

THE AW MORROW GASTROENTEROLOGY AND LIVER CENTRE

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8 January 2017

Dr Lian-Sheng Ma,
President and Company Editor-in-Chief
Baishideng Publishing Group Inc
8226 Regency Drive, Pleasanton, CA 94588, USA
Email: esps@wjgnet.com

Dear Dr Ma,

Re: Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 31288
Title: Patients with non-viral liver disease have a greater tumour burden and less curative treatment options when diagnosed with Hepatocellular Carcinoma
Author Name: Waled Mohsen

Thank you for providing the reviewers' responses and an opportunity to resubmit our manuscript for publication in World Journal of Gastroenterology. We have provided the following specific responses to the reviewers' comments and hope that our manuscript is now determined to be suitable for publication.

Reviewer's code: 00503530: Reviewer's country: Japan

Suggestions:

- Comparison with other countries including Asia
- Use or non use of anti viral therapy

Response:

- We thank the reviewer for his/her comments. We have analysed a large cohort that is much more heterogenous with regard to aetiology than many studies from either Asia or western countries. We have acknowledged this difference with other studies from Asia in our discussion, and do not feel that expanding on this issue will alter the findings or interpretation of our study.

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- Unfortunately, we do not have consistent data on the use of antiviral treatments in this cohort, and are therefore unable to analyse the impact of antiviral treatment on outcomes or presenting features of HCC.

Reviewer's code: 00053950: **Reviewer's country:** Finland

Suggestions:

- Exclude patients without NAFLD or alcoholic liver disease from the non-viral liver disease cohort.
- The discussion is a bit long and some repetition is seen

Response:

- We hoped to study the entire cohort of patients with non-viral liver disease. This is in keeping with our aims and the title of our study. The majority of patients in the non-viral cohort without alcoholic liver disease or NAFLD had hereditary haemochromatosis as their predominant liver aetiology. There is little data about how well this group of patients are screened for HCC. This group of patients may not have regular contact with a gastroenterology service and HCC screening may be overlooked, especially if the liver disease is not severe.

We acknowledge that the patients with autoimmune aetiology may be screened more effectively and be more engaged with a liver unit when compared to patients with NAFLD or alcoholic liver disease. In our cohort only 17 patients (1.5%) of the entire cohort had autoimmune aetiology: including autoimmune liver disease, primary sclerosing cholangitis and primary biliary cirrhosis.

Furthermore, the proportion of patients that did not have alcoholic liver NAFLD in our entire cohort was only 3%. Excluding them made no difference to our statistical analysis or conclusions.

Questions:

- If HCC was diagnosed in a person with active alcohol use, was the treatment offered immediately despite this fact? Or was the patient treated first with thermoablation or TACE

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and only thereafter with liver transplantation?

Response:

- With regards to HCC and active alcohol use, in Australia we do not offer liver transplantation to patients with alcoholic liver disease if there has been alcohol use in the last 6 months.
- With regards to alcohol use and other treatment modalities for HCC such as local regional therapy and surgery. This is usually determined on a case by case basis. Following discussion in a multi-disciplinary meeting with surgeons, interventional radiologists, Hepatologists and HCC clinical nurse consultants.

Reviewer's code: 00008736: **Reviewer's country:** Germany

Suggestion: The manuscript is acceptable for rapid publication

Response: We thank the reviewer for his or her extremely supportive comments

Reviewer's code: 00058405: **Reviewer's country:** Brazil

Suggestion:

- The authors should shorten the introduction to make it less descriptive and more focused on the aims of the study
- The authors should make clear the inclusion and exclusion criteria for the study and should detail the variables included in the data bank.

Response:

- We thank the reviewer for his or her supportive comments
- We have shortened the introduction and outlined the inclusion and exclusion criteria as suggested.

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Yours sincerely,

A handwritten signature in black ink, appearing to read "Simone Strasser".

Associate Professor Simone Strasser

A handwritten signature in black ink, appearing to read "Waled Mohsen".

Dr Waled Mohsen