



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67746

Title: Non-alcoholic fatty liver disease and extrahepatic comorbidities: Inflammatory cross-talk that needs a multidisciplinary approach

Reviewer's code: 02445854

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Research Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Spain

Manuscript submission date: 2021-05-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-21 01:41

Reviewer performed review: 2021-05-21 08:16

Review time: 6 Hours

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|---------------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| Peer-reviewer statements | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

This review is interesting, however the title is misleading and must be modified. I would have expected that this article was about all extrahepatic comorbidities in NAFLD, instead it is focused just on some of them, i.e. inflammatory bowel disease, obstructive syndrome apnea and psoriasis. There are too many abbreviations, and they affect the flow of reading. I'd suggest to limit their use to those most frequently used in this review article and spell out all the others. It is preferable to spell out the abbreviations in the headings of each section as well. Introduction It must be specified that alcohol consumption is a criterion to exclude NAFLD. As stated here, it seems a positive criterion. Please reword. What does it mean "imbalance in favor of proinflammatory/anti-inflammatory cytokines"? In favor of which ones? The proinflammatory cytokines or the anti-inflammatory cytokines? This phrase is unclear. IBD A recent study in rats has suggested a potential molecular mechanism for the comorbidity of NAFLD and IBD [Kwon J, et al. DSS-induced colitis is associated with adipose tissue dysfunction and disrupted hepatic lipid metabolism leading to hepatosteatosis and dyslipidemia in mice. *Sci Rep* 2021;11:5283]. "control attenuation parameter" is not a probe. It is an algorithm that estimates the attenuation of the ultrasound beam in dB/m, and is available on the FibroScan device (Echosens, France) together with transient elastography, which estimate the stiffness that is related to fibrosis. By the way, the results of this study are questionable. In fact, recent studies have reported that the control attenuation parameter threshold for the diagnosis of liver steatosis (NAFLD) is much higher than the one used in the cited study [Eddowes PJ, et al. *Gastroenterology* 2019; 156: 1717-30; Petroff D et al. *Lancet Gastroenterol Hepatol* 2021; 6:185-98.]. Therefore, an overestimation of NAFLD is likely. NAFLD and OSA Page 10: give reference(s) for the statement: the decrease in oxygen tension that occurs during



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nocturnal apnea-hypopnea episodes primarily affects hepatocytes in zone 3 etc. NAFLD and psoriasis Several sentences need references.



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Title: Non-alcoholic fatty liver disease and extrahepatic comorbidities: Inflammatory cross-talk that needs a multidisciplinary approach

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Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Netherlands

Author's Country/Territory: Spain

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|---------------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| Peer-reviewer statements | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

The manuscript of Perez-Carreras et al. is an interesting review on the link between NAFLD and three common diseases. It was a pleasant read and I think only a few things need to be addressed.

1. In the abstract, the authors mention 'algorithms' for screening for NAFLD in the 3 diseases. This is however not mentioned in the manuscript itself. I think the authors mean that the physicians treating IBD, OSA or PS should be aware that their patients have a higher chance to develop NAFLD.
2. On page 8 'experimental studies' are mentioned. What exactly is this: animal and in vitro studies? Please clarify/specify.
3. Please explain the different markers/scores for NAFLD: FIB-4, NAFLD disease score, PASI score.
4. On page 9 it is mentioned that 32.8% of the IBD patients had NAFLD and 24.6% significant fibrosis. Is this a higher prevalence than in the general population? Or was this not tested? If the latter is the case, no conclusion can be drawn from this study.
5. On page 12: 'Patients in the group with PS and NAFLD were older and had a higher body mass index,.... score).' To which group were these patients compared? And what can be concluded from this? Does this mean that age is associated with NAFLD? And is this not a general phenomenon?
6. The first sentence on page 13 is not clear at all: '..., means the same patient having both diseases cannot be seen as totally independent.' Please rephrase this!
7. In the part on the treatment of PS I feel that the authors forgot to mention the topical use of corticosteroids which are known to provoke NAFLD.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67746

Title: Non-alcoholic fatty liver disease in patients with intestinal, pulmonary or skin diseases: Inflammatory cross-talk that needs a multidisciplinary approach

Reviewer's code: 02445854

Position: Editorial Board

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Professional title: Doctor, Research Assistant Professor

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Review time: 1 Hour

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|---------------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Peer-reviewer statements | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |

SPECIFIC COMMENTS TO AUTHORS



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The Authors have satisfactorily addressed all reviewer's concerns.