

Rebuttal Letter

First, we would like to thank the Editors, Editor-in-Chief and all the reviewers for their generous comments. All reviewer comments were addressed accordingly.

Reviewer 1 comments:

Scientific	Quality: Grade	B	(Very	good)
Language	Quality: Grade	A	(Priority	publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The manuscript entitled ‘Metabolic complications of Hepatitis C virus infection’ discuss the disease in the context of systemic abnormality. The contents are well-organized, interesting and suggestive and deserves publication in World Journal of Gastroenterology as a review article. Minor comments 1. In lines 12-13 of Abstract, ‘these three organs’ may be ‘these organ and tissues’. 2. In line 14 of Abstract, ‘Liver’ may be ‘liver’. 3. In the text, there are too many abbreviations. List of abbreviations will be helpful. And following may be avoided because of low repetition and low popularization; SMML (skeletal muscle mass loss), TG (triglyceride), SVR (sustained virologic response). 4. Please define LDL-C (P.10, Line 8 from the top) and IRS2 (P.10, Line 6 from the bottom). 5. In Table 1, please add a brief explanation to NS3 ‘a serine protease’ to account for the nature. Please define NS5 as NS5A, NS5B, or both, and add a brief explanation as well as NS3. 6. In Figure 1, please define ‘IR’ and ‘Adv. (is this ‘advanced’?)’. In addition, ‘fibrinogenesis’ under ‘Chronic HCV’ may be started with ‘F’. 7. In Figure 2, please define ‘FFA’, ‘IR’, and ‘ADV.’

Answers to Reviewer 1:

1. In lines 12-13 of Abstract, ‘these three organs’ may be ‘these organ and tissues’. – Addressed in the highlighted revision.

2. In line 14 of Abstract, ‘Liver’ may be ‘liver’. – Addressed

3. In the text, there are too many abbreviations. List of abbreviations will be helpful. And following may be avoided because of low repetition and low popularization; SMML (skeletal muscle mass loss), TG (triglyceride), SVR (sustained virologic response). – Changes made and other less used abbreviations were also removed. A list of abbreviations as suggested is available.

4. Please define LDL-C (P.10, Line 8 from the top) and IRS2 (P.10, Line 6 from the bottom). – LDL was defined on (P. 5, line 6 from the bottom) and LDL-C was defined again as suggested. IRS2 was defined as suggested.

5. In Table 1, please add a brief explanation to NS3 ‘a serine protease’ to account for the nature. Please define NS5 as NS5A, NS5B, or both, and add a brief explanation as well as NS3.- Changes made in table 1 as suggested

6. In Figure 1, please define ‘IR’ and ‘Adv. (is this ‘advanced’?). In addition, ‘fibrinogenesis’ under ‘Chronic HCV’ may be started with ‘F’. 7. In Figure 2, please define ‘FFA’, ‘IR’, and ‘ADV.’- Changes made, all abbreviations are defined with figure title.

Reviewer 2 comments:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This review highlights knowledge on the metabolic manifestations of Hepatitis C and the potential pathways in which these metabolic changes can influence the natural history of the disease. In this paper, more attention is paid to the influence of hepatitis C on metabolic problems, while the influence of metabolic diseases on hepatitis C is less mentioned, which may be related to the major of the author. This is also the crux of this article is not comprehensive.

Answers to Reviewer 2:

“the influence of metabolic diseases on hepatitis C is less mentioned”- Addressed

The authors talked briefly on this issue under the subheading ‘Impact of metabolic disease on CHC disease progression’ by mentioning the systematic review by Dyal et al.

Another paragraph was added at the end of the same section to further address this comment on metabolic disease impacting on Hepatitis C infection and its liver complications.

Reviewer 3 comments:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: In this review, the authors highlights and provides useful information about the metabolic derangement of Hepatitis C and its potential pathways to influence the natural history of the disease. It will remind physicians to pay close attention to the metabolic parameters in HCV patients especially cirrhotics and patients on the waiting list for transplantation. Thus, this is a meaningful review to be published.

Answers to Reviewer 3:

Thank you very much for the encouraging comments about our paper and the kind review.

Reviewer 4 comments:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: There is a close association between CHC virus infection and its metabolic complications. In this paper, the authors conduct a review on the interplay between HCV major proteins and the liver-muscle-adipose axis, and highlight current knowledge on the metabolic manifestations of Hepatitis C and the potential cellular and molecular mechanisms. The review is interesting and comprehensive, which could help us understand the systemic effects of CHC with its hepatic and metabolic complications. The manuscript and figures are well displayed.

Answers to Reviewer 4:

Thank you very much for the encouraging comments about our paper and the time taken for the expert review

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

Science editor: 1 Scientific quality: The manuscript describes a review of the metabolic complications of hepatitis C virus infection. The topic is within the scope of the WJG. (1)

Classification: Three Grades A and Grade B; (2) Summary of the Peer-Review Report: The manuscript discusses the disease in the context of systemic abnormality. The contents are well-organized. The questions raised by the reviewers should be answered; and (3) Format: There is 1 table and 3 figures. A total of 126 references are cited, including 21 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Four Grades A. The authors are native English speakers. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG. 5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (2) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. *World J Gastroenterol* 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable; and (3) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study. 6 Recommendation: Conditional acceptance.

Answers to Science Editor:

Thanks for all the comments and suggestions. We have addressed all the issues in the revision and formatted the revised paper as per the Journal requirements

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.

Response to Company Editor-in-Chief:

Thanks for the conditional acceptance of this paper and we have revised the paper to meet the high quality of the Journal and we are sure that this article shall be a cutting edge paper