Reviewer’s report

Title: Apolipoprotein E Gene Polymorphism and the Risk of Cardiovascular Disease and Type 2 Diabetes

Version: 0 Date: 10 Jun 2019

Reviewer: Lupe Furtado-Alle

Reviewer’s report:

The article Apolipoprotein E Gene Polymorphism and The Risk of Cardiovascular Disease and Type 2 Diabetes in Hakka Population consists in an investigation of APOE polymorphism role in TDM2 and CV. The relevance of the subject is well presented and the study has a clear aim. Besides these favorable points, the entire text requires careful language review and some important issues must be discussed.

Statistical analysis

1) Authors should inform if data distribution were tested for normality (p values included). Suitable tests must be applied for parametric or non-parametric data.

2) Hardy-Weinberg equilibrium of genotype distribution must be tested.

3) Authors should include the use of blood pressure control medicaments as a correction factor in multivariate regression analysis.

4) Authors did not inform if comparisons of biochemical variables between groups had taken into account the use of blood pressure control, cholesterol or glycemic control medicaments.

Results

1) The term "Baseline characteristics of subjects" may be misleading by suggesting that this is a follow up study. The authors show only patients and control variables which were used in the association analysis.

2) The indiscriminate use of terms CVD and CAD is confusing.

3) Lines 153 to 156: "At the same time, a significant sex difference was found between controls and T2DM patients without CVD, CVD patients without T2DM, T2DM patients with CVD, respectively, which suggested that women are more likely to develop cardiovascular disease or T2DM." This information/suggestion is not supported by data shown in table 1. The only sex ratio difference is found in the control group, but not in
any of the patient's group. It is not correct to compare patients sex ration with control sex ratio because control sample was selected by the authors and should had been designed to match a 50:50 male: female proportion.

4) Line 179 to 182: "In CVD+T2DM patients, the frequency of E3/E3 genotype was lower (p = 0.556), while the frequency of E3/E4 genotype and epsilon 4 allele were higher than that of CVD group (p = 0.070 and 0.124, respectively)." These differences are not significant and the authors should say so.

5) Line 182 to 183: "In addition, compare with controls, ε2 allele was significantly lower in T2DM, CVD without patients, T2DM with CVD patients (p = 0.003)" This sentence is difficult to understand and must be rewritten.

6) Lines 208 to 222: "Relationship between Lipid profiles and ε4 allele" The analysis presented in this topic should take into account the use of cholesterol control drugs.

Discussion/Conclusion

1) Lines 225 to 249: Authors present a lot of information that does not really discuss their findings. Some of this information could be in the Introduction section of the article.

2) I believe there is an error in control sample composition, because authors included age and sex bias by not matching properly controls and patents regarding these variables. Considering this problem, authors should not suggest age and sex as risk factors based on their association analysis.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

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