

## PEER-REVIEW REPORT

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

**Manuscript NO:** 80959

**Title:** Lower alanine aminotransferase levels are associated with increased all-cause and cardiovascular mortality in nonalcoholic fatty liver patients

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 04213276

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Doctor

**Reviewer's Country/Territory:** Greece

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-02-05

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-02-28 13:59

**Reviewer performed review:** 2023-03-01 09:55

**Review time:** 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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

This manuscript presents a significant conclusion, that very low ALT levels may be indicative of higher overall mortality in patients with NAFLD, due to higher incidence of cardiovascular incidents. While there is significant association for patients with ALT < 0.5 ULN, many patients have normal but closer to ULN levels. The authors must state how many patients were in each of the groups according to ALT levels and also present an analysis that shows differences between elevated and normal ALT patients and not just patients with very low ALT. Additionally, the authors showed that higher proportion of patients with normal ALT levels had advanced fibrosis. Can there be an analysis regarding the correlation of ALT levels and level of fibrosis. Also, if this correlation is sound, how do the authors explain that in this study most patients (174/202) with NAFLD and advanced fibrosis have normal transaminases?

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**Reviewer's code:** 04091933

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Senior Researcher

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-02-05

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-02-27 06:50

**Reviewer performed review:** 2023-03-11 21:45

**Review time:** 12 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The study is relevant because the authors are the first to examine ALT levels and all-cause and specific-cause mortality in patients with NAFLD and show that normal or reduced ALT levels may be associated with an increased risk of mortality. The authors logically discussed the possible mechanisms of the association between ALT levels and mortality, as well as the limitations of the study. The clinical significance of the study is that clinicians should be aware of low ALT levels associated with an increased risk of death, and not just high ALT levels associated with liver damage. Thus, the authors recommend being more vigilant in NAFLD patients with ALT levels <0.5ULN. The tables are convincing and confirm the correctness of the authors' conclusions. References are relevant. The manuscript can be recommended for publication without further revision.