Reviewer 1 Comments and Suggestions for Authors

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: In this review, the authors discussed the underlying molecular and cellular mechanisms of gestational diabetes mellitus (GDM) and the possible influential factors, as well as the predictive and preventive measures based on the basic and clinical studies which investigated the etiology, pathophysiology and management of GDM. The review is well written and informative, containing the current research progress in this field, which may help understand the principles of current drug actions and provide a clue to recognize new treatment targets.

On behalf of the authors, I appreciate the invitation of submission from *World Journal of Diabetes* and the decision of potential acceptance from *Academic Editor*, as well as the positive comments from reviewers. Also, thank you very much for your careful and thoughtful review of our manuscript. As an author, reviewer, and editorial board member of journals, I know how much time you have to spend in reviewing manuscripts. Your comments inspire and instruct us a lot. I and my colleagues have made efforts to address the concerns raised by all reviewers and have revised the manuscript to improve its readability. Please see the revised manuscript for details. We hope the explanation and revision we have made can address reviewers' concerns. (the revised text is highlighted in red color).

Reviewer 1 Comments

1. I suggest that this review be accepted for publication after the following minor issues are addressed. 1. Line 6 on page 4, the unit 'gm' should be 'g', and there should be a space between '75' and the unit 'g'. 2. The gene names should be italicized. Some gene names are not stardardized, e.g., 'PrlR' should be 'Prlr'. Please pay attention to these issues.

Response: Thank you very much. According to the comments, we have corrected the text you mentioned above. Please see revised test for details (page 4, line 4-6; page 12, line 19-20).

Thank you again for your valuable comments on our manuscript. The review offers evidence-based information with the aim of providing researchers and clinicians with an insight and understanding the molecular and cellular mechanisms, actions, prediction, prevention and treatments of gestational diabetes. We consider these summaries and suggestions to be interesting, practical, and constructive for researchers, clinicians, and healthcare providers who are devoted to promoting quality and efficiency of pregnancy care. Of raising concern in women health, we believe that our manuscript will be of interest to the readers of *World Journal of Diabetes*. We have revised our manuscript, and look forward to a favorable response from you.

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Guest Editor, Clinical and Experimental Obstetrics and Gynecology *(SCI)*

Reviewer 2 Comments and Suggestions for Authors

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: This is a nice article encompassing a molecular overview of prediction and prevention of GDM. The article is well written and interesting.

On behalf of the authors, I appreciate the invitation of submission from *World Journal of Diabetes* and the decision of potential acceptance from *Academic Editor*, as well as the positive comments from reviewers. Also, thank you very much for your careful and thoughtful review of our manuscript. As an author, reviewer, and editorial board member of journals, I know how much time you have to spend in reviewing manuscripts. Your

comments inspire and instruct us a lot. I and my colleagues have made efforts to address the concerns raised by all reviewers and have revised the manuscript to improve its readability. Please see the revised manuscript for details. We hope the explanation and revision we have made can address reviewers' concerns. (the revised text is highlighted in red color).

Reviewer 2 Comments

1. I am happy with publication of the article after a minor revision in which I would like the authors to do an effort to summarize major concepts of treatment in the discussion along with a recent major reference (ref 1). I would reccomend adding a brief sentence stating that we should update current treatment of GDM which is very frequently suboptimal and citing ref.2. More so the effect of COVID-19 on the risk of GDM should be mentioned given its relevance of this end and major recent evidences emerging from the Intercovid study (ref 2). This would add importance to the issue of vaccination for COVID 19 which improves substantially both maternal and pregnancy outcome (ref 3)

   References 1. Chatzakis C, et al. Gestational Diabetes Mellitus Pharmacological Prevention and Treatment. Curr Pharm Des. 2021;27(36):3833-3840. doi: 10.2174/1381612827666210125155428. PMID: 33550962. 2. Eskenazi B, et al. Diabetes mellitus, maternal adiposity, and insulin-dependent gestational diabetes are associated with COVID-19 in pregnancy: the INTERCOVID study. Am J Obstet Gynecol. 2022 Jul;227(1):74.e1-74.e16. doi: 10.1016/j.ajog.2021.12.032. Epub 2021 Dec 20. PMID: 34942154; PMCID: PMC8686449. 3. Villar J, et al.; INTERCOVID-2022 International Consortium. Pregnancy outcomes and vaccine effectiveness during the period of omicron as the variant of concern, INTERCOVID-2022: a multinational, observational study. Lancet. 2023 Feb 11;401(10375):447-457. doi: 10.1016/S0140-6736(22)02467-9. Epub 2023 Jan 17. PMID: 36669520; PMCID: PMC9910845.

