Author's response to reviews

Title: Clinical characteristics and beta cell function in Chinese patients with newly diagnosed type 2 diabetes mellitus with different levels of serum triglyceride

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Author's response to reviews: see over
Dear Professor Fernanda Ortis,

We thank the reviewers for their constructive comments regarding our manuscript and appreciate your willingness to review our revised manuscript entitled “Clinical characteristics and beta cell function in Chinese patients with newly diagnosed type 2 diabetes mellitus with different levels of serum triglyceride” by Hu et al. (MS: 1896638514159308). Attached is our revised manuscript that has incorporated responses to reviewers’ comments. Our point by point response to each reviewer’s concern is followed:

Reviewer #1 (Professor Junia Santos-Silva):

Overviews
The aim of this manuscript was to determine whether there is a functional correlation between plasma TG levels and T2DM progression in Chinese patients. There are some suggestions for manuscript improvement.

Major Comments/Critics
1. The manuscript in general is very difficult to read and follow, so someone needs to carefully read the entire manuscript to make sure everything is understandable with only a single reading. I strongly suggest an English review.
   Answer: Thank you for your sincere advice and now we have made our manuscript reviewed by Professor Yunli Zhou from Neuroendocrine Unit, Massachusetts General Hospital, Harvard Medical School and we want to do our best to make sure everything is understandable with only a single reading. If there is still anything difficult to read or follow, please let us know and we would make a further revise.

2. The expression ‘drug native’ for T2DM (lines 35, 63, 74 for example) should be explained.
   Answer: Thank you for your useful advice. We are so sorry that we have made a mistake in...
the spelling. In fact, we really want to use the words “drug naive” to express the meaning that these patients with newly diagnosed T2DM didn’t have diabetes drug treatment before the research. The wrong words “drug native” have already been changed to “drug naive” in the manuscript.

3. Since all individuals enrolled into this study had newly diagnosed T2DM, authors should avoid saying that only to the group who presented higher TG content.

Answer: Thanks for your advice. In this research, all participants were patients with newly diagnosed T2DM, and all comparisons among different groups according to TG levels were under the background of newly diagnosed T2DM. So in this manuscript, “the group who presented higher TG content” really refers to patients with newly diagnosed T2DM and with higher TG content at the same time. We have changed some unsuitable sentences in the manuscript.

4. Authors should mention the number of the Ethical Committee Approval.

Answer: Thanks for your advice. The number of the Ethical Committee Approval is Renjikls N026. Now, the number of the Ethical Committee Approval has been added into the manuscript.

5. Results and Discussion:

5.1 Why not divide the groups into 4, as done in table 2 and figure 2? By dividing into 4 groups, the statistical differences remains between groups (BMI, HDL-C, LDL-C, HbA1c etc) in table 1 and figure 1?

Answer: Thank you for an important question. In fact, we have considered the division of four groups before. The table in the next page showed the results according to the quartile of TG level. We could see the statistical differences remains among groups (BMI, HDL-C, LDL-C, HbA1c etc). However, the differences between group1 and 2 or between 3 and 4 were not that obvious. So we think maybe it was more reasonable to divide the patients into two groups, namely newly diagnosed T2DM with normal and high TG (TG≤ 1.70mmol/L and >1.70mmol/L) (details in Table 1). After the analysis of the data divided into two groups, we found HOMA-beta and HOMA-IR had no significantly difference in the two groups, which made the results doubtable. So in order to have a further understanding of the relationship between triglyceride level and beta cell function of these patients, we divided these patients into four groups according to the quartile of TG concentrations and finally found the differences (details in Table 2).
Group was defined by the quartile of serum TG. Group 1: newly diagnosed T2DM with TG up to 1.13mmol/L; Group 2: newly diagnosed T2DM with TG of 1.14 to 1.56mmol/L; Group 3: newly diagnosed T2DM with TG of 1.57 to 2.27mmol/L; and Group 4: newly diagnosed T2DM with TG of 2.28 to 11.65mmol/L.

* P< 0.05 versus Group 1; # P< 0.05 versus Group 2; + P< 0.05 versus Group 3

5.2 Authors should include the total n for each group in table 1.

Answer: Thank you for your useful advice. The total number of normal TG group was 348, and the total number of High TG group was 276. Now we have added the number of each group in Table1. Please see the details in the Table1.

