Peer Review File

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Reviewer A

Prenatal growth assessment is an important part of prenatal care and predicting fetal growth restriction will improve obstetric care. However I am unable to find novelty in the findings from what is already known.

Major comments:

1. A clear statement about what this research adds to the current clinical practice is missing and should be addressed.

Reply 1: We have added a clear statement in the conclusions about what this study adds to current practice. (see Page 15, line 322-326)

2. One of the conclusions of this manuscript is the fact that when FGR occurs the changes of low birth weight are higher, which is stating the obvious.
3. In coherence with the comment above (nr 2) the relevance of table 2 should be reconsidered.

Reply 2, 3: Thank you for your reminder and suggestion. We considered infant characteristics other than low birth weight, such as gender, length, and score, together with maternal characteristics, to be included in the multiple regression model to explore their influence on the occurrence of FGR. Therefore, the content of univariate analysis of infants in Table 2 will be retained.

4. No statement about genetic abnormalities are given in this manuscript, not in the exclusion criteria or elsewhere in the material and methods section. However I think the presence or absence of genetic abnormalities is very important factor concerning fetal growth restriction.

Reply 4: We had ruled out genetic disorders such as trisomy13, 18 and 21 but forgot to mention them. It has now been added in Section 2.2.2 and Figure 1. (see Page 6, line 113-114)

5. In the material and method section numerous definitions are lacking. The definition of PROM, fetal distress, premature delivery and oligohydramnios should be given.

Reply 5: Thanks for your reminder, we have added the definitions of PROM, fetal distress, premature delivery, and oligohydramnios. (see Page 6, line 118-124)

6. No information is given about which growth chart is used.

Reply 6: According to the growth chart information in the Chinese health industry standard WS/T 800-2022 on the growth standard for newborns by gestational age, the diagnosis information of FGR was given. (see Page 5, line 99-105)

7. The definition of low birthweight should be adjusted for the gestational age ate

delivery, not solely based on birthweight.
Reply 7: Thank you for reminding us that the definition of low birth weight is too simple, so we redefined low birth weight based on industry standards and clinical diagnosis. (see Page 5-6, line 108-112)

8. The savings for preferred strategies should be quantified.
Reply 8: Yes**,** thank you for reminding us, we have considered it.

9. Congenital defect are an exclusion criteria, only prenatally detected, or also postnatally?
Reply 9: Congenital defects were 13, 18, 21 trisomy and other genetic diseases. (see Page 6, line 113-114)

10. Based on ISUOG guidelines the cut off for NT measurements is 3.5mm, why did the researches choose for 2.5mm?
Reply 10: According to many industry standards and national standards, we have set the measurement cutoff value of NT as 3.5mm. (see Page 7, line 135)

11. Is there information about the reason for premature delivery? Is this excluding the iatrogenic cases?
Reply 11: Preterm birth was divided into spontaneous preterm birth, premature rupture of membranes, and iatrogenic preterm birth, and iatrogenic preterm birth was excluded from this study.

12. Information about Doppler measurements is missing.
Reply 12: We have added the Doppler measurements. (see Page 7, line 136-140)

13. Although the researchers conclude that maternal serum screening markers in the first trimester in combination with third trimester characteristics the give no clinical suggestion in which way this can improve pregnancy outcomes. Prescribing aspirin could be a suggestion.
Reply13: The clinical diagnostic value and recommendations of this study have been added in the conclusion section. (see Page 15, line 322-326)

Minor comments:
1. Rephrase the first sentence into correct English.
Reply 1: Yes, we have done it.

2. Head 2.4: Statistical method (start with a capital).
Reply 2: OK.

3. Page 9, line 275: pregnant women with FGR were more likely to give FGR?
Reply 3: We have amended this statement: when FGR occurs the changes of low birth weight are higher, which is stating the obvious.

4. Page 15, table 1: multiple pregnancies n=1 in FGR group, however this is an exclusion criteria?

Reply 4: Yes, thank you for reminding us, so we have removed it.

5. The use of reference 28 is incorrect, because in this particular paper a different subgroup is analyzed.

Reply 5: Yes, we have deleted it.

Reviewer B

This is a retrospective cohort study that aims to determine whether first trimester biochemical markers are predictive of later FGR.

Abstract:

The authors report associations between several markers and FGR but do not report predictive efficacy – which is out of step with the title of the paper and the concluding statement of the abstract.

Reply: We added the combined predictive effect of markers in the results section of the abstract. (see Page 2, line 24-25)

Introduction:

The literature review describing previous work on first trimester prediction of FGR is incomplete.

Reply: Thanks for the reminder that we have described previous FGR prediction work in more detail. (see Page 3, line 50-56)

The main aim of the paper could be more clearly expressed at the end of the introduction.

Reply: Yes, we have expressed clearly at the end of the introduction. (see Page 4, line 70-73)

Methods:

How were the controls matched?

Reply: We randomly paired the FGR groups in a 1:4 ratio.

I am surprised the authors have chosen to define FGR as birthweight <2500g rather than a centile. This limits the value of the data – for example, all preterm babies will be 'FGR' using this definition. This makes the whole paper less valuable and although I recognise this is fundamental to the project, I would recommend reviewing this decision.

Reply: We have redefined low birth weight and macrosomia in the diagnostic criteria section, which was based on the Chinese industry standard for growth chart information of infants born at different gestational ages. The definition of FGR was given in the introduction. (see Page 5-6, line 108-112)

Results:
The statement that macrosomia and/or low birth weight are related to FGR (3.4) is a bit odd and suggests the authors haven't thought about the appropriateness of statistical correlation.
Reply: We have removed macrosomia in Table 4.

Discussion:
The paragraph on preterm birth needs to account for a fixed FGR cut-off.
Reply: We supplemented the diagnostic values for FGR in the corresponding sections. (see Page 11, line 268-269)

The paragraph on mode of delivery is really irrelevant to the data that are presented and should be removed.
Reply: OK.