

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71488

Title: Non-alcoholic fatty liver disease and hepatocellular carcinoma: Clinical challenges of an intriguing link

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05065581

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Singapore

Author's Country/Territory: Greece

Manuscript submission date: 2021-09-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-10 03:41

Reviewer performed review: 2021-09-10 04:00

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input 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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

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
-------------------------------------	---

SPECIFIC COMMENTS TO AUTHORS

A nicely written review about the HCC prevalence and pathogenic pathways in patients with NAFLD, and potential impact on disease prognosis, surveillance and prevention.

One minor comments is that it would be good to update the global prevalence information in introduction with more recently references. Reference 2 is an example.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71488

Title: Non-alcoholic fatty liver disease and hepatocellular carcinoma: Clinical challenges of an intriguing link

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05458463

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Thailand

Author's Country/Territory: Greece

Manuscript submission date: 2021-09-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-13 15:54

Reviewer performed review: 2021-09-21 10:16

Review time: 7 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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
-------------------------------------	---

SPECIFIC COMMENTS TO AUTHORS

This review article is about an overview of non-alcoholic fatty liver disease (NAFLD) and progressive stages of NAFLD, its impact on public health worldwide, risk factors, pathogenesis, the prevention strategies, and the healthcare policies regarding NAFLD-related hepatocellular carcinoma (HCC). The authors provided the discussion detail in each section as followings; The first section, the authors discussed the brief background knowledge focused on NALFD. Secondly, the authors described the prevalence of various disorders related to HCC, i.e., type II DM, vital hepatitis, obesity, metabolic syndrome. The third part was about the pathogenic pathway and risk factors. The authors mentioned only the possible some risk factors such as smoking, alcohol, genetic variations related to HCC. The remaining possible pathways were seen in the supplementary file. The prognosis of the disease was discussed in the fourth part. Even though the controversial findings were reported, it could be assumed that HCC with NAFLD is the most risky when compared with the others. However, these patients have received less attention than the other groups, then the higher risk of mortality while waiting for lung transplant were observed in this patient group. The recent guideline and the proposed future surveillance guideline in NAFLD patient were then discussed in this section. The diagrams were shown in Figure 2 and Figure 3, respectively. The preventive strategies were discussed under the prevention section, including the weight management, diets, alcohol limitation, and medications. Some pharmaceutical treatments including aspirin, statins, metformin were recommended to reduce the progression of HCC. In conclusion part, the authors' point of concern is regarding an inappropriate surveillance latest guideline for NAFLD related HCC patients. In order to



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

identify an appropriate implementation, the authors further suggested the proposed guideline for HCC surveillance in NAFLD patients based on future perspectives. Overall, the title, abstract and keywords reflect the focus point of the review manuscript. The detail of literature used in the review is mentioned in the literature search section. The manuscript detail is in logical organization and provide the in-depth discussion in each section. There are some of the following points should be considered for minor editing. 1. Lots of abbreviations throughout the main manuscript (MS), the authors should provide abbreviation lists in the front page then it make the readers easy to follow. 2. The authors included the pathogenic pathway review in the supplementary file, it would be better for giving main concepts of the related pathways in either the main MS or the legend explanation in Figure 1. The remaining of the pathway can still be in the supplementary file.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71488

Title: Non-alcoholic fatty liver disease and hepatocellular carcinoma: Clinical challenges of an intriguing link

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03208726

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Greece

Manuscript submission date: 2021-09-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-12 07:03

Reviewer performed review: 2021-09-24 00:15

Review time: 11 Days and 17 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Language quality	<input checked="" type="radio"/> Grade A: Priority publishing <input type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input type="radio"/> Accept (High priority) <input checked="" type="radio"/> Accept (General priority) <input type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection
Re-review	<input checked="" type="radio"/> Yes <input type="radio"/> 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

SPECIFIC COMMENTS TO AUTHORS

Non-alcoholic fatty liver disease (NAFLD) can develop into non-alcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma (HCC), and HCC can also occur in NAFLD patients without cirrhosis. With the effective treatment of viral hepatitis and the global prevalence of obesity and type 2 diabetes mellitus (T2DM), NAFLD has become the most common liver disease worldwide. Therefore, NAFLD is expected to become the main cause of HCC all over the world. This review summarizes the latest data concerning the epidemiology, pathogenesis, risk factors, prognosis, surveillance and prevention of NAFLD-related HCC patients. Although other articles on similar topics(Huang et al., 2020; Margini and Dufour, 2016) have been published, the literature listed by the author is more representative, and some contents are summarized in figures and tables. This article has clear logic, excellent language ability and strong readability. Finally, from my point of view, in the section of "Pathgenetic pathways and risk factors", it's better that if the author can list some representative pathogenic molecular pathways involved in the development of NAFLD-related HCC then add details to the supplementary document. References Huang, D.Q., El-Serag, H.B., and Loomba, R. (2020). Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. *Nature Reviews Gastroenterology & Hepatology* 18. Margini, C., and Dufour, J.F. (2016). The story of HCC in NAFLD: from epidemiology, across pathogenesis, to prevention and treatment. *Liver International Official Journal of the International Association for the Study of the Liver* 36.