Response: Thank you again for the review. In response to your comments, we have added three paragraphs as mentioned below. The first paragraph is a summary of major concepts of treatment in oral and injection form, which emphasizes that current treatment of GDM is very frequently suboptimal [77]. The second paragraph focuses the roles of diabetes mellitus and overweight or obesity as risk factors for COVID-19 infection in pregnancy, as well as the importance of vaccination for women with these comorbidities. The third paragraph furthermore states that COVID-19 in pregnancy is associated with increased risk of severe maternal morbidity

and mortality, especially among symptomatic and unvaccinated women. Women with complete or boosted vaccine doses have reduced risk for severe symptoms, complications, and death. Vaccination coverage among pregnant women remains a priority. We believe that the novelty and practicality of this review will be largely improved by adding these descriptions and references [77-79] as follows:

To update, the current treatment of GDM is very frequently suboptimal. The most common oral pharmacological interventions that have been assessed are metformin, probiotics, and vitamin D administration. However, no intervention appears to be universally superior to placebo/no intervention for the prevention of GDM [77]. Currently, insulin injection is the preferred medication for treating hyperglycemia in gestational diabetes mellitus. Metformin and glyburide are not regarded as first-line agents, as both cross the placenta to the fetus. Even though there are sufficient data confirming the safety and effect of metformin in women with GDM, there are very limited data concerning the long-term effects of metformin on the offspring. Furthermore, glyburide should be used with caution, as it increases the risk of neonatal hypoglycemia. Some studies also show that it increases the risk of macrosomia. Overall, oral agents may be a therapeutic option in women with GDM after a discussion of the known risks and the need for more long-term safety data in the offspring [77].

A study (INTERCOVID) investigated the role of overt or gestational diabetes mellitus and high body mass index as risk factors of COVID-19 infection in pregnancy. Conducted between March 2020 and February 2021 in 43 institutions from 18 countries, the study enrolled 2184 pregnant women aged ≥18 years. Each woman diagnosed with COVID-19 was matched with 2 nondiagnosed women delivering or initiating antenatal care at the same institution [78]. The results revealed that COVID-19 was associated with preexisting diabetes mellitus (relative risk [RR] 1.94; 95% CI 1.55-2.42), overweight or obesity (RR 1.20; 95% CI 1.06-1.37), and gestational diabetes mellitus (RR 1.21; 95% CI 0.99-1.46). The gestational diabetes mellitus association was specifically among women requiring insulin, whether they were of normal weight (RR 1.79; 95% CI 1.06-3.01) or overweight or obese (RR 1.77; 95% CI 1.28-2.45). A somewhat stronger association with COVID-19 diagnosis was observed among women with preexisting diabetes mellitus, whether they were of normal weight (RR 1.93; 95% CI 1.18-3.17) or overweight or obese (RR 2.32; 95% CI 1.82-2.97) [78]. In conclusion, diabetes mellitus and overweight or obesity were risk factors for COVID-19 diagnosis in pregnancy, and insulin-dependent gestational diabetes mellitus was associated with the disease. Therefore, it is essential that women with these comorbidities are vaccinated [78].

Subsequently, a large prospective and observational study (INTERCOVID-2022) involving 41 hospitals across 18 countries, enrolled 4618 pregnant women from Nov 27,

2021 to June 30, 2022. During pregnancy, each woman with a COVID-19 diagnosis was matched with two women without COVID-19. Overall, women with a diagnosis had an increased risk for MMMI (RR 1.16; 95% CI 1.03-1.31), SPMMI (RR 1.21; 95% CI 1.00-1.46) and SNMI (RR 1.23; 95% CI 0.88-1.71), compared with those without a diagnosis [79]. Moreover, severe COVID-19 symptoms in the total sample increased the risk of severe maternal complications (RR 2.51; 95% CI 1.84-3.43), perinatal complications (RR 1.84; 95% CI 1.02-3.34), and referral, ICU admission, or death (RR 11.83; 95% CI 6.67-20.97). Notably, vaccine effectiveness (all vaccines combined) for severe complications of COVID-19 in all women with a complete regimen was 48% (95% CI 22-65) and 76% (47-89) after a booster dose [79]. Concludingly, COVID-19 in pregnancy was associated with increased risk of severe maternal morbidity and mortality, especially among symptomatic and unvaccinated women. Women with complete or boosted vaccine doses had reduced risk for severe symptoms, complications, and death. Vaccination coverage among pregnant women remains a priority [79].

