



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 112388

Title: Recent advances in the diagnosis of celiac disease

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 08729366

Position: Peer Reviewer

Academic degree and professional title: MD

Reviewer’s Country/Territory: China

Author’s Country/Territory: China

Manuscript submission date: 2025-07-25

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-08-04 15:20

Reviewer performed review: 2025-08-04 15:55

Review time: 1 Hour

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? No</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> <p>Is the content of the Introduction adequate? Yes</p>
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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? **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 A (Excellent)
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 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
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This editorial by Wang and Wu provides a timely and well-structured overview of recent advances in the diagnosis of celiac disease (CD), with a valuable emphasis on serum biomarkers. The authors effectively synthesize current knowledge on both established immunological biomarkers (tTG-IgA, DGP antibodies, EMA-IgA) and



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promising non-immune biomarkers (I-FABP, Citrulline, BUN), highlighting their respective merits, limitations, and evolving roles in diagnosis and monitoring. It successfully underscores the critical need for improved diagnostic strategies, particularly given the high prevalence of underdiagnosis. The inclusion of specific data relevant to the Chinese population (e.g., reported adult incidence, the Xinjiang cohort study on diagnostic delay) adds significant regional context and relevance for the journal's readership. The discussion on tTG-IgA thresholds for non-biopsy diagnosis is clinically pertinent, and the exploration of newer biomarkers like I-FABP and Citrulline offers insight into potential future diagnostic avenues. The novel link between elevated Blood Urea Nitrogen (BUN) and diagnostic delay, highlighted by referencing Li et al. (also in WJG), is a particularly interesting and clinically applicable point. The conclusion appropriately calls for large-scale validation studies to refine biomarker panels and move towards less invasive precision medicine approaches. While concise, the editorial fulfills its purpose as an overview. It effectively translates complex immunological and biochemical concepts into clinically relevant information. The core tip aptly summarizes the key message regarding the importance of serum biomarkers complementing traditional methods. The references are generally current and support the presented arguments. Overall, this editorial is scientifically sound, well-written, addresses a clinically significant topic, and is suitable for publication in its current form. It provides a useful update for clinicians and researchers alike. This editorial outlines the scientific merits and potential limitations of serum biomarker assays for CD diagnosis, offering additional avenues for clinical research. Furthermore, it provides clinicians with practical insights into the applicability of these diagnostic tools across varying clinical scenarios.



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Academic degree and professional title: MD

Reviewer’s Country/Territory: Italy

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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? No</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> <p>Is the content of the Introduction adequate? Yes</p>
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Do authors omit important references? **No**

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Yes



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Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade B (Very 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	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The manuscript is clearly written and provide an extensive review of available biomarkers for Celiac disease. The topic is of special interest due to several reasons:

- the increasing prevalence of Celiac Disease world-wide, mostly due to the extension of available diagnostic test to a wider range of patients with "non-classical" presentation;
- the current interest of clinical research towards potential pharmacological treatment for



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patients with Celiac Disease;

- the limitation of the current most validated biomarker (anti-transglutimaniase IgA) in a not uncommon subset of patients (association of IgA deficiency and Celiac Disease).

The introduction is concise and informative.

The following section focuses on the various biomarkers. The first section focuses on serological markers, defined by the authors as "immune biomarkers"; the authors clearly review current evidence on ttg-IgA, DPG-IgG and EMA-IgA antibodies. I would only recommend, if possible, to further extend the revision to less used but potentially interesting biomarkers, like ttg-IgG, proposed by the European Society for the Study of Celiac Disease as a possible alternative to DPG-IgG in patients with IgA deficiency.

The second section describes the evidence surrounding promising non-immune biomarkers, namely I-FABP and BUN. I would suggest to implement this section giving some space to intestinal permeability markers, such as urine lactulose/mannitol ratio and lactoferrine, if possible.

The conclusion is concise, but I think it could be improved if the authors give some space to the role of biomarkers in clinical research. Notably, most clinical trials evaluating the efficacy of treatments for non-responsive celiac disease have to recur to the histological evaluation of mucosal damage, which represent an invasive procedure. Furthermore, non-responsive celiac disease (differently from refractory celiac disease) is not always nor lineary associated with the presence of histological damage. This scenario further indicates the need for a non-invasive and widely validated biomarker.

All in all, the manuscript quality is good, however I would recommend the revision of the following minor flaws to improve it:

- 1) extend the revision of serological markers to anti-transglutimaniase IgG, as they represent a novel potential biomarker for Celiac Disease associated with IgA deficiency;
- 2) extend the revision of non-immune biomarkers to markers of intestinal permeability;



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3) in the conclusion, the authors should highlight how the absence of universally validated biomarkers represent a strong limitation in the design of clinical trials investigating potential treatments for Celiac Disease alternative to gluten-free diet. Current and past trials were widely heterogeneous in the choice of non-invasive biomarkers, making it difficult to compare the results of the different investigated molecules.