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Letter to the Editor

Authors' reply to the letter: "Low bone mineral density in rare metabolic disorders: data from a Turkish cohort of patients with glycogen storage disorders and organic acidemias"

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We sincerely thank the authors of the Letter to the Editor for their interest in our study and for the opportunity to clarify the methodological basis of our bone mineral density (BMD) assessments. In our study, all DXA results were interpreted in accordance with the 2019 Pediatric Official Positions of the International Society for Clinical Densitometry (ISCD), which define the current global standard for pediatric densitometry.[1] An explicit and essential statement from the ISCD 2019 pediatric positions is the following: "Z-scores should be generated from reference data matched to age, sex, and the manufacturer's reference database used by the DXA system." ISCD does not state or imply that country-specific or locally developed pediatric reference data should be used.

Although the 2006 reference curves were generated using a Hologic device, these curves are not part of Hologic's embedded pediatric reference database. Therefore, despite being a valuable national dataset, the 2006 Turkish pediatric BMD reference values[2] cannot be technically applied within an ISCD-compliant DXA workflow and were not used in our study, as doing so could result in inaccurate or non-standardized Z-score interpretation. Moreover, the 2006 Turkish reference curves were developed exclusively from healthy, normally growing children. ISCD emphasizes that growth patterns and body composition in children with chronic illnesses differ substantially from those of healthy peers, and therefore normative datasets derived from healthy populations may lead to misleading Z-score interpretation in chronically ill groups.

A review of current Turkish pediatric DXA practices also supports the methodological approach used in our work. Several recent theses evaluating BMD in chronic pediatric conditions have consistently relied on DXA-derived Z-scores generated from the manufacturer's reference database and have interpreted them using ISCD definitions and cut-off values. In recent theses[3-6] conducted on pediatric patients in Türkiye, the assessment of bone mineral density has been based on ISCD guidelines. In these studies, the ISCD-recommended Z-score threshold (≤ –2 SD) has been used to define low BMD, and measurements have been interpreted using device-specific reference databases provided by the DXA manufacturer. Moreover, many of these works explicitly highlight adherence to ISCD standards as a methodological strength. This demonstrates that contemporary academic research in Türkiye consistently employs ISCD- and manufacturer-based DXA interpretation in line with international standards, rather than utilizing the 2006 national reference curves. In addition, it is evident

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that the ISCD criteria have also been used in an academic study conducted in Türkiye.[7] International practices further support this approach. For example, Brazil has a national pediatric BMD reference dataset.[8] Nevertheless, Brazilian clinical studies evaluating BMD in hepatic glycogen storage disease and published in Nutrients (high-impact journal) in 2021 calculated Z-scores exclusively using ISCD 2019 recommendations and manufacturer-specific reference data rather than their national curves.[9] This demonstrates that even countries with strong population-specific datasets prioritize ISCD-compliant Z-score generation to ensure device compatibility and international comparability. In rare metabolic disorders such as glycogen storage diseases and organic acidemias, where study populations are small and global harmonization of data is essential, adherence to ISCD methodology is particularly critical.

In light of these considerations, our use of the ISCD 2019 pediatric positions and Hologic's manufacturer-calibrated pediatric reference database reflects current international best practice, aligns with ISCD expectations for device-specific DXA interpretation, and is consistent with contemporary Turkish and global pediatric literature. For these reasons, although scientifically valuable, the 2006 national pediatric BMD reference curves could not be applied methodologically or technically within an ISCD-compliant framework. We hope that this explanation clarifies the rationale underlying our methodological choices and contributes to constructive scientific dialogue.

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Conflict of interest

The authors declare that there is no conflict of interest.

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