Author's response to reviews

Title: Association between lipids profile and thyroid parameters in euthyroid diabetic subjects: A cross-sectional study

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Author's response to reviews: see over
Dear editor,

I am so apologized for the delay of revised manuscript. With great thanks for the time and effort you and reviewers expend on this paper and important and helpful comments, which makes the manuscript more interesting and informative, we read carefully and modified our paper after thinking and discussing your comments. This is our responses (in **BOLD** type). The page and line numbers refer to our revised manuscript.
Reviewer: Tien-Chun Chang

Specific comments:

1. No page number appeared in the manuscript.

   Response: The page number had been added at the bottom of each page.

2. Abstract: Results: “TSH was higher in females than males” is reasonable. However, why TSH was associated with HDL-C and also with LDL-C.

   Response: In my opinion, the association between TSH and HDL-c might just be a statistic association with no meaning. And the association lost its statistic significance in the partial correlation analysis, adjusted for age, sex, duration of diabetes, fasting glucose and BMI.

3. Abstract: Results: “Lipid levels were lower in TPO-Ab positive patients” is contradictory to what we expected. How can that be explained?

   Response: Yes this result is contradictory to what we expected. But the difference had no statistics significance. So this suggested that chronic autoimmune thyroiditis per se might not be a risk factor of dyslipidemia in our sample of euthyroidism diabetic patients. Or this might result from the small sample size of TPO-Ab positive patients (only 6 patients in this group).

4. Background: Hyperthyroidism was also associated with increased risk of dyslipidemia? Then how can you explain in the next 2 sentence that autopsy showed atherosclerosis decreased in hyperthyroidism?

   Response: The first sentence came from the reference[2], but it was not well explained in the text. So we have moved this sentence away, and we will make more effort to find a reasonable explanation. Could you give us some advice?

5. Results: 106 patients had anti-TPO antibody determined. If there is relationship between autoimmune disease and TSH levels, the numbers are enough to prove.

   Response: Yes our result did not support the concept that chronic autoimmune
thyroiditis per se might be a risk factor of dyslipidemia. But as only 6 patients in the TPO-Ab positive group, statistic bias could not be excluded. Larger scale studies were still needed to further confirm the role of thyroid antibodies in atherosclerosis.
Reviewer: Altan Onat

Though the topic is worth investigating and findings are of interest, following concerns need addressing.

1. Own salient findings should be stated with greater clarity.
   
   **Response:** Yes we have revised the statement of results in Abstract and Conclusion part.

2. A table needs to be constructed replacing the current Table 1 showing the distribution of variables stratified to gender and dichotomous TSH and fT3, with the purpose of better understanding the lipid and BP differences.
   
   **Response:** Thanks a lot for your good advice and we have had the table revised, hoping it could show the differences of lipid and BP clearly (Page 16). And the results had been added in the Results part. (Page 7, Paragraph 2-4)

3. Table 2 is best to be omitted, simple coefficients for the whole sample being added to Table 3.
   
   **Response:** Thanks a lot for your advice and we have put the two tables together (Page 17). And some changes had been made in Results part according to the revise of the table (Page 7, Paragraph 3-4).

4. One explanation to a positive association of TSH with total and LDL cholesterol may be both being a consequence of autoimmune activation involving Lp(a), with ensuing “reduced” Lp(a) levels, a determinant of new-onset diabetes, and accompanied by low circulating total and LDL cholesterol and autoimmune complex involving TSH as well. Among euthyroid patients with established diabetes, the stated variables may tend to normalize secondary to a decline in autoimmune processes and in the reduction of Lp(a) levels, fT3 may be the globulin to aggregate with TSH, similar to apo A-I aggregating with Lp(a) [please, consult Onat A, Anadolu Kardiyl Derg 2013; 13: - ], thus explaining the significant correlation with HDL-cholesterol.
   
   **Response:** Thanks a lot for your good advice. I have studied the papers you recommended carefully, and added this explanation in our Discussion part (Page 9,
Paragraph 2).

5. Sex distribution should be stated in Table 4. Patients exhibiting TPO-Ab seropositivity and disclosing TSH-correlated lower DBP and TC levels, and fT3-correlated lower HDL and Trg levels…Can this be explained better?

Response: The sex distribution had been stated in Table 4 (Page 18). For these correlations lost their significance when adjusted for age, sex, duration of diabetes, fasting glucose and BMI, we did not fully detailed.

6. Numerous grammar and language errors exist, requiring correction.

Response: The manuscript had been read again carefully and revised.
Reviewer: Jiajun Zhao

Reviewer's report:

Authors have addressed my suggestions adequately. But I wonder how long did it take to recruit the 389 subjects? and the subsequent 73 individuals? It is not easy to persuade one patient to attend the study, even more difficult to select proper subjects according to your strict inclusion and exclusion criteria. In addition, the titles of table 2 and table 3 are not consistent with the contents.

Response: The first group of 389 subjects was recruited for about 2 years (January 1, 2012 to December 31, 2013), and the subsequent 73 individuals were recruited for about 7 months (January 1, 2014 to July 20, 2014). We plan to do more study about this topic, so the study will be continued.

Table 2 and table 3 had been combined and the title had been revised. (Page 17)
Thanks again to you for the thoughtful and thorough review. Hopefully we have addressed all of your concerns. If there are any problems, please don’t hesitate to tell us.

Sincerely yours,

ZHANG Yun and XIAO Xinhua