

Review Form 3

Journal Name:	Asian Journal of Immunology
Manuscript Number:	Ms_AJI_126461
Title of the Manuscript:	Endotyping Cellular and Humoral Immunoreactivity against Tartrazine in Allergic Patients. A Retrospective Study.
Type of the Article	Original Research Article

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PART 1: Review Comments

Compulsory REVISION comments	Reviewer's comment	Author's Feedback <i>(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Please write a few sentences regarding the importance of this manuscript for the scientific community. Why do you like (or dislike) this manuscript? A minimum of 3-4 sentences may be required for this part.	This manuscript is valuable for the scientific community as it addresses the diagnostic challenges surrounding non-IgE-mediated hypersensitivity to tartrazine, a common azo dye. By evaluating the Tube Titration of Precipitins (TTP) and the Leukocyte Adherence Inhibition Test (LAIT), it offers promising methods for endotyping humoral and cellular immune responses, which could enhance personalized treatment for patients with chronic allergic conditions. I appreciate the manuscript's approach, as it provides preliminary evidence for using TTP and LAIT to classify immunoreactivity levels, adding depth to allergy diagnostics. However, the study's retrospective nature and absence of a prospective design leave room for further research to strengthen these findings.	Thank you very much for your appreciation. Our next step is to design a prospective study to further strengthen these preliminary findings.
Is the title of the article suitable? (If not please suggest an alternative title)	The current title, "Endotyping Cellular and Humoral Immunoreactivity against Tartrazine in Allergic Patients: A Retrospective Study," is generally suitable, as it reflects the focus on immunoreactivity against tartrazine and indicates the study's retrospective nature. However, a slightly more precise title could improve clarity and capture attention. An alternative title might be: "Evaluation of TTP and LAIT for Diagnosing Non-IgE-Mediated Tartrazine Hypersensitivity: A Retrospective Study in Allergic Patients" This suggested title highlights the diagnostic methods (Tube Titration of Precipitins and Leukocyte Adherence Inhibition Test) and clarifies the study's emphasis on non-IgE-mediated hypersensitivity, which may better convey the study's focus to readers.	Thank you very much for your suggestion, however we are obliged to decline. In fact, this is very tempting, however there are some reasons to not modify the title: A) The abbreviations "TTP" and "LAIT" did not make sense in the title, since they are not universally recognised, so we should write the whole name of the assays, what would make the title very large. B) The assays employed did not necessarily evaluate "hypersensitivity", since tolerance mechanisms may also be involved, and are not evaluated by these procedures. C) as a consensus with the other reviewer who opted for keeping the title unaltered.
Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.	The abstract is comprehensive, covering essential elements such as the study's background, aim, methodology, results, and conclusion. However, a few adjustments could enhance clarity and focus: Condense the Methodology: Some technical details could be streamlined. For example, rather than specifying each patient condition individually, summarizing them as "various non-IgE-mediated allergic conditions" could improve readability. Results Section: Adding concise statistics (e.g., mean and standard deviation values) directly in the abstract would strengthen its clarity and impact. Emphasize Conclusions: The conclusion could better highlight the study's implications for clinical practice and potential for future research, such as the need for prospective studies or validation. Suggested Deletion: Consider removing the location and duration details from the abstract (e.g., place and dates of the study), as these are less critical in conveying the study's relevance. These adjustments would help focus the abstract on the study's core findings and implications for the scientific community.	Thank you very much for your considerations, we are performing the adjustments suggested. We introduced a new section at the end of the paper named: 7. FUTURE DIRECTIONS AND RECOMMENDATIONS FOR CLINICAL PRACTICE
Are subsections and structure of the manuscript appropriate?	Yes, the subsections and structure of the manuscript are appropriate and well-organized. The manuscript follows a logical flow, with clear sections for the Introduction, Materials and Methods, Results, Discussion, Limitations, and Conclusion, which enhances readability and helps readers understand the study's progression. Each section provides sufficient detail and is adequately subdivided, especially in the methodology, where step-by-step descriptions of the TTP and LAIT procedures support reproducibility. Additionally, the limitations section effectively addresses the study's retrospective nature and potential biases. This structure is well-suited to presenting complex immunological research findings and makes the manuscript accessible to a broad scientific audience.	Thank you very much for your appreciation.
Please write a few sentences regarding the scientific correctness of this manuscript. Why do you think that this manuscript is scientifically robust and technically sound? A minimum of 3-4 sentences may be required for this part.	The manuscript is scientifically robust and technically sound, as it employs established immunological assays—the Tube Titration of Precipitins (TTP) and the Leukocyte Adherence Inhibition Test (LAIT)—to assess cellular and humoral immunoreactivity, supported by appropriate statistical analysis. The methods are well-documented, ensuring reproducibility and transparency in data collection and analysis. Furthermore, the study's use of retrospective data over several years provides a meaningful	Thank you very much for your appreciation.

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	sample size that reinforces the validity of its findings. The manuscript's scientific rigor is also enhanced by its clear identification of limitations, such as the need for prospective studies, which adds to its credibility and encourages further research in this area.	
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form. :	The references in this manuscript are generally sufficient and include a mix of foundational and recent sources on tartrazine hypersensitivity, diagnostic immunology, and the specific methodologies (TTP and LAIT) used. Many references are recent, with a few publications from 2023 and 2024, which supports the study's relevance to current research. However, additional references on recent advancements in non-IgE-mediated allergy diagnostics and endotyping could further strengthen the discussion. Specifically, recent reviews or studies on precision medicine in allergy diagnostics and the clinical application of immunological tests in non-IgE-mediated allergies might add valuable context. Including these could provide a more comprehensive perspective on how TTP and LAIT fit within the broader framework of allergy diagnostics and personalized immunology.	Thank you very much for your appreciation.
<u>Minor</u> REVISION comments Is the language/English quality of the article suitable for scholarly communications?	The language and English quality of the article are generally suitable for scholarly communication; however, minor revisions could improve readability and flow. Some sentences, particularly in the introduction and discussion sections, are lengthy and could benefit from being simplified or divided to enhance clarity.	Thank you very much for your appreciation. We are conducting a grammar review according with your suggestions.
<u>Optional/General</u> comments	<p>Overall, this manuscript provides a valuable contribution to the field of allergy diagnostics by exploring practical methods for detecting non-IgE-mediated immunoreactivity against tartrazine. Its retrospective design offers meaningful insights, though prospective studies would further validate these preliminary findings. Additionally, while the study's methodology and statistical approach are sound, readers would benefit from a clearer emphasis on the potential clinical applications of TTP and LAIT, particularly for developing cost-effective and accessible allergy diagnostics. Including a brief section on future directions or recommendations for clinical practice could strengthen the paper's relevance and impact within the scientific community.</p> <p>No significant ethical issues are evident in this manuscript. The study was conducted retrospectively, and data were analyzed from patient records with institutional review board approval, ensuring compliance with ethical standards. Additionally, the authors state that informed consent was provided collectively by the institution's ethics committee in line with the Declaration of Helsinki. Given these considerations, the study appears to have adhered to appropriate ethical guidelines for research involving human data.</p> <p>The manuscript does not indicate any competing interest issues. The authors have not disclosed any conflicts of interest that might bias the study's design, findings, or interpretations. This neutrality adds to the credibility of the research, suggesting that the study's results and conclusions are presented objectively.</p>	Thank you very much for your appreciation. These are very good ideas which we are including the new section on the text.

PART 2:

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Are there ethical issues in this manuscript?	<u><i>(If yes, Kindly please write down the ethical issues here in details)</i></u>	