Reviewer's report

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

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Reviewer: Altan Onat

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Authors evaluated cross-sectionally the association between elevated ALT (>40 U/L) and cardiometabolic risk factors in over 11,500 rural men and women from Northeast China. In logistic regression analyses they showed that female gender, age group 45-54 years, high TC and triglycerides, overall or abdominal obesity and hyperuricemia were significantly associated with elevated ALT. Authors pointed to that women diverged from men in exhibiting no significant relation to these parameters and concluded that ALT can be considered a cardiometabolic risk factor.

Following concerns arise in the interpretation of data.

1. The way findings stand in this large population-based study, there is hardly any novelty, since similar associations had been reported regarding γ-glutamyltransferase, demonstrating additionally relationship to several outcomes (Onat A. Obesity 2012; 20: 842-8).

2. The main finding should be that elevated ALT is associated in each gender with the “hypertriglyceridemic waist” (HtgW) phenotype, initially described by JP. Després and associates (from Montreal, Am J Cardiol 2007; 99:369-73) and found as a major determinant of cardiometabolic risk among Turks (Onat A. Eur J Clin Invest 2013; 43:1129-39). Authors might benefit assessing via a logistic regression the independent association of log ALT values with HtgW, adjusting for age, sex, total cholesterol and uric acid.

3. The paragraph on Definitions should specify whether former and never smokers are treated as one category.

4. Table 2 may be much condensed by omitting data on crude OR and focusing on age- and sex-adjusted ORs.

5. Dyslipidemia in the initial paragraph of the Discussion is to be specified as Htg and low HDL-C.

6. A notable finding that should be highlighted (yet seems concealed) is that sex- and age-adjusted current smoking is independently associated with lower likelihood of elevated ALT. This is not surprising as smoking has been reported to lower the risk of type-2 diabetes presumably by inhibiting autoimmune processes (Onat A, Atherosclerosis 2007; 193:380-8; Rasouli B. Diabetes Care 2013; 36:604-10).
7. The finding that elevated ALT was not associated with prevalent diabetes: a) requires reevaluation by combining men and women which may allow appearance of statistical significance; b) merits a brief comment. Diabetes is predicted inversely by lipoprotein(a) (Mora S. Clin Chem 2010; 56:1252-60; Onat A. Current Pharm Design 2014; 20:575-82; Onat A. Exp Clin Endocrin Diabet 2015; 123:11-8) and is strongly predicted by HtgW which is also predicted inversely by lipoprotein(a). One may presume that ALT is collinear with Lp(a) and thereby acts as a mediator for CV risk factors including HtgW.

8. Refs. 19 and 20 on line 149 do not recommend cutoffs and are not related to Chinese people. It is surprising why 102 cm was selected as threshold for male abdominal obesity in Chinese.

9. Some linguistic improvements may be sought such as line 58, the sentence on line 229, lines 238-240,

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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