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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 72515

Title: MAFLD from childhood to adulthood: state of art and future directions

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05040445
Position: Editorial Board
Academic degree: MD

Professional title: Associate Professor, Chief Physician, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 05:35

Reviewer performed review: 2021-10-25 07:25

Review time: 6 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors intended to interpret the differences of MAFLD and NAFLD in both children and adults. However, I don't think there are much information for children, I suggest that authors should considered to delete those about children. And the whole manu need to completely re-edit. and the authors need to more conclusive than just see this study and that study so so. There are too many paragraphs in the manu and may be the authors should try to combine those tell the same topic.

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Manuscript NO: 72515

Title: MAFLD from childhood to adulthood: state of art and future directions

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02536349
Position: Editorial Board
Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: Italy

Manuscript submission date: 2021-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 05:36

Reviewer performed review: 2021-10-29 14:04

Review time: 10 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for compilng the recent status of MAFLD in children. I will recommend for publishing. Two minor typographic errors (comma after Similarly-Similarly,... or Similar to...) and change coline to choline "phosphatidylcholine instead of phosphatidylcoline)

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Name of journal: *World Journal of Hepatology*

Manuscript NO: 72515

Title: MAFLD from childhood to adulthood: state of art and future directions

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05264112
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-20 04:47

Reviewer performed review: 2021-10-31 22:25

Review time: 11 Days and 17 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In the present study, the authors reviewed the roles of several factors (including genetics, inflammation, metabolic abnormalities, insulin resistance, obesity, prenatal determinants, and gut liver axis) in MAFLD pathophysiology, the adaptability of MAFLD diagnostic criteria for children, and current available data on the feasibility of MAFLD definition in clinical practice. This review is interesting. However, several aspects need to be modified as follows, 1.The key words should reflect the focus of the manuscript. 2.The statement of diagnostic criteria in Page 4 needs to be more closely aligned with the original guidelines. For example, 1) MAFLD diagnosis is based on histological (biopsy), imaging or blood biomarker evidence of fat accumulation in the liver (hepatic steatosis), but not only the radiological evidence. Actually, for detection of steatosis, ultrasound is the most widely used first-line diagnostic modality and is recommended by the guidelines. 2) The standard of waist circumference is varied in Caucasian men and Asian men. 3) It's the plasma high-sensitivity C-reactive protein (hs-CRP) level instead of C-reactive protein (CRP) level is recommended in the guidelines for metabolic at-risk criteria. These subtle differences have very different meanings in the clinical practice of diagnostic criteria. 3.In Page 8, in regard to the Yamamura et al. studies (in reference 64), the results should be stated. Actually, Yamamura et al concluded in this report that in patients with MAFLD, even mild alcohol intake was associated with an increase in the prevalence of significant fibrosis (25.0% vs 15.5%; P = .0181). 4.In Page 9, in regard to the study in a large cohort of 954 of Italian children with obesity (in reference 16), the results of the article deserve a more accurate explanation. Actually, Sessa et al showed that that the MAFLD diagnosis based on "overweight/obesity" criteria in obese children were less accurate in identifying patients at higher cardiometabolic risk compared with the

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diagnosis of MAFLD based on "evidence of metabolic dysregulation" and "overweight/obesity" criteria. Sessa et al emphasized the usefulness of MAFLD diagnostic criteria in adequately stratifying young patients in a specific context such as obesity having an intrinsic greater cardiometabolic risk. 5.The statement of previous research results can be more concise and more logical.

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Manuscript NO: 72515

Title: MAFLD from childhood to adulthood: state of art and future directions

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02811953
Position: Editorial Board
Academic degree: PhD

Professional title: Associate Professor, Director

Reviewer's Country/Territory: United States

Author's Country/Territory: Italy

Manuscript submission date: 2021-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-24 02:31

Reviewer performed review: 2021-11-02 03:25

Review time: 9 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript (#72515) entitled "MAFLD from childhood to adulthood: state of art and future directions" is a manuscript by Francesca Lanzaro, et al. The authors aimed to investigate the proposed replacement of the term of Non-alcoholic fatty liver disease (NAFLD) with metabolic associated fatty liver disease (MAFLD). Main comments 1. The abstract does not really reflect what the authors have done. Please describe what and how you have summarized the current state of MFLAD. 2. Please differentiates MFLAD and metabolic syndrome (MetS). What are their similarities and what are the differences? 3. Section two (PATHOPHYSIOLOGY) contains many paragraphs with only one sentence. Please summarize those genes in a table and describe them according to their functions or pathways. 4. In the third paragraph of the third section (EVIDENCE ON MAFLD: FROM CHILDHOOD TO ADULTHOOD), please define older and younger in terms of age in years before you use them and conclude that MAFLD patients are older. 5. NAFLDD has stages. Does MAFLD leads to hepatoma or tumorigenesis? 6. Please use a table or graph to compare NAFLD and MAFLD. 7. Please include a section to describe the treatment options and strategies for MAFLD if any.

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Manuscript NO: 72515

Title: MAFLD from childhood to adulthood: state of art and future directions

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03805186
Position: Peer Reviewer
Academic degree: PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-18 23:52

Reviewer performed review: 2021-11-03 00:35

Review time: 15 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This minireview describes the relevance of genetic factors, inflammation, fat distribution, and microbial alterations to metabolic disorders in MAFLD patients, and compares the differences between MAFLD and NAFLD.It highlights that using the definition of MAFLD allows for better identification of liver fibrosis, metabolic disorder diseases, and kidney injury diseases compared to NAFLD. This review provides an overview of the latest findings in this field of research in humans, summarizes the progress of research on MAFLD in adults as well as in children, and raises the thorny issues that remain to be addressed. On the one hand, I found the paper to be overall well written and much of it to be well described. I felt confident that the authors performed careful and thorough literature search and information collection, which reflects the current status of MAFLD in a more comprehensive way. On the other hand, I found some of the description of the paper not to be too detailed, while the description of some very important points were inadequate or completely missing. Therefore, I recommend that a minor revision is warranted. I explain my concerns in more detail below. 1. This article describes the latest diagnostic criteria for MAFLD in adults, but is inadequate for the diagnosis of metabolic disorders. 2. The title of the article is about MAFLD in children and adults, but the manuscript lacks a definition of age-appropriate MAFLD in children based on sex and age percentiles. 3. There are similarities and differences in the etiology, natural history and prognosis of fatty liver in children compared to adults. This article does not described in sufficient detail and rigorously. 4. Page 8, lines 24. How do you define significant fibrosis? 5. Page 5, lines 5-9. I suggest adjusting this sentence to use a transitive logical relationship to emphasize the higher cardiovascular risk of MUO compared with MHO. 6. It is suggested to add statistical data at the main findings in the

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table to more visually represent the strength of the association. 7. There are not enough comments on the outlook for future research in children and adults with MAFLD, and I suggest enriching the insights into this aspect.