References:

[77] Chatzakis C, Cavoretto P, Sotiriadis A. Gestational diabetes mellitus pharmacological prevention and treatment. Curr Pharm Des 2021; 27: 3833-3840. doi: 10.2174/1381612827666210125155428.

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[79] Villar J, Soto Conti CP, Gunier RB, Ariff S, Craik R, Cavoretto PI, Rauch S, Gandino S, Nieto R, Winsey A, Menis C, Rodriguez GB, Savasi V, Tug N, Deantoni S, Fabre M, Martinez de Tejada B, Rodriguez-Sibaja MJ, Livio S, Napolitano R, Maiz N, Sobrero H, Peterson A, Deruelle P, Giudice C, Teji JS, Casale RA, Salomon LJ, Prefumo F, Cheikh Ismail L, Gravett MG, Vale M, Hernández V, Sentilhes L, Easter SR, Capelli C, Marler E, Cáceres DM, Albornoz Crespo G, Ernawati E, Lipschuetz M, Takahashi K, Vecchiarelli C, Hubka T, Ikenoue S, Tavchioska G,

Bako B, Ayede AI, Eskenazi B, Thornton JG, Bhutta ZA, Kennedy SH, Papageorghiou AT; INTERCOVID-2022 International Consortium. Pregnancy outcomes and vaccine effectiveness during the period of omicron as the variant of concern, INTERCOVID-2022: a multinational, observational study. Lancet 2023; 401: 447-457. doi: 10.1016/S0140-6736(22)02467-9.

Thank you again for your valuable comments on our manuscript. The review offers evidence-based information with the aim of providing researchers and clinicians with an insight and understanding the molecular and cellular mechanisms, actions, prediction, prevention and treatments of gestational diabetes. We consider these summaries and suggestions to be interesting, practical, and constructive for researchers, clinicians, and healthcare providers who are devoted to promoting quality and efficiency of pregnancy care. Of raising concern in women health, we believe that our manuscript will be of interest to the readers of *World Journal of Diabetes*. We have revised our manuscript, and look forward to a favorable response from you.

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Editorial Board, *International Journal of Environmental Research and Public Health (SCI)*
Guest Editor, Clinical and Experimental Obstetrics and Gynecology *(SCI)*

Reviewer 3 Comments and Suggestions for Authors

Reviewer #3:
Scientific Quality: Grade D (Fair)
Language Quality: Grade C (A great deal of language polishing)
Conclusion: Major revision
Specific Comments to Authors: This review aims to discuss the underlying molecular and cellular mechanisms of GDM and the possible influential factors, as well as the predictive and preventive measures based on the clinical studies which investigated the

etiology and management of GDM. Overall, this is an interesting study, which may be beneficial to the clinical management of GDM.

On behalf of the authors, I appreciate the invitation of submission from *World Journal of Diabetes* and the decision of potential acceptance from *Academic Editor*, as well as the positive comments from reviewers. Also, thank you very much for your careful and thoughtful review of our manuscript. As an author, reviewer, and editorial board member of journals, I know how much time you have to spend in reviewing manuscripts. Your comments inspire and instruct us a lot. I and my colleagues have made efforts to address the concerns raised by all reviewers and have revised the manuscript to improve its readability. Please see the revised manuscript for details. We hope the explanation and revision we have made can address reviewers' concerns. (the revised text is highlighted in red color).

