

Round 1

Dear Editor:

Thank you for the scientific review of our manuscript entitled “Partners in diabetes epidemic: a global perspective- (Manuscript NO.: 86654, Review).” We appreciate the insightful comments from the reviewers and your decision for us to revise this manuscript, all of which will substantially improve our paper. All re-writing, editing, and research questions have been addressed in body text, figures, and legends with deep revision. Highlighted final copy of the revised manuscripts is included for the convenience of your further review.

The Major Changes in the revision are summarized as follows:

- 1) Given the work of **Ranjit R Parhar** in revising the manuscript, we consider her as one of the authors. The order of author is changed. We added **Ranjit R Parhar** in the “submit revised manuscripts” system online . We confirm that the manuscript has been read and approved by all named authors.
- 2) Some grammatical and typographical errors in the MS were corrected by Randy Gaugler, one author of this manuscript. Randy Gaugler is a English speaking expert (A distinguished professor) who was born and bread in USA, did all the schooling here and has been in the editorial board of many scientific journals.
- 3) We added some short paragraph, great comment and some new references in the revised manuscript acoding to the reviewers’ suggestion. All revised portions were marked in pink text.

Our responses/ rebuttals to each and every question raised by the reviewers are depicted as follows:

Responses to reviewers’ critiques

Reviewer 1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The manuscript entitled Partners in diabetes epidemic: a global perspective has been reviewed with the following observation. 1. Title: The title is suitable and it reflect the main subject of the manuscript. 2. Abstract. The abstract summarize and reflect the work described in the manuscript. 3. Key Words. The key words are suitable MeSHs and reflect the focus of the manuscript .

[Comment 1]

Reviewer: 4. Background. This review is not based on focused question. And The protocol of the systematic review has not been registered in Prospero. So, this article is better to be called as scoping review instead of systematic review. The background of diabetes mellitus and its present status are not adequately described in the manuscript.

Response: As suggested, change has been made directly in the manuscript. A new paragraph on diabetes mellitus has been added (with the reference) directly in the manuscript.

[Comment 2]

Reviewer: 5. Methods. Data sources and search strategy are described in adequate detail. But reproducibility of the search with the given keywords is in question. As all the included articles may be included in the reference list. The present reference list shows PMID in all articles. This represents that articles are indexed in Medline data bases only.

Response: A few new key words have been added according to the reviewer's suggestion.

[Comment 3]

Reviewer: 6. Results. The search findings may be described under subheading Result which is lacking in the manuscript. It should also include critical view point and gap analysis.

Response: Changes have been made as suggested

[Comment 4]

Reviewer: 7. Illustrations and tables. Figures 1 and 2 may be revised. Figure 1 should be modified as per PRISMA flow chart. Figure 2 does not reflect correctly the relationship among insulin signaling and risk factors.

Response: Changes have been made as suggested

[Comment 5]

Reviewer: 8. References. As the manuscript includes publications up to 2019. So the latest articles are not included.

Response: We have added some new references-with updated information-2019 and onward.

[Comment 6]

Reviewer: Quality of manuscript organization and presentation. The manuscript is required to be concisely and coherently organized and presented as instructed. There is scope of language improvement and grammatical error correction in the manuscript.

Response: We have carefully revised the manuscript as suggested. Some grammatical and typographical errors in the MS were corrected by Randy Gaugler who are a native English-speaking.

[Comment 7]

Reviewer: 10. Research methods and reporting: the manuscript may be re written following PRISMA guidelines for scoping review.

Response: The manuscript has been re-organized following PRISMA guidelines for scoping review.

Reviewer 2:

[Comment 1]

Reviewer: Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: In the manuscript titled "Partners in diabetes epidemic: a global perspective," the authors searched 3,359 articles in databases such as PubMed and 128 articles that explored the substantial links between insulin signaling, genetics, environment, mitochondria, and obesity and diabetes. This review contains some interesting findings and the authors elaborate on the causes of diabetes, but the differences between genetic and environmental as well as cellular and animal models and human biology limit the applicability of these models to mechanistic studies and therapeutic interventions in diabetes. This review contains some interesting findings and the authors elaborate on the causes of diabetes, but the differences between genetic and environmental as well as cellular and animal models and human biology limit the applicability of these models to mechanistic studies and therapeutic interventions in diabetes. However, too much of this manuscript reviews previous experiments, and this review only investigates studies up to 2019, and the availability of recent new findings and original explorations are major shortcomings of this manuscript. Therefore, major revisions must be made before this manuscript can be accepted for publication in World Journal of Diabetes.

