Author’s response to reviews

Title: Association between thyroid-stimulating hormone and maternal hemodynamics in hypertensive disorders of pregnancy: An observational study

Authors:

Yu Liu (liuyuwow512@163.com)
Bo Gao (michellbo@163.com)
Xin Zeng (august555482@126.com)
Jing Yang (yangjingnjsfy@163.com)
Lei Zhang (zlnjfy@163.com)
Ganwei Xu (30418964@qq.com)
Ruizhe Jia (rzjia9599@163.com)
Zhengfeng Xu (xzfnjfy@163.com)

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Author’s response to reviews:

Dear editor,

This was a revision for manuscript PRCH-D-19-00859R1, entitled ‘Association between thyroid-stimulating hormone and maternal hemodynamics in gestational hypertensive disorders: An observational study’. Thank you very much for your comments and suggestions. We have carefully studied the comments and made corrections accordingly, which were highlighted in bold and green color in the revised version of the manuscript. The detailed responses are listed. We would like to re-submit this revised manuscript, and wish it is acceptable for publication in your journal.

Looking forward to hearing from you.

Best regards,

Zhengfeng Xu
The detailed responses to the editor’s and reviewers’ comments:

First of all, we thank the editor and the reviewers for their careful review and the positive and constructive comments and suggestions. The point-to-point responses to the comments were listed below.

Editor comments

1. There seems to be confusion between the chi-squared test, and the Pearson’s correlation coefficient. Line 51-52 of the abstract states that correlations between thyroid hormones and maternal hemodynamic parameters were assessed by the Pearson’s chi squared test. The Chi squared test examines the relationship between categorical variables, not correlation between linear variables. Please ensure that the correct test is specified. The same comment applies to the statistical methods section.

Response:

Thank you for your careful review. We are sorry for this mistake. The correlations between thyroid hormones and maternal hemodynamic parameters were assessed by Pearson’s correlation coefficient, instead of Pearson’s chi squared test. These mistakes were corrected both in the abstract section (Line 54, P3) and methods section (Line 184, 186, P9).

2. GHD is not a standard abbreviation. Please eliminate this abbreviation from the manuscript. Also, please replace this term with the more commonly used term “Hypertensive disorders of pregnancy” and specify whether women with the remaining to forms of this disorder (chronic hypertension in pregnancy and preeclampsia superimposed on chronic hypertension) are included in this study.

Response:

Thank you for your advice. We have eliminated all of the non-standard abbreviations of GHD and replaced with HDP (hypertensive disorders of pregnancy). Patients with chronic hypertension in pregnancy and preeclampsia superimposed on chronic hypertension were excluded from the study. These criteria were supplemented in the Patients and Methods Section-Patients Section (Line 132-133, P6-7).
3. Please state what summary statistics are presented in the abstract (i.e. mean SD, median IQR, value with 95% CI, etc.).

Response:

We really appreciated your suggestions. We have added the detailed summary statistics presented in the abstract in the methods section of the abstract. Normally distributed variables were expressed as mean± standard deviation (SD) and skewed variables were expressed as median (25th percentile, 75th percentile). Correlations between thyroid-stimulating hormone (TSH) or free thyroxine (FT4) and maternal hemodynamic parameters were assessed by Pearson’s correlation coefficient and 95% confidence interval (95%CI). Logistic regression models were applied to confirm the associations with odd ratio (OR) and 95%CI. (Line 51-52, 54-55, P3)

4. Please ensure that the criteria for “Reduced CO” is defined at first use in the abstract, and again at first use in the manuscript. The abbreviation for cardiac output is not defined in the abstract. It may be clearer for readers to refer to this subset of patients as the “Low CO group”.

Response:

We are sorry for this mistake. The criterion for ‘reduced CO’ was defined in the Methods Section-Maternal hemodynamic monitoring Section of the manuscript (L154-155, P7-8). This criterion was added at the first use in the abstract in the revised manuscript (Line 59, P3). The abbreviation for cardiac output at first use was added in the abstract in the revised version (Line 59, P3).

5. Page 5, line 104 – please replace the informal abbreviation Jan with January

Response:

We are sorry for this mistake. The informal abbreviation Jan has been replaced by January.

6. Please eliminate the non-standard abbreviation ICG.

Response:

Thank you very much for your advice. We have eliminated all the non-standard abbreviation ICG from the revised manuscript.
7. Page 5 lines 106-108 – was gestational hypertension diagnosed on the basis of a single elevated blood pressure, or persistent elevations in blood pressure (>2 measurements at least 4-6 hours apart as required by most guidelines)? Were diagnostic criteria for GH and PE (hypertension, proteinuria) confirmed by review of medical records, or through other methods?

Response:

We are sorry for the confusion. The elevated blood pressure was confirmed by at least 2 measurements at intervals of at least 4-6 hours apart. This was added in the Patients Section (Line 130-131, P6). HDP patients in this study were prospectively enrolled in the study in the third trimester. They were enrolled once diagnosed by the medical reports of blood pressure measurements and proteinuria test at routine prenatal examination at our hospital.

8. For RRIDs of antibodies and ELISAs, please eliminate the space between RRID: and AB to conform to standard RRID notation (RRID:AB…).

Response:

We apologize for the informal expression of RRID notation. We have eliminated the space between RRID: and AB to conform the standard RRID notation (Line 161-163, P8).

9. Please remove the final sentence of the paper, which states that “routine and longitudinal monitoring of TSH levels during pregnancy should be considered”. This type of clinical recommendation requires careful analysis of risks, benefits, costs and burdens for patients and the healthcare system, which was not the focus of the current study. The authors could replace this sentence with a general statement about the need for further study, as long as there is no clinical recommendation.

Response:

We appreciated for your valuable advice. We have removed the final sentence of the paper. Instead, we added ‘Mechanisms of the associations between TSH and reduced CO warrants future investigation’ to the final sentence (Line 299-300, P14).

10. Table 3: Please reorganize columns as r, then 95% CI, then p values.

Response:

Thank you for your advice. We have reorganized the columns of Table 3 in the order of r, 95%CI and p values.
11. Table 4: GFR has a p-value <0.05, however was not included in the multivariate model.

Response:

We apologize for this misleading. GFR has a p-value less than 0.05 in the univariate regression analysis, it was pooled into the multivariate model. However, GFR has no significant association with reduced CO and the results were not presented in the table. Here, we added the results of GFR in the multivariate regression analysis in Table 4. GFR was not significantly associated with reduced CO (OR=0.987, 95%CI: 0.970-1.004, p=0.141).

12. Table S1: Gravidity, parity and GHD should be listed as n (%), however only n appears on the table. Please provide sample sizes in the headers for the Normal CO and Low CO groups and specify what summary statistics are shown in the table legend.

Response:

We are sorry for this mistake. The proportions of gravidity, parity and GHD have been added in Supplementary Table 1. The sample sizes of Normal CO and Low CO groups were added in the headers of the table. The details of the summary statistics were added in the table legend of Supplementary Table 1.

Reviewers’ comments:

Reviewer 1: No further comments

Response:

Thank you for your careful review and the positive comments.

Reviewer 2: No further comments

Response:

Thank you for your careful review and the positive comments.