Reviewer 3 Comments

However, I have several concerns as follow:

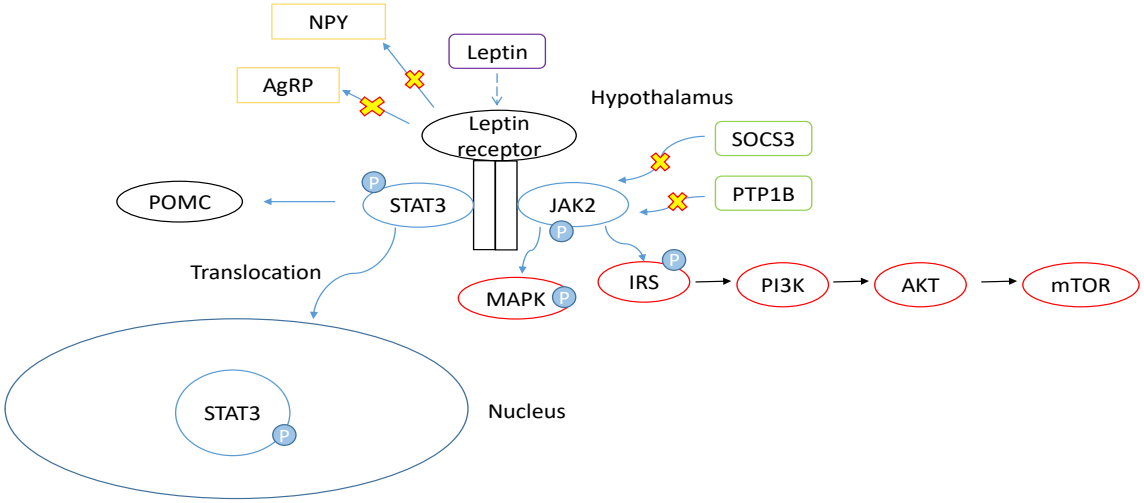
1. The figure 2 is helpful. However, it is far away from the major point of the review. GLUT4 is only one important part of this review. It is important to have tables/figures to summarize the potential factors for GDM. It should also be clarified in the manuscript. More detailed subtitle will be helpful.

Response: Thank you very much for your comments. Other than the GLUT4 translocation pathway, we have added two additional paragraphs/figures to describe and illustrate another important pathophysiologic mechanisms of GDM including the leptin signaling pathways (Sec. 5.4; Figure 3) and the nuclear factor kappa B (NF-kB) signaling pathway in the Inflammatory process (Sec. 5.5; Figure 4). It is shown in the revised manuscript as follows:

5.4 Dysfunction of leptin signaling pathways

Another important etiology which should be responsible for GDM is dysfunction of leptin signaling pathways (Figure 3). Leptin signaling is mediated by the JAK2/STAT3 pathway to exert its anorexigenic effect. Binding to the leptin receptor, leptin can activate JAK2, STAT3, and

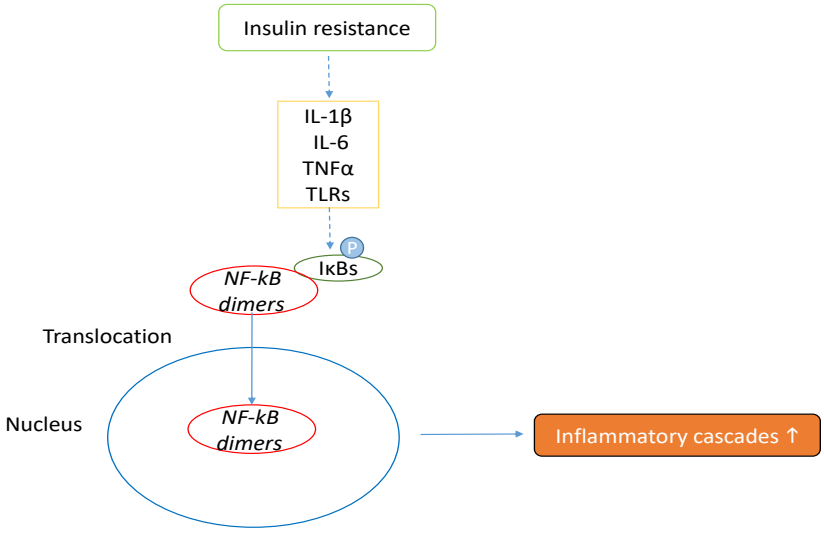
MAPK via phosphorylation of different sites on the leptin receptor and subsequent binding to downstream molecules [36,37]. Thus, the JAK2 and Signal transducer and activator of transcription (STAT) 3 are phosphorylated. The activated STAT3 translocates to the nucleus and activates the transcription of the target genes, which mediates the anorexigenic effect of leptin. The negative regulators of JAK2 including suppressor of cytokine signaling 3 (SOCS3) and protein tyrosine phosphatase 1B (PTP1B), both of which act as a feedback inhibitor of leptin signaling, have been reported to promote obesity and diabetes. On the other hand, leptin also regulates MAPK and phosphatidylinositol 3 kinase (PI3K) signaling through insulin receptor substrate (IRS) phosphorylation. In addition, leptin inhibits appetite-stimulators neuropeptide Y (NPY) and agouti-related peptide (AgRP), and thus activates the anorexigenic polypeptide pro-opiomelanocortin (POMC) [36,37].



