# PEER-REVIEW REPORT

**Name of journal:** *World Journal of Hepatology*

**Manuscript NO:** 75457

**Title:** Fibrosis regression following Hepatitis C antiviral therapy

**Provenance and peer review**: Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06076623

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Egypt

**Manuscript submission date:** 2022-01-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-01-29 11:40

**Reviewer performed review:** 2022-02-04 05:05

**Review time:** 5 Days and 17 Hours

| Scientific quality | [ ] Grade A: Excellent   [ ] Grade B: Very good   [ Y] Grade C: Good   [ ] Grade D: Fair   [ ] Grade E: Do not publish |
| --- | --- |
| Language quality | [ ] Grade A: Priority publishing   [ Y] Grade B: Minor language polishing   [ ] Grade C: A great deal of language polishing   [ ] Grade D: Rejection |
| Conclusion | [ ] Accept (High priority)   [ ] Accept (General priority)   [ Y] Minor revision   [ ] Major revision   [ ] Rejection |
| Re-review | [ Y] Yes   [ ] No |
| Peer-reviewer | Peer-Review: [ Y] Anonymous   [ ] Onymous |

| statements | Conflicts-of-Interest: [    ] Yes    [ Y] No |
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## SPECIFIC COMMENTS TO AUTHORS

My detailed comments are as follows: 1.Could you review more about the specific pathophysiological mechanisms of liver fibrosis regression after Hepatitis C therapy? 2.Could you draw diagrams or tables about the key points of the article?

## PEER-REVIEW REPORT

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| **Scientific quality** | [  ] Grade A: Excellent   [  ] Grade B: Very good   [ Y] Grade C: Good [  ] Grade D: Fair   [  ] Grade E: Do not publish |
| **Language quality** | [  ] Grade A: Priority publishing   [  ] Grade B: Minor language polishing [ Y] Grade C: A great deal of language polishing   [  ] Grade D: Rejection |
| **Conclusion** | [  ] Accept (High priority)   [  ] Accept (General priority) [  ] Minor revision   [ Y] Major revision   [  ] Rejection |
| **Re-review** | [ Y] Yes   [  ] No |
| **Peer-reviewer** | Peer-Review: [ Y] Anonymous   [  ] Onymous |

| statements | Conflicts-of-Interest: [   ] Yes   [ Y] No |
|---|---|

## SPECIFIC COMMENTS TO AUTHORS

In the manuscript "Fibrosis regression following hepatitis C antiviral therapy", Elsharkawy et al. presented a review of the literature focused on the topic of the possible regression of liver fibrosis in patients with chronic HCV infection after viral eradication. The topic is of great interest, especially in light of the need for more information on the correct management and follow-up of patients with SVR. The authors carefully analyze most aspects of the topic. However, the paper can be improved, both in content and form.  Specifically, main issues are:  - An extensive revision of English is required. Many sentences appear unclear and the vocabulary needs to be implemented.   - At the end of the paragraph "HCV and liver fibrosis", a sentence is repeated consecutively. Moreover, the meaning of this sentence and the following ones (up to the end of the aforementioned paragraph) appears unclear and must be better explained, in order to avoid errors of understanding.  - Many studies evaluating the regression of hepatic fibrosis (and liver stiffness) after viral eradication have been omitted. A more careful analysis of the relevant literature is needed. As an example: Rosato V et al. Factors affecting long-term changes of liver stiffness in direct-acting anti-hepatitis C virus therapy: A multicentre prospective study. J Viral Hepat. 2022 Jan;29(1):26-34. doi: 10.1111/jvh.13617. PMID: 34582610.   - Similarly, several studies evaluating the clinical significance of liver stiffness regression following clearance of HCV have been omitted. For example Rinaldi et al. show how the degree of improvement in liver stiffness after SVR can be a predictor of HCC risk (Rinaldi L et al. Role of Liver Stiffness Measurement in Predicting HCC Occurrence in Direct-Acting Antivirals Setting: A Real-Life Experience. Dig Dis Sci. 2019 Oct;64(10):3013-3019. doi: 10.1007/s10620-019-05604-8. PMID: 30937719).   - In the paragraph "Fibrosis regression following HCV treatment:

