LETTER TO THE EDITOR
https://doi.org/10.1590/1806-9282.67.Suppl1.20201094

Comments on "Kawasaki and COVID-19 disease in children: a systematic review"

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Dear Editor,

Gonçalves et al.[1] presented a systematic review of the association of Kawasaki Disease and COVID-19 in children. While benefiting from an interesting topic, there were some methodological issues that we thought we might address.

This systematic review included only one case report, leading to no further discussion on the topic. Although there is no restriction for the number of included studies in a systematic review, the outcome should add some scientific value to the reviewed topic, which might be of interest for the scientific community[2]. A systematic review, including only one study and one patient, seems to lack any additional scientific value.

The primary goal of a systematic review is to search all sources of evidence in order to find all relevant studies, in response to a clear and formatted research question[3]. In the search strategy of the current study, it would be better if the free keyword "kawasaki syndrome" was accompanied by other terms (i.e., kawasaki disease, kawasaki), along with other equivalent free keywords and MeSH terms like Mucocutaneous Lymph Node Syndrome, in order to prevent unintentional missing of the relevant articles. Also, since most of the cases reported in this field do not entirely fit in the diagnostic criteria of Kawasaki Disease, some new medical terms have been introduced by researchers and clinicians in this state to replace the term "Kawasaki Disease" in order to better define the current inflammatory syndrome, including Multisystem Inflammatory Syndrome in Children (MIS-C), Pediatric Inflammatory Multisystem Syndrome (PIMS), and Kawasaki-like Disease, which should be included in the search strategy to acquire more accurate results[4]. The PICO components, presented in Table 1, are not defined according to the review question. Suppose the study is considered as a systematic review on prevalence/incidence. In that case, the question should follow the CoCoPop format (Condition: Kawasaki disease, Context: COVID-19 infection, and Population: children), if the review is aimed to determine the etiology and risk, the question should follow the PEO format (Population: children, Exposure: infection with SARS-CoV-2, and Outcome: Kawasaki Disease), and if none, the question should follow PICO in the following form: 1. Population: children, Intervention/exposure: COVID-19 infection, Comparator/control: no COVID-19 infection, and Outcome: Kawasaki Disease[5]. "Association" is not an appropriate comparator and "coronavirus" is definitely not an outcome. Additionally, in all questions, the "children" should be defined in exact age ranges. Besides, the authors have mentioned in Table 1 that only "Descriptive/Cross-sectional/Observational studies" will be included, while the "Controlled clinical trials" are in among the inclusion criteria in Table 2, and "randomized controlled trials", "clinical trial", and clinical trial-related terms (e.g., "random allocation", "double-blind method", etc.) are included in the search strategy. Again, in contrast, the PRISMA[6] Flow Diagram of the study (Figure 1) indicates that some studies have been excluded during the eligibility phase, for being "interventional studies".

Moreover, an exclusion criterion of "Poorly described or inappropriate" studies has been mentioned in Table 2 of the study. The criteria for considering a study "inappropriate" should be clearly defined to prevent further misinterpretations. Also, assessing the quality of the studies is not something that could be performed during the screening phase of a study; this is the exact reason that there is a quality assessment (critical appraisal or risk of bias assessment) step in conduction of systematic reviews. Speaking of

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Conflicts of interest: the authors declare there are no conflicts of interest. Funding: none.
Received on December 11, 2020. Accepted on December 13, 2020.

the risk of bias assessment, the authors addressed that the quality of the studies was assessed using the Pithon et al.[7] protocol. We believe that the protocol that the authors are addressing is not compatible with the quality assessment of the current study, and the authors might have made mistakes in choosing and also use of this protocol due to the following reasons: 1. The protocol is developed for dental studies (several items related to mouth wash are mentioned in the checklist), 2. The case studies were clearly excluded from the Pithon et al.[7] study, therefore, the protocol is not compatible with quality assessment of the case studies, 3. The authors claim that any study with less than six scores was excluded, where the only included study obtains hardly four points from the protocol.

The Figure 1, representing the PRISMA Flow Diagram of the study, is completely different from what the article text represents; the authors have mentioned that "Initially, 840 articles were identified, of which three qualified and passed to the stage of abstract assessment. Of these, two were excluded because they did not answer the guiding question.", while the PRISMA Flow Diagram indicates that from 840 studies (837 without duplicates), 6 studies were selected after abstract assessment, where four of them did not pass the full-text assessment.

We believe that the addressed issues might have drawn the study away from the PRISMA statement[6] and clearly affected the quality of the systematic review.

AUTHORS' CONTRIBUTIONS

MSH: Conceptualization, Data Curation, Writing – Original Draft. **MAA:** Writing – Review & Editing.

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