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## Peer Review File

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### Reviewer A

This is a well written and interesting discussion of why PIMS-TS/MIS-C was not recognised in China and other Asian countries before its recognition and description in EUROPE and USA. The authors suggest that as MISC is a rare response to SARSCov2 there may not have been sufficient cases in the population in China to have the new inflammatory disease emerge.

The letter will stimulate debate and further research.

my only suggestion is the DIAMONDS should be referred to as the EU funded DIAMONDS study.

Reply: Thank you for your comments.

Changes in the text: “DIAMONDS study funded by Europe Union” in line 66

### Reviewer B

This editorial discusses the differences between COVID-19 patterns in Asia and other countries, with regards especially to MIS-C. This manuscript raises some key points and questions.

Reply: Thank you for your comments.

### SPECIFIC COMMENTS

1. Unfortunately, a number of the sentences in the manuscript are awkward, hard to read or poorly worded. Extensive revision is required to enhance this aspect of the work and to improve readability

Reply: We had read through the manuscript to improve the expression.

Changes in the text: We try our best to revise the manuscript.

2. There are also typographical errors (e.g. Aisa should be Asia)

Reply: Sorry for that mistake.

Changes in the text: in line 37, we revised as “Asia”.

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3. References are misplaced in several places: references should be placed at the end of sentences unless following Author et al.

Reply: We moved them to the right place.

Change in the text: we revised them in line 34, 37 and 69.

4. Wikipedia is not considered a website of authority. References to data from WHO should be supported by inclusion of a website or other source, so that others can review the same data directly.

Reply: We only use some demography data like population of city from the Wikipedia to calculate the prevalence rate. We use the case number data from the WHO website.

Changes in the text: We explained it in line 76.

5. Fig 1 is interesting as a pictorial depiction of the reports of COVID-19. Details of the search may be required. In regards the case reports mentioned, do the percentages listed refer to the number of reports or the number of subjects included in those case reports?

Reply: We offered the search strategy as a supplementary material. The percentages refer to the reports.

Changes in the text: We added in line 88 as: (The details of the search strategy can be found in the Supplementary material 1)

### **Reviewer C**

The authors of this short commentary or Editorial mention some potential reasons why MIS-C has not been described in Asia as compared to Europe, North America, and now Latin America. Overall, this manuscript fails to support strong arguments to test this hypothesis and many speculations were made.

Are there any reports or manuscripts from China by researchers or public health authorities going back to databases, clinical reports, and discharge diagnosis to see if Asian patients may actually have in fact MIS-C (utilizing the current knowledge and symptoms? Why did the authors do not mention if there were or not increased reports

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on myocardial dysfunction, shock or other similar conditions that eventually had been MIS-C?

Reply: We did a general search in PubMed and did not catch related research about retrospective case study on MIS-C. But we heard some researches was doing this work. We revised the case report mentioned and realized it may meet the MIS-C diagnosis.

Changes in the text: revised the line 30 as: We now consider it a suspicious case of MIS-C as the patient had multiple organs involvement.

Why did the authors do not comment about Asian patients from those cohorts from Europe and North America? Certainly, there are Asian patients among those series.

Reply: Actually, we did a systematic review for MIS-C case study and found out that the Asian children in the case series, but the incidence varies.

Changes in the text: We added it in line 44: but the relationship between ethnicity and susceptibility of MIS-C was inconclusive. Despite cohorts from Europe and North America have showed high proportion of children of black origin, there were certain amounts of Asian patients (5).

The title is weak and not very attractive. I rather would suggest:

Why MIS-C has been less commonly described in Asia?

Reply: Thank you for your suggestion.

Changes in the text: We changed the title.

Some other comments:

Lines 27, 28: As per September 2020, it is true that most publications have been in adults; however, we have now enough pediatric clinical and epidemiological publications from all main regions of the world to obtain significant and important considerations of COVID-19 in children and adolescents. Certainly, still many things to be discovered.

