Author’s response to reviews

Title: Heterogeneous Neurodevelopmental Disorders in Children with Kawasaki Disease: What is New Today?

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Author’s response to reviews:

The revised parts in the text were shown in bold and gray-shading formatting.

Response to reviewers:

Ying-Hsien Huang (Reviewer 1): Lin et al. have designed a study of KD patients were followed up to estimate the prevalence of epilepsy and associated NDDs in comparison with the prevalence in general pediatric population in Taiwan and worldwide. They found KD patients have higher risk of NDD, epilepsy and Tourette syndrome. However, the quality would be further improved if the following points were addressed properly.

Major
1. The major concern is no comparable controls for this study. The authors should do population-based cohort study and use the database of National Health Institute to prove their novel findings.
Reply: We conducted an additional control by using National Health Insurance Research Database and remade Table 2. The section of method (2.2) and results (3.3) have been revised accordingly.
2. In the section 3.3, there is no corresponding reference in each sentence. The authors only cited as " [12-54]." in the last sentence. This is not a good scientifical manner.
Reply: We broke down the “references [12-54]” and placed them in the appropriate location in the paragraph 3.3
3. The prevalence of epilepsy in KD is 2.61 % and it is almost 8 folds higher compared to references. However, there is no similar literature to say it. The authors should try the best to prove it.
Reply: We added a short but in-depth discussion into “discussion section, paragraph 3” to elaborate our findings:
“Brain involvement of systemic autoimmune disorders commonly causes seizures as a presenting symptom [61]. Recent studies have shown a trend that many autoimmune disorders, including multiple sclerosis, diabetes mellitus, celiac disease, thyroid disease, systemic lupus erythematosus, antiphospholipid syndrome, rheumatic arthritis, Behçet's disease and Sjögren syndrome, possibly increase the risk of epilepsy [62]. KD, essentially a vasculitis autoimmune, was indicated in our results to have 8-fold increased risk of epilepsy than the references. This phenomenon echoes recent research that autoimmune disease have been implicated as causative factors of seizures and epilepsy [63,64].”

4. The figure 2 is not helpful in this article.
Reply: We removed the Fig 2 and changed the Fig 3 to Fig 2

Semra Cetinkaya (Reviewer 2): This article is beneficial and new information for literatur.

My critisizms:
1. ...should be added subgroup analysis: (NDDs according to cardiovascular findings and the duration of IVIG therapy).
Reply: We added a subgroup analysis (Table 3) as your suggestions and made a supplementary explanation in the “results section (3.3)”

“Table 3 further compares the possible confounders in children with KD with the development of different neurodevelopmental disabilities. No significant differences were found in terms of whether the children had cardiovascular findings at diagnosis and the timing of IVIG treatment”

2. ...should be removed Figure 2.
Reply: We removed the Fig 2 and changed the Fig 3 to Fig 2
3. ...should be changed Figure 3 as Table (to be more understandable).
Reply: In order to balance the number of figure and table, we have retained Fig 2(original Fig 3), however, we remade that figure to make it more understandable.