Reviewer's report

Title: Association between elevated Serum Alanine Aminotransferase and Cardiometabolic Risk Factors in Rural Chinese Population: A Cross-Sectional Study

Version: 4  Date: 10 March 2015

Reviewer: Ole-Petter Hamnvik

Reviewer's report:

Overall comments:
In this study by Chen et al, an impressively large number of subjects living in rural China were metabolically characterized, and the association between ALT and metabolic risk factors were investigated. The study is overall well executed with appropriate design of the analyses. The authors will need to better describe how their study advances the field and how it fits in with prior data, as well as discussing any clinical or research implications of their findings in some more detail. With this in mind, I have some specific comments:

Major compulsory revisions:
- 1. Background: In general, the background accurately discusses what is known about ALT and metabolic risk factors – ALT may be a marker of NAFLD and has been found to be associated with most metabolic risk factors already. However, it is unclear to me why the authors embarked on this study. What is new about this study? The authors claim that “Although several studies have reported the close associations between elevated ALT and metabolic diseases, uncertainty still exists whether elevated ALT is independently associated with cardiometabolic risk factors”. What is the uncertainty? Several studies have shown this, many reference by the authors, other include PMID 24726813. The population also does appear to be novel - the Chinese population has already been studied (as shown by references number 2, 12 and 26). The gender analyses appear a bit more novel, but from the background it is unclear to my why these analyses were performed – is there information in the literature to suggest that there would be a difference?

- 2. Methods: What factors were controlled for in the multivariate analysis? Based on information presented later, it seems that sex and age were the only confounders that were included. I think a more inclusive model should be presented in addition to this simple model (similar to the model used for the gender analyses). With such a high number of subjects, a large number of confounders can be included without affecting the stability of the model to any great degree.

- 3. Results: For the gender analysis, it would be helpful to know if there was any difference in male / female demographics and anthropometrics (perhaps as additional columns in Table 1)? Also, how many men vs. women had high ALT –
could the lack of association in women be simply due to smaller numbers?
- 4. Table 1: Include information on how many individuals had diabetes, HTN, etc.
- 5. Table 2/3: I would clarify the referent category for all variables – this is implicit in names such as “High WC”, but how about race? Or variables with multiple levels such as education and income?
- 6. Discussion: Overall, the discussion attempts to place the findings in the context of prior studies. However, there is little or no discussion about the significance of the findings. Is there a biologic rationale for the findings? Why is the high-ALT group is significantly younger, more likely male, higher educated with a higher income? Any clinical / research implications?

Minor essential revisions:
- 7. Abstract: Clarify that the high-ALT group had LOWER HDL cholesterol (as it appears now, it appears as if they had HIGHER levels).
- 8. Methods: Were alcohol intake, smoking, race self-reported? For physical activity, please reference WHERE the detailed methods for assessing this can be found. For summary statistics, were any of the data significantly non-normally distributed? If so, it may make sense to present median and 25th, 75th percentiles. The logistic regression analysis mentions analyses that are not presented – association between dyslipidemia and depression?
- 9. Discussion: The authors report incidence of high ALT of 10.5% in men and 4.8% in women, but in Table 2, the odds ratio for high ALT is almost 3 for women. These statements appear to be contradictory – should the odds ratio be 3 for men? As a limitation, it should be mentioned that there are known causes of ALT elevations that were not tested for, such as alcohol abuse (the alcohol consumption was by self-report and not quantified), chronic viral hepatitis, and other illnesses. I would not include the phrase “Serum ALT can be considered as a cardiometabolic risk factor” (also used in the abstract). There were no cardiac outcomes studied so it is unclear if ALT is associated with any cardiac disease beyond the associated with cardiac risk factors. A better conclusion would be “Elevated serum ALT is associated with a worse cardiac risk profile”, or something like that. If the authors have data on cardiac disease, then this would be relevant to include in this paper

Discretionary revisions: None

Minor issues not for publication:
- 10. General: Rather than “general obesity”, I would change throughout to “BMI above 25 kg/m2”.
- 11. Background: What do the authors mean by “in addition to the related epidemiological studies of DM and obesity in this population”? I am not sure what they are trying to say.
- 12. I would remove “dramatically” from line 200 and “extremely” from line 180.
- 13. What is meant by this sentence (lines 238-240): “Given the sex-related data, it is known whether the cardiometabolic risk factors associated with elevated serum ALT level exists difference in both genders”

- 14. In general, there are some very minor grammatical errors throughout that can be corrected by the editor or by a native English speaker.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests