

Peer Review File

Article information: <https://dx.doi.org/10.21037/pm-22-19>

Reviewer A

General comment

The authors presented a manuscript with the main aim to provide an up-to-date information about COVID-19 related mortality and relevant risk factors in children and young people (CYP). The design of the study was a narrative review. They conducted a literature search using Pubmed and Web of Science specifically for papers about COVID-19 related mortality and relevant risk factors in CYP. According to the report, it was estimated that 99.995% of infected children and young people survived the infection, with wild-type and Alpha being the predominant variants. Currently, the Omicron variant has shown to be more transmissible and less virulent than previously circulating variants. They found that those who are, with multiple co-morbidities, from non-white ethnic groups, and in low- and middle-income countries have increased risk of intensive care unit admission and death. This is an interesting study. However, the study has several limitations that should be addressed by the authors

Specific comments

Comment 1: The Abstract section needs a complete overhaul. The “Key Content and Findings” subsection should focus on the results of the analysis and not on general comments.

Reply 1: Thank you for the comment and the abstract part is reorganized as requested. (Line 19-37)

Changes in the text: Background and Objective: Coronavirus disease 2019 has been a most important global issue since December 2019. Although for children, the clinical course of Coronavirus disease 2019 is milder, it may still cause a multi-system inflammatory syndrome and has rendered 22,000 deaths among children and young people. The objective of this review is to provide an up-to-date information about Coronavirus disease 2019 related mortality and relevant risk factors in children and young people.

Methods: This study provides a narrative review of Coronavirus disease 2019 related mortality and relevant risk factors in children and young people.

Key Content and Findings: With the Omicron being the dominant circulating variant, the absolute risk of death from Coronavirus disease 2019 is extremely low in children and young people. We found that those who are with multiple co-morbidities, from non-white ethnic groups, and in low- and middle-income countries might have increasing risk of intensive care unit admission and death. And vaccination is always critical to reduce the incidence of severe Coronavirus disease 2019 cases.

Conclusions: This review provides an overview of the Coronavirus disease 2019 related mortality and relevant risk factors. Understanding of this disorder continues to evolve, and prompt diagnosis and treatment allow for the best

possible outcome for patients with Coronavirus disease 2019.

Comment 2: I don't understand where the 99.995% value came from.

Reply 2: Thank you for the comment and we have modified the expression (line 29-30).

The value of 99.995% was quoted from one research with a more strict evaluation criteria to differentiate between children and young people who died of SARS-CoV-2 infection and CYP who died with a positive SARS-CoV-2 test as a coincidental finding. (Smith C, Odd D, Harwood R, Ward J, Linney M, Clark M, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. Nat Med. 2022 Jan;28(1):185–92.)

Changes in the text: the absolute risk of death from Coronavirus disease 2019 is extremely low in children and young people.

Comment 3: Methods

This section also needs a complete overhaul. I suggest including a narrative literature review flowchart showing the records included and excluded from the analysis.

Reply 3: Thank you for the comment. We have provided a detailed search strategy summary in table 1. As a narrative review, we only kept the record of included studies. And we are sorry that the inclusion and exclusion flowchart of the analysis is unavailable yet.

Comment 4: Discussion

My major concern is with the scope of the research. A quick analysis shows the absence of relevant studies with representative cohorts from different regions of the world. For example, Oliveira et al. reported data on more than 20,000 Brazilian children and adolescents with COVID-19 (Lancet Child Adolesc Health. 2021;5(8):559-568 J Pediatr. 2022;244:178-185 e173); Cloete et al. reported the first cohort of children infected during the omicron period in South Africa (Lancet Child Adolesc Health. 2022;6(5):294-302). These are some examples that the scope of the research should be reassessed by the authors. The contents of Table 1 seem a little disjointed to me. I really feel that Table 1 could be better organized. For example, the Table should include the setting where cohorts were pooled (hospital or outpatient)

Reply 4: Thank you for the comment. We have reviewed the search strategy and added some researches, however, the reported mortality rate and the dynamic trend of mortality still remained the same. And As the table 1 serves to show the mortality rate from different regions of the world, we have presented a varying mortality rate in the main text and included the table 1 into supplemental material. (Line 67-69)

Change in the text: Previous studies have revealed that between 1% and 5% of all COVID-19 cases occur in children(6,9), with an varying mortality rate between less than 1% to 8% in hospitalized children(10–22).

Comment 5: Conclusion

The Conclusion section is vague and did not address the main purpose of the study.

Reply 5: Thank you for the comment. We have modified the conclusion part as requested. (Line 165-168)

Change in the text: Since the clinical and demographic characteristics varies when different variants circulate, understanding of this disorder continues to evolve, and prompt diagnosis and treatment allow for the best possible outcome for patients with COVID-19.

Reviewer B

Comment 1: missing references about the five variants - introduction - line 47 to 50.

“So far, there have been five variants of concern (VOCs): Alpha (B.1.1.7, U.K. variant), Beta (B.1.351, South Africa), Gamma (P.1, Brazil), Delta (B.1.617.2, India), and Omicron (B.1.1.529, Africa).”

Reply 1: Thank you for the advice, we have added reference. (Line 44)

Changes in the text: So far, there have been five variants of concern (VOCs)(2). (Reference 2. World Health Organization. Tracking SARS-CoV-2 variants [Internet]. Available from: <https://www.who.int/activities/tracking-SARS-CoV-2-variants>)