

---

Dear Editor,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate the editor and the reviewer very much for their positive and constructive comments and suggestions on our manuscript entitled **"Nonalcoholic Fatty Liver Disease: Showing Significant Sex Dimorphism"(NO: 72084)**. Based on these comments and suggestions, we have made careful modifications on the original manuscript (see those in red), which we hope meet with approval. We hope that these revisions are satisfactory and that the revised version will be acceptable for publication in World Journal of Clinical Cases. Below you will find our point-by-point responses to the reviewers' comments.

We would like to express our great appreciation to you and the reviewer for your comments on our paper. Looking forward to hearing from you.

Thank you and best regards.

Nov 21th, 2021

Lili Zhang MD, PhD, Professor,

zhanglili.jl@foxmail.com

Department of Endocrinology, The Second Affiliated Hospital  
of Chongqing Medical University, No.74, Linjiang Rd, Yuzhong Dist,  
Chongqing, 404100,

***Response to the reviewer 1***

*Comments: The authors present a review on the gender differences in the*

---

*pathogenesis, epidemiology and clinical course of MAFLD. It is an interesting topic, with potentially clinical impact, for which I commend the authors. However, I think the manuscript needs major rewriting, in order to be easier to read and to convey a more clear message. The organization is a bit confusing. For example, it is not clear the difference of chapters pathogenesis and pathophysiology. I believe both words have similar meaning. The chapter on hepatocellular carcinoma is particularly confusing. The abstract should be completely reviewed. For example, it is not logic to say that men have more severe fibrosis, but women have faster fibrosis progression. Also, what do the authors mean when stating that men benefit more from treatment, what treatment? Furthermore, the sentence “the development and prognosis are worse among women than among men” is difficult to interpret, since before the authors said before men had higher prevalence of MAFLD and advanced fibrosis. MAFLD is not exactly the same as NAFLD. Also, MAFLD does not manifest as NAFLD or NASH. It could be said MAFLD manifests as simple steatosis or steatohepatitis with different degrees of liver fibrosis.*

---

**Response:** Thanks for your constructive comments.

1. According to your suggestion, we have revised the subtitle to make it more clear.
2. For *the chapter on hepatocellular carcinoma is particularly confusing*, we have revised that chapter and hope it is more clear.
3. We have revised our abstract based on your constructive comment.
4. We have re-written the corresponding part.
5. As we reviewed in our manuscript: From treatments like Very low-carbohydrate ketogenic diets, Protein tyrosine phosphatase 1B inhibition and lose weight etc al, men benefit more than women.
6. We agree with you that MAFLD is not exactly the same as NAFLD. And, MAFLD does not manifest as NAFLD or NASH. It could be said MAFLD manifests as simple steatosis or steatohepatitis with different degrees of liver fibrosis. Therefore, we changed those places that may not suitable.

---

**Response to the reviewer 2**

*Comments: Thank you for this well-prepared review. I t deserves publisment. I want to raise few points. 1- MAFLD has not been fully replaced NAFLD completely. There are still a debate on subject. NAFLD is still being used. (<https://easl.eu/event/digital-nafld-summit-2021/>) Actually MAFLD has many advantages, but Lean-NAFLD cases without any metabolic disturbances are not covered by this replacement. Maybe non-MAFLD will be used instead of lean NAFLD without MAFLD. So, adding "NAFLD with metabolic criteria" will justify the issue still under debate. 2- A typographic error " Kupfer" to "Kupffer" 3- "some people believe that " sentence needs citation.*

**Response:** Thanks very much for your positive comments!

1. We have changed “MAFLD” to “NAFLD” in the article.
2. Thank you for you kind reminding. We have corrected the typographical errors.
3. We have quoted relevant literatures in the “some people believe that”sentence.

---

### ***Response to the reviewer 3***

*Comments: This reviewer should congratulate authors for approaching this interesting topic. Some suggestions to let readers have a broader view of the issue. The key point is this..... a study showed that women with NAFLD lost the protective effect that women have against cardiovascular disease...thus the hormonal factor seems to play a reduced role. Authors are requested to comment on this aspect. Could glucocorticoids have some effects in sexual dimorphism, at the light of their key role in pathogenesis of NAFLD, as evident in..World J Gastroenterol. 2013 Oct 28; 19(40): 6735–6743. Authors should speculate on this alternative Hypothesis*

**Response:** Thanks very much for your positive comments! We have revised our manuscript according to your constructive comments.

1. We have added some comments on that topic.
2. For *Sexual dimorphism of glucocorticoids in the pathogenesis of NAFLD*. we added further hypothesis on that topic.