Dear editor,

The authors would like to thank the referees for their careful review. Undoubtedly, the comments have greatly contributed to enhancing our work. All remarks and suggestions have been addressed point by point. Every modification to the manuscript's text has been directly incorporated into the document and are highlighted in yellow. Please, do not hesitate to contact us in case of any further doubt.

Kind Regards,

Mauro F F Mediano, PhD

Evandro Chagas National Institute of Infectious Disease/ Oswaldo Cruz Foundation

---

Reviewer A:

Recommendation: Revisions Required

---

1. Relevance of the title to the content of the article

Regular

Remarks

The title is: A descriptive study of COVID-19 clinical profile in children and adolescents: a Brazilian experience in patients admitted to a pediatric public reference center in the city of Rio de Janeiro during the first pandemic wave.

The title is long, it is suggested that the authors make it shorter by including the population, place of study and the period, for example: Clinical profile during the first pandemic wave in children and adolescents with COVID-19 at pediatric public hospital, Rio de Janeiro, Brazil

Authors´ reply: The authors accepted the suggestion and modified the title in the manuscript.

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Regular

Remarks

The number of words is optimal.

Authors´ reply: Thank you.

Background: It would be appropriate to include the period of the first wave of the pandemic, because not all readers know this information about Brazil.

Authors´ reply: We appreciate the reviewer for this comment. In Brazil, the first COVID-19 wave included the period between February 25, 2020, to November 5, 2020 and the second COVID-19 wave included the period from November 6, 2020, to April 30, 2021. Since our study included patients

from March 2020 to March 2021, we corrected this information in the manuscript including the second pandemic wave in Brazil according to the following reference: Zeiser et al. First and second COVID-19 waves in Brazil: A cross-sectional study of patients' characteristics related to hospitalization and in-hospital mortality. Lancet Reg Health Am. 2022 Feb:6:100107.

Methods: It would be good to check if the population was under 18 years old or less than or equal to it. Usually all patients greater than or equal to 18 years of age are considered adults in most countries. It is important to mention in the methods section what type of analysis was performed (descriptive, bivariate analysis, etc.), the use of the p value or 95% CI.
Authors´ reply: The authors reviewed the information regarding the age range of the patients and incorporated all suggestions into the abstract text.

Results: It is important to mention the frequency of admission to the ICU or the use of mechanical ventilation to see the severity of the disease.
Authors´ reply: The information regarding the frequency of admission to the ICU was incorporated into the abstract.

Conclusion: The authors could start the sentence with, in our hospital… because their data cannot be extrapolated to generalize…
Authors´ reply: The authors incorporated this suggestion into the abstract text.

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner
Regular

Remarks
The authors mention that the clinical characteristics are controversial in children and adolescents. This statement is not entirely correct, because according to the waves and specifically the predominance of the variant, some characteristics have been clearly determined.
It is necessary to describe in a paragraph why it is important to describe the characteristics of the patients during the first wave (justification of the study).
It is also important to mention some studies that describe the clinical characteristics of patients during the first wave in some other studies and the results of these (admission to the ICU, use of mechanical ventilation, mortality), to give the reader the context that the results will be presented.
Authors´ reply: We have rephrased the introduction section to improve the manuscript comprehension and better contextualize the readers.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.
Regular

Remarks

Study Design

The age must be reviewed. Have the authors truly considered patients over 18 years of age? Or were they all under 18 years of age? That is, up to 17 years, 11 months and 29 days.

Authors´ reply: The authors corrected the information related to the patients' age range.

Population

It is suggested to include the approximate population of patients treated per year and how much it represents of the total child population of Rio de Janeiro, so that the reader can understand that it is a hospital that receives a large influx of patients. It is also important to mention if they have critical service specialties (ICU) and if they receive patients from other regions of Brazil.

Authors´ reply: The following information was included in the manuscript: This is the largest pediatric reference center in the public health system in the state of Rio de Janeiro. On average, the hospital conducts 6,000 outpatient consultations from several medical specialties, 300 hospital admissions, and 190 surgeries per month.

There is no mention of the inclusion and selection criteria of patients. If a patient was referred from another institution, was he or she entered the analysis? Were there patients excluded?

Authors´ reply: This information was included in the manuscript.

It is important to mention of all the patients who had Covid-19 infection in the emergency, how many patients were hospitalized and whether this was their total sample.

Authors´ reply: Unfortunately, since this is a retrospective study, we do not have this information. This is described as a limitation of the study.

What criteria were used to hospitalize a patient; did they all have to have some respiratory complication?

Authors´ reply: At the time of the study conduction (in the beginning of the pandemic period), the criteria used to hospitalization was not fully determined and was mostly based on clinical judgement about the patient's symptoms. This information was included in the manuscript.

If a patient had a COVID-19 infection but did not develop pneumonia, and some other disease that was not respiratory (for example, pyelonephritis), were they included in the study?

Authors´ reply: All patients < 18 years old, with confirmed diagnosis of COVID-19 by nasopharyngeal or oropharyngeal RT-PCR swab test for SARS-CoV-2, that needed to be hospitalized based upon medical discretion were included in the study. The reason for hospitalization was COVID-19.

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

Yes

Authors´ reply: Thank you.

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.
Regular

Remarks
I cannot view the tables in the document.
Authors´ reply: We apologize for that. All tables were included at the end of the manuscript.

It would be interesting to describe the comorbidities found in that 32.4%, because COVID-19 had a worse outcome in those people with these characteristics (comorbidities, for example, heart disease, chronic lung disease, etc.).
Authors´ reply: The comorbidities were described at table 1.

It is important to mention whether all hospitalized patients used supplemental oxygen, and what type of non-invasive ventilation they used (high-flow nasal cannula, CPAP). Were there patients with mechanical ventilation?
Authors´ reply: The number of patients that needed non-invasive mechanical ventilation was described in table 1. Unfortunately, information on the type of non-invasive ventilation was not available.

Did any of the patients have, apart from Covid-19 infection, any other illness that was the main reason for the patient's admission?
Authors´ reply: The main reason for hospitalization was COVID-19.

Were there patients who developed multisystem inflammatory syndrome? And if there were criteria (WHO-CDC) used for diagnosis and what organ damage there was (a characteristic in misc in the elevated d-dimer, but they mention that none of the participants had elevation of this marker).
Authors´ reply: Only one case was observed. This information was included in the body of the manuscript and is also presented in table 1.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.
Regular

Remarks
The first paragraph should only mention the main findings and implications of these results.
The comparison with other studies may correspond to the second paragraph onwards.
Although studies from Europe are important, they must be complemented with studies from Latin America or Brazil itself, so that the reader understands the context of the epidemiology of covid-19 in this region.

Authors´ reply: We appreciate the reviewer for this comment. We proceed with the changes suggested by reviewer. We also included some additional references of studies conducted in Brazil to better contextualize the readers about the epidemiology of COVID-19 in Brazil.

More important than sex is to describe age and compare with other studies. Because the restrictions according to each country made the pediatric population less affected because they did not go out and had no contact, that may explain that about a quarter of the population is only children under 10 years old. It would be important to mention what the health restrictions were like in Rio de Janeiro and how this could have influenced the fact that only more adolescents have been hospitalized than children.
Authors´ reply: In Brazil, preventive measures for COVID-19 were established for the entire population in the initial period of pandemic. Schools were closed for both children and adolescents without distinction. Our study demonstrated a greater number of hospitalized children in comparison to adolescents. This finding was also observed in a previous study that demonstrated 25% lower odds of hospitalization among adolescents in comparison to children, despite a higher severity of COVID-19 among adolescents (Antoon et al., 2021). This may indicate a compassionate concern of health professionals with the clinical management of children with COVID-19 in the beginning of the pandemic period, where no previous information about the management of the disease was available. This information was included in the manuscript.

It is mentioned that 38.2% had pneumonia, which means that there were patients hospitalized for other causes that are not necessarily attributed to COVID-19, this must be clarified in the methodology and results. Was it possible to have tests for other viruses, such as influenza, VSR, adenovirus concomitant with covid-19? This should also be mentioned.
Authors´ reply: COVID-19 was the cause of hospitalization for all patients. This information was included in the methods section. The information of 38.2% refers to associated bacterial pneumonia nd this information was included in the manuscript.

Did all patients have a chest x-ray, ultrasound or tomography? Since it is a limited sample, it is important to mention the patients who underwent the examination and the denominator, to know exactly what the percentage refers to.
Authors´ reply: Information about complementary exams are included in table 1.

It is important to clarify whether all the patients who were admitted to the ICU were due to COVID-19 or because they decompensated due to their comorbidities or another condition. Not every COVID-19 infection predisposes admission to the ICU. This should be clear in those two patients with diabetes, whether they were admitted to the ICU for pneumonia or diabetic ketoacidosis. “The two adolescents with diabetes required ICU admission, reinforcing the need for greater care in children and adolescents with this condition due to the risk of complications (18).”
Authors´ reply: We appreciate the reviewer for giving us the opportunity to clarify this aspect of the study. In our study, we only included patients that were hospitalized due to COVID-19. This information was included in the methods section, as follows:

There was a high frequency of oseltamivir use (90%), were there patients with other viral coinfections, for example influenza? Was there any hospital protocol that indicated its use? Did those patients who did not have COVID-19 pneumonia still receive oseltamivir? That should be mentioned.

