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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 111309

Title: Advances in gestational diabetes mellitus screening: Emerging trends and future directions

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08279645
Position: Peer Reviewer
Academic degree and professional title: Associate Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Türkiye

Manuscript submission date: 2025-06-26
Reviewer chosen by: Hong-Xin Jiang
Reviewer accepted review: 2025-06-27 08:38
Reviewer performed review: 2025-07-02 12:25
Review time: 5 Days and 3 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? **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? **Not Applicable** Is the description of the experiments clear and complete? **Not Applicable** Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable** Are the experimental data of the Results true and reliable? **Not Applicable** 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** 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? **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**

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	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 A (Excellent)
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	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Enhance Machine Learning Section: The section on machine learning-based predictions for GDM and its progression to type 2 diabetes mellitus (T2DM) is promising but could be strengthened by including specific examples or case studies of successful clinical implementations. For instance, discussing a study where machine learning improved diagnostic accuracy in a real-world setting would add practical context. Additionally, elaborating on challenges, such as data standardization or model validation, would provide a more balanced perspective. Consider citing recent studies, such as those

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available on PubMed, to support this section.

Deepen Biomarker Validation Discussion: The biomarker section categorizes metabolic, inflammatory, placental, genetic, and urinary markers effectively. However, including more details on their validation—such as performance in large-scale cohort studies or ongoing clinical trials—would enhance credibility. For example, discussing the sensitivity and specificity of biomarkers like PAPP-A2 or microRNAs in diverse populations could clarify their clinical utility. Resources like ClinicalTrials.gov may provide relevant trial data to reference.

Highlight Unique Contributions: To emphasize the manuscript's originality, consider adding a brief comparison with existing GDM reviews. For instance, how does this review differ from or build upon prior works in terms of scope, focus on emerging technologies, or integration of machine learning? A short paragraph in the introduction or discussion could address this, citing key reviews from journals like Diabetes Care or The Lancet Diabetes & Endocrinology.

Expand Future Directions: The conclusion mentions integrated, multi-omic approaches, which is forward-thinking. Expanding this section with specific research suggestions—such as interdisciplinary collaborations between bioinformaticians and clinicians or studies focusing on underrepresented populations—would strengthen its impact. For example, proposing research on machine learning models tailored to high-risk ethnic groups could address current gaps.

Verify Reference Completeness: The reference list is assumed to be comprehensive, but ensure it includes the most recent studies, particularly in fast-evolving areas like

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biomarkers and machine learning. A quick check for seminal papers from 2023–2025, accessible via Google Scholar, could confirm this. Avoid over-reliance on older references or self-citations, ensuring a balanced representation of the field.

Image and Box Quality: The figures and boxes are described as clear and necessary, with consecutive numbering (e.g., Figure 1, Figure 2; Box 1–4). However, please confirm that image resolution meets journal standards (e.g., 300 dpi for print). Additionally, ensure no redundancy exists between text and visual content, as this could streamline the manuscript.

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Manuscript submission date: 2025-06-26

Reviewer chosen by: Li Li

Reviewer accepted review: 2025-08-01 03:34

Reviewer performed review: 2025-08-06 06:24

Review time: 5 Days and 2 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? **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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Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Thank you for submitting your revised manuscript, "Advances in gestational diabetes mellitus screening: Emerging trends and future directions," to the *World Journal of Diabetes*. Your thorough responses to the reviewers' comments and the subsequent revisions have significantly strengthened the manuscript. Below are specific comments addressing the revised content, the quality of the revisions, and suggestions for further refinement to ensure the manuscript meets the journal's standards for publication.

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1. Response to Reviewer Comment 1: Enhancing the Machine Learning Section

Your inclusion of Zaky et al. (2025) and Kaya et al. (2024) as examples of real-world applications of machine learning (ML) for early GDM prediction is commendable. These additions effectively illustrate the diagnostic potential of ML models and address implementation challenges, such as data standardization and external validation. However, to further enhance this section, consider briefly discussing the specific ML algorithms used in these studies (e.g., random forests, neural networks) and their performance metrics (e.g., AUC, sensitivity, specificity) to provide readers with a clearer understanding of their practical utility. Additionally, a brief mention of how these models could be integrated into clinical workflows would strengthen the practical context. For example, you could note whether these models are deployable in resource-limited settings or require advanced computational infrastructure.

