

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Gestational diabetes mellitus refers to different degrees of abnormal glucose metabolism that develops or is first found during pregnancy, which has shown a significant increasing trend due to the change of life style and the fertility policy. To address this challenge, in this study, the authors aimed at exploring the value of combination of insulin aspart and metformin for GDM treatment. The authors used primary clinical data, blood analysis, outcome measures on patients in groups of observation/control, and statistical method to organize their manuscript. The results showed that, after treatment, the levels of FBG, 2h PG, HbA1, Hcy, TNF- α , IL-6 and CRP in both groups were significantly decreased ($P < 0.05$), and the levels of FBG, 2h PG, HbA1, Hcy, TNF- α , IL-6 and CRP in the OG were lower than in the CG ($P < 0.05$). The study design is reasonable, and the results reflects the conclusion as well. I recommend its acceptance after the minor revision. The detailed comments are: Comments 1: In my opinion, this study focused on the effects of insulin aspart and metformin on gestational diabetes mellitus. So, the title of this paper can be simplified. Comments 2: In the "Inclusion and exclusion criteria" part, why did the authors exclude patients with multiple pregnancies?

Response:

1. Thank you for your suggestion. The title has been simplified.
2. The exclusion of patients with multiple pregnancies is due to the fact that multiple pregnancies present a higher risk of complications and may confound the results of the study. Additionally, the management and treatment of gestational diabetes will differ in multiple pregnancies compared to singleton pregnancies. Therefore, excluding patients with multiple pregnancies helps to ensure that the study results are more accurate and applicable to a broader

population.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors made a retrospective study to investigate the effects of insulin aspart and metformin on gestational diabetes mellitus. After reasonable grouping the patients into observation and control groups, the authors showed that the baseline data of the two groups were similar, including the factors of age, maternal category, and educational level. However, the observation group showed lower level of blood-glucose-related indexes [fasting blood glucose (FBG), 2-h postprandial glucose (2h PG) and hemoglobin A1c (HbA1c)], serum related factor (Hcy), serum inflammatory cytokines (TNF- α , IL-6 and CRP). In short, the topic of this manuscript is timely and interesting. The authors have organized the manuscript rationally, with good methodology and well-written English. However, some important editing needs to be done before publication: 1. What is the most commonly used treatment for gestational diabetes mellitus in clinic? Compared with that, what are the key advantages of the combination of insulin aspart and metformin? 2. In this study, the drug treatment for patients lasted until delivery. Then, how long will the patient's status be tracked after delivery? 3. The authors should add ethical statement in the manuscript.

Response:

1. The most commonly used treatment for gestational diabetes mellitus in clinics is dietary modification and physical exercise. However, if these lifestyle interventions are not sufficient to control blood glucose levels, the use of insulin therapy is often recommended. Compared to insulin monotherapy or metformin monotherapy, the combination of insulin aspart and metformin has several key advantages. Firstly, it can achieve better glycemic control with a

lower risk of hypoglycemia compared to insulin therapy alone. Secondly, metformin can reduce insulin resistance and has been associated with a lower risk of preeclampsia in women with GDM. Thirdly, insulin aspart can provide more flexible dosing and better postprandial glucose control. Lastly, the combination therapy may have a potential protective effect on the developing fetus, which may lead to better pregnancy outcomes.

2.Unfortunately, the patients in this study were not followed up, so the long-term prognosis of this combined treatment on mothers and fetuses is not clear. Therefore, we hope to conduct more experiments and follow-up in subsequent studies to improve our research conclusions.

3.Thank you for your suggestion. An ethical statement has been added.