5.5 Inflammation underlying GDM: the Nuclear factor kappa B (NF-kB) signaling pathway

A detailed mechanism can be explained by the Nuclear factor kappa B (NF-kB) signaling pathway in the inflammatory process (Figure 4). The proteins in the NF-kB family combine each other to form homodimers or heterodimers to exert stimulative or repressive function after transcription. As suppressors, the inhibitory regulators of NF-kB (IκBs) can bind to the NF-kB dimers to form a complex, which remains sequestered and inactive in the cytoplasm of non-stimulated cells [38]. Under the status of insulin resistance,

pro-inflammatory cytokines including IL-1β, IL-6, and TNFα are increased to initiate the NF-kB signaling pathway. After receiving stimulation from the aforementioned cytokines and toll-like receptors (TLRs), the Iκ*B*s are rapidly phosphorylated, ubiquitinated, and then degraded to expose a nuclear localization sequence on the NF-kB proteins. Thus, the NF-kB dimers translocate to the nucleus to regulate gene transcription and induce inflammatory cascades [38]



References:

[36] Park HK, Ahima RS. Leptin signaling. *F1000Prime Rep* 2014; 4: 73. doi: 10.12703/P6-73.

[37] Vilmi-Kerälä T, Palomäki O, Kankkunen P, Juurinen L, Uotila J, Palomäki A. Oxidized LDL, insulin resistance and central blood pressure after gestational diabetes mellitus. *Acta Obstet Gynecol Scand* 2016; *95:* 1425–1432. https://doi.org/10.1111/aogs.13029

[38] de Mendonça ELSS, Fragoso MBT, de Oliveira JM, Xavier JA, Goulart MOF, de Oliveira ACM. Gestational diabetes mellitus: the crosslink among inflammation, nitroxidative stress, intestinal microbiota and alternative therapies. *Antioxidants 2022: 11:* 129. https://doi.org/10.3390/antiox11010129

2. Please also reduce the size of conclusion. The reviewer suggests to move some part of conclusion forward as “discussion”. The conclusion has to briefly summarize the major point/result of the whole review.

Response: Currently, some parts of the Conclusion have been removed forward as Discussion. Moreover, we have removed redundant words and sentences in the section of Conclusion to make it concise to read as follows: (one paragraph; Page 30-31)

GDM is a complex condition of pregnancy with significant implications for both the mother and the fetus. Currently, no scientific consensus has been reached on how best to diagnose GDM, either by one-step or two-step OGTT. The pathophysiology of GDM probably involves genetic variants, pancreatic β-Cell depletion or dysfunction, and aggravated insulin resistance due to failure in the plasma membrane translocation of GLUT4. It is also associated with the negative regulation of leptin signaling pathways, and the actions of chronic low-grade inflammation which involve the nuclear factor kappa B (NF-kB) signaling pathway. Currently, leptin and body mass ratio have been used as markers for predicting the occurrence of GDM during pregnancy. For preventing GDM, physical activity and dietary control are considerable interventions. Nevertheless, many detailed cellular and molecular mechanisms underlying GDM, as well as prediction and prevention, remain unexplored and warrant further investigation.

3. There is only 1 paragraph in “introduction”. The authors were suggested to divide it. Moreover, the size can also be reduced, if possible.

Response: For your comments, we have divided the section of Introduction into five paragraphs, and shortened its size. Please see the revised manuscripts for details.

4. Moreover, it is helpful to further consider the advantage and disadvantage of each strategy in table/text. It is more friendly to the readers.

