Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-026-06507-z

CORRESPONDENCE

Comparative Cytokine Profiles in Enthesitis-Related Arthritis and Adult Spondyloarthritis: Authors' Reply

Nebahat Zeynep Özaslan[1] · Mehtap Kalçık Unan[2] · Hüseyin Uzuner[3,4] · Gamze Dilek[2] · Nihal Şahin[1] · Aynur Karadenizli[4] · Neslihan Gökçen[2] · Kemal Nas[2] · Hafize Emine Sönmez[1]

Received: 12 September 2026 / Accepted: 7 October 2026
© The Author(s), under exclusive licence to Dr. K C Chaudhuri Foundation 2026

To the Editor: We thank Ying for thoughtful and constructive comments regarding our study comparing cytokine and chemokine profiles in enthesitis-related arthritis (ERA) and adult spondyloarthritis (SpA) [1, 2].

We agree that pubertal stage and anthropometric characteristics may influence circulating biomarkers, particularly NRG4, which has been associated with adiposity and metabolic parameters in children [3]. These variables were not systematically collected and therefore could not be incorporated into our analyses. Nevertheless, our study included age- and sex-matched healthy pediatric and adult control groups, allowing disease groups to be compared with developmentally appropriate controls. Thus, although residual confounding by pubertal or anthropometric factors cannot be excluded, age-related differences alone are unlikely to fully explain the observed biomarker patterns.

Importantly, our findings also demonstrated associations with disease activity. GM-CSF strongly correlated with JSpADA in ERA ($\rho=0.825$, $p=0.001$) and with BASDAI ($\rho=0.868$, $p=0.001$) and CRP ($\rho=0.872$, $p=0.001$) in adult SpA. CXCL16 and PF4 also correlated with CRP in ERA. These findings support an inflammatory component to these biomarker elevations, while not establishing disease specificity or causality.

We acknowledge that symptom-to-sampling interval and psychosocial variables were not systematically recorded and may represent potential confounders. All patients, however, were treatment-naïve and sampled at diagnosis, minimizing treatment-related effects.

We also agree that clinical assessment may underestimate or misclassify enthesitis in children. Ultrasonography can identify subclinical entheseal abnormalities not detected clinically, although standardized pediatric definitions remain an area of ongoing development [4].

Accordingly, our results should be interpreted as hypothesis-generating rather than definitive evidence of disease-specific biomarker signatures. Future multicenter longitudinal studies integrating pubertal staging, anthropometrics, symptom duration, objective entheseal imaging, and psychosocial assessment will be important to validate these findings.

Funding The original study was supported by Kocaeli University (Grant No. TSA-2024-3720). No additional funding was received for this correspondence.

Declarations

Conflict of Interest None.

References

1. Ying Q. Comparative cytokine profiles in enthesitis-related arthritis and adult spondyloarthritis: Correspondence. Indian J Pediatr. 2026. https://doi.org/10.1007/s12098-026-06506-0
2. Özaslan NZ, Unan MK, Uzuner H, et al. Comparative cytokine profiles in enthesitis-related arthritis and adult spondyloarthritis. Indian J Pediatr. 2026;93:1046–51.
3. Wang R, Zhou W, Zhu X, et al. Differences in Neuregulin 4 expression in children: Effects of fat depots and obese status. Endocr Res. 2020;45:190–201.
4. Weiss PF, Chauvin NA, Klink AJ, et al. Detection of enthesitis in children with enthesitis-related arthritis: dolorimetry compared to ultrasonography. Arthritis Rheumatol. 2014;66:218–27.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

✉ Nebahat Zeynep Özaslan
zeynepgozaluludag@gmail.com

[1] Department of Pediatric Rheumatology, Faculty of Medicine, Kocaeli University, Kocaeli, Türkiye

[2] Department of Physical Medicine and Rehabilitation, Division of Rheumatology and Immunology, Sakarya University School of Medicine, Sakarya, Türkiye

[3] Department of Medical Services and Techniques, Kocaeli Vocational School of Health Services, Kocaeli University, Kocaeli, Türkiye

[4] Department of Medical Microbiology, Molecular Research and Antibody Laboratory, Faculty of Medicine, Kocaeli University, Kocaeli, Türkiye

Published online: 23 October 2026