Authors´ reply: Information of other infections during the hospitalization can be found in table 1. Regarding the use of oseltamivir, as discussed in the 8th paragraph of the discussion section, patients included in this study were infected during the first year of COVID-19 pandemic in Brazil (March 2020 to March 2021), in which medical knowledge about clinical management of COVID-19 was uncertain. Therefore, the medications used to treat patients at that time may noy reflect the best therapeutical treatment options to treat patients with COVID-19 nowadays.

Among the limitations, it is important to mention the selection bias since the patients came from a tertiary center and may have only managed moderate to severe complicated patients.

Authors´ reply: This was included as a limitation of the study.

It would be appropriate to see which variant was identified in the first wave in Rio de Janeiro and whether or not this can explain the moderate to severe cases of the patients.

Authors´ reply: Unfortunately, since this is a retrospective study, it is not possible to identify the variant of each case included in the study.

What would be the strengths of your study?

Authors´ reply: The strength of the study is described in the last sentence of the limitation paragraph, as follows: On the other hand, because COVID-19 prognoses are better in pediatric populations, hospitalizations are not common, reinforcing the originality of the – albeit only descriptive – study findings.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Regular

Remarks

The conclusion addresses the terms mild/moderate COVID-19, but nowhere in the methodology does it describe how that classification was made. It is understood that the severe cases were those who were admitted to the ICU, but who were the mild ones? This must be clarified and how it was classified to give that conclusion.

Authors´ reply: We agree with this important comment from the reviewer. Since we did not use a specific criterion to classify the severity of COVID-19 and also considering that severe cases were those that requires admission to ICU, we changed our conclusion to "To conclude, COVID-19 was not severe in most of the children and adolescents in the study."

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Good

Remarks

The references are appropriate.

Authors´ reply: Thank you.

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Acceptable

Authors´ reply: Thank you.

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it.

The main weakness is the limited population, but this can be overcome by addressing the public health aspects that Rio de Janeiro carried out and how this could influence the epidemiology of covid-19 in children in its institution.

Authors´ reply: Thank you.

General comments

The article is important because it shows the cases and the initial management of the pandemic in a tertiary hospital in Rio de Janeiro. I leave some comments to improve the quality of the article and the interpretations it may have for readers.

• I suggest reducing the length of the title

• Improve the writing of summary methods

• Improve the justification: why is it important to describe the characteristics of the first wave patients?

• Some characteristics of the hospital should be mentioned (how many patients they treat per year, and if they receive referrals from other centers, and if they have a complete intensive care unit).

• Mention the inclusion and exclusion criteria of the study and, above all, if all patients who were admitted for symptoms other than Covid, but who had a positive PCR-COVID-19 result, were included in the analysis.

• In the discussion, the measures that Rio de Janeiro had to avoid contagion by covid-19 should be mentioned and how this could explain its results. In addition, they should add the strengths of their study and compare the results with regional studies, which could having had a similar situation in terms of human or logistical resources for managing the pandemic.

• If they are going to mention the term mild, moderate or severe, they must include this classification within the methodology.

Authors´ reply: We appreciate the reviewer for this comprehensive evaluation. We tried to address all aspect that were raised by the reviewer with the certainty that all these aspects will improve the quality of our manuscript.

Reviewer C:

Recommendation: Revisions Required

---

1. Relevance of the title to the content of the article

Good

Authors´ reply: Thank you.

Remarks

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Good

Authors´ reply: Thank you.

Remarks

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Regular

Remarks

improve the justification of the problem, explaining why it was decided to carry out a covid 19 study in a population that did not present high mortality.

Authors´ reply: We appreciate the reviewer comment. We have included an additional paragraph to better justify the study.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

Good

Authors´ reply: Thank you.

Remarks

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

No

Authors´ reply: Please, see page 5 – ethical aspects.

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Good

Remarks

Authors´ reply: Thank you.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Regular

Remarks

improve the purpose of the article, emphasizing the contribution of the results to the current knowledge of the problem.

Authors´ reply: Discussion was improved, as suggested by reviewer.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Good

Remarks

Authors´ reply: Thank you.

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Good

Remarks

Authors´ reply: Thank you.

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Needs some language corrections

Authors´ reply: Manuscript was reviewed from a native English speaker.

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

Justify why you chose a population with very low covid 19 mortality and what new contributions will reach those already known.

Authors´ reply: Aspects related to this were included in the introduction section to better contextualize the study.
