Response to Reviewers and Editors

Dear Reviewers and Editors,

Many thanks for your valuable comments regarding our review article entitled "**Pediatric metabolic liver diseases: evolving role of liver transplantation**". We appreciate your interest and valuable time spent in going through our article. We have now revised our manuscript taking in to account the comments, critiques and questions highlighted in your reviews and editors. We believe that the revised manuscript now reads well and fulfils the requirements for publication in World journal of Transplantation. If you have any further queries or comments, please do not hesitate to contact us.

Kind Regards

Mukul vij

Reviewer comments

Reviewer #1: With the current paper the authors summarized the role of liver transplantation for children suffering from metabolic liver diseases. The paper is well written and covers a very important aspect in paediatric liver transplantation. I have the following comments on the manuscript:

1. It would be helpful to include prevalence of the different metabolic diseases

Authors Response: We have added prevalence of the different metabolic diseases in the manuscript

2. Abstract: APOLT is not really a novel technique. It has been performed in some centres many years ago.

Authors Response: We have revised our manuscript

3. Alpha-1 antitrypsin deficiency: I do not agree that „serum levels of A1AT may not help in diagnosis as it is an acute phase reactant….". Only homozygous patients are candidates for

liver transplantation and they all have definitely serum levels below 30 mg/dl. So the diagnosis in homozygous patients can be established just by determining the serum level.

Authors Response: Corrections are done in the manuscript and following sentence is added: Serum levels of A1AT can help in diagnosis of A1AT deficiency, as it is very low in those who are homozygous

4. Why is the risk for hepatic artery thrombosis and IgA nephropathy increased in children with AATD post Ltx?

Authors Response: A higher incidence of hepatic artery thrombosis is noted in these patients as the blood vessel integrity is defective in these patients due to deficiency of A1AT and a disruption of the vessel wall can happen during clamping. Liver impairment resulting from A1AT deficiency may directly contribute to renal abnormalities resembling IgAN.

5. Primary hyperoxaluria: It should be mentioned that there is a new medical treatment option (LUMASIRAN)

Authors Response: A novel FDA approved small interfering ribonucleic acid called Lumasiran decreases hepatic oxalate production by inhibiting the enzyme glycolate oxidase and hence has been found to reduce systemic oxalate load, thereby decreasing renal excretion of oxalates.

6. Maple Syrup Unine Disease: Domino-Tx should be discussed in more detail

Authors Response: Domino-Tx is discussed in more detail now.

7. Auxilliary Partial Liver Transplantation (APOLT): The heterotopic technique should also be discussed (Pros and Cons)

Authors Response: Auxilliary Partial Liver Transplantation (APOLT) is discussed in detail in the manuscript.

Editor comments

1 Scientific quality: The manuscript describes a review of the pediatric metabolic liver diseases. The topic is within the scope of the WJT.

(1) Classification: Grade C;

(2) Summary of the Peer-Review Report: The authors summarized the role of liver transplantation for children suffering from metabolic liver diseases.

It is well written and covers a very important aspect in pediatric liver transplantation. However, the questions raised by the reviewer should be answered; and

(3) Format: There are 2 tables and 6 figures.

(4) References: A total of 113 references are cited, including 24 references published in the last 3 years;

(5) Self-cited references: There are 16 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

Authors Response: We have removed some of the self-cited references. The self-citing rate is < 10% now.

(6) References recommend:

The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Authors Response: The peer reviewer has not recommended to add any improper reference.

2 Language evaluations: Classification: Grade B.

3 Academic norms and rules: No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJT.

5 Issues raised:

(1) The title is too long, and it should be no more than 18 words;

Authors Response: The title only has 9 words

(2) The “Author Contributions” section is missing. Please provide the author contributions;

Authors Response: the author’s contribution section is added in the manuscript

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Authors Response: All original pictures are now included

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and

Authors Response: PMID and DOI are added to the references

(5) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. 6

Authors Response: All images are original and are from the author’s cases only.