

Number ID: 03967085

Publication Name: World Journal of Diabetes

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Title: Effectiveness and safety of COVID-19 vaccines in patients with diabetes as factors for vaccine hesitancy

Running title: COVID-19 vaccines for diabetes patients

Manuscript Type: Minireviews

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:

Dear Editor,

Dear reviewers,

Thank you for your time to review our Manuscript ID: 76715, Authors: Georgi Vasilev, Plamena Kabakchieva, Dimitrina Miteva, Hristiana Batselova, Tsvetelina Velikova. We acknowledge that our paper might have some issues in the conformity with the reviewers' comments.

We have taken into account all of the suggestions made by the reviewers. Those changes are highlighted in green within the manuscript. Please see below, in blue, for a point-by-point response to the reviewers' comments. All page numbers refer to the revised manuscript file.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This paper brings an extensive review about the effectiveness of the Covid-19 vaccines for diabetes patients. The authors discuss important issues related to the

potential causes of hesitancy for vaccination in this particular group of patients, i.e., diabetic population. In overall, the paper is well-written, and it flows logically. Technically, the authors provide a complete review concerning the benefits of the available immunizers for diabetes patients, which includes the investigation of the vaccine adverse effects.

➤ Thank you for the overall evaluation of our paper as good.

Despite the good analyzes and review process, I believe that the topic “Vaccine hesitancy” could be improved, by presenting a deeper review on this subject since vaccine hesitancy is one of the most interesting topics in this paper.

➤ Thank you very much for the valuable note. We completely agree that this is important topic. Therefore, we added paragraphs on the topic where applicable.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The authors described in their review the safety and efficacy of COVID-19 vaccination in patients with diabetes mellitus.

➤ Thank you for the overall evaluation of our paper as good.

Here's some points I would like to raise for improvements:

1. Routine vaccine for diabetes patients (page 6 & 7) may be out of scope for this review. Suggest to remove the entire section.

➤ Thank you very much for the suggestion. We acknowledge that this part of the paper may seem like out of scope of the review. However, we believe that this background is absolutely needed for development of new vaccines, thus it should be mentioned.

➤ Additionally, patients with diabetes and their physicians may remind themselves the
➤ However, we would like to implement the suggestion, thus, we added an explanatory paragraph why this information is needed in the review.

2. Similarly, autoimmune diseases (page 8 & 9) are too general, potentially out of scope for this review. Unless there is explanation for that, suggest to remove it too.

- Thank you for the note. We agree that these pages are devoted on the general problem. We believe that this is important for the readers to figure out once again why vaccination is a priority for patients with autoimmune diseases.

3. Suggest to add in a section to explain why and how diabetes mellitus affects the immune system, with figures. And how immunodeficient state could potentially affect the efficacy of a vaccine, particularly COVID-19 vaccine in this context.

- Thank you for the valuable note. We agree that it is important to focus on the immunological alterations in patients with diabetes, furthermore, it could affect the efficacy of vaccination. We have provided a figure that summarizes the effects of diabetes characteristics on the immune system and its function.

4. It would be interesting to include also a summary of the numbers of diabetic patients contracted with COVID-19 after vaccination – to see the real efficacy of the vaccination.

- Thank you for the valuable comment. We searched for data on the topic to add as information on page 16. However, we did not find studies that cited particular numbers of re-infected diabetes patients after COVID-19 vaccination. If the referee pointed out a certain article, we would appreciate to find out which is it.

5. Will the severity of diabetes mellitus affect the selection, efficacy, effectiveness, side effects etc of a COVID-19 vaccine? Discuss that.

- Thank you focusing on this point. We agree with the referee that these factors can also influence the efficacy of COVID-19 vaccines, thus, we added this information where we found such in the literature, and where it was applicable. By extending this part of the paper, we believe that we increased significantly the scientific value of the paper.

6. The authors mentioned about the strict glycaemic control could increase the efficacy of COVID-19 vaccine. Explain this works at cellular level.

- Thank you for the great suggestion. We have added the missing information.

7. “Patients with diabetes are more prone to have pronounced side effects of COVID-19 vaccination than healthy people”. This phrase needs a reference.

- Thank you for noticing this. We have corrected it, since we meant the opposite “are not more prone”. We have also provided the reference in the section before the conclusion,

8. The review is a bit too wordy. Suggest to include one or two figures to summarise part of / entire review.

- We agree with the referee that some of the passages in the text are more explanatory and large. However, we believe that the text is concise and all of the provided information will be valuable for the readers. We agree with your suggestion about including a figure and crafted one,
- Additionally, by providing a summarizing table of existing studies so far along with a figure, we believe that the paper has become more comprehensive and readable.

9. Lastly, there are many reviews on efficacy of COVID-19 vaccine on diabetes patients published in the English literature. I just wonder, what additional information/ novelty in this review add up to the existing knowledge in this area. Please explain further.

- We summarize all of the existing data on studies of COVID-19 vaccines, their safety and effectiveness profile, along with the factors associated with vaccine hesitancy. As far as we know, there is no such review combining these two topics.

6 EDITORIAL OFFICE’S COMMENTS

Authors must revise the manuscript according to the Editorial Office’s comments and suggestions, which are listed below:

(1) Science editor:

The manuscript is well-written. The questions raised by the reviewers should be answered.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

(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. Please be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site: <https://www.referencecitationanalysis.com/>. Please 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.

- Thank you for the overall evaluation of our paper as good. We revised the manuscript according to the reviewers' and editors' comments to improve the quality of our paper.
- We used RCA to find proper papers to cite, and also, we revised the table according to the journal requirements.

(1) 76715-Answering Reviewers

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