

Ying Dou,

Science Editor, Editorial Office of Baishideng Publishing Group Inc

Name of journal: World Journal of Clinical Cases

Manuscript NO.: 44587

Column: Retrospective Cohort Study

Title: Clinical presentation and early predictors for poor outcomes in pediatric myocarditis

Dear Professor Dou:

Please find attached a revised version of our manuscript, which we would like to resubmit for publication in World Journal of Clinical Cases. Your comments and those of the reviewer were highly insightful and led us to thoroughly review the subject and consequently to improve the quality of our manuscript. Please find in the following pages our responses to each of the comments of the reviewer as well as your own comments. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication World Journal of Clinical Cases. We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

Moises Rodriguez-Gonzalez, MD.

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Responses to the comments of Reviewer #1 (Reviewer's code: 02520738)

- Comment 1: Please discuss the role of care manager in such a context. Please consider the paper from Ciccone MM et al. Vasc Health Risk Manag. 2010 May 6;6:297-305.

Author response: In the first version of the manuscript we had discussed yet the role of the care manager in the context of pediatric myocarditis in the emergency department setting. The care manager of patients with pediatric myocarditis is to have a high index of clinical suspicion because of the challenging diagnosis of this entity, mainly due to its heterogeneous and unspecific presentation, usually mimicking to common viral infections in pediatrics. We have read with interest the paper from Ciccone MM et al as suggested. It resulted very interesting but we think that it does not fit well with our pediatric study in the setting of an acute disease (this paper refers to adults with chronic cardiovascular conditions such as diabetes and heart failure). Therefore we would decline the suggestion of the reviewer to add to the references list. Thank you very much for your revision.

Responses to the comments of Reviewer #2 (Reviewer's code: 03702209)

- Comment 1: They found increased troponin in a minority of cases. It would be useful to clarify the type of troponin they measured. Was it high sensitivity troponin?

Author response: We agree that it is remarkable that not all patients with myocarditis, a condition where myocytes destruction usually occurs, presented elevated levels of cardiac Troponin T. We found increased Troponin T levels according to our laboratory's reference levels in up to 62% of children with myocarditis. Although this is consistent with the literature there are 2 facts that could explain this finding:

- 1) Not all cases diagnosed as myocarditis were real myocarditis as stated in the limitations section.
- 2) There are only a few data on cardiac troponin I (cTnI) and T (cTnT) levels in pediatric patients with cardiac disease. We believe that this lack of clinical and experimental evidences is especially due to low sensitivity of cTnI and cTnT immunoassay methods. Only very recently, the set-up of a new high-sensitivity method allowed the measurement of cTnI in more than 80% of apparently healthy neonates, infants, children, boys and girls (Caselli et al. Biomark Med 2016;10(4):357-65; Caselli et al. Clin Chim Acta 2016;458:68-71). We believe that this high-sensitivity immunoassay method for cTnI will have a great clinical relevance in pediatric cardiology. Unfortunately this immunoassay method was not available at our institution during the study period. We state in the methods section that cardiac Troponin T was determined by a non-high sensitivity immunoassay.

- Comment 2: The use of English is rather fair and I took the liberty to correct the manuscript (corrections appear in red) and attach it.

Author response: Thank you very much for your corrections. A native English speaker have revised this new version.

Responses to the comments of the Editor:

- Comment 1: Core tip should less than 100 words.

Author response: The core tip is now 90 words in length.

- Comment 2: Please modify the referenced references in this format

Author response: Done.

- Comment 3: Please write the article highlight section accordingly. Please don't copy from the main text.

Author response: We have written the article highlights section without copying from the main text.

- Comment 4: Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

Author response: We have done it. However, We could not find the doi of References number 2 and number 16, so we provide the first page of both papers as solicited as an attachment.

Finally, we submit the revised manuscript and all required documents, including the audio core tip, and the signed Copyright Assignment form in PDF format, after checking that the information in the signed document (i.e., the manuscript title, the authors' list, and the corresponding author) is identical to the information presented in the final version of the manuscript.

We really hope that these explanations, based on your constructive comments and helpful suggestions, clarify enough your doubt. We also want to thank you for your time and courtesy in the editorial management of our manuscript.

Sincerely yours,

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