August 31, 2016

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The Editor
World Journal of Gastroenterology

Dear Sir,

Re: **Variable Outcome in Infantile-Onset Inflammatory Bowel Disease in an Asian Cohort**

Many thanks for the review and constructive comments and suggestions by the esteemed reviewers of the above manuscript. The authors found these comments very helpful in improving the quality of the manuscript.

The authors would like to address the issues raised by the reviewers, as follow:

Reviewer 1 (Reviewer code 00036810, Japan)

1. The authors readily acknowledge that only four of the six infants with infantile-onset inflammatory bowel disease (IO-IBD) had mutational analysis for IL10 or IL10R performed. The other two infants who both had phenotype similar to ulcerative colitis did not have mutational analysis. The main reason was that in our reading of the literature, IO-IBD secondary to mutation in IL10 or IL10R genes usually present with a phenotype similar to severe Crohn's disease. Therefore mutational analysis was not performed in the two infants with IO-IBD who had ulcerative colitis phenotype. This has been emphasized again in the revised manuscript.

2. Many thanks for this helpful suggestion. The authors have consulted some statistical experts, and have concluded that multivariate analysis is not applicable in this case. As shown in Table 2, the number of children with IO-IBD which has discontinuation of immunosuppression was only 3, which was lower than the minimum expected frequency of 5.

Reviewer 2 (Reviewer code 03476256, Poland)

1. The authors agree that wrong conclusions have been made in the original abstract. This has been corrected in the amended manuscript.

2. The total number of IO-IBD presented in the manuscript was six. This has been clarified in the amended manuscript.

3. Many thanks for this helpful suggestion. The sections on 'demography, phenotypic characteristics, clinical presentation and associated anomalies' have been shortened considerably to avoid any repetition with those information presented in Table 1.

4. Many thanks for pointing out this mislabeling of diagnosis. The diagnosis has been changed to postnatal CMV infection.

5. Conclusions: the authors agree that the conclusions made were overstated and that as compared to patients with late onset disease, patients with IO-IBD were not more likely to discontinue immunosuppression.

6. References 23 has been updated.

Reviewer 3 (Reviewer code 03473365, South Korea)

1. Many thanks for this constructive comments. The authors agree that the number of patients described in the present cohort is quite small as IO-IBD is indeed an uncommon condition. Therefore the result of analysis for the present study would not be truly representative of the characteristics of this rare condition. Nevertheless the authors believe that the data presented would be useful to clinicians in this part of the world as most of the patients with IO-IBD described in the literature are from the Middle East or Caucasian population. This has been emphasized in the manuscript (page 17, paragraph 3).

2. The authors agree with the observation that there may be selection bias in comparing the outcome of IO-IBD and patients with late-onset IBD as there is no matching of baseline data between the two groups. This has been added in the amended manuscript (page 17, paragraph 2).

3. Many thanks for pointing out that the only mutational analysis performed for the present study was for IL-10 or IL-10R mutation. Further mutational analysis for other possible genetic defects are not available. This potential weakness has been highlighted in the amended manuscript.

4. Many thanks for the suggestion of adding any significant family history of IBD or other autoimmune conditions in patients with IO-IBD. This information has been added in the amended manuscript (page 8, paragraph 4).

5. Many thanks for suggesting to add some comments on the role of ASCA in early onset IBD. A new paragraph on the sero-positivity rate of IBD in early onset Crohn's disease, as well as its implication has been added in the amended manuscript (page 16, paragraph 4).

6. Minor point: insufficient histopathological description. Many thanks for this helpful suggestion to improve the quality of this manuscript. More information on the histopathological findings of the six patients has been added in the amended manuscript (Table 1).

Thank you,

Yours truly,

Dr WS Lee
On behalf of all authors