

## Peer Review File

**Article information:** <http://dx.doi.org/10.21037/tp-20-211>.

### Reviewer A

#### Comment1:

Thank you for providing me the chance to review this important manuscript that is approaching an important area related to maternal and newborn health.

However, I think the manuscript in the current status is just reporting some observations and neglecting the role of covariates that might lead to the same results of the study. For example, the authors neglected completely any information about the mother's health during pregnancy, which has a great impact on the pregnancy outcome. Maternal dietary carnitine deficiency or genetic causes can lead to decreased carnitine levels in the newborn. Similarly, increased glycine level in the newborn might be due to other causes than pregnancy-induced hypertension.

The study needs more information about maternal health status during pregnancy, then adjusting for all the co-variates including PIH to acknowledge that these results are solely due to PIH or at least PIH has higher influence than other covariates.

**Reply1:** We thank the reviewer's valuable comment. As requested by reviewer, we revised the description in our manuscript as follow. We added some data about our inclusion criteria and modified our exclusion criteria.

**Changes in the text: Page 4 line 98-109.**

#### Comment2:

A general comment is checking the English language of the entire manuscript, with a special focus on the tenses. The author should use past tense when writing about their study.

**Reply2:** We thank the reviewer's comments and we apologize for the incorrect tense in our manuscript. We had re-checked the full text and modified their tenses.

# EDITORIAL CERTIFICATE

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Manuscript Title:

The influence of pregnancy-induced hypertension syndrome on the metabolism of newborns

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### **Comment3:**

Methods:

Page 3, lines 91-94: Is the 56 mothers the total number of all women who delivered in this hospital during this period? The type of the sample is not clear. What are the criteria for selection?

**Reply3:** We thank the reviewer's valuable comment. For the first question, all the participants were delivered in our hospital during Sep. 2010 to Aug.2012. For the second, we had added the criteria for selection in our manuscript.

**Changes in the text: Page 4,98-102.**

### **Comment4:**

Page 4, line 136: "The quantitative data not conforming to normal distribution were described by M (P25, P75)." What is (M), if the authors mean the median; they should write the word "Median" followed by the abbreviation (M).

**Reply4:** We thank for the reminding of reviewer and we apologize for the incorrect description in our manuscript. (M) indeed mean the median. We have already modified it in the article.

**Changes in the text: Page 6 line 152.**

**Comment5:**

Page 4, lines 137-138: “The data of qualitative data were described by frequency, and chi-square test was used for comparison between groups.” Was there any “qualitative data” in the study or this was a spelling mistake? If there was, how can qualitative data be described by frequency and chi-square test? Please explain what you mean.

**Reply5:** We thank the reviewer’s valuable comment. The gender of newborn (the frequency of male) was the qualitative data in our manuscript. Qualitative data is a group of written descriptive data that represents the nature of things and defines their categories. It cannot be quantified, but can only be qualitative. It is described by frequency, and chi-square test is commonly used for comparison between groups

**Changes in the text: Page 7 table 2.**

**Comment6:**

Results:

A general comment, what test the authors used to test the normality of the data. Were data of weight and height of 58 women normally distributed? The same question applies to the control group data of weight and height.

**Reply6:** Thanks for reviewer’s comment. We used Kolmogorov-Smirnov and Shapiro-Wilk test to test the normality of the data. The weight and height of 58 women were normally distributed. The same as the control group.

**Changes in the text: Page 6 line 148-149.**

**Comment7:**

Table 1: Why you didn't calculate BMI to detect obesity among these mothers. Presenting weight and height didn't inform the reader by any important information.

However, presenting BMI can give good information, particularly, according to the presented means of weight and height; these women were more likely to be overweight. Overweight and obese women are at higher risk to develop PIH.

**Reply7:** We thank the reviewer's valuable comment. We added the data of BMI to detect obesity among these mothers in table 1. The result showed that overweight women were at higher risk to develop PIH.

**Changes in the text: Page 7 table 1.**

**Comment8:**

Page 5, lines 167-168: "The average gestational age, weight and body length of PIH were lower than those of newborns with normal pregnancy." There is an English language problem in the writing that requires substantial revision. This sentence should be written as: "The average gestational age, weight and body length of newborns of mothers with PIH were lower than those of newborns of mothers with normal pregnancy."

**Reply8:** We thank the reviewer's valuable comment. We had modified this sentence.

**Changes in the text: Page 8 line 188-189.**

**Comment9:**

In table 2, 3, please add the full value of p rather than  $<0.05$ .

All the analysis is descriptive. However, these results might be due to other factors (covariates) that affected this outcome. Were the mothers' blood examined for the level of anemia for example. Low birth weight—a study outcome in table 2—could be the result of many other factors other than PIH; anemic pregnant women for instance give birth to low birth weight infants.