2. Response to Reviewer Comment 2: Deepening Biomarker Validation Discussion

The expanded discussion on microRNA biomarkers, incorporating Juchnicka et al. (2022) and Ye et al. (2022), is a valuable addition. The inclusion of AUC values and mechanistic associations with GDM pathophysiology enhances the credibility of the biomarker section. However, to further improve this section, consider adding a brief comparison of microRNA biomarkers with other biomarker categories (e.g., metabolic or inflammatory markers) to clarify their relative predictive power. For instance, are microRNAs more sensitive or specific than HOMA-IR or inflammatory markers like CRP? Additionally, referencing ongoing clinical trials from ClinicalTrials.gov, as suggested by the reviewer, could further validate the clinical utility of these biomarkers. If no relevant trials are available, a statement acknowledging this gap would demonstrate thoroughness.

3. Response to Reviewer Comment 3: Expanding Future Directions

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The revised conclusion effectively highlights limitations in current ADA-recommended screening strategies and proposes biomarker-based and ML-driven approaches for individualized risk stratification. The focus on shifting from conventional diagnostic thresholds to personalized models is forward-thinking and aligns well with emerging trends in precision medicine. To further strengthen this section, consider specifying one or two high-risk ethnic groups (e.g., South Asian or Hispanic populations) and discussing how ML models could be tailored to address their unique risk profiles. Additionally, a brief mention of potential barriers to implementing multi-omic approaches (e.g., cost, accessibility, or regulatory challenges) would provide a more balanced perspective.

4. Response to Reviewer Comment 4: Verifying Reference Completeness

The updated reference list, incorporating studies from 2022–2025, demonstrates a robust effort to reflect current research in biomarkers and ML. The inclusion of recent studies such as Zhao et al. (2025) and Zaky et al. (2025) strengthens the manuscript's relevance. However, to ensure a truly balanced representation, consider checking for any seminal papers from underrepresented research groups or regions (e.g., Africa or South America) to address global perspectives on GDM. A quick Google Scholar search for 2023–2025 studies from these regions could confirm whether additional references are needed. Additionally, ensure that self-citations, if present, are minimal and justified to avoid potential bias.

5. Response to Reviewer Comment 5: Image and Box Quality

Your confirmation that all figures meet the journal's 300 dpi resolution standard and that redundancy between text and visual content has been minimized is appreciated. The consecutive numbering of figures (e.g., Figure 1, Figure 2) and boxes (e.g., Box 1–4) is clear and appropriate. However, based on the provided PowerPoint file ("111309-Image

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File-revision.pptx"), the content on Page 2 lists biomarker categories (e.g., metabolic, inflammatory, placental, genetic, urinary) but contains a duplication of "Genetic Biomarker S" and "Urine Biomarker S." This appears to be an error and should be corrected to avoid confusion. Additionally, consider adding a brief caption or legend to Figure 2 (Biomarkers in GDM) in the manuscript to clarify the abbreviations (e.g., SII, SIRI, FABP4) for readers unfamiliar with these terms. If not already included, ensure that all figures are referenced in the text to guide readers effectively.

6. General Comments on Manuscript Quality

The manuscript is well-structured, with a clear introduction, detailed pathogenesis section, and comprehensive discussion of biomarkers and ML-based approaches. The core tip and abstract succinctly summarize the manuscript's contributions, emphasizing precision diagnostics and individualized care. The scientific quality and significance are high (Grade A), as the manuscript synthesizes current evidence and identifies critical gaps in GDM screening. However, the novelty and creativity (Grade B) could be further enhanced by explicitly addressing how the proposed approaches differ from existing reviews or by proposing a novel framework for integrating biomarkers and ML in clinical practice.

7. Suggestions for Further Improvement

Clarify Ethnic Variability: Given the global variability in GDM prevalence (6–20%), consider adding a brief subsection or paragraph discussing how biomarkers and ML models perform across diverse populations (e.g., Asian vs. Caucasian vs. African cohorts). This would address the reviewer's suggestion to focus on underrepresented populations and enhance the manuscript's global relevance.

Streamline Biomarker Section: The biomarker section is comprehensive but lengthy.

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Consider consolidating overlapping content (e.g., metabolic and inflammatory markers) into a table summarizing key biomarkers, their predictive performance (e.g., sensitivity, specificity), and validation status. This would improve readability and allow readers to quickly compare biomarker utility.

Visual Aids: If feasible, include a simple chart to visualize the performance of ML models (e.g., AUC values from Zaky et al. and Kaya et al.) or biomarker sensitivity/specificity across studies. This would enhance the manuscript's visual appeal and support the reviewer's emphasis on practical context.

Example Chart for ML Model Performance (if desired):

If you would like to include a chart comparing the performance of ML models from Zaky et al. (2025) and Kaya et al. (2024), I can generate one. For example, a bar chart could display AUC values for each model. Please confirm if you would like me to produce this chart, and provide specific AUC values if available (or I can note that these should be extracted from the cited studies).

