

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 57335

Title: Cannabis Use History is Associated with Increased Prevalence of Ascites Among Patients with Nonalcoholic Fatty Liver Disease: a Nationwide Analysis

Reviewer's code: 05091450

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: United States

Manuscript submission date: 2020-06-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-06-04 01:52

Reviewer performed review: 2020-06-11 09:28

Review time: 7 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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 Grade E: Do not publish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 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

SPECIFIC COMMENTS TO AUTHORS

Remarks to the author: Increased incidence of and excess weight lead to an increased incidence of Non-alcoholic fatty liver disease (NAFLD) has been demonstrated to have highly correlation with obesity. The evidence of weight gain and related metabolic alterations caused by cannabis consumption have been proved in psychosis patients, which may be at greater risk of presenting fatty diseases, such as NAFLD. Therefore the meta-analysis of observational studies of cannabis use and the risk of NAFLD is a critical issue. In this manuscript, the authors report the cannabis is associated with liver-related complications of NAFLD, however, the previous studies on the likely effect of cannabis on liver steatosis has been investigated, which aimed to explore if cannabis consumption had an effect on hepatic steatosis (doi: 10.1016/j.pnpbp.2019.109677). Although previous investigation reduces the novelty of this study, this analysis was performed with a large population database to measure clinical outcomes at the national level. This cohort-analysis has several limitations that need to be addressed before being re-evaluated for its publication. Major comments 1. The purpose of this article focus on the effect of cannabis on clinical outcomes and in-patient mortality in patients with NAFLD, therefore the time effect of the period and dose-dependent analysis with an increase of the cumulative defined daily doses (cDDD) compared with nonusers will be necessary in this study. 2. What kind of strategies was applied in this article for the study quality examination? The random-effect model need to be used to calculate the overall risk ratio (RR) with a 95% confidence interval (CI), and the heterogeneity among the studies need to be assessed. 3. To detect population bias and heterogeneity, the pooled analysis or subgroup analyses are required, and all the included cases need to be adjusted with the same and potential confounding factors Minor comments 1. The structure of introduction are very weak, the authors need to provide more information



**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

about the cannabis and NAFLD. 2. Table 1: The total number of patients in each variable is different and needs to be confirmed. For instance, cannabis use group N=9,735, but total number 9,225 in race, 9,715 in primary payer; non-cannabis N=18,440, total number 18,530 in elixhauser comorbidity index. 3. Table 1: The item and number should be aligned in order to facilitate reading. For example, household median income data of two groups are not aligned. 4. Discussion : “A likely explanation for the variations is the differential effects of active cannabinoids extracted from various types of cannabis strains with different concentrations.” This description to convince readers that further data is needed. In addition, is it related to the activation and inhibition of cannabinoid receptors? 5. References mark should be consistent, such as ref 2 and 4 are inconsistent. Please overall recheck each of them.

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Title: Cannabis Use History is Associated with Increased Prevalence of Ascites Among Patients with Nonalcoholic Fatty Liver Disease: a Nationwide Analysis

Reviewer's code: 02997291

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Research Scientist, Senior Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2020-06-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-06-04 05:45

Reviewer performed review: 2020-06-22 05:22

Review time: 17 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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
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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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160, Pleasanton, CA 94566, USA
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<https://www.wjgnet.com>

SPECIFIC COMMENTS TO AUTHORS

The ms could be of potential interest, but has severe limitations. 1. we cannot find why these patients assumed cannabis, which type, and how (orally, inhalant, etc) 2-. patients are typically not routinely tested for cannabis use upon admission, and the diagnosis of cannabis use is often made from patient reports. 3. is cannabis prescribed or freely consumed? The authors made some interesting conclusions, but do not give them in a logic and rational presentation, rather in a chaotic way. The authors should give some hypothesis on their results, not simply wrote them down, like the laundry list

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 02997291

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Research Scientist, Senior Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2020-06-04

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-08-27 12:19

Reviewer performed review: 2020-08-27 13:23

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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
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The revised manuscript has ameliorated in general quality of presentation and in the logical terms of sequence. The findings are not irrelevant, even if authors failed to detect a possible motivation of their relevant data on ascites. It should be expanded any hypothetical reason for the fact that Cannabis was associated with higher rates of ascites, but there was no statistical difference in the prevalence of portal hypertension, varices and variceal bleeding, and cirrhosis. Authors limited to give this observation, without any personal comment.