



PEER-REVIEW REPORT

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Title: Gastrointestinal involvement in paediatric COVID-19 – from pathogenesis to clinical management: A comprehensive review

Reviewer's code: 00008869

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Italy

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Comments on the abstract: 1.- In the first paragraph of the page 2, it says that "the majority of them are children", this can imply 2 scenarios, are the most frequent infected patients children? Or infected children are more willing to expose gastrointestinal symptoms? A more targeted and strong statement should be made. 2.- From the abstract based on my first read, it is explicit that the Gastroenterological manifestations are not a "risk factor" for severe COVID-19 disease, this aspect from my own perspective and dependent on the way the Journal style, should be entailed to a more closed open questions to make it more "attractive" to the readers. Comments on the Main text: 1.- On page 3, first paragraph of the introduction, the authors should state a reference in the aspect of when it was listed as a pandemic? Who declared the pandemic? Make more specific argument on the cause and declaration of the pandemic. 2.- On page 3, second paragraph, it says that children with MIS-C "often" presents with abdominal pain, which is ambiguous, abdominal pain is a diagnostic criteria for the syndrome. 3.- On page 4, my best idea would be to make more emphasis on how viral infection from SARS-CoV-2 induces a elevation of liver enzymes and bilirubin, since this is a review paper focused on gastrointestinal symptoms, more emphasis should be made on the causes and try to dig more on the "cytokine storm". 4.- On page 5, the paragraph about clinical manifestations from my perspective is lacking more information regarding the severe evolution of patients with COVID-19 in pediatric age, although it is mentioned in a Spanish source, a more strong statement should be made since this is one of the "hooks" of the abstract and one of the justifications to issue this review. 5.- On page 5 the second paragraph after diagnosis, they describe in detail the laboratory values etc, but should this not be included in the clinical manifestations? Diagnosis can have many optics, one can describe what tools do you use to diagnose the disease? Others and most



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likely the only tool that has been used to diagnose SARS-CoV-2 are RT-PCR, NAAT and those, my best bet is that lymphocyte count, etc. are not part for a clinician to detect if the patient has or not the virus? From my point of view, this information regarding the clinical laboratory values should be included in the "clinical manifestation segment" and the rest for example page 6 4th paragraph should be left here as they are the only means to detect and diagnose the virus, the others are just clinical manifestations and consequences of the disease itself. 6.- On page 9, last paragraph, please correct "partecipants" to participants. My point of view that more emphasis should be made on why celiac patients have a susceptibility to get infected with bacteria or virus? And how does that translate to SARS-CoV-2? How about addressing a potential bias in respect as patients with previously diagnosed gastrointestinal disease are more exposed to physicians and more leaning towards receiving standard of care? 7.- On page 11, the first paragraph needs reference on the last statement as per "IBDs tend to be more extensive and severe in children than in adults". Main consensus: From my personal point of view, the strongest segment of the paper is where the characteristics to each chronic gastroenterological conditions are made: such as IBD, Celiac Disease, Transplant, Abdominal surgery; I really enjoyed reading those and most specially how the practice of medicine in each of the area of the specialty have been impacted and how that has changed the epidemiological-clinical picture of patients. Although this is a review, more emphasis should be made on clinical manifestations and a reorganization of the laboratory values which are part of the disease manifestations and not of diagnosis. I guess this review should be used as a bridge to issue key recommendations for own "each scenario" in respect of each chronic gastrointestinal disease in the pediatric age; both clinicians and patients can benefit from it. Page 2 line 44 paediatric patients, correct it through out the paper Page 8 line 169 NPS in order to identify SARSCoV2. Spell out NPS