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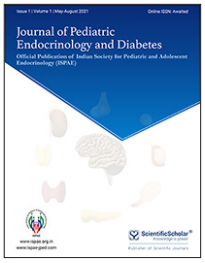

Editorial

Bone health assessment in children with type 1 diabetes using dual-energy X-ray absorptiometry scans: What is known and the way forward

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Childhood and adolescence are critical periods for bone development and peak bone mineral accrual.[1] An insult to the developing skeleton (chronic illness such as diabetes mellitus, inflammatory disorders, myopathies, malnutrition, dietary deficiencies, and medications such as glucocorticoids) can affect bone strength and increase fracture risk in the short- and long-term. The studies in adults with type 1 diabetes mellitus (DM) show an increased risk of fractures,[2] a modest reduction in bone mineral density (BMD),[3] and low bone turnover.[4] The studies in children with type 1 DM, on the other hand, show conflicting results primarily due to differences in study design and patient characteristics.

Ravishankar *et al*. have studied the prevalence of vitamin D deficiency, bone biochemistry, bone turnover markers, and BMD using dual-energy X-ray absorptiometry (DXA) in 37 children with type 1 DM and age-matched controls.[5] Children with type 1 DM were more likely to have vitamin D deficiency when compared to controls. However, there was no difference in the bone turnover markers or BMD between the two groups.

A recent meta-analysis of BMD and bone mineral content (BMC) in youth with type 1 DM included 2617 patients and 3851 matched controls. Patients with type 1 DM had lower BMD and BMC, measured by different modalities such as DXA, peripheral quantitative computed tomography (pQCT), and quantitative ultrasound.[6]

Another meta-analysis of nine studies reporting BMD Z-scores using DXA also showed a similar reduction in BMI in youth with type 1 DM.[7] However, it is important to note the heterogeneity of included studies in both meta-analyses regarding pubertal stage, gender, ethnicity of the children, and methods used to measure BMD, limiting extrapolation of the results to a broader group.

A caveat of DXA is the inability to distinguish between cortical and trabecular bone involvement. Because the two compartments are superimposed in DXA, the selective involvement of one can be missed. For example, the studies using pQCT, which can separate the two compartments, show low trabecular bone BMD in children with type 1 DM and normal or higher cortical BMD when compared to controls.[6]

Interestingly, in the present study, 38% of the children with type 1 DM were underweight, and 24% were stunted. DXA results should be interpreted cautiously in children with short stature. The bone is a three-dimensional structure. However, DXA is a two-dimensional projection that

measures the amount of mineral content in a given area of bone. Since areal BMD is affected by the size of the bones and the child, it can be falsely low in short children, while the converse is true in taller children.[8]

Several mathematical techniques of varying complexity have been developed to overcome this limitation. Height for age Z-scores adjusted BMC and BMD Z-scores can overcome the influence of stature on BMD measurements.[8] Furthermore, since DXA discounts the depth of bone in its measurements, it cannot estimate the true volumetric BMD (vBMD). However, vBMD can be calculated from the DXA data by estimating the approximate depth of the bone. The bone mineral apparent density thus derived has been shown to correlate with fracture risk.[9] The three-step "Mølgaard" model is an additional technique that we routinely use to adjust BMC and BMD for the size of the child; it takes into account the (a) height for age, (b) bone area for height, and (c) BMC for the bone area. This helps distinguish the effects of stature, bone size, and lightness on BMD.[8] Since there is a strong correlation between lean body mass (LBM) and bone mass, BMC adjusted for LBM is particularly useful in conditions like spinal muscular atrophy where sarcopenia can confound BMD measurement.[8] While no particular method can be recommended over the other, it is vital to remember the limitations of DXA in certain situations and use size-adjusted DXA data to make critical clinical decisions.

For the clinician, fracture risk is a more relevant outcome of interest. Unfortunately, there are insufficient data in the literature. A population-based cohort study from the United Kingdom reported a hazard ratio of 1.14 (95% CI 1.01–1.29) for fractures in males and 1.35 (95% CI 1.12–1.63) in females with type 1 DM between 0 and 19 years of age.[10] The studies in the future, therefore, should include fracture incidence as an outcome measure to shed more light on this crucial aspect. While long bone fractures have a dramatic clinical presentation, vertebral fractures can be insidious and overlooked if not actively screened. DXA-based vertebral fracture assessment (VFA) can provide valuable information about the axial skeletal involvement.[11]

With the increasing global incidence of type 1 diabetes, physicians need to recognize the musculoskeletal complications that can arise in this setting and proactively implement measures to improve musculoskeletal health.[12]

Accumulating evidence suggests that type 1 DM adversely affects the musculoskeletal system in children. However, there are many unknowns, and available literature is ***not robust enough to recommend routine DXA measurements*** in the absence of fractures, to assess bone health in children and adolescents with type 1 DM outside a research setting.

Modifiable factors that improve musculoskeletal health, such as correcting vitamin D deficiency, ensuring adequate dietary calcium intake, and encouraging regular physical activity, should be optimized in all children with type 1 DM.[13] Disease-specific targets such as achieving glycemic control and managing comorbid conditions such as celiac disease and hyperthyroidism are also crucial to improving bone health.

We would like to stress that the diagnosis of osteoporosis in children and adolescents ***should not be*** based on the results of DXA measurements alone. A BMC/BMD Z-score of more than –2.0 does not rule out the possibility of skeletal fragility and increased risk of fracture and a Z-score of <–2.0 does not confirm osteoporosis and should not be used for commencing bone-strengthening medications (e.g., bisphosphonates). On the contrary, osteoporosis in children and adolescents is defined as follows: In the absence of high energy trauma (a) two or more long bone fractures by the age of 10 years, (b) three or more long bone fractures by the age of 19 years, or (c) one or more vertebral crush fractures.[14] The occurrence of long bones fractures can be elicited from history but, not all children with vertebral fractures will present with pain and, therefore, it is our practice that during DXA measurements, we always perform lateral DXA imaging of the spine, which provides higher resolution images with very low radiation compared to standard lateral spine radiographs. Taking the above points into consideration, in both clinical and research settings, DXA measurements in children and adolescents should be accompanied by a history of long bone fractures and VFA, preferably using DXA so that a diagnosis of osteoporosis could be made.

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