

MDPI Reviewer Report

Manuscript Title: Are All Incretin Therapies Equal for the Kidney? Comparative FAERS Analysis of Tirzepatide and Semaglutide

Journal: Journal of Clinical Medicine (JCM)

Reviewer Recommendation: Accept after minor revision

1. Summary of the Manuscript

This manuscript presents a comparative pharmacovigilance study assessing acute kidney injury (AKI) signals associated with tirzepatide versus semaglutide using the FDA Adverse Event Reporting System (FAERS) from January 2022 to September 2025. Using disproportionality metrics (Reporting Odds Ratio and Proportional Reporting Ratio), the author shows that semaglutide exhibits a higher proportional reporting signal for AKI than tirzepatide. The study provides valuable real-world insights differentiating renal safety profiles between two incretin-based agents.

2. Major Strengths

- Novelty and Relevance: Addresses an emerging comparative safety question between two widely used incretin-based therapies.
- Methodological Rigor: Uses standard disproportionality analysis methods (ROR, PRR) and FAERS-based case definitions aligned with MedDRA terminology.
- Clear Presentation: Results are clearly summarized with well-structured tables and figures.
- Balanced Interpretation: Avoids causal claims and acknowledges limitations inherent to spontaneous reporting systems.

3. Major Comments (for Authors)

- Provide greater detail on duplicate case handling and clarify how FAERS unique case IDs were managed.
- Include the exact list of MedDRA Preferred Terms for AKI in supplementary materials for reproducibility.
- Add the 2×2 contingency table for transparency in ROR/PRR calculations.
- Add a brief subsection on mechanistic implications in Discussion (GLP-1–mediated volume depletion vs tubular effects).
- Add numerical values and confidence intervals on Y-axes and in figure legends.
- Light English proofreading to improve sentence flow and reduce repetition.

4. Minor Comments

- Specify the MedDRA version used (e.g., v26.0).
- Confirm that no financial conflicts of interest existed.

- Add a short clinical implications paragraph at the end of Discussion.
- Ensure uniform DOI formatting and punctuation in references.

5. Ethical and Editorial Considerations

No plagiarism or duplicate publication detected. Ethical approval not required as FAERS data are public and de-identified. Author declarations are satisfactory and no conflicts of interest are evident.

6. Overall Recommendation

Accept after minor revision.

The manuscript is scientifically sound, clinically meaningful, and well-presented. Only minor revisions to methodological transparency, figure annotation, and language flow are suggested before acceptance. Once these edits are implemented, the paper will be suitable for publication in the Journal of Clinical Medicine.