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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 109385

Title: Inflammatory biomarkers in the pathogenesis of pancreatic cancer: A literature review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06636544

Position: Editorial Board

Academic degree and professional title: Associate Professor, MD, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Pakistan

Manuscript submission date: 2025-05-08

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-05-11 00:24

Reviewer performed review: 2025-05-12 05:43

Review time: 1 Day and 5 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 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**

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

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**

Do the selection and design of the figures and tables



	follow the principles of necessity and clarity? Not Applicable Does the research scope comply with ethics? Not Applicable
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: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	

SPECIFIC COMMENTS TO AUTHORS

This manuscript presents a mini-review exploring the role of various inflammatory biomarkers in the pathogenesis and clinical management of pancreatic cancer, particularly pancreatic ductal adenocarcinoma (PDAC). The authors aim to summarize



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the involvement of biomarkers such as CRP, IL-6, haptoglobin, serum amyloid A, calprotectin, ferritin, and others, drawing from a broad literature base. While the topic is of high clinical relevance and the review includes an extensive collection of cited studies, the manuscript requires significant revision in the areas of focus, clarity, structure, scientific depth, and linguistic accuracy.

1. The manuscript reads more like an exhaustive list of inflammatory markers with brief summaries of associated studies than a critically synthesized mini-review. The review would benefit from clearly structured sections that group biomarkers by biological pathways (e.g., cytokine signaling, acute-phase proteins, immune-modulatory functions), or by clinical utility (e.g., diagnostic, prognostic, predictive biomarkers), instead of treating each marker in isolation.
2. The review often presents data uncritically. For example, conflicting results from studies on the same marker (e.g., CRP, IL-6) are presented without analysis of potential causes (e.g., differences in study design, stage of disease, assay methodology). There is minimal discussion of limitations, heterogeneity of findings, or gaps in the literature.
3. The manuscript inadequately contextualizes how these biomarkers relate to current diagnostic or therapeutic standards in PDAC. How do they compare with CA19-9? Are any approved for clinical use? Are they integrated in current treatment algorithms or trials?
4. The manuscript contains numerous grammatical issues, awkward phrasings, and repetition. For example, the abstract includes "However, this review article summarized...", which should be rephrased for clarity.
5. Several references appear inconsistently formatted and should follow the World Journal of Clinical Oncology style precisely.
6. The treatment for pancreatic cancer should be introduced (PMID: 34078087). TGF-beta is also an important biomarker (PMID: 33812073).



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7. "Approved immune checkpoint inhibitors include antibodies that block Programmed Cell Death 1 (PD-1), Programmed Cell Death ligand 1 (PD-L1), and Cytotoxic T lymphocyte-associated protein 4 (CTLA-4)." lacks reference such as doi.org/10.1016/j.cej.2024.152175.
8. The manuscript oscillates between general "pancreatic cancer" and specific "pancreatic ductal adenocarcinoma" without clarification.
9. It is suggested to condense and streamline the main text, eliminating overly detailed study descriptions that do not add value.
10. Emphasize how this review differs from previous literature or systematic reviews in the field.



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05292374

Position: Editorial Board

Academic degree and professional title: Associate Professor, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Pakistan

Manuscript submission date: 2025-05-08

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-05-12 00:10

Reviewer performed review: 2025-05-18 15:11

Review time: 6 Days and 15 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 content of the Materials and Methods complete?

Yes

Is the content of the Introduction adequate? **Yes**

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? **No**

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 Conclusion reasonable? **Yes**

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

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

Do authors omit important references? **Yes**

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? **No**

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? Not Applicable
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 B (Very 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?	Yes
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	

SPECIFIC COMMENTS TO AUTHORS

This comprehensive review examines the role of inflammatory biomarkers—including erythrocyte sedimentation rate, plasma viscosity, procalcitonin, calprotectin, haptoglobin, serum amyloid A (SAA), ferritin, and fibrinogen—in the pathogenesis of pancreatic ductal adenocarcinoma (PDAC). The authors synthesize evidence from clinical and molecular studies to highlight how chronic inflammation contributes to



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tumor initiation, progression, and metastasis. Strengths include the systematic evaluation of diverse biomarkers, integration of recent clinical data (e.g., prognostic scores combining CRP and CA19-9), and emphasis on translational implications, such as biomarker-guided therapy. The inclusion of figures summarizing biomarker mechanisms adds visual clarity. A notable innovation lies in exploring understudied markers like calprotectin and fibrinogen, offering fresh insights into their diagnostic and prognostic utility in PDAC. However, some potential issues need to be addressed before accept for publish.