5.3 Since no statistical differences were observed in FPG levels, authors cannot say that the levels of FPG were increased (lines 150-151).

Answer: Thank you for you useful advice. We have deleted the description about FPG level in the manuscript since no statistical differences were observed.

5.4 Authors state that insulin action (figure 2f) is increased in the group 1 and “stayed the same” in groups 2, 3 and 4. They should discuss the results in comparison to the literature and, as the graph shows, the insulin action reduces when TG levels raised, therefore, did not remain the same.

Answer: Thanks for your advice. In figure 2f, we could observe IAI was high in group 1 and the difference was statistical compared with group 2, 3, and 4. However, there were no statistical
difference among group 2, 3, and 4. So we make the conclusion that “stayed the same”, which we really mean was “not deteriorate”. IAI (insulin action index) is an index to reflect the degree of insulin sensitivity. In this research, we used HOMA-IR and IAI to evaluate the degree of insulin resistance. The results showed insulin resistance didn’t become worse as the further rise of TG (the results of group 2, 3, and 4), which were, to some extent, comparable with Ma et.al.’s study. Their studies indicated that the Chinese patients of newly diagnosed T2DM with hyperlipidemia had no statistical differences in insulin sensitivity compared with patients of newly diagnosed T2DM without hyperlipidemia.

5.5 Instead of saying that more studies are needed, authors should propose a mechanism by which better management of dyslipidemia could improve glucose homeostasis in T2DM.

Answer: Thank you for your good advice. According to our clinical experience and animal experiments, we believe lipotoxicity is an important cause of T2DM and a better management of dyslipidemia could reduce the effect of lipotoxicity to diabetes and thereby improve glucose homeostasis in T2DM patients. So we propose that a better management of dyslipidemia may, to some extent, reduce the effect of lipotoxicity, thereby improving glucose homeostasis in patients with newly diagnosed T2DM. Now we have added our clinical and animal studies about lipotoxicity to diabetes in Discussion (line199-204). In addition, the revision of the conclusion has also been made in the Conclusions section.

Reviewer #2 (Professor Carla CRC Carvalho):

Overviews

The authors present a well done study, with appropriated methods, clear and well balance discussion, and short term future perspective to use the knowledge acquired herein, particularly due to ethnic considerations. I am not native English spoken, but I considered the manuscript had no spelling mistakes.

Answer: Thank you very much for your prompt review.
Editor’s Additional Request:

1. Please change the 'Aims' to 'Background' in the Abstract Section.

Answer: Thank you for your good advice. We have changed the word “Aims” to “Background” in the Abstract Section.

2. Requesting to re-upload the Figure Legends

Figure legends must be included in the main manuscript text file at the end of the document, rather than being a part of the figure file. For each figure, the following information should be provided: Figure number (in sequence, using Arabic numerals - i.e. Figure 1, 2, 3 etc); short title of figure (maximum 15 words); detailed legend, up to 300 words. Please note that it is the responsibility of the author(s) to obtain permission from the copyright holder to reproduce figures or tables that have previously been published elsewhere.

Answer: Thank you for your good advice. We have added the figure legends in the main manuscript text file at the end of the manuscript. And the details of the figures (including number, title and legend) have been revised according to the information above. We are sure that we haven’t put figures or tables in this manuscript that have previously been published elsewhere.

3. STROBE guidelines

In accordance with BioMed Central editorial policies (http://www.biomedcentral.com/about/editorialpolicies#StandardsofReporting), could you please ensure your manuscript reporting adheres to STROBE guidelines(http://www.strobe-statement.org/) for reporting observational research. This is so your methodology can be fully evaluated and utilised. Can you please include a completed STROBE checklist as an additional file when submitting your revised manuscript.

Answer: Thank you for your good advice. We have finished the STROBE checklist and it will be uploaded as an additional file when we submitting our revised manuscript.

We greatly appreciate the opportunity to revise our manuscript and hope that it is now acceptable for publication in BMC Endocrine Disorders.

Sincerely,

Yaomin Hu, M.D., PhD