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Dr. Subrata Ghosh
Dr. Andrzej Tarnawski
Editors in Chief, World Journal of Gastroenterology

Dear Drs. Ghosh and Tarnawski, and the Editorial Board,

Thank you for your consideration of our article, newly titled: **“Clinical Considerations in the Management of NASH Cirrhosis Pre- and Post-Transplant: A Multi-System Challenge.”** Non-alcoholic steatohepatitis (NASH) is the most common chronic liver disease worldwide and is projected to become the leading indication for liver transplantation in the next two decades. This article presents a comprehensive review of the multi-system comorbidities that make NASH patients a unique and challenging patient population. We appreciate the reviewers’ and editorial board’s time and critique of this article. We have edited the manuscript and present our point-by-point response to specific comments below. We hope this revised manuscript meets all requirements and is suitable for publication.

Best,

Justin Steggerda, MD

Mazen Nouredin, MD

Reviewer Comments

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: In this interesting paper, the authors provide a comprehensive review of the conditions and challenges facing patients with NASH cirrhosis undergoing liver transplantation; moreover they provides recommendations for evaluation and management to optimize them before liver transplantation in order to have a good outcome. The paper is well structured and well conducted. REFERENCES are OK IMAGES and TABLES are Ok.

LANGUAGE is ok. Only minor mistakes in typesetting. This review is a good summary, which has a high application value for a large number and variety of clinicians. It is recommended that this review will be published first.

We thank Reviewer #1 for their consideration of this article. We have attempted to correct all mistakes in typesetting throughout the document.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The relevance of the issue is beyond doubt. The prevalence of NAFLD, obesity, and type 2 diabetes is currently high and is likely to continue to increase. In the United States, liver transplantation for non-alcoholic steatohepatitis takes a leading position in comparison with other reasons for this procedure. The article is written in a good style, easy to read and contains a lot of valuable information. There is no doubt that the article will be very useful for hepatologists and transplantologists in various regions of the world. The main comment on the article: the content of the article does not match its title. There is practically nothing in the article that would correspond to the term “management”. The article is a description of the clinical manifestations in patients with NASH before and after liver transplantation. Therefore, the reviewer suggests the authors to change the title of the article to “Clinical aspects of NASH Cirrhosis Pre- and Post-Transplant: A Multi-System Challenge”. If the authors are capable and want to completely rewrite the article so that it matches the term “management”, then no one has the right to refuse their desire. A few comments. In the article, it is important to focus on specific indications for liver transplantation. It would be useful for practitioners to know the specific likelihood of deaths depending on the condition of the patient before transplantation. It is advisable to implement these ideas in the article in the form of schemes or figures. I think that in the case of a change in the title of an article, a manuscript with

moderate changes can be published in the journal.

We thank Reviewer #2 for their consideration of this article for publication. We appreciate the pointed critique and provide our response here:

- The reviewer has asked that we consider changing the title of this article because of concern that the article does not address patient management. We have changed the title to “Clinical Considerations in the Management of NASH Cirrhosis Pre- and Post-Transplant: A Multi-System Challenge,” reflecting that the focus of the article is on the clinical conditions that make patients with NASH cirrhosis a unique and challenging patient population. Nonetheless, we do provide recommendations (*see Table 2*), many of which are in-line with published guidelines regarding the management of clinical conditions common with NASH. Furthermore, we posit that understanding the pathophysiology of NASH and its comorbidities will improve the management and optimization of these patients to maximize outcomes following liver transplantation.
- Secondly, the reviewer has asked about specific likelihood of death depending on the condition of the patient before transplantation. We have addressed this comment in the section titled “NASH and the Waitlist” in which we had previously discussed patient factors associated with waitlist mortality. Furthermore, we added a comment regarding scoring systems—to date, no scoring system has been developed that estimates mortality specifically in patients with NASH. Rather, MELD score remains the most validated scoring system for estimating mortality in patients with cirrhosis and waiting liver transplant.

Editor’s Comments

The author must revise the manuscript according to the Editorial Office’s comments and suggestions, which listed below:

(1) *Science Editor:* 1 Scientific quality: This is a review of the management of NASH cirrhosis. The topic is within the scope of the WJG. (1) Classification: Grade A and Grade B; (2) Summary of the Peer-Review Report: Reviewer#03358964 thinks this is an interesting paper. The authors provide a comprehensive review of the conditions and challenges facing patients with NASH cirrhosis undergoing liver transplantation. The paper is well structured and well conducted. This review is a good summary, which has a high application value for a large number and variety of clinicians. Only minor mistakes in typesetting should be corrected. Reviewer# 02861303 thinks the topic of the article is certainly relevant. The article is written in a good style, easy to read, contains a lot of valuable information for practitioners. The main comment on the article: The manuscript lacks information that allows the use of the term “management” in the title of the article. The questions raised by the reviewers should be answered; and (3) Format: There are 2

tables and 1 figure. A total of 178 references are cited, including 30 references published in the last 3 years. There are 2 self-citations. 2 Language evaluation: Classification: Grade A and Grade A. The manuscript is from United States. 3 Academic norms and rules: The authors provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an invited manuscript. The study is without financial support. The topic has not previously been published in the WJG. The corresponding author has published 3 articles in the BPG. 5 Issues raised: (1) I found there is no “Author contribution” section. Please provide the author contributions; and (2) I found the authors did not provide the original figures. 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. 6 Re-Review: Not required. 7 Recommendation: Conditionally accepted.

(2) Editorial Office Director: I have checked the comments written by the science editor.

(3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.

We thank the editor for their time and consideration of the article. We would like to note that during revisions to meet reference requirements with regards to formatting, we noticed that a few references had been inappropriately placed in the initial manuscript and therefore missed in the reference section. We have corrected this and now report a total of 181 references (previously 178). Additionally, we have addressed the comments of Reviewer #2 (see above).