Response: For your comments, we have added two paragraphs describing the advantages and disadvantages of both exercise and diet control strategies, respectively. We believe that the novelty and practicality of this review will be largely improved by adding these descriptions and references [50,58,72-76] as follows:

Physical exercise

In addition to the advantage of preventing GDM, some physiological studies have reported that exercise in pregnant women improved cardiovascular functions such as fitness, blood pressure, and peripheral edema. An ACOG report also showed that exercise improved the symptoms of constipation, bloating, fatigue and insomnia in pregnant women. For the fetus, the benefits of moderate exercise included an increase in amniotic

fluids, increase in placenta viability and volume, improvement in neurological system development, and reduction in body fat percentage. However, excessive exercise might elevate the incidence of antepartum hemorrhage and the risk of preterm birth. In consideration of the disadvantage, physical exercise should be avoided in the pregnant women with restrictive lung disease, preeclampsia, persistent bleeding in second or third trimester, incomplete cervix, placenta previa, hemodynamically significant heart disease, and high order multiple gestations (≥ triplets) [50]. (Page 23)

Diet

The advantages of low GI food include lowering postprandial glucose, preventing excessive rise in postprandial insulin, and inducing satiety, all of which may contribute to weight loss. To date, there is no marked influence on the obstetric, maternal or fetal outcomes such as maternal weight gain, neonatal birth weight, proportion of LGA, and macrosomia [72]. Current evidence has suggested that low GI nutritional approach is reasonably safe in GDM. However, further research is needed to develop tools to facilitate patient adherence to treatment goals, individualize interventions and improve the results [73].

The low-carbohydrate diet results in a lower postprandial glucose, lower daytime mean glucose concentrations, lower area under the curve of 2 hours postprandial glucose, and lower 24 hours total glucose area under the curve, when compared with the 60% carbohydrate diet. However, there were some results revealing that lower carbohydrate intake will often lead to an increased intake of fat, which, outside pregnancy, has been associated with an increase in serum fatty acids, insulin resistance, increased fetal fat accretion and infant adiposity [58]. These disadvantages might have limited further use of the low-carbohydrate diet as a means of diet intervention.

The MedDiet may reduce the risk of GDM by alleviating systemic oxidative stress [74]. The MedDiet might downregulate circulating inflammatory biomarkers and favor glucose homeostasis, improving insulin sensitivity and glycemic postprandial response. Moreover, the Mediterranean diet has a high content of fiber, which can increase satiety and control weight gain [F]. Similar to the MedDiet with a low-glycemic index [75], the DASH diet in pregnant women with GDM was associated with a decreased number of macrosomic babies. It also led to a lower mean of weight and head circumference and ponderal index

of the newborns, but did not affect the length and Apgar score of the infants [76]. However, the disadvantages of diet control as mentioned above lie in the adherence to diet interventions in pregnant women. (Page 25-26)

References:

[50] Padayachee C, Coombes JS. Exercise guidelines for gestational diabetes mellitus. World J Diabetes 2015; 6: 1033–1044. https://doi.org/10.4239/wjd.v6.i8.1033

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5. Although the study has language certificate, it still needs carefully editing by someone with expertise in technical English writing, preferably from a native English speaker with appropriate research background.

Response: The revised manuscript has been reviewed again by a native English speaker who is skilled at medical English writing. Please see the revised manuscript and the recent language certificate (issued 09/May/2023 in the attached file) for details. Your understanding is highly appreciated.

Thank you again for your valuable comments on our manuscript. The review offers evidence-based information with the aim of providing researchers and clinicians with an insight and understanding the molecular and cellular mechanisms, actions, prediction, prevention and treatments of gestational diabetes. We consider these summaries and suggestions to be interesting, practical, and constructive for researchers, clinicians, and healthcare providers who are devoted to promoting quality and efficiency of pregnancy care. Of raising concern in women health, we believe that our manuscript will be of interest to the readers of *World Journal of Diabetes*. We have revised our manuscript, and look forward to a favorable response from you.

