe there is a significant difference between CD and UC in terms of COVID-19 infection risk and outcome. For instance, an initial analysis of 525 IBD patients from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD), an international registry developed in order to collect information from IBD patients globally with confirmed COVID-19 infection and its clinical characteristics, outcomes and complications, showed that increasing age, comorbidities, and corticosteroids were associated with higher risk of complications of COVID-19. In a Multivariable regression, diagnosis of CD was not associated with higher risk of experiencing a composite outcome of ICU admission, ventilator support, and/or death as compared with UC/IBD unspecified (Odds Ratio [95% CI] 0.76 [0.31–1.85],  $p=0.54$ ) <sup>[2]</sup>.

**References:**

1. Marcela V, Marina M, Caio F, Fabio T, Liliana C, Rogerio S-H, et al. P059 Corticosteroids, Aminosalicylates and Gastrointestinal Symptoms Are Associated With the Need of Hospitalization in Patients With Inflammatory Bowel Diseases and COVID-19. Off J Am Coll Gastroenterol | ACG 2020;115.
2. Brenner EJ, Ungaro RC, Gearry RB, Kaplan GG, Kissous-Hunt M, Lewis JD, et al. Corticosteroids, but not TNF Antagonists, are Associated with Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results from an International Registry. Gastroenterology 2020 Aug;159(2):481-491.e3.