Comments:

While the introduction details pancreatic cancer mortality in the United States, it lacks global and Asian-specific data. Pancreatic cancer incidence and mortality vary significantly across regions, with rising rates in Asia due to lifestyle and genetic factors. Incorporating updated global statistics (e.g., GLOBOCAN 2022) and regional disparities would strengthen the epidemiological relevance.

Structural and Logical Flow: The manuscript suffers from dense, monolithic paragraphs, particularly in the introduction and main text. Subdividing sections with descriptive subheadings (e.g., "Inflammatory Microenvironment and Stromal Interactions" or "Clinical Translation of Biomarkers") would enhance readability.

Figure Optimization: Figures 2–4 contain excessive text, diminishing their interpretability. Key pathways or mechanisms should be visualized through simplified diagrams (e.g., flowcharts, heatmaps) with minimal annotations. For example, Figure 2 (haptoglobin) could use arrows to depict fucosylation's role in tumor-stroma crosstalk, supplemented by brief legends rather than verbose descriptions.

Updated References: The global cancer burden discussion cites GLOBOCAN 2020; updating to GLOBOCAN 2022 (Filho et al., 2025) enhances timeliness and aligns with current trends. While the introduction addresses U.S. pancreatic cancer mortality, it



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lacks global/Asian data. As Asian-based authors, incorporating pancreatic cancer incidence, survival rates, and biomarker profiles (e.g., SAA/ferritin level disparities vs. Western cohorts) contextualizes findings broadly. Regional incidence/mortality disparities—including Asia’s rising rates (lifestyle/genetic links)—warrant inclusion to strengthen epidemiological relevance.

Language and Syntax: Some sections feature repetitive phrasing and convoluted sentences. Streamlining language and avoiding redundancy—particularly in biomarker-specific subsections—would improve clarity.

Conclusion Depth: The conclusion briefly reiterates findings but lacks a forward-looking perspective. Expanding on unresolved questions (e.g., biomarker validation in multiethnic cohorts, therapeutic targeting of SAA or fibrinogen) or clinical challenges (e.g., biomarker specificity in early-stage PDAC) would add critical depth.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 109385

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06636544

Position: Editorial Board

Academic degree and professional title: Associate Professor, MD, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Pakistan

Manuscript submission date: 2025-05-08

Reviewer chosen by: Yu Bai

Reviewer accepted review: 2025-07-18 08:55

Reviewer performed review: 2025-07-18 08:57

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? **Not Applicable**

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? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Not Applicable**

Is the content of the Discussion reasonable? **Not Applicable**

Is the Conclusion reasonable? **Not Applicable**

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

Do authors omit important references? **Yes**

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

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



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	<p>Is the manuscript's text correct, concise, and clear? Yes</p> <p>Will the manuscript's content be of interest to readers? Yes</p> <p>Are additional experiments needed for the study? Yes</p> <p>Does the research scope comply with ethics? Not Applicable</p>
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 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	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

I AGREE THE PUBLICATION



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 109385

Title: Inflammatory biomarkers in the pathogenesis of pancreatic cancer: A literature review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05292374

Position: Editorial Board

Academic degree and professional title: Associate Professor, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Pakistan

Manuscript submission date: 2025-05-08

Reviewer chosen by: Yu Bai

Reviewer accepted review: 2025-07-18 04:23

Reviewer performed review: 2025-07-18 15:37

Review time: 11 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 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? **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? **No**

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**



	Does the research scope comply with ethics? Not Applicable
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 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?	Yes
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

I sincerely thank the authors for their diligent revisions in response to the previous review comments. The majority of concerns have been adequately addressed in the revised manuscript. However, upon reviewing the updated figures provided within the answering-reviewers file, I remain concerned that the textual elements within the figures appear overly dense and could impede visual clarity. I strongly recommend further optimization to reduce text redundancy, simplify labeling, or utilize graphical cues



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where possible to enhance readability without compromising essential information. Additionally, please ensure the finalized figures are embedded directly within the main manuscript file or supplementary materials, as appropriate, rather than solely within the “109385-answering-reviewers”, to facilitate proper evaluation by readers and the editorial team. With these minor adjustments, the manuscript would be significantly strengthened.