**AUTHOR'S RESPONSE TO PEER-REVIEW / EDITORIAL REPORT**

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 75518

**Title:** Divergent Trajectories of Lean versus Obese Non-alcoholic steatohepatitis patients from Listing to Post-Transplant – A retrospective cohort study

Dear Editor,

Thank you for reviewing our manuscript submitted to the *World Journal of Gastroenterology* and giving us the opportunity to submit a revised draft. We are thankful to all the reviewers for providing constructive feedback and insightful comments on our manuscript. Please find below a point-by-point response to reviewer comments. All page numbers refer to the revised manuscript file with tracked changes.

**REVIEWER 1** *Retrospective studies are prone to be influenced by bias and enlarging the size sample or set comparison may be effective ways to avoid it. But I am sorry this manuscript does not meet these requirements, so the reliability of the conclusions remains elusive.*

**Author's response:** We agree with the reviewer that retrospective single-center studies do have potential for bias and have acknowledged this in our limitations. Nonetheless, we should note that our experience comes from the largest liver transplant centre in North America with 200 liver transplants a year, where patients are followed from the time of listing to follow-up post-transplant. The sample size was limited due to strict selection criteria of duration of MELD-Na era (2012 onwards) and exclusion of patients listed with exception points, in order to follow waitlist outcomes. As the primary objective of this study was to compare the outcomes of NASH (Non-alcoholic steatohepatitis) patients based on their BMI (Body Mass Index), we divided them into two groups (lean vs obese) instead of a non-NASH control arm.

**Manuscript changes:** None

**REVIEWER 2:** *The authors retrospectively analyzed the role of BMI on outcomes of NASH cirrhosis transplants. The results of the study revealed paradoxical correlation of lean NASH with wait-list outcomes, and graft and patient survival post-liver transplantation. The study is very interesting and focuses on the importance of healthy food and physical exercise before and after liver transplantation. The authors correctly described the limitations of the study, but some deeper insight of the mechanism linking lean NASH and better outcome of graft and patients is necessary.*

**Author's response:** Thank you very much for your kind feedback. Regarding your comment on the mechanisms linking lean NASH and outcomes, dysfunctional adipose tissue (in particular, visceral adiposity) is related with increased cardiometabolic risk in lean NAFLD (Non-Alcoholic Fatty Liver Disease). Further, alterations in TM6SF2, a gene conferring susceptibility to NASH and fibrosis, are shown to be increased in lean NAFLD as compared to obese NAFLD patients. However, there is a paucity of data on post-transplant outcomes in lean patients specifically. There is still much that is not known or understood, and hence it is challenging to explain the underlying molecular mechanisms linking lean NASH with worse outcomes post liver transplantation.

**Manuscript changes:** We have addressed this important point in the discussion section and the changes are highlighted in yellow, (page 10, paragraph 2 and page 11 paragraph 1)

**REVIEWER 3:** *This is a well-written study that demonstrated that lean NASH has worse outcomes than obese NASH. Unfortunately, there is limited data on long term survival. Looks like obese NASH patients have higher incidence of cardiac disease than lean NASH patients. Would their long-term patient survival thus be shorter than lean NASH due to cardiac events?*

**Author's response:** We thank the reviewer for their helpful feedback. Though numerically it appears that the incidence of diabetes and hypertension were higher in obese group at 1 and 5 years, this difference was not statistically significant. Further, the incidence of cardiovascular events was similar between the two groups. We agree that further expansion of follow up to 10 years might show a statistically meaningful difference. However, this analysis was not possible in the current study. Given the selection criteria with start of study from Nov 2012, none of the patients achieved the 10-year benchmark.

**Manuscript changes:** We have addressed this in the discussion section and the changes are highlighted in yellow (page 11, paragraph 2).

**EDITORIAL OFFICE'S COMMENTS**

***(1) Science editor:*** *It is an interesting observational study rather than retrospective study given the lack of control cohort of a non-NASH arm. The manuscript accurately describes many limitations, that I believe are enough to limit value of stated conclusions. Larger number, longer follow up and a control group would reelevate the manuscript's impact.*

**Author's response:** Please find above our response to Reviewer 1's comment.

**Manuscript changes:** None

***(2) Company editor-in-chief:***

- *I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, 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.*

  *Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".*

  **Author's response:** Thank you for your kind consideration of our manuscript. The appropriate changes have been made in the figure legends.

- *Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.*
- *Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned.*

*Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.*

**Author's response:** Appropriate changes have been made in the figures and tables.

- *In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.*

  **Author's response:** All the figures in the manuscript are original.

Thank you again for your interest and for providing us this opportunity to revise our work. We look forward to hearing back from you.

Sincerely,

Fakhar Ali Qazi Arisar, MBBS, MRCP (UK), FCPS (Pak)
Mamatha Bhat, MD, FRCPC
Ajmera Transplant Program, University Health Network