Reply: It's true. We just showed the situation in the early pandemic.

Changes in the text: We change the "To date" to "In the early pandemic"

**Reviewer D**

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This is an interesting letter. As mentioned, Kawasaki disease is the most common in Japan and many people have wondered why MIS-C is not prevalent there and in the rest of Asia. I do not think that people are suggesting that Asian paediatricians are missing MIS-C however, but rather wondering whether other factors such as ethnicity, genetics, environment or infection rate associate with the disease. The letter should perhaps focus more on a thoughtful discussion on these possibilities, as it come across as a bit defensive. The figure is not referenced and not representative of a full systematic review.

Reply: Thank you for your comments.

Changes in the text. We offered a search strategy as an appendix to support this figure in line 88.

Line 20- ‘recently some paediatricians’ – grammar- you do not need the word ‘some’

Reply: Thank you. We deleted the word.

Change in the text: deleted “some” in line 20.

Line 22- there are many more references and reported areas than just Italy- probably best to include some of these- ie UK, US, Africa etc

Reply: We added a references here.

Change in the text: Added reference 2-3.

Line 23- ‘Various speculations have then emerged on this issue, and some even doubt that Asian pediatricians missed the diagnosis of MIS-C in the early epidemic...’

Perhaps the word doubt should be changed to ‘suspect’ or ‘suggest’

Reply: We revised it.

Change in the text: line 22, we use “suspected” instead of “doubt”.

Line 27- ‘To date, the published data on COVID-19 in children remain limited, and most case reports originate from Asia (mainly from China, Fig 1).’ I don’t think that this conclusion holds without a proper systematic review of the data- ie with search methods, results etc..also- all these cases need to be referenced.

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Reply: 1. We only said the situation in the early pandemic; 2. We offered a search strategy as appendix.

Change in the text: revised the line 27 as: In the early epidemic when.

Line 37- ‘We analyzed that the reason why MIS-C cases were not discovered in Aisa is probably related to the different prevalence rates of COVID-19’ This was not analysed or shown here and is an opinion - probably best to say, ‘We suspected/postulated/theorised that the reason...’

Reply: We revised it.

Change in the text: in line 35, we use the “postulated”.

Line 39-42- all of these statements need references

Reply: We use the case number data and local population data to calculate the rate.

Change in the text: We explained the data resources in line 75.

Line 43- ‘Besides, differences in ethnic genetic background and SARS-CoV-2 subtypes may lead to the different COVID-19 prevalence and incidence of MIS-C.’ - I suspect that this is the case and probably the majority of the reason that cases weren’t seen in Asia- all other literature shows that MIS-C is highly skewed towards children of black origin. This should warrant careful and sensitive discussion.

Reply: Actually, Asian children is also the case series in the Europe and North American, so it’s too complicated.

Change in the text: We mentioned Asian children also is in the case series in line 44.

Line 57- ref needed – ‘In addition, Tokyo, the worst affected city in Japan, has an infection rate of only 0.1% and a case fatality rate of 4.4%.’

Reply: The same as above “line 39-42” question.

Line 63- ‘As advocated by WHO, pediatricians around the world should strengthen the surveillance of MIS-C during the COVID-19 pandemic’ needs reference

Reply: We add the reference.

Change in the text: added reference 9 in line 64.

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Line 66 – may need to reference and further explain DIAMONDS

Reply: We explained it.

Change in the text: We revised line 66 as: **DIAMONDS study funded by Europe Union.**

Line 68 – guideline is problematic- is this for COVID-19 in children or MIS-C in children? Not really sure of relevance. Definitely not relevant if IVIG is not included.

Reply: This is for children with COVID-19. We suppose that the recommendation had limitation. The question and recommendation are: Should intravenous immunoglobulin (IVIG) be used to treat children with severe COVID-19?

Recommendation7: Intravenous immunoglobulin (IVIG) should not be used to treat children with severe COVID-19.

Change in the text: we did not change.