

Comment on dynamic plasma biomarker trajectories in pediatric sepsis

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Dear Editor,

The study by Tian et al. on the prognostic value of dynamic plasma biomarker trajectories in pediatric sepsis was read with great interest.¹ The prospective design and the use of systematic serial measurements are clear strengths of the study. At the same time, it is believed that several aspects related to the study population, analytical strategy, and biological framework merit further consideration in order to better place the findings within a clinical context.

First, the study population primarily consists of children with early-recognized, mild-to-moderate sepsis. Low Pediatric Sequential Organ Failure Assessment Score (pSOFA) scores at admission, infrequent intensive care unit admissions, limited need for invasive organ support, and the absence of mortality indicate that the cohort represents a relatively narrow severity spectrum.¹ This may limit the applicability of the findings to children with more severe forms of sepsis. In higher-acuity settings, factors such as delayed presentation, immune dysregulation, endothelial injury, and exposure to advanced organ support therapies are known to substantially influence biomarker behavior and its prognostic meaning.^{2,3} From this perspective, the high discriminative performance reported for the proposed two-step algorithm should be interpreted cautiously,

as it may partly reflect derivation from a low-risk and relatively homogeneous population.

Second, the model focuses exclusively on inflammatory and coagulation biomarkers, resulting in a somewhat limited biological scope. Increasing evidence suggests that pediatric sepsis is a heterogeneous condition involving not only inflammation but also metabolic failure, endothelial dysfunction, and immune exhaustion.^{3,4} In more severe clinical phenotypes, traditional inflammatory markers may lose discriminatory capacity. Incorporating biomarkers that reflect additional pathophysiological pathways could therefore improve the clinical relevance and robustness of the proposed approach.

Finally, although the authors emphasize the prognostic significance of serial declines in biomarker levels, the analyses presented are primarily associative. In clinical environments with early recognition and standardized sepsis management, reductions in inflammatory biomarkers may simply parallel clinical improvement rather than serve as independent predictors of outcome. This raises questions regarding the directionality of the observed associations between biomarker trajectories and clinical endpoints.^{2,5} Furthermore, the lack of analyses demonstrating incremental prognostic value beyond established clinical variables and

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severity scores makes it difficult to determine whether serial biomarker measurements meaningfully influence bedside decision-making.⁵

In summary, Tian et al.¹ provide valuable descriptive insights into biomarker kinetics in pediatric sepsis. However, interpretation of the proposed algorithm should consider the study's methodological and biological constraints. The restricted severity range of the cohort, the largely associative analytical approach, and the limited breadth of the biomarker panel may temper the generalizability and clinical impact of the findings. Future studies that include broader and more severe patient populations, rigorously assess the added prognostic value of biomarker kinetics beyond clinical evaluation, and integrate complementary biomarker domains may further advance both understanding and clinical application in this complex area.

Author contribution

The author confirms contribution to the paper as follows: Study conception and design: MÇ; data collection: MÇ; analysis and interpretation of results: MÇ; draft manuscript preparation: MÇ. The author reviewed the results and approved the final version of the manuscript.

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Conflict of interest

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REFERENCES

1. Tian J, Song J, Wang F, Liu F, Jiang L. Predictive value of dynamic plasma biomarkers for clinical outcomes in pediatric sepsis. *Turk J Pediatr* 2025; 67: 818-828. <https://doi.org/10.24953/turkpediatr.2025.6251>
2. Wong HR. Pediatric sepsis biomarkers for prognostic and predictive enrichment. *Pediatr Res* 2022; 91: 283-288. <https://doi.org/10.1038/s41390-021-01620-5>
3. Esposito S, Mucci B, Alfieri E, Tinella A, Principi N. Advances and challenges in pediatric sepsis diagnosis: integrating early warning scores and biomarkers for improved prognosis. *Biomolecules* 2025; 15: 123. <https://doi.org/10.3390/biom15010123>
4. Matics TJ, Sanchez-Pinto LN. Adaptation and validation of a pediatric sequential organ failure assessment score and evaluation of the sepsis-3 definitions in critically ill children. *JAMA Pediatr* 2017; 171: e172352. <https://doi.org/10.1001/jamapediatrics.2017.2352>
5. Leonard S, Guertin H, Odoardi N, et al. Pediatric sepsis inflammatory blood biomarkers that correlate with clinical variables and severity of illness scores. *J Inflamm (Lond)* 2024; 21: 7. <https://doi.org/10.1186/s12950-024-00379-w>