

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39345

Title: Pathogenesis of Non-alcoholic Fatty Liver Disease in children and adolescence:
From “two hit theory” to “multiple hit model”

Reviewer's code: 00160002

Reviewer's country: Iran

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-13

Date reviewed: 2018-04-21

Review time: 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear Author (s): I have read the review. It is an update and thorough review in the field and is well organized. The only issue that is not clear to me in the title is that why did you add the phrase “in children and adolescents” there. The review is a general one and



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does not clarify the differences and similarities between these 2 groups; I think this phrase can be deleted with no harm to the manuscript. If accepted the key words referring to them can be deleted and others like pathogenesis, pathophysiology, genetic etc. can be added I do understand that the manuscript is a narrative review, and no structured methodology is defined, but I recommend you to clarify the method for the paper selection/ search for the readers.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39345

Title: Pathogenesis of Non-alcoholic Fatty Liver Disease in children and adolescence:
From “two hit theory” to “multiple hit model”

Reviewer's code: 00007076

Reviewer's country: Italy

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-13

Date reviewed: 2018-04-23

Review time: 10 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review article aims to addresses the pathogenesis of Non-alcoholic Fatty Liver Disease in children and adolescence. Although the target is of clear relevance, the review does not, unfortunately, hit the target. Main critiques 1. The several pathways



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described in the pathophysiology of NALFD/NASH is reported in an acritical way. Much more perspective needs to be inserted to explain what is known, what is not and what we need to explore next. 2. In the title is mentioned that focus was put on children and adolescents as data indicate that the clinical course in these subjects may be quite different and more severe than in adults. Unfortunately, this issue is marginally (at least) addressed. The only potentially novelty of the Ms is the difference between pediatric and adult NAFLD; several recent and less recent extensive review papers have been published on NAFLD/NASH 3. The Ms needs to have much more illustrations as the only Figure is inadequate to give the message.

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BPG Search:

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- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39345

Title: Pathogenesis of Non-alcoholic Fatty Liver Disease in children and adolescence:
From “two hit theory” to “multiple hit model”

Reviewer's code: 03022389

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-13

Date reviewed: 2018-04-26

Review time: 13 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors provide a review of factors that contribute to the pathogenesis of progressive NAFLD. Discussion of these factors is framed as a transition in mechanistic understanding of the disease from the classic “two hit hypothesis” to the



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more current “multiple hit model”. The manuscript is well written and provides a good summary of the field’s current understanding of several different factors that contribute to NAFLD development and progression. While the title implies a focus on pediatric NAFLD, this specific focus is somewhat lacking throughout the manuscript, a point that could be addressed by changing the title or adding some specific comparison and contrast to adult NAFLD. Overall, I do not have any major issues with the manuscript, but there are several minor issues (see attached "Comments to Authors" document) that could be addressed to improve its clarity and comprehensiveness.

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