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Letter to the editor

Response to "Methodological Considerations for Assessing the Impact of Gastrointestinal Symptoms in Patients with COVID-19"

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Dear Editor,

Regarding Dr. Azañero-Haro's comments on our article "Morbidity and Mortality in COVID-19 Patients With and Without Gastrointestinal Symptoms," we, the authors, believe his analysis provides valuable considerations that enrich the scientific discussion on this topic.

Concerning the study period, it is important to clarify that our data were collected between March 2020 and September 2021—a time when understanding of COVID-19 and its multisystemic impact was still emerging. Although our article was published in 2024, the analysis was based on the information and management guidelines available during that earlier period. As we all know, the pandemic represented a dynamic clinical scenario in which evidence and therapeutic strategies evolved progressively as new studies and recommendations emerged[1,2].

We understand the author's concerns about liver function and its potential relationship with COVID-19 severity. At the time, altered liver markers were considered potentially relevant for prognosis[3,4]. However, the scientific community has since refined this interpretation, and it is now recognized that elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels may reflect a patient's clinical status without necessarily predicting outcomes.

Furthermore, COVID-19 management has changed substantially since the pandemic's onset[2]. During our cohort's data collection period, various therapeutic strategies were employed—some of which, such as certain antivirals or immunomodulators, are no longer part of standard treatment. This may have influenced the interpretation of results related to liver function. Current management has been simplified and focuses primarily on corticosteroids in selected cases, reinforcing the need to interpret our findings within their original temporal context[5].

Regarding sample size and statistical power, as is common in scientific research, our initial calculations were based on certain epidemiological and statistical assumptions whose validity could only be confirmed after data collection. Therefore, for outcomes with lower-than-expected frequency (such as mortality and bacterial coinfection), the analytical capacity—particularly statistical power—may have been affected. The knowledge-building process inherently involves refining such assumptions, and our study provides a valuable starting point for future research.

We appreciate this opportunity for academic exchange and reiterate the importance of continued investigation into COVID-19's multisystemic effects. Evidence in this field

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continues to evolve, and future studies may address these questions with updated information and optimized methodological designs.

We thank Dr. Azañero-Haro for his comments and the editorial committee for allowing us to participate in this valuable discussion.

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