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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 108724

Title: Impact of the COVID-19 outbreak on the seasonality and incidence of type 1 diabetes mellitus: A nationwide cohort

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08424558

Position: Peer Reviewer

Academic degree and professional title: MD, PhD, Postdoctoral Fellow

Reviewer's Country/Territory: China

Author's Country/Territory: Israel

Manuscript submission date: 2025-04-23

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-05-11 12:06

Reviewer performed review: 2025-05-11 12:22

Review time: 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **Yes**

Do authors only cite their own earlier publications? **Yes**

Are all references related to the topic of the manuscript? **Yes**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **Yes**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

This manuscript investigates the impact of the COVID-19 pandemic on the incidence and seasonality of type 1 diabetes mellitus (DM1) in a nationwide pediatric cohort in Israel. By leveraging a large longitudinal dataset, the authors compare DM1 trends before and during the pandemic, exploring correlations with respiratory virus prevalence. The findings indicate an increased DM1 incidence and a weakened seasonal pattern during the COVID-19 period, potentially supporting a role for respiratory viruses in DM1 pathogenesis. The study is timely and relevant, addressing a question that has gained attention during the pandemic. Its key strengths include the use of



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nationwide data, a robust time series analysis, and integration of viral testing records. The innovation lies in combining seasonality modeling with real-world viral circulation data to indirectly assess viral triggers of DM1. However, several methodological and interpretational issues need to be addressed before the manuscript can be considered for publication. Major Revisions: 1. The use of "two insulin prescriptions" as a proxy for new-onset DM1 is potentially problematic. Please clarify whether additional criteria (e.g., ICD codes, clinical records) were used to exclude misclassification, especially in distinguishing type 1 from type 2 diabetes in adolescents. 2. The observed changes in DM1 incidence during COVID-19 may also reflect altered healthcare-seeking behavior, diagnostic delay, or reduced access to care. These factors should be acknowledged and discussed as possible alternative explanations. 3. The method by which viral PCR data (population-level) were linked temporally or epidemiologically to DM1 diagnoses (individual-level) should be elaborated. This is crucial for interpreting the correlation results and IRR estimates. 4. While the use of Fourier terms is appropriate, the biological interpretation of changes in sine and cosine coefficients is unclear to a general medical audience. Please provide a clearer explanation or visualization of what these changes imply for clinical seasonality. 5. The conclusion that respiratory viruses "may play a role" in DM1 development is plausible but speculative. The language throughout should be revised to avoid overinterpretation of weak correlations, particularly given the ecological nature of the viral data.



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Peer-review model: Single blind

Reviewer's code: 07838429

Position: Peer Reviewer

Academic degree and professional title: PhD, Postdoctoral Fellow

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: Israel

Manuscript submission date: 2025-04-23

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-05-10 04:10

Reviewer performed review: 2025-05-11 17:00

Review time: 1 Day and 12 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the Conclusion reasonable? **No**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

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Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

This study presents a thoughtful and timely investigation into how the COVID-19 pandemic affected the incidence and seasonal patterns of Type 1 Diabetes Mellitus (DM1) in a pediatric population. A large, population-based nationwide healthcare system data enhances the study's credibility and generalizability. The authors should be commended for their methodological rigor, clear articulation of aims, and novel focus on seasonality and viral correlations, topics of significant clinical and epidemiological importance. I would like to appreciate the authors' valuable contribution to the ongoing scientific efforts to understand the broader impacts of the COVID-19 pandemic on



non-communicable diseases such as DM1. The work provides an important foundation for future studies on environmental and infectious triggers in autoimmune diseases. The authors are advised to address the following points before proceeding with this manuscript further; 1. First, the author is advised to make minor changes in the title. A suggested title is given as follows: "The Impact of the COVID-19 Outbreak on the Seasonality and Incidence of Type 1 Diabetes Mellitus: A Nationwide Cohort Study". 2. Clarify how the COVID-19 period (only one year) allowed inference on seasonality, which typically requires multiple cycles. 3. Consider refining this sentence: "The increased incidence of new-onset DM1 and the disruption of its seasonal pattern..." To "An increase in new-onset DM1 and disruption of its typical seasonal pattern during the COVID-19 lockdown..." 4. On the second page, change the term "Objective" to "Introduction or Background" and provide a solid background on DM1 etiology, seasonal patterns, and viral triggers. 5. Include more discussion on COVID-19 as a direct potential trigger of autoimmunity in the pancreas, referencing proposed mechanisms (e.g., molecular mimicry, beta-cell tropism). 6. "The COVID-19 (Coronavirus Disease) pandemic began in March 2020..." Better phrased as: "The COVID-19 pandemic, which began in March 2020, led to..." 7. Add a clear description of the study design, population, and data sources. 8. Address potential misclassification more clearly: using insulin prescription as a proxy may include misdiagnosed T2DM cases, even in younger children. 9. Presents detailed demographic and virological data and incorporates appropriate statistical models and visual interpretation of seasonality. 10. Include confidence intervals (CIs) and p-values for all incidence rate comparisons. 11. Expand slightly on potential biological mechanisms for COVID-19 or other respiratory viruses triggering DM1. 12. If possible, include a brief discussion on post-pandemic trends or mention whether follow-up studies are ongoing. 13. Correct the statements that follow as; "and therefore may have a role" consider improving for fluency: "and may therefore