does fibrosis really regress?", no reference was made about the potential impact of the damage cofactors (eg: obesity, diabetes mellitus) in influencing the regression of fibrosis. In my opinion this concept is crucial and needs to be discussed.  - The paragraphs "Antiviral treatment for HCV" and "Evaluation of fibrosis" show contents that need to be anticipated for the correct reading and understanding of the manuscript. It is therefore advisable to insert these paragraphs (or part of them) in the first part of the paper.  - The acronym LSM at the end of the paragraph "Fibrosis regression following HCV treatment: does fibrosis really regress?" it has never previously been fully explained  - In the section "Effect of fibrosis regression on clinical outcomes" the impact of viral eradication on some of the most important HCV-related extrahepatic manifestations (eg diabetes and atherosclerosis) is omitted. Numerous works deal with this theme. Eg:  - Adinolfi LE, et al. Reduced incidence of type 2 diabetes in patients with chronic hepatitis C virus infection cleared by direct-acting antiviral therapy: A prospective study. Diabetes Obes Metab. 2020 Dec;22(12):2408-2416. doi: 10.1111/dom.14168. PMID: 32761721. - Adinolfi LE, et al. Impact of hepatitis C virus clearance by direct-acting antiviral treatment on the incidence of major cardiovascular events: A prospective multicentre study. Atherosclerosis. 2020 Mar;296:40-47. doi: 10.1016/j.atherosclerosis.2020.01.010. PMID: 32005004.  - Finally, in my opinion, it is necessary to better explain why the interpretation of the improvement of liver stiffness must be evaluated with caution and not assimilated to the regression of liver fibrosis. In particular, it is necessary to better explain the role of steatosis and especially inflammation, which appear to significantly influence liver stiffness.   For all these reasons, I would re-evaluate this manuscript for publication in "World Journal of Gastroenterology" after major revision.

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**Provenance and peer review**: Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 02942289

**Position:** Editor-in-Chief

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Research Associate

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** Egypt

**Manuscript submission date:** 2022-01-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-02-06 10:49

**Reviewer performed review:** 2022-02-06 11:02

**Review time:** 1 Hour

| Scientific quality | [ ] Grade A: Excellent   [ ] Grade B: Very good   [ Y] Grade C: Good [ ] Grade D: Fair   [ ] Grade E: Do not publish |
|---|---|
| Language quality | [ ] Grade A: Priority publishing   [ ] Grade B: Minor language polishing [ Y] Grade C: A great deal of language polishing   [ ] Grade D: Rejection |
| Conclusion | [ ] Accept (High priority)   [ ] Accept (General priority) [ ] Minor revision   [ Y] Major revision   [ ] Rejection |
| Re-review | [ Y] Yes   [ ] No |
| Peer-reviewer | Peer-Review: [ Y] Anonymous   [ ] Onymous |

| statements | Conflicts-of-Interest: [   ] Yes   [ Y] No |
|---|---|

## SPECIFIC COMMENTS TO AUTHORS

Dear Editor,   The paper by Elsharkawy et al. entitled "Fibrosis regression following hepatitis C antiviral therapy" is a mini review of literature on regression of liver fibrosis in patients with chronic HCV infection after SVR.   The paper can be improved.   - An extensive revision of English is required.   the meaning of several sentence appears unclear and must be better explained.   - Many studies evaluating the regression of hepatic fibrosis (and liver stiffness) after viral eradication have been omitted. Please add a table on the outcome reported in different study.   -And please add a second table on the histological outcome in this setting. - better explain the Histopathological features of fibrosis regression, ad the role of overlapping   -better explain the pathogenesis and the burden of liver steatosis and inflammation on the liver stiffness, and in the regression I would re-evaluate this manuscript for publication in "World Journal of Gastroenterology" after major revision.

# RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Peer-review model:** Single blind

**Reviewer's code:** 06076623

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Docor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Egypt

**Manuscript submission date:** 2022-01-29

**Reviewer chosen by:** Li-Li Wang

**Reviewer accepted review:** 2022-04-29 04:35

**Reviewer performed review:** 2022-04-29 07:56

**Review time:** 3 Hours

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

## SPECIFIC COMMENTS TO AUTHORS

The revised version refines the article.