



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 67173

Title: Circulating microRNA 9-3p and serum endocan as potential biomarkers for hepatitis C virus-related hepatocellular carcinoma

Reviewer's code: 02441274

Position: Editorial Board

Academic degree: FACG, FASGE, MD

Professional title: Adjunct Professor, Professor

Reviewer's Country/Territory: India

Author's Country/Territory: Egypt

Manuscript submission date: 2021-04-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-18 05:12

Reviewer performed review: 2021-04-27 10:37

Review time: 9 Days and 5 Hours

| | |
|---------------------------------|---|
| 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 Grade E: Do not publish |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 type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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

Please find the review for the manuscript "Circulating microRNA 9-3p and serum endocan as potential biomarkers for hepatitis C virus-related hepatocellular carcinoma " below:

1. The sentence "To the best of our knowledge, the roles of miR-9-3p and endocan have not been evaluated in HCC" seems incorrect. eg. Higashi T, Hayashi H, Ishimoto T, et al. miR-9-3p plays a tumour-suppressor role by targeting TAZ (WWTR1) in hepatocellular carcinoma cells. *British journal of cancer*. 2015 Jul;113(2):252-8.
2. How was the sample size calculated in each group ? What were the inclusion and exclusion criteria ?
3. Was matching done between the case and control groups ?
4. As cirrhosis was diagnosed based on history, clinical examination, laboratory results, and imaging that included abdominal ultrasonography and CT, it would be more appropriate to use the term chronic liver disease
5. The aim and objectives of the study need to be more clear and specific.
6. The sentence "In the HCC group, 62.9% of patients were classified as grade A according to Child-Pugh classifications; and four (11.4%) patients were in BCLC stage, 18 (51.4 %) patients in stage B and 13 (37.1%) patients were in stage C " seems to be incomplete. BCLC staging and CHILD class should be mentioned separately. Also in table, please include all BCLC and CHILD class even if a particular group has no patients.
7. Limitations of the study needs to be mentioned. eg. only HCV related cirrhosis and HCC were included in the study
8. The cost and availability of tests like "Endocan" and "miR-9-3p" need to be discussed.



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 67173

Title: Circulating microRNA 9-3p and serum endocan as potential biomarkers for hepatitis C virus-related hepatocellular carcinoma

Reviewer's code: 04770380

Position: Editorial Board

Academic degree: DSc, PhD

Professional title: Professor

Reviewer's Country/Territory: Russia

Author's Country/Territory: Egypt

Manuscript submission date: 2021-04-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-19 16:12

Reviewer performed review: 2021-04-28 18:40

Review time: 9 Days and 2 Hours

| | |
|---------------------------------|---|
| 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 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 type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input type="checkbox"/> Yes <input checked="" 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 entitled “Circulating microRNA 9-3p and serum endocan as potential biomarkers for hepatitis C virus-related hepatocellular carcinoma” by Wahb et al. focuses on the investigation of expression levels of miR-9-3p and endocan and their correlation with clinicopathological parameters and survival rates in HCV-related hepatocellular carcinoma (HCC). The authors showed that miR-9-3p was downregulated, and endocan was upregulated in HCC patients. Also, the authors found the better performance of miR-9-3p and endocan as compared to AFP in discriminating HCC from cirrhosis and healthy controls. The submitted manuscript may be of interest for the journal audience. However, there are some concerns. They are as follows: Major concerns: 1. It is not clear from the study, can miR-9-3p target endocan gene? Since the expression levels of miR-9-3p and endocan are inversely correlated, it would be useful to study the ability of miR-9-3p to target ESM1. Minor concerns: 1. It is recommended to subdivide the “Results” section into subsections. 2. MiR-9-3p has been identified in HCC as a tumor suppressor. Therefore, it would be useful to discuss this in “Introduction” and “Discussion” sections (for example, see Higashi T, Hayashi H, Ishimoto T, Takeyama H, Kaida T, Arima K, Taki K, Sakamoto K, Kuroki H, Okabe H, Nitta H, Hashimoto D, Chikamoto A, Beppu T, Baba H. miR-9-3p plays a tumour-suppressor role by targeting TAZ (WWTR1) in hepatocellular carcinoma cells. *Br J Cancer*. 2015 Jul 14;113(2):252-8. doi: 10.1038/bjc.2015.170. Epub 2015 Jun 30. PMID: 26125451; PMCID: PMC4506379). 3. It would be better to capture data presented in Table 4 as a figure. 4. There are some technical errors in the text: (i) Introduction, paragraph 1, line 2: HCC is the third leading cause of cancer death, not the fourth one; (ii) Introduction, paragraph 2, line 2: The word “epigenetic” should be removed. (iii) The authors use both terms “microRNA” and “miRNA” – this should be unified. (iv)



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Introduction, last paragraph: since endocan is implicated in inflammation and HCV is associated with inflammation, this linkage between endocan and HCV-related YCC should be emphasized in the last sentence.