

PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 74901

Title: A Systematic Review of Factors Early in Life Associated with Hepatic Steatosis

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03538879

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Singapore

Manuscript submission date: 2022-01-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-11 13:28

Reviewer performed review: 2022-01-13 02:45

Review time: 1 Day and 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input 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 Grade E: Do not publish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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

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

SPECIFIC COMMENTS TO AUTHORS

NAFLD is becoming a new global epidemic, which obtains potential risks of cardiovascular diseases and end-stage liver diseases. NAFLD, especially in adolescents, is a serious clinical problem, which will affect the physical and mental health of adolescents. Generally, we believe that unhealthy lifestyles in adolescence, such as high-fructose intake, high calorie diet, sedentary work and lack of sleep, are the main risk factors. This review provides a new understanding on adolescent NAFLD, and points out the effects of maternal factors, paternal factors, intrauterine factors, especially the maternal metabolic factors are crucial, which provides guidance for the early intervention on these risk factors in adolescent NAFLD patients. Ref 12 suggests the existence of a malnourished NAFLD, which has no significant correlation with the dominating adolescent NAFLD with malnutrition. It is not proper to be included this literature.

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Manuscript NO: 74901

Title: A Systematic Review of Factors Early in Life Associated with Hepatic Steatosis

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05847926

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Singapore

Manuscript submission date: 2022-01-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-18 15:20

Reviewer performed review: 2022-01-25 06:34

Review time: 6 Days and 15 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input 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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statementsConflicts-of-Interest: [] Yes [**Y**] No**SPECIFIC COMMENTS TO AUTHORS**

The manuscript aims to review the early developmental factors associated with NAFLD. These factors include maternal and paternal factors, intrauterine factors, postnatal factors such as breastfeeding, lifestyle factors in adolescence including sleep, physical activity, nutrition and presently still non-modifiable factors such as genetic polymorphisms. According to the author's results, interventional strategies to ameliorate the developmental programming of NAFLD may thus potentially be more efficacious during the critical windows of developmental plasticity, negating the need for strategies to reverse NAFLD later in life. The topic of the manuscript is very interesting and meaningful, and also conforms to the idea of DOHaD theory. However, there are still several issues to be clarified. The first, NAFLD itself is a characteristic of metabolic syndrome with complex etiology, which is closely related to obesity. The author also repeatedly mentioned obesity in the discussion part, but did not analyze the internal relationship between them. Second, whether there is a definite definition and scope of "developmental plasticity" and "developmental reprogramming", which needs to be clarified. Also, There are many risk factors for NAFLD, and the author focuses on the early stage of life, and you should pay more attention to the key points rather than discussing in general.