**Reply9:** We thank the reviewer's valuable comment. We added the full value of p. Our inclusion criteria had limited any diseases or other pathologic conditions except for PIH. Therefore, the mothers were no anemia. And we had a good reason to believe that the low birth weight of the newborn was the result of PIH.

**Changes in the text: Page 7 table 2; Page 11 table 3.**

**Comment10:**

In the same table 2: what is the scientific significance of comparing newborn gender of both groups? Please explain.

**Reply10:** We thank the reviewer's valuable comment. Considering the gender of the newborn may have an effect on its blood metabolites, we compared the gender of the two groups of newborns simultaneously.

**Comment11:**

Discussion:

A general comment on the discussion: it needs substantial revision and editing.

Page 11, line 266: "Therefore, the results of this study may be related to pregnancy-induced hypertension." How the authors can reach this conclusion from a descriptive analysis without any advanced regression analysis?

**Reply11:** We thank the reviewer's valuable comment and we apologize for the incorrect statement. Through literature review, we knew that mothers with PIH were prone to preterm birth. Our result also showed that PIH women likely to preterm birth. We just wanted to showed the same conclusion. We had modified the sentence.

**Changes in the text: Page 14 line 296-297.**

**Comment12:**

Page 11, lines 268-288. This section is discussing complications of PIH, however, the study showed nothing about maternal health during this pregnancy. All what the authors mentioned about the mothers is their weight and height! As it is well known that the discussion section is for discussing the study outcome compared to other results rather than a place for literature review. Absence of information of maternal health during this pregnancy renders this section irrelevant and misallocated in the discussion section.

**Reply12:** We thank the reviewer's valuable comment. Most of the study we mentioned in this part were single factor analysis. We controlled other factors except for PIH when we chose samples. We had added something about maternal health

during this pregnancy. We wanted to showed the consistence between our study and researches at home and abroad, so we listed some literatures.

**Changes in the text: Page 14 line 281-282.**

**Reviewer B**

This is a translational study done to evaluate the differential metabolomics of infants born to mothers with and without PIH. Blood samples were analyzed from these groups and the authors report a significant relationship between the metabolic fingerprint with increased glycine and decreased C14DC, C22, C4DC, C5:1, C6DC, C5-OH, Proline, C14-OH in blood samples.

**Comments**

In general there are many grammatical mistakes and awkwardly worded sentences in the manuscript which makes it difficult to read and follow. Some of them are described below, however it is beyond the scope of this review to correct them all in the manuscript.



**Comment1:**

Page 1 line 36: The conclusion is not worded well and does not make sense, it needs to

be rewritten. Also, use of words like ‘proven relationship’ is too strong. This study does not definitely prove, but merely suggests a relationship. You need to be careful about what you are concluding.

**Reply1:** We thank the reviewer’s valuable comment and apologize the incorrect description. We had modified the word.

**Changes in the text: Page 2 line 42-43.**

**Comment2:**

Page 2 line 51- ‘delay’ in childbearing age is incorrect. You can say increase in maternal age or more mothers with advanced maternal age.

**Reply2:** Thanks for the reviewer’s correction. We had modified this sentence.

**Changes in the text: Page 3 line 58.**

**Comment3:**

Page 2 line 54 – “The high level of blood pressure in pregnancy” should be replaced with pregnancy induced hypertension and/or chronic hypertension to show what pathology are you focusing on and to include the entire spectrum.

**Reply3:** Thanks for the reviewer’s value comment. We had modified this sentence.

**Changes in the text: Page 3 line 62.**

**Comment4:**

Page 3 line 78 – “almost blank” in this sentence has no meaning. You can use the word scant.

**Reply4:** Thanks for the reviewer’s value comment. We had modified this word.

**Changes in the text: Page 3 line 82-83.**

**Comment5:**

Page 4 line 87-88: ‘blood samples were obtained from the informed consent of the family members of the newborn’. The sentence has no relevant meaning.

**Reply5:** Thanks for the reviewer's value comment. We wanted to show that the blood samples of newborns were obtained after their parents had provided written informed consent. We had modified this sentence.

**Changes in the text: Page 4 line 94-95.**

**Comment6:**

Page 4 line 93- were selected as what??? I assume the authors want to say 'cases'

**Reply6:** Thanks for the reviewer's value comment. 56 patients with pregnancy-induced hypertension...were selected as cases. We had modified this sentence.

**Changes in the text: Page 4 line 112.**

**Comment7:**

Page 4 line 95: It should be 'were excluded'. This has already happened, please mind the tense. Similarly, throughout the manuscript the author describes the methods as if the study has been planned for the future and not as something that has already been accomplished. This is confusing.

**Reply7:** Thanks for the reviewer's value comment. We had modified the sentence and the tense of all manuscript.

**Changes in the text: All manuscript.**