Author’s response to reviews

Title: A cohort study of the association between maternal serum inhibin-A and adverse pregnancy outcomes A population-based study

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Reviewer reports:

Parvin Abedi, PhD (Reviewer 1):

1. Introduction: it is better that authors start this section with the screening tests not with the down syndrome.
Response: This is edited as suggested, as highlighted.

2. Introduction: line: 40: please state the name of the country.
Response: The name of the country is added, as highlighted.

3. Introduction: line 53-57: please cite these sentences. Also the following sentence needs to be cited: Additionally, the results from previous studies are inconsistent.
Response: The sentences are now cited, as suggested.

4. Introduction: what is the mechanism for the increase or decrease of inhibin-A as a component of quad test?
Response: The mechanism is unclear but we the hypothesis is explained in the fourth paragraph of “Discussion” section?
5. What was the hypothesis of this study, please mention at the end of the introduction.

Response: The hypothesis of the study is added at last paragraph of “Introduction”, the last second sentence.

6. Method: we need to have more information about the initial cohort study, e.g. when did it start with how many participants?

Response: The information is added as suggested, as highlighted.

7. Statistical analysis: please state that in which level of significantly variables were entered to the logistic regression. And what were the confounding variables that you adjusted for them.

Response: The information is added in the last paragraph of “Methods” section, as highlighted.

8. Method: please mention the normal range of inhibin-A.

Response: The normal levels of inhibin-A are specific for individuals, varied with gestational age and body weight and the measured values were converted to MoM automatically after adjusted for gestational age and body weight calculated by the built-in software model. Therefore we apologize that we could not provide the normal range.

9. Method: please cite all pregnancy outcome definitions (preterm labor…).

Response: The reference is provided.

10. Please explain the procedure for the measuring PPH.

Response: The information is now added.

11. Results: table 1: please state that how did you categorizes the socio-economic status of participants? And why you do not have any medium category?

Response: The socio-economic status was based on their occupations. This is indicated at the footnote of the table 1, in the revised manuscript. We have categorized into just only two groups.

12. Why authors in table 2 used relative risk and in table 3 they used OR in the logistic regression? If it is possible, please show the crude and adjusted OR in one table. And please indicate which factors you adjusted.

Response: Table 2 shows outcomes of the cohort study of which relative risk is preferred. Table 3 shows logistic regression analysis of which odd ratio is preferred. In the revised manuscript, crude OR and adjusted OR are shown in the same Table 3.

13. Discussion: please cite line 6-9, also 14-17 and 26-29.

Response: They are now cited as highlighted.

14. One of the limitations of this study is: participants were not enrolled randomly and cannot be
generalized to the whole population of the country.

Response: The limitations are added in the part of limitation at the last second paragraph of the “Discussion” section, as highlighted.

Reviewer 2:
Thank you for the opportunity to read and review your paper. It addresses an important subject, and your study appears to have been an interesting one. There are some problems with the paper which mean it doesn't present your study as well as it could. My comments regarding aspects that need attention are listed below.

1. The entire paper needs proof reading for consistency and readability as some of the terms used are inconsistent and some of the material is a hard to understand.

Response: English and typographical errors are now checked and edited by a professional English native speaker.

2. In order for this paper to be ready for publication it requires extensive work in relation to all sections, which is the introduction, methods, result and discussion.

Response: The manuscript has been reviewed and corrected.

3. In the background part, the authors mention about their project "we have implemented a screening program for the fetal Down syndrome with serum markers in second-trimester pregnant women, as a pilot study project. All of the participants underwent quad test free of charge, supported by the government. Under the project, baseline data, laboratory results and pregnancy outcomes were followed-up and prospectively collected. To take advantage of Down syndrome screening, we could also have a great opportunity to study on the correlation between various serum biomarkers and adverse pregnancy outcomes". It will be clearer if the authors explain about the result of the study rather than explain about the procedure of the last study.

Response: These sentences aimed to clarify the original project (Down syndrome screen) which based this study, not to show the result of the original project but we emphasize the prospective nature of the original project which make our new study more reliable.

4. The objective of this study is not quite clear. The authors explained that the study aimed to determine the association between Inhibin-A level in the second trimester and rates of adverse pregnancy outcomes, however, in the result part the authors analyzed about comparison of the pregnancy outcomes between the high Inhibin-A group and the normal inhibin -A group. I do not understand why?

Response: We have rewritten the objective “To compare the rates of adverse pregnancy outcomes between women with normal and abnormal inhibin-A levels”.

5. The material and methods used in this study is not clearly explained and difficult to follow, I suggested that the authors make it a simple one and will be easy to understand.

Response: We try to make it simple to follow in the revised manuscript.
6. Results and discussion, the authors need to make sure about what is the study aimed. In addition in some part of result is confusing and difficult to follow.

Response: We try to make it simple to follow in the revised manuscript.

7. In the discussion part, is it the study about the association of maternal serum markers and adverse pregnancy done by authors?

Response: Yes, but we have rewritten to make it clearer. The objective is to compare the rates of adverse pregnancy outcomes, in particular preeclampsia, preterm birth, fetal growth restriction and low birthweight, between women with normal and abnormal inhibin-A levels.