8. Formatting and Minor Edits

Ensure consistency in terminology (e.g., "GDM" vs. "gestational diabetes mellitus") throughout the manuscript to avoid redundancy. For instance, after defining GDM, use the acronym consistently unless introducing a new section.

In the abstract, consider replacing "multi-dimensional biomarkers" with "multimodal biomarkers" for clarity and alignment with scientific terminology.

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Double-check the reference format to ensure compliance with the *World Journal of Diabetes* guidelines (e.g., correct PMID and DOI formatting).

Conclusion:

The revised manuscript is of high scientific quality and addresses the reviewers' comments effectively. The additions to the machine learning and biomarker sections, along with the expanded future directions, significantly enhance the manuscript's impact. Addressing the minor issues noted above (e.g., correcting the duplicated biomarker categories, adding captions for figures, and considering ethnic variability) will further polish the manuscript for publication. I recommend **acceptance with minor revisions**. Please clarify whether you would like a chart generated for ML model performance or any other specific additions.

Thank you for your diligent work on this important topic. I look forward to seeing the final version of your manuscript.

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Peer-review model: Single blind

Reviewer's code: 08415436
Position: Peer Reviewer
Academic degree and professional title: Assistant Professor, PhD
Reviewer's Country/Territory: Türkiye
Author's Country/Territory: Türkiye

Manuscript submission date: 2025-06-26
Reviewer chosen by: Li Li
Reviewer accepted review: 2025-08-25 06:57
Reviewer performed review: 2025-08-30 21:19
Review time: 5 Days and 14 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? **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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	Are the experimental data of the Results true and reliable? **Not Applicable** Are the quality and resolution of the images up to standard? **Yes** Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable** Is the description of the experiments clear and complete? **Yes** Is the content of the Materials and Methods complete? **Yes** Is the content of the Introduction adequate? **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** 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? **Not Applicable** 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? **Yes** Is the manuscript's text correct, concise, and clear? **Yes** Will the manuscript's content be of interest to readers? **Yes**

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	Are additional experiments needed for the study? **No** Does the research scope comply with ethics? **Yes**
Scientific quality	Grade C (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 C (Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

1. A comprehensive range of content is presented, from pathophysiology to classical OGTT-based screening protocols, from biomarkers to artificial intelligence applications.
2. The detailed analysis of metabolic, inflammatory, placental, genetic, and epigenetic biomarkers, in light of current literature, provides a multidisciplinary perspective.
3. The emphasis on the high predictive power of microRNAs (miRNAs) and machine learning models provides guidance for future personalized healthcare.

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4. The tables and figures are quite well-executed; presenting the reader with a comparative overview of different screening criteria, biomarkers, and risk prediction models enhances the understandability and visual appeal of the text.

5. The multidisciplinary approach brings together the fields of nutrition, endocrinology, perinatology, and data science.

Limitations:

1. Nutritional interventions are not adequately addressed in the article. More emphasis on the preventive effects of simple sugar consumption and dietary and lifestyle interventions (e.g., low-glycemic-index diet, Mediterranean diet, exercise) could have enriched the article. I believe adding a few paragraphs or headings would also increase your citation count.

2. Numerous AUC values, logistic regression results, and statistical data are presented. These details are excessive in a review format, distracting the reader, and giving the text a thesis-like feel. (for example, this section: Recent meta-analysis evaluated 25 studies that developed and validated ML-based models for GDM prediction, demonstrating an overall pooled area under the receiver operating characteristic curve of 0.8492, indicating strong discriminatory power. Among the various ML techniques analyzed, non-logistic regression models, including gradient-boosting decision trees (DT), support vector machines, and artificial neural networks, outperformed traditional logistic regression models, achieving an area under the receiver operating characteristic of 0.8891 compared to 0.8151 for logistic regression.

Other examples: BCAAs demonstrated predictive performance of AUC ≥ 0.67 with sensitivity above 76%, adipokines varied widely with AUCs between 0.337 and 0.836, and vitamin D deficiency showed a sensitivity of 81% but low specificity (44%)[60].

Different ML algorithms, including logistic regression, DT, random forest, Naïve Bayes, and Cox models were compared. Among these, random forest exhibited the highest

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predictive accuracy (χ2: 0.88, 95%CI: 0.81-0.94), whereas logistic regression models showed slightly lower performance (χ2: 0.81, 95%CI: 0.75-0.88). these explanations are too long and distracting)