Response: Great comment-Some new references have been added as suggested.

[Comment 2]

Reviewer:Major comments:

1. 52 Diabetes may become the leading cause of death in 2030 [1]. Diabetes will become one of the most significant diseases or major diseases in the future.
2. 81 We identified studies that discussed diabetes including Type 1 Diabetes (T1D) and Type 2 Diabetes (T2D), The full name is required at the first occurrence of the abbreviation.
4. 132 Suppresses lipolysis, and perhaps stimulates de novo fatty acid synthesis [19]. References are spaced from the text.
6. 168 While gene expression profiling of pancreatic islets obtained from T2D individuals, Gunton et al. (2005) 41.Citation format error

Response: Corection has been made as suggested.

[Comment 3]

Reviwer: 3. This statement needs reference: 106 Gestational diabetes develops during pregnancy; it causes high blood glucose that can affect pregnancy and baby' s health.

7. This statement needs reference: 239 Even living under the same environment some individuals are more vulnerable to diabetes risk because of some inherited factors suggesting that T2D occurs because of intense interactions between many genes and the environment.

8. This statement needs reference: 325 KLF extensively expressed throughout larval development and during adulthood with a predominant expression in intestine, a major endocrine system positioned close to sexual organs and engaged in nutrient sensing and energy metabolism.

Response: The reference has been added.

[Comment 4]

Reviewer: 5. 139 They reported an increased adiponectin levels in insulin-resistant patients with T1D, and a reduced levels in patients with T2D [24]. Why are adiponectin levels different in T1D and T2D patients, so there is an appropriate range for adiponectin levels?

Response: The increased adiponectin levels in insulin-resistant patients with T1DM, in contrast to the reduced levels found in patients with T2DM showed an undefined relationship of adiponectin to insulin resistance in humans [24]. This explanation has been added directly on the manuscript.

[Comment 5]

Reviewer: 9. The authors showed Factors responsible for T2D incidence in Fig. 2, why not show TD1 as well?

Response: Fig. 2 was rewritted according to the reviewer's comment.

[Comment 6]

Reviewer: 10. As far as I know, intestinal flora changes as well as inflammatory factors and lipid metabolic processes can also have an impact on diabetes, which the authors can supplement with recent research articles to support.

Response: Some short paragraph, great comment, and some new references has been added in the revised manuscript.

Sincerely,

Huan Wang, Ph D.

Round 2

Dear Editor, Thank you very much for your e-mail regarding the submission and some comments about our manuscript. Your comments have improved both the quality and the clarity of the manuscript. We carefully read the comments, and have now completed a revision MS. The relevant regulations in the revision had been made according to the comments, and the major revised portions were marked in pink text according to the first-round review, and in blue text according to the second-round review.

Sincerely,

Huan Wang

Response to the second-round review

[Reviewer 1] [Comment] In the manuscript titled " Partners in diabetes epidemic: a global perspective," the authors searched 3,375 articles in databases such as PubMed and following the (PRISMA) guidelines for 143 articles that explored the substantial links between insulin secretion, insulin resistance, insulin signaling, genetics, environment, mitochondria, and obesity, gut microbes and diabetes. This review contains some interesting findings and the authors elaborate on the causes of diabetes, contributing to the acceleration of medical advances in the treatment and prevention of diabetes as well as its application in diabetes control. Therefore, this revised manuscript is acceptable for publication in World Journal of Diabetes.

[Response] Thank you very much.

[Reviewer 2] [Comment] The revised manuscript titled Partners in diabetes epidemic: a global perspective has the following observations 1. The manuscript has been revised as per given suggestions that may be considered as satisfactory. 2. In abstract, the given below statement may be rewritten keeping in view the following queries. a. Whether laboratory research, systematic reviews, and clinical trials are databases or articles categories. b. Which reporting terms were followed? c. The same information is not present in the manuscript. We searched relevant articles in PubMed, google scholar, laboratory research, systematic reviews, clinical trials, and epidemiological data that connected insulin signaling, genetics, environment, lipid metabolism dysfunction, mitochondria and the gut microbiota as the major determinants in diabetes, and followed the preferred reporting terms for this review. 3. the methods section says The databases were searched in 2018 and 2019 but the articles included in this study were published between 1981 and 2021. How is it possible?

[Response] These comments mentioned above have been corrected and addressed in the revision of MS.