Author's response to reviews

Title: Apolipoprotein A1/ high density lipoprotein-cholesterol ratio is an important risk factor in type 2 diabetes?

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Author's response to reviews: see over
Cover letter

Dear Editors

We had made revisions in this version of the manuscript. If I can be of any assistance at all in clarifying any points in the manuscript, please do not hesitate to contact me. Thank you for your help and I look forward to your response.

Reviewer: Evangelos Rizos

Major comments

1. Provide an explanation why ApoB/LDL is differently associated with diabetes in men compared with women. (p14, line 231-241)

For unadjusted univariate analysis in Table 2 and 3, all ApoA1/ HDL, ApoB/LDL, ApoB/ApoA1 and LDL/HDL were significantly associated with diabetes. When they were separately put into multivariate model for analyses, ApoA1/HDL remained significant in both sexes and top tertile of ApoB/LDL was only significant in women. In Table 4, all ApoA1/ HDL, ApoB/LDL, ApoB/ApoA1 and LDL/HDL were put into the same model for analysis. The lipid index of ApoA1/ HDL was significantly associated diabetes with a linear response in both genders. Only top ApoB/LDL tertiles conferred risk for diabetes at approximately 2-fold ORs in women but not in men, independently of other confounders. There are apparently gender differences which are worthy of further survey

2. One of the criteria to diagnose diabetes was HbA1c > 6%? Why? Please explain. (p16, line 270-274)

According to American Diabetes Association, HbA1c has been used to diagnose diabetes with a cut point of 6.5%. However, the approximate mapping between HbA1c values (%) and estimated average glucose measurements is given by the following equation.

Estimated average glucose (mg/dl) = 28.7 \times \text{HbA}_1c \ - \ 46.7 \quad [1].

The translation of HbA1c to estimated average glucose is shown in table below. HbA1c of 6 is approximated as estimated average glucose of 126 mg/dl. Although we adopted HbA1c \geq 6 as one of selection criteria in the present study, we tried to put HbA1c \geq 6.5 into analysis and the results was similar (Data not shown).
3. Rewrite the tables according to univariate and multivariate regression. State clearly the covariates used for the multivariate models. (p11, line 177-198; p24, Table 2; p25, Table 3)

We had rewritten the tables and stated the covariates used for the multivariate models.

4. Rephrase the manuscript so that the term prediction is substituted by association/relation. These are not prediction factors but only association models.

We had substituted the term prediction for association/relation in the manuscript.

**Minor comments**

1. Background: rephrase lowering to reduction: (p6, line 89)

We had rephrased lowering to reduction in the background.

2. Discussion: rephrase capability of anti-atherosclerotic to anti-atherogenic properties. (p15, line 246)

We had rephrased capability of anti-atherosclerotic to anti-atherogenic properties in the discussion.
Reference

Reviewer: Gerald H Tomkin

Reviewer's report:

1. The title of this article is intriguing. I initially thought the authors were going to look at risk of complications of diabetes but the purpose of the paper is not stated in the background. Instead the authors just state that the authors analysed lipid, lipoproteins and other variables to determine the potential roles as predictors of diabetes" Thus the study is a cross sectional study investigating lipids, lipoproteins and other variables in order to discover abnormalities in diabetes as compared to non-diabetic subjects. (p1, line 1-2)

We had substituted the title, Apolipoprotein A1/ high density lipoprotein-cholesterol ratio is an important risk factor in type 2 diabetes, for “The association between the apolipoprotein A1/ high density lipoprotein -cholesterol and diabetes in Taiwan-A cross-sectional study.”

2. Diabetes mellitus is so named because blood sugar makes the diagnosis of diabetes so the study is a study of lipid abnormalities in diabetes as compared to the general population. Lipoprotein abnormalities are so well described in diabetes that it has been suggested that diabetes mellitus should be renamed diabetes lipidus. There is ample literature to confirm low HDL, high triglycerides as the major lipid abnormality in diabetes. The interesting new finding in this paper is that apo A1/HDL cholesterol is more likely to be abnormal in diabetic than non-diabetic patients. Thus the authors show that if you have not got the ability to measure blood sugar to diagnose diabetes, you might suspect diabetes by an abnormal apo A1/HDL cholesterol at least in a Taiwanese population. What would be interesting to find in the future is whether this ratio can predict the development of diabetes prior to hyperglycaemia occurring. (p17, line 286-290)

While existing glucose based diagnostic criteria remain obscure, diabetes might be suspected by an abnormal ApoA1/HDL-C in a Taiwanese population. ApoA1/HDL-C in the development of diabetes by a cohort study is required, as susceptible individuals are increasingly being considered as candidates for appropriate interventions.

3. Some attention needs to be paid to spelling and grammar.
Now our manuscript is under the language correction by a native-English speaker with scientific expertise.

4. The abstract should perhaps be slightly altered and it should be made clear that the study is about identification of new patients with diabetes rather than predicting the risk of developing diabetes in the future. **(p4, line 45-67)**

We had made alterations in our abstract.

Best regards,

Sincerely,

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