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Editorial Board, Technology in Cancer Research and Treatment *(SCI)*
Editorial Board, *International Journal of Environmental Research and Public Health (SCI)*
Guest Editor, Clinical and Experimental Obstetrics and Gynecology *(SCI)*

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.
Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade B (Very good)

Dear Science Editor:

On behalf of the authors, I appreciate the invitation of submission from *World Journal of Diabetes* and the decision of potential acceptance after appropriate revision, as well as the positive comments from reviewers. Also, thank you very much for your careful and thoughtful review of our manuscript. As an author, reviewer, and editorial board member of journals, I know how much time you have to spend in reviewing manuscripts. All of the comments inspire and instruct us a lot. I and my colleagues have made efforts to address the concerns raised by all reviewers and have revised the manuscript to improve its readability. Please see the response to the reviewers' comments and the revised manuscript for details. We hope the explanation and revision we have made can address reviewers' and your concerns. (the revised text is highlighted in red color).

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Again, we appreciate your efforts to disseminate new knowledge to readers, which in turn may benefit everyone worldwide and the next generation. Thank you very much for your time and consideration in reviewing our manuscript.

Kuo-Hu Chen, MD, PhD

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Editorial Board, Technology in Cancer Research and Treatment *(SCI)*
Editorial Board, *International Journal of Environmental Research and Public Health (SCI)*
Guest Editor, Clinical and Experimental Obstetrics and Gynecology *(SCI)*

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Dear Company Editor-in-Chief:

On behalf of the authors, I appreciate the invitation of submission from *World Journal of Diabetes* and the decision of potential acceptance after appropriate revision, as well as the positive comments from reviewers. Also, thank you very much for your careful and thoughtful review of our manuscript. As an author, reviewer, and editorial board member of journals, I know how much time you have to spend in reviewing manuscripts. All of the comments inspire and instruct us a lot. I and my colleagues have made efforts to address the concerns raised by all reviewers and have revised the manuscript to improve its readability. Please see the response to the reviewers' comments and the revised manuscript for details. We hope the explanation and revision we have made can address reviewers' and your concerns. (the revised text is highlighted in red color)

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

→ Done! All figures (Figure 1-4) are prepared using PowerPoint.

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→ Added in each figure!

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

→Done in Table 1.

If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

→ We confirm that all figures and table(s) are original and made by ourselves without external copyright issues.

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

→ According to the reviewers’ comments and your suggestions, we have added 12 new references with the latest cutting-edge research results to enhance the novelty of the review. We believe that the novelty and practicality of this review will be largely improved by adding these new references (main text: 7306 words; total references: 79; please see the reference list in the revised manuscript for details).

.The review offers evidence-based information with the aim of providing researchers and clinicians with an insight and understanding the molecular and cellular mechanisms, actions, prediction, prevention and treatments of gestational diabetes. We consider these summaries and suggestions to be interesting, practical, and constructive for researchers, clinicians, and healthcare providers who are devoted to promoting quality and efficiency of pregnancy care. Of raising concern in women health, we believe that our manuscript will be of interest to the readers of *World Journal of Diabetes*. We have revised our manuscript, and look forward to a favorable response from you.

Again, we appreciate your efforts to disseminate new knowledge to readers, which in turn may benefit everyone worldwide and the next generation. Thank you very much for your time and consideration in reviewing our manuscript.

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JournalChiefEditorReviewReport

1. Specific Comments To Authors: First of all, this review has been written well. I am glad to see that one out of 3 reviews made significant comments to improve the quality of review. Although authors replied to all reviewers' comments nicely and mentioned that they revised the manuscript according to the comments made by reviewers, the revised manuscript file has been sent without highlighted text for the revised section so it is difficult to identify the revision. So I suggest to send me the revised version of manuscript with the revisions highlighted with different coloured text.
--> We are grateful to the Chief Editor for the decision of minor revision. Currently, the revised version of manuscript has been sent back with the revisions highlighted with

different coloured text (red).

Secondly, although authors made significant efforts to improve the quality of figures, I suggest that the Figure 2-4 needs to be even improved by drawing with cell structures showing the different section of cell and cell signalling pathways in the appropriate section of the cell. Language is acceptable so once the figures 2-4 are revised as per my above comments, please send me the document to have a final look to make a decision. Regards, Prof. Islam.

--> In the revised manuscript (DOC) and figures (PPT), we have re-illustrated Figure 2-4 by using the Professional Software BioRender to draw cell structures showing the different section of cell and cell signalling pathways in the appropriate section of the cell.