

Answers to Reviewers

Reviewer #1

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a great observation that this study concluded. It pinpoint the importance of autoimmune/allergic/toxic/inflammatory process in NASH pathophysiology. The researchers should include the the BMI in table one and the existence of other chronic disease manly DM or HTN. Also, it would be great if by any chance they can look into LPS, TNF-alpha or IL-6 levels in these patients. Overall, unique and novel and brave study. I congrats them.

Reply to reviewer:

Thank you for your favourable review. Regarding BMI and co-morbidities, these were not included into the main manuscript tables as we only have data for 77% of patients, of which the mean BMI was 30.61 and Diabetes Mellitus was present in 45.02%. As mentioned in the discussion, one of the limitations of our study was that data for co-morbid conditions was not available for all patients.

Unfortunately, we did not look into inflammatory markers such as LPS, TNF-Alpha or IL-6 as these are difficult to measure and not readily available.

Science editor: There are 2 figures and 2 tables. The format of the tables is not within required standard. Table 1, Line "Metavir Fibrosis score" format stated "Mean; (range)" does not correspond with the format provided (probably, Mean (\pm SD)). Standard abbreviation "SD" should be given in capital letters. P-value of patients' ethnicity is not provided. In the table 1 the format of Subjects' age and NAS is "Median (IQR)"; however, ALT and AST are shown as "Mean(\pm SD)" – this should be explained or revised for the data presentation format. (4) There are 23 literature references, neither of them are published in last 3 years (2 most recent references are published in 2018). (5) There is no self-citing. (6) References recommendations The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially those published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately 2 Language quality: Classification: Grade A. No language certificate is provided. Although the paper is well-written, formal statement of either native English speaking, or certificate supporting correctness of English should be provided. 3 Academic norms and rules: Institutional Review Board Approval Form is not correctly provided. Certificate issued on 06AUG2019 by the Health and Disability Ethics Committees stated that the submitted data are not within the scope of HDEC review (but no submission letter is provided); it recommends contacting institutional ethics committee before the study begins. Prospective studies requires Ethics Committee approval. It is not clear, when the study began. Some information provided by the authors, suggests that the study was initiated in 2005 and lasted up to 31DEC2017. Thus, it is not clear, why the HDEC issued their response in 2019. There is no information on the study registration, which is required per ICMJE

recommendations; no letter to obtain an exempt is provided. Biostatistics Review Certificate is issued by one of the authors, that seems inapplicable. Google search shows no similar titles. 4 Supplementary comments: This is unsolicited manuscript, it has no financial support 5 Issues raised: The paper described as a prospective trial contain signs of retrospective design. This should be appropriately clarified. STROBE Statement checklist is not provided. There are some comments that were not raised by the reviewer, however require attention. There is no information on the NASH diagnostic criteria used in the study; this is important to verify heterogeneity of the group and the correctness of data obtained. In this regard, liver steatosis may be a result of medications used for comorbid diseases; however, this information was not mentioned as an exclusion criterion. More details are required on certain criteria of "other aetiologies such as viral hepatitis, alcohol, autoimmune and hereditary causes"; this is especially important for autoimmune-associated diseases, as some of them may have similar manifestation on the liver histology. Whether IgG4-associated disease was excluded also? Per methods' description, IgG levels were indirectly measured, at least in some cases. The number of samples with calculated levels should be provided and this approach should be addressed in the discussion. It is advisable to add the data on the presence of insulin resistance and glycosylated hemoglobin level to patients' baseline characteristics in addition to the data mentioned by the reviewer. There is no information on the data processing (i.e. data available for the final analysis with the reason of non-inclusion). The manuscript would benefit, if patients' flow chart was provided. Another point to mention is that the authors did not take into the account the possible influence of the treatment provided to the patients on the outcome measures; this may significantly influence the results. METAVIR is an abbreviation and should be given in capital letters. Please, delete extra spaces in the literature references list. I would suggest sending the manuscript for additional reviews. 6 Re-review: required 7 Recommendation: Conditional acceptance.

Reply to Editor:

The tables have been amended. The authors are native English speaking from Singapore and New Zealand. Anonymized, de-identified data of patients with liver biopsy proven non-alcoholic steatohepatitis were prospectively collected from 2005 to 2016 in a combined database from both hospitals. Institutional Review Board (IRB) Approval with waiver of informed consent was sought and approved in 2017 to use the database for research when our group felt there were enough numbers to start analysis. As we were not able to complete the project in the stipulated time, an IRB renewal was applied for in 2019 and approved, hence there are 2 IRB forms submitted. The manuscript has been amended to clarify some of the points mentioned about NASH diagnostic criteria and exclusion criteria. Please see above replies to the reviewer, limitations of the study were mentioned in the discussion.

(2) *Company editor-in-chief:* I have reviewed the Peer-Review Report, 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.