

## PEER-REVIEW REPORT

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 00068420

**Reviewer's country:** India

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-10-24

**Date reviewed:** 2017-11-02

**Review time:** 8 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 checked="" 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 checked="" 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		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

The study entitled "Risk factors for hepatic steatosis in adults with cystic fibrosis: similarities to non-alcoholic fatty liver disease" submitted for publication in WJH, has been reviewed and found with some serious deficiencies; This study was planned to investigate whether cystic fibrosis may be consider as an important cause of NASH progressing to cirrhosis of liver. It was conducted in patients with cystic fibrosis with various abnormal liver function markers. The results of this study could not demonstrate an association of hepatic steatosis with gender, age, homozygous/ heterozygous genotypes, hypertension, hyperlipidemia, CFKD, use of alcohol, insulin resistance and pancreatic insufficiency, etc. in this group of patients. As such it is difficult to determine whether this study provides any message at this stage particularly, when authors claim that sample size is not adequate to conclude the findings. In addition, this study plan has

some methodological abbreviations also 1. The assays used do not describe details of various estimations made. 2. How mutations were tested, is not clear. 3. Tables and figures are given the manuscript are neither meticulous nor informative.

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 02529007

**Reviewer's country:** Iran

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-10-24

**Date reviewed:** 2017-11-04

**Review time:** 10 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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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

The Manuscript ID: 36787 entitled, "Risk factors for hepatic steatosis in adults with cystic fibrosis (CF): similarities to non-alcoholic fatty liver disease" describes a cross-sectional study on the clinical, biochemical and imaging characteristics of adult CF patients with hepatic steatosis by a retrospective review of 114 adult CF patients in an academic outpatient setting during 2016. Results indicated that 14.9% had hepatic steatosis with higher ALT levels and overweight (BMI >25) and higher percent of predicted forced expiratory volume in 1 second (ppFEV1) were associated with hepatic steatosis. However, no association with hepatic steatosis and CF related liver diseases could be identified. Authors concluded that Hepatic steatosis might be clinically and phenotypically distinct from CF related liver diseases while the lack of association with malnourishment and the significant association with higher BMI and higher ppFEV1

demonstrate similarities with NAFLD. Comments: In general, findings of this articles are in the scope of the Hepatology journal and might be of interest for its audience. The manuscript is well-written and is clearly presented. The methods, results and conclusions are also well-described. However, manuscript could be further benefited by considering the role of blood fatty acids in CF. In this context, authors are advised to consider this parameter in their analyses (if possible) or consider some related articles in the background information (introduction) and discussion section. For example some following manuscripts that discusses the potential role of blood fatty acid (FA) composition in cystic fibrosis (CF) related to liver diseases might be considered: - Drzymala-Czyż S et al, Determinants of Serum Glycerophospholipid Fatty Acids in Cystic Fibrosis. *Int J Mol Sci.* 2017 Jan 18;18(1). - Van Biervliet et al, Fatty acid composition of serum phospholipids in cystic fibrosis (CF) patients with or without CF related liver disease. *Clin Chem Lab Med.* 2010 Dec;48(12):1751-5. - Lebensztejn et al, Cytokeratin-18 and hyaluronic acid levels predict liver fibrosis in children with non-alcoholic fatty liver disease. *Acta Biochim Pol.* 2011;58(4):563-6. In addition, the figure 1 might need a complete description (figure legend) to explain the five separate figures (which might need to be specified separately by letters).

## PEER-REVIEW REPORT

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 00071662

**Reviewer's country:** Turkey

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-11-06

**Date reviewed:** 2017-11-06

**Review time:** 6 Hours

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [ Y] Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

Interesting study Further studies needed

## PEER-REVIEW REPORT

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 03262379

**Reviewer's country:** Iran

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-11-06

**Date reviewed:** 2017-11-06

**Review time:** 11 Hours

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

## COMMENTS TO AUTHORS

Hello, I reviewed the manuscript entitled "Risk factors for hepatic steatosis in adults with cystic fibrosis: similarities to non-alcoholic fatty liver disease". Authors included patients with CF for assessment of liver diseases and steatosis. While none of the patients had signs of liver disease, a proportion of patients had liver steatosis. The liver steatosis in the CF patients was associated with higher BMI. Authors concluded that the liver steatosis is the same as the condition observed in NAFLD patients and liver steatosis is not the underlying disease for development of CFLD. This is a well-designed study presenting novel and important findings. Regards

## PEER-REVIEW REPORT

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 03646816

**Reviewer's country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-11-06

**Date reviewed:** 2017-11-13

**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

Overall well-written manuscript characterizing the profile of steatotic CF patients. Comments below: 1. Authors argue that CF hepatic steatosis is more similar to NAFLD than CFLD. However, they refer to steatosis as a hepatic manifestation of CFLD in the introduction - this should be clarified. 2. Are US, CT, and MRI comparable techniques for the detection of steatosis? The authors should provide a more in depth discussion of the validation of these techniques. 3. CF steatosis patient characteristics are given compared to non-steatosis CF patients, but how do these patients look compared to non-CF steatosis or NAFLD patients? This would better make the authors' point. 4. Authors mention that none of the patients with steatosis met criteria for CFLD. Did any of the other CF patients in the cohort meet criteria? 5. More discussion on the ppFEV1 finding is warranted. What do the authors think this means? Also, how do the authors



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explain the lower AAR value in steatosis patients? These elements should be added to the discussion.



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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 029417

**Reviewer's country:** Turkey

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-11-06

**Date reviewed:** 2017-11-15

**Review time:** 9 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input 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 checked="" 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

the text is well written and deals with steatosis in the cystic fibrosis patients. Actually the authors have found BMI and ppFEV1 as the risk factors for steatosis development. The flow of knowledge very well but steatosis developed in the obese individuals which is also what NAFLD is basically. Therefore the significance of the findings should be clarified and furthermore did the authors make any kind of liver biopsy to correlate the results.

## PEER-REVIEW REPORT

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

**Manuscript NO:** 36787

**Title:** Risk factors for hepatic steatosis in adults with cystic fibrosis: Similarities to non-alcoholic fatty liver disease

**Reviewer's code:** 02444941

**Reviewer's country:** Philippines

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-11-06

**Date reviewed:** 2017-11-22

**Review time:** 16 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

The authors present the results of their cross sectional study looking at hepatic steatosis in CF patients. Studies evaluating liver disease in CF are needed to advance our knowledge of CFLD so this study can contribute to the body of knowledge on CFLD.

1. It is important to highlight the lack of histologic confirmation of steatosis as a limitation which the authors did. 2. It might also be useful for the authors to mention that other measures of insulin resistance like the HOMA-IR can be obtained to determine the presence of absence of insulin resistance but was not obtained in this study. 3. Can the authors expound on the finding of a lower mean AAR in the hepatic steatosis group? Why would the group without hepatic steatosis have a higher AAR indicating more fibrosis or higher propensity to fibrosis? Is this an indication that they might have other forms of CFLD or another liver disease altogether? 4. Corollary to #3, were markers of

chronic viral infection checked? If not, perhaps indicate in the discussion this fact and account for it.