

**Re: Manuscript NO: 71160; Association of Maternal Obesity and Gestational Diabetes Mellitus with Overweight/Obesity and Fatty Liver Risk in Offspring**

**Dear Editor-in-Chief**

We would like to thank the editor and reviewers for their constructive comments and good suggestions. We have made point-by-point response at the bottom of the file and revised our manuscript accordingly. Attached please find the revised manuscript.

Thanks so much in advance for your kindly consideration.

Yours sincerely,

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## **Responses to the comments of Reviewer #1**

The paper has some interesting findings on the association between maternal overweight and GDM and fatty liver risk in offspring. This study will raise the awareness of complications associated with being overweight and GDM. The manuscript is well-written, technically sound, contains all the necessary information on the study. The study design is straightforward, statistical analysis is appropriate, limitations are listed, and conclusions are based on collected data. The references are sufficient.

**Comment 1:** The authors should specify the time frame of the study. The dates (at least a year and a month) of the first and last woman enrolled in the study should be listed as well as the time frame of the follow-up.

**Reply:** Thank you for raising this important point. We have mentioned the dates of the first and last woman enrolled in the study in the revised manuscript.

**Comment 2:** There was a particular number and date of the ethics committee decision on the study design; it could be included in the text (e.g., protocol N 119, 2021-11-19).

**Reply:** Thank you for noting this. We have added the number and date of the ethics committee decision in the revised manuscript.

**Comment 3:** The sentence "The specific offspring characteristics were as follows: birth weight: 3.40 (0.48) kg and 210 (48.8%) boys." could be re-written for easier reading.

**Reply:** Thank you for the thoughtful suggestion. We have re-written the sentence by "The mean birth weight of the group of offspring was  $3.40 \pm 0.48$  kg and 210 (48.8%) children were male gender."

**Comment 4:** Table 1. The CAP abbreviation should be mentioned in the footnotes.

**Reply:** Thank you for raising this important point. We have mentioned the CAP abbreviation in the footnotes in Table 1 of the revised manuscript.

**Comment 5:** Table 2 lacks links to footnotes (a, b, c, d).

**Reply:** Thank you for noting this omission. We have added the links to footnotes in the Table 2 of the submitted version.

**Comment 6:** Tables 2, 4 would be easier to read with each value descended in the same value (e.g., one line for the value and one for CI in each row).

**Reply:** This is a good suggestion. We have revised each value descended in the same value (one line for the value and one for CI in each row) in Tables 2, 4 accordingly.

## **Responses to the comments of Reviewer #2**

In this manuscript Zeng J and Colleagues describe the association of maternal obesity and GDM with overweight/obesity and fatty liver risk in offspring at 8 years of age. The topic is interesting. The major strength of this study relies on its clear aim and study design. However, some issues should be raised.

**Comment 1:** Abstract The phrase «This study indicates that maternal BMI and GDM status both increase the odds of overweight/obesity and fatty liver in offspring» seems not quite correct. According to the described results, isolated GDM was not significantly associated with fatty liver (model 1 OR 2.39 (0.91-6.29)).

**Reply:** Thank you for finding the mistake. We have modified this sentence into “This study indicates that maternal obesity can increase the odds of overweight/obesity and fatty liver in offspring, and GDM status only increase the odds of overweight/obesity in offspring”.

**Comment 2:** Work Definitions Please provide exact numbers (cutoffs) for the diagnosis of GDM , Offspring overweight/obesity and fatty liver.

**Reply:** Thank you for your good advice. We have provided the exact cutoffs for the diagnosis of GDM and offspring fatty liver in the revised manuscript. As the offspring overweight/obesity were defined by using the International Obesity Task Force age- and gender-specific cutoff points, the exact cutoff points change dynamically with age and gender, which could thus not shown in the submitted version.

**Comment 3:** Results The authors write «Maternal GDM was also positively associated with childhood overweight/obesity, with an OR of ... Further adjusting for ... GDM status of the mother and birth weight (Model 3) did not change the associations.» It seems impossible to adjust for GDM if you explore the association of GDM with childhood overweight/obesity.

**Reply:** In fact, you are right. We have corrected the writing mistake in the revised manuscript. Thank you so much again.

**Comment 4:** Discussion The phrase «Our prospective cohort demonstrated that in the Chinese population, maternal obesity and GDM did not increase the risk of liver fibrosis in school-age children» contradict the results of the study. Maternal obesity did increase the risk of fatty liver. It would be good to provide a more comprehensive overview of possible mechanisms of the lasting impacts of maternal obesity and impaired glucose metabolism on offspring weight and hepatic health. Eg., the influence of intrauterine hyperglycemia via altered expression of predisposing genes (eg., [doi.org/10.1155/2018/6481658](https://doi.org/10.1155/2018/6481658), [doi.org/10.1017/S0016672318000010](https://doi.org/10.1017/S0016672318000010)).

**Reply:** Thanks for your kindly suggestion. We have revised the discussion section based on some related articles and also added those articles in the references.

**Comment 5:** Table 4 looks disorderly. Please add visible lines in the table.

**Reply:** Thank you for noting this. We have added visible lines in the Table 4 for easier reading.

**Comment 6:** It is unclear what for did the authors made adjustments listed in model 4.

**Reply:** Thank you for raising this important point. We have made the adjustments listed in model 4 with the consideration of the associations between E values and CAP values. After careful consideration, we have deleted the inappropriate adjustments in the revised version.