



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 38203

**Title:** Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic liver disease with advanced fibrosis

**Reviewer's code:** 02861131

**Reviewer's country:** Moldova

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-01-31

**Date reviewed:** 2018-02-01

**Review time:** 21 Hours

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

Manuscript Number: 38203 Manuscript Title: MILD DRINKING HABIT IS A RISK FACTOR FOR HEPATOCARCINOGENESIS IN NON-ALCOHOLIC LIVER DISEASE WITH ADVANCED FIBROSIS Comments To Authors GENERAL COMMENTS (1)

The importance of the research and the significance of the research contents; The authors of this article have been assessed the influence of a mild drinking habit on liver carcinogenesis from non-alcoholic fatty liver disease (NAFLD), which may support the theory of connection between liver carcinogenesis and mild drinking habit (less than 20ml/day). The importance and significant of the research is high because research on NAFLD/NASH pathogenesis and carcinogenesis is ongoing and till now we do not have clarity in this point. (2) The novelty and innovation of the research; The author compare incidence of hepatocellular carcinoma (HCC) in NAFLD/NASH patients with



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abstinence (0 ml/day alcohol) and with a mild drinking habit. There are no reports to date investigating the influence of a mild drinking habit on NAFLD/NASH patients. (3) Presentation and readability of the manuscript; Original article is well organized. (4) Ethics of the research. This study was carried out in accordance with the World Medical Association Helsinki Declaration and was approved by the ethics committee of Shinshu University School of Medicine (approval ID: 2802). **SPECIFIC COMMENTS**  
Title: accurately reflects the major topic and contents of the study. Abstract: it is not gives a delineation of the research background. The methods are presented clear. Results contain important information and numbers, with understandable abbreviation Conclusion reflect the result. Introduction: present relevant information about prevalence of NAFLD, pathogenetic mechanism of alcohol implication in liver carcinogenesis. Classically, in this part need to include aim of the study. Methods: clear delineated how subjects were selected, how clinical data was collected, how were performed histological evaluation and statistical analysis (methodology) many persons were evaluated before the selection patients for this study? Results: authors present interesting and original result, compare mild drinking group with non-drinking, HCC and non-HCC group, evaluated factor of liver carcinogenesis for NAFLD patients, compared patients for risk for HCC in dependence of level of fibrosis and presented factor that related to carcinogenesis in case of advantage fibrosis in NAFLD. Too many section in result- not bad to merge section Comparison of clinicopathological features at the time of biopsy between the HCC and non-HCC groups With Factors related to hepatocarcinogenesis in all NAFLD patients And Comparison of clinicopathological features at the time of biopsy between the HCC and non-HCC groups in NAFLD patients with advanced fibrosis With Factors related to hepatocarcinogenesis in NAFLD patients with advanced fibrosis Discussion is clear and well organased Conclusions: Conclusion reflect the result. References: references are appropriate, relevant, and updated. Tables and Figures: (1) The tables reflect the major findings of the study (2) The tables designed to present the maximal amount of information in the most concise and clear manner



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**Title:** Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic liver disease with advanced fibrosis

**Reviewer's code:** 03262379

**Reviewer's country:** Iran

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-02-02

**Date reviewed:** 2018-02-09

**Review time:** 7 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

**COMMENTS TO AUTHORS**

Hello, I reviewed the manuscript entitled "Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic liver disease with advanced fibrosis". The authors assessed the risk of hepatocarcinogenesis in NAFLD individuals consuming alcohol less than 20 g in comparison to those without alcohol consumption. They found that the risk of HCC is marginal in the whole cohort however in the patients with advanced fibrosis the drinking habit was significantly associated with increased risk of HCC. This study is presenting interesting and important results regarding life style of patients with NAFLD and can greatly contribute in the management of patients with NAFLD. I have few minor point which should be considered before publication. Minor Comments: 1. In the title, "non-alcoholic liver disease" should be replaced by "non-alcoholic fatty liver disease". 2. In comparison of the groups (drinking and non-drinking) the fibrosis was



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not significantly different however I guess if the authors compare the cirrhosis (F4) between the 2 groups they will see a significant difference between the groups. I suggest the authors to check it and add it to results. 3. In figures 1, 2 and 3, the title of parameters of X and Y axes is missing. I suggest authors to add them. Regards



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**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 38203

**Title:** Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic liver disease with advanced fibrosis

**Reviewer's code:** 00069130

**Reviewer's country:** United States

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-02-02

**Date reviewed:** 2018-02-16

**Review time:** 13 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
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		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

I have read the m/s titled "Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic liver disease with advanced fibrosis" by Kimura T et al. This is an interesting study. The study is well conceived and the manuscript is well written. There is a paucity of literature in this area: whether small amount of alcohol has a carcinogenic effect in a compromised liver. This is very logical. A cirrhotic liver has undergone multiple rounds of futile regenerative cycles and the cells have already accumulated many mutations. In this primed context, if they are exposed to ethanol even in small amounts it will cause great stress-oxinent stress, cell death and replicative stress. Which can cause more mutations (multiple hits) and epigenetic changes resulting in cancer. It is important to note that, the amount of alcohol per hepatocyte is much more in a cirrhotic patient because the total number of healthy hepatocytes are few. The



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authors are requested to check the tables once again.