Author’s response to reviews

Title: Comparison between clinical features and prognosis of malignancy- and non-malignancy–associated pediatric hemophagocytic lymphohistiocytosis

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Author’s response to reviewers:

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Comparison between malignancy- and non-malignancy-associated HLH in terms of clinical features and prognosis in children” (ID: BPED-D-18-00244). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and made corrections which we hope meet with approval. Revised portion are marked in red in the paper. The main correction in the paper and the responds to the reviewers’ comments are as following:

Responds to the reviewer’s comments:

Reviewer 2#

Response to comment: There are some grammatical errors through the text. Please correct all them (e.g. "were is" in the abstract section)

It needs to be revised in conclusion sentence

Response: We have corrected all the grammatical errors and revised in conclusion sentence.
Reviewer 3#

1. Response to comment: “Abstract is written essentially as a mini-paper, with a very detailed and elaborate, but ambiguously worded description (for example the Results section of the Abstract starts with “The median age of these two groups was 3.60 (0.25-13) and 1.20(0.25-13) years, respectively (p=0.027).” - which 2 groups? Does 3.6 relate to malignancy associated or non-malignancy associated?.

Methods section of the abstract does not contain meaningful methods data, instead focusing on detailed description of the analyzed groups ”.

Response: a. The median age of these two groups was 3.60 (0.25-13) and 1.20 (0.25-13) years in malignancy-associated and non-malignancy-associated HLH respectively.

b. “The Mann–Whitney U and Chi square tests were used to compare the clinical features of two groups. Overall survival time was compared by both log rank and Mann–Whitney U tests.” has been added in methods section of the abstract.

2. Response to comment: “The short abstract (the 1t page of the document sent for peer review) contains some unreadable parts, especially this sentence“It is called known as malignancy-associated HLH. Non-malignancy-associated were HLH is defined as having secondary hemophagocytic lymphohistiocytosis HLH other than a neoplasm”.”

Response: We have deleted “It is called known as malignancy-associated HLH. Non-malignancy-associated were HLH is defined as having secondary hemophagocytic lymphohistiocytosis HLH other than a neoplasm”. We have added “The objective of this study was therefore to describe the clinical characteristics, prognostic factors and survival outcomes of HLH when associated to a malignant disease, and comparing them to those not-malignancy associated.”

3. Response to comment: “Discussion is overly bloated, resembling a review paper. I suggest removing parts that are not directly relevant to the study, focusing on how the findings integrate into the existent web of knowledge, rather than aiming to provide a broad overview of the HLH field.”

Response: We have removed parts that are not directly relevant to the study.

4. Response to comment: “The Conclusion section should state the conclusions, rather than repeating results and background”.

Response: We have removed parts of results and background in the Conclusion section.

5. Response to comment: “Statistical analysis should include multiple group corrections.”
Response: We have done multiple group corrections in Statistical analysis.

6. Response to comment: “The Method section states that p<0.01 is considered significant. However, some comparisons with higher p value are stated as significant, for example ‘presence of albumin<25 g/L (p=0.017), HGB<60 g/L (p=0.027), and bone marrow hemophagocytosis (p=0.034) were correlated with poor prognosis.’ This discrepancy needs to be resolved.”
Response: We have stated that p<0.05 in the Method section.

7. Response to comment: “The background states that:”The combination of HLH and malignancy is very rare.”. How does it reconcile with that 22 out of 91 patients had HLH associated with malignancy. ~ 25% does not fit a “very rare” bill.”
Response: We have deleted the sentence “The combination of HLH and malignancy is very rare.”

8. Response to comment: “Consider to have more consistency between numerical and alphabetical presentation of numbers. Sticking to numerical presentation would make more sense to me.”
Response: We have changed alphabetical presentation of numbers to numerical presentation.

9. Response to comment: “It would be useful to add information on the cause of death, to get a sense to what extent HLH was directly contributing to mortality.”
Response: Because of the time, we can't do this at present, but in future writing, we will consider adding information on the cause of death.
Thank you and best regards.

Sincerely Yours,

Hua Pan