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contribute to the development of DM1." and "Further research is needed to explore..." perhaps specify: "...to explore causal pathways and preventative strategies." 14. Carefully format the citations and references as per the guidelines of "World Journal of Diabetes". 15. The conclusion section is too brief and misses the opportunity to restate major findings and implications. Consider revising this section as follows; Conclusion "This study suggests that reduced seasonal variation in type 1 diabetes incidence during the COVID-19 lockdown, combined with an overall increase in new cases, may reflect the role of respiratory viruses, including SARS-Cov-2, as environmental triggers of DM1. These findings highlight the need for further studies to confirm causality and inform preventive approaches."



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 108724

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Peer-review model: Single blind

Reviewer's code: 07838429

Position: Peer Reviewer

Academic degree and professional title: PhD, Postdoctoral Fellow

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: Israel

Manuscript submission date: 2025-04-23

Reviewer chosen by: Yu Bai

Reviewer accepted review: 2025-06-04 04:20

Reviewer performed review: 2025-06-05 05:43

Review time: 1 Day and 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

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Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers? **Yes**

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Dear authors, After a careful re-evaluation of this manuscript I'm satisfied with the content and the revisions made by the authors. Furthermore, the points that I have highlighted in the previous version have been addressed properly. Therefore, I would like to accept this manuscript in its present form and recommend its further processing for publication in this journal. Thank you for the opportunity to review your study.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree and professional title: MD, PhD, Postdoctoral Fellow

Reviewer’s Country/Territory: China

Author’s Country/Territory: Israel

Manuscript submission date: 2025-04-23

Reviewer chosen by: Yu Bai

Reviewer accepted review: 2025-06-05 11:13

Reviewer performed review: 2025-06-05 11:23

Review time: 1 Hour

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? Yes</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes</p> <p>Are the Key Words complete? Yes</p>
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Will the manuscript's content be of interest to readers? **Yes**

Are additional experiments needed for the study? **Yes**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: Yes

SPECIFIC COMMENTS TO AUTHORS

This manuscript presents a retrospective study based on a nationwide Israeli database, systematically analyzing the incidence and seasonality of type 1 diabetes mellitus (DM1) before and during the COVID-19 pandemic. The results show an increased incidence of DM1 during the pandemic, accompanied by a weakening of the previously observed seasonal pattern. These findings suggest that respiratory viruses, especially COVID-19, may act as potential environmental triggers for DM1. The study holds significant public health relevance and demonstrates a degree of theoretical innovation. Strengths and Innovations of the Manuscript 1. Large-scale data: The study covers a nationwide population over a long duration (9 years) and includes multiple types of respiratory



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viruses, ensuring strong representativeness. 2. Robust methodology: The use of time-series modeling, Poisson regression, and Fourier decomposition for analyzing the seasonality of DM1 is methodologically sound. 3. High public health relevance: It provides important population-level evidence on the potential impact of COVID-19 and other viruses on the incidence of DM1. 4. Clear narrative: The manuscript is logically structured, the narrative is coherent, and the conclusions are consistent with the results.

Minor Revision Suggestions

1. The terms “pre-COVID-19 period” and “COVID-19 period” are somewhat redundant. It is recommended to standardize these as “pre-pandemic” and “pandemic period” and to clarify them in the Introduction.
2. The term “seasonality” of DM1 is central to the study but is not clearly defined in the Introduction. It is suggested to briefly explain the concept of seasonality and the analytical indicators used (e.g., Fourier terms) to help readers better understand the analytical logic.
3. Certain expressions should be revised for academic precision. For instance, instead of “suggest COVID-19 may be a DM1 trigger,” it would be more appropriate to say “suggest a potential triggering role of COVID-19 in new-onset DM1.”