

Dear Editor and Reviewers,

We thank the reviewers for their comments. We have now modified the manuscript in accordance to the reviewer comments. The changes made are highlighted in yellow. Further, we have answered the questions raised by the reviewers below. Kindly note that there is also a change in the order of names.

We hope that the revised manuscript is now acceptable to be published in WJD.

Best Regards

Chellakkan. S. Blesson

Reviewer 1:

73855 Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

This is an interesting review paper, which really gives a great overview on feedbacks between the maternal low protein diet and the lean type 2 diabetes. However, these references are not comprehensive enough for such a sweeping statement. The authors need to add the research progress related to the relationship between intestinal microflora and maternal low-protein diet and lean type 2 diabetes.

*We wish to thank this reviewer for the positive comments. We agree with this reviewer that there are some literature available in connection with intestinal microflora, maternal LP diet, and T2D. Upon scrutiny, we think that the evidences are limited and inconclusive. Further, in this review our focus is to consolidate the literature on low protein programming and the development of type 2 diabetes, we think that relationship between intestinal microflora and lean type 2 diabetes is beyond the scope of this review.*

Reviewer 2:

03460306 Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

This is a review article regarding maternal low protein diet and fetal programming of lean T2D. Overall, the topic is timely and the manuscript was written well.

*We thank the reviewer for the positive comments.*

There are some comments. 1. Beta cell failure is critical to develop diabetes. Lower beta cell mass in subjects with low birth weight has been reported recently (Sasaki et al. Diabetologia, 63:1199-1210, 2020). The authors may cite and discuss this paper.

*We thank the reviewer for pointing this out; we have now included this reference in the revised manuscript (Lines 281-283)*

2. Ethnicity, especially Asians, appears to strongly associate with lean T2D. Ethnic difference in the pathogenesis of lean T2D should be discussed in the manuscript.

*We thank the reviewer for bringing this valid point, we have now briefly mentioned about this aspect in the revised manuscript (Lines 151-154)*

3. The authors stated that vegan diet is associated with higher risk of T2D in offspring. Is there any evidence for this statement?

*We are thankful for this comment. This is a very interesting concept that we are proposing in this review. Although there are no direct evidence for this statement, there are strong circumstantial evidence and so we have made a case for this. We and others have clearly shown that prenatal low protein diet programs the offspring to develop T2D later in life. It is hard to study this aspect in human, however, there are plenty of data that shows that vegetarian and vegan diet has low protein content and children born to vegetarian and vegan mothers have low birthweight just like we see in animal model. Further, various literature show that low birth weight is a hallmark of metabolic syndrome in adult life. Taken together, we can postulate that low protein vegan and vegetarian diet during pregnancy will make the offspring susceptible for T2D later in life.*