

Dear Editor and reviewers, thanks for considering and reviewing our manuscript, and thanks for your valuable comments. This is a point to point response to your comments; we are hoping that it will satisfy your valuable queries and comments, thanks.

Reviewers comment

Reviewer 1

- in Abstract section, author mentioned insulin resistance in Keywords section, however, reviewers do not identify the explanation of insulin resistance does not found in the abstract section, please clarified and revised

Answer: thanks for your comments. We modified it and added insulin resistance in the abstract section.

- author should mention the full name and abbreviation of HCC in the second paragraph of abstract

Answer: thanks for your comments. We modified it

- please mention the VLDL by full name in the page number 8

Answer: thanks for your comments. We modified it

- page number 9. Please add vitamin D by the **role of Vitamin D**

Answer: thanks for your comments. We modified it

- please mention more detail the acknowledgments

Answer: thanks for your comments. We modified it

- please add the DOI in the reference number 10, 17, 20, 21, 22, 27, 32, 38, 4153,

Answer: thanks for your comments. We modified all.

- please make sure the graphical abstract is more visualize and more attractive. The current version is not well organized, please fixed, such as iron metabolism reproductive status and menopause and insulin resistance does not have figures.

Answer: thanks for your comments. We modified it

Reviewer 2

Title: well presented

Abstract: needs language revision

Answer: Thanks, the article benefited from language editing by a professional once again

Introduction: generally well written but few grammatic errors are present The present study is minireview summarizing the metabolic effects of HCV infection. The quality of the article is very well but language is the main problem and needs revision

Answer: thanks for your comments. We modified it

Reviewer 3

I was asked to review the paper entitled : "Metabolic Aspects of Hepatitis C Virus". It is an interesting paper, however I think there are some things that can be improved; Major comments:

1. Page 5, last paragraph: You say " In this context, a high prevalence of cirrhosis and non-SVR was observed among patients with diabetes and CHC". It should be mentioned that the rate of SVR is indeed lower in patients with insulin resistance, but only in Interferon based treatment. It seems that SVR rates following DAA are not influenced by IR (PMID: 30024489)

Answer: thanks for your comments. We modified it

2. Page 6, end of first paragraph you say: "Consequently, further evidence from long-term follow-up studies is still required to determine if successful eradication of HCV can help to ameliorate IR and improve glycemic control and clinical outcomes in patients with established DM2.28, 29". Several studies have proven better control of DM and amelioration of IR following SVR and I think they should be discussed (DOI: 10.1080/14787210.2018.1505500; DOI: 10.1016/S1665-2681(19)31578-9; <https://doi.org/10.1371/journal.pone.0209216>)

Answer: thanks for your comments. We modified it and added these two articles.

3. Page 7, first paragraph, you say: "Studies reported that steatosis may improve and even disappear following successful antiviral treatment with interferon and ribavirin; however, data on direct acting antivirals are still limited. 34, 35". References you quoted refer to peg IFN treatment only, not DAA.

Suggested references that should be discussed: DOI: 10.15761/JTS.1000194; doi: 10.1097/MEG.0000000000001106; <https://doi.org/10.1038/s41598-021-93881-7>; <https://doi.org/10.1371/journal.pone.0209615>

Answer: thanks for your comments. We modified it and added those articles.

Minor comments:

1. Paragraph with Insulin resistance, you say: "IR is associated with HCV infection in up to 80% of cases", I think that correct wording is "HCV infection is associated with IR in up to 80% of cases"

Answer: thanks for your comments. We modified it.

2. English polishing is needed to avoid awkward wording such as:

- page 5, first paragraph: "the systemic burden of hepatitis C infection surpasses its liver disease burden because it is a major burden on the overall health of the human body, causing increased economic burden to patients and healthcare systems" - page 6, second paragraph: "Not only are IR and DM are more prevalent in the course of HCV infection..." - page 8, last paragraph: "Plausible explanations include the feasibility of adipose tissue to promote fatty substrates..."

- page 9, last paragraph: "HCV infection can be an independent risk factor for increased carotid IMT⁴⁹ and cerebrovascular deaths⁵⁰, as reported in many types of study; ..."

- page 11, second paragraph: "There is a high incidence rate of sarcopenia, of up to 70%, in patients with cirrhosis. Dasarathy S. Cause and management of muscle wasting in chronic liver diseases."

Answer: thanks for your comments. We modified it.

Thanks again for your valuable comments and the meticulous revision of our manuscript.