



Comment on: Emerging Evidence on Multisystem Inflammatory Syndrome in Children Associated with SARS-CoV-2 Infection

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We read Sood et al.’s article on “Emerging evidence on multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection: a systematic review and meta-analysis” [1]. This article is timely and essential, given much is still uncertain about how COVID-19 affects children. The authors summarized the pathogenesis of multisystem inflammatory syndrome in children (MIS-C) resulting from SARS-CoV-2 infection and the therapeutics administered to treat the condition. Unfortunately, this review had several methodological issues and failed to provide valid systematic evidence that can affect the inferences made from the review’s findings.

The authors did not indicate the guidelines they used to report this review. The International Committee of Medical Journal Editors recommends the authors follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 guidelines to conduct and report systematic reviews. When we assessed the reported items in the review with the PRISMA 2009 checklist, 22 of the 27 items were not reported at all or partially reported causing concern about the overall conduct of the review [2]. Alternatively, Sood and colleagues could have used the Meta-analysis Of

Observational Studies in Epidemiology (MOOSE) to report this review. When applied, we found that 27 of the 33 MOOSE checklist elements were not reported in this review [3]. The gross omission of information significantly impacts the quality and overall conclusions of this review.

While the authors stated they would summarize the evidence of MIS-C and available therapeutics, there was no explicit research question stated, making the objective of this review unclear. While the population of interest is assumed to be children given the title and information in the introduction, there is no additional information on the PICOT characteristics of interest to guide the search for studies. For example, the age category of the children should be defined. The roles and contributions of each author were also not addressed. There was no mention of inclusion or exclusion criteria for this review and no evidence of how authors resolved study selection discrepancies. Additionally, there was no indication that this review’s protocol was registered with PROSPERO; protocol registration is imperative to ensure the integrity of the review procedures, reduce research duplication, and minimize reporting and publication bias. All these factors undermine the transparency of the review process.

There was also a discrepancy in what databases were used to search studies. The authors do not list PubMed as a database searched in the abstract or methods section; yet, it is listed as a database in their PRISMA diagram. The authors also potentially omitted critical databases to search for studies, such as EMBASE, CENTRAL, or Cochrane Reviews, resulting in evidence selection bias. These databases could have identified additional studies to be included in the review. However, the authors provide a partial list of the search terms used in this review given the statement “and related terms.” Without an exact search string, it is impossible to replicate this review. Furthermore, the authors do not provide details on how articles were screened, what data was abstracted, and how the data were abstracted from the studies. It is unclear whether more than one author screened the articles independently and

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how discrepancies were resolved. Having a single author execute the article screening and data abstraction introduces reviewer bias, which can subsequently bias the results of the research.

The authors state that they used the STROBE reporting guidelines to assess risk of bias. The STROBE statement was developed to improve the reporting of observational studies [4]. It is an inappropriate and ineligible tool to use to assess the risk of bias. Notwithstanding, data on the risk of bias within studies presumably conducted was not provided in this review. The quality of primary studies is critical to the internal validity of a systematic review and meta-analysis. Failure to disclose the quality of evidence of the included studies undermines the results and conclusions drawn from the review. Reviewing the supplemental material, it was observed that 15 of the 17 studies were case series or a case report. Case series have the lowest quality of evidence. Again, low quality of evidence weakens the strength of recommendations based on the quality of evidence and affects the validity of the findings [5]. Since the authors failed to discuss the risk of bias assessment, the quality of evidence generated by this review is questionable.

Additionally, the authors do not provide information on control/comparison groups and outcomes of interest. This missing information, coupled with the ambiguity in this review's objective, makes it hard to understand the purpose of reported results. The authors report a pooled meta-analysis of patient characteristics. However, no details are provided on how the data was handled, how the results of studies were compiled, issues of heterogeneity, or excessive influence from a single study. We noticed that the authors combined non-peer reviewed articles with peer reviewed articles and reported very high levels of heterogeneity. However, no information is provided on how they tested for heterogeneity, nor an assessment to identify the causes for the high heterogeneity. Internal validity of results depends on the methodological and statistical rigor of the included studies. The authors do not discuss any limitations of their review or the studies they reviewed. The blatant failure to critically appraise the included studies and document the statistical methods used compromises this review's internal validity.

Overall, we commend Sood et al. for conducting a review on an important topic. However, this review suffers from major methodological failures that cannot be ignored, and the evidence generated by this review lacks internal validity. Due to the significant implications of systematic reviews for clinicians and policymakers in addressing the COVID-19

pandemic, systematic reviews must be carried out with methodological rigor. Readers should carefully consider these limitations and interpret the evidence of this review with extreme caution.

Authors' Contribution All authors have contributed to the critical revision of the manuscript for important intellectual content.

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Code Availability Not applicable

Declarations

Ethics Approval and Consent to Participate This article does not contain any studies with animals or humans performed by any authors. This letter is a response to an already published article. Informed consent section was not applicable for this manuscript; this letter is a response to an already published review.

Consent for Publication Not applicable

Conflict of Interest The authors declare no competing interests.

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