Comment on: Endocrinopathies complicating transfusion-dependent hemoglobinopathy. *Need for better assessment of skeletal complications*

To the Editor

I have read with interest the recent publication by Al-Agha et al[1] that highlights the multitude of serious endocrinopathies associated with repeated blood transfusions in patients with various hemoglobinopathies. Reduced bone strength, as reflected by osteoporosis or osteopenia, is among the major complications identified in their study. Bone weakness and resultant fractures have a detrimental impact on the quality of life (QoL) in general and particularly in the context of hemoglobinopathy wherein osteoporosis and osteopenia associated with multiple transfusions can further increase the negative impact of hemoglobinopathy on QoL. Recent evidence has shown increased fracture risk even in transfusion-naïve patients.[2] Therefore, accurate diagnosis and management of these skeletal problems are essential for a holistic approach aimed at improving the QoL of such patients.

In their study, Al-Agha et al[1] have used Z-score measurements based on bone mineral densitometry (BMD) as the diagnostic criteria for osteoporosis or osteopenia. Bone mineral densitometry provides a 2 dimensional (2D) areal measurement of bone mass and it is employed as an indirect indicator of fracture risk. However, BMD only account for up to 50% of bone strength, thus making BMD an inadequate marker of skeletal ability to resist fractures.[3] The ability of bone to resist fracture depends not only on the amount of bone but also the 3 dimensional (3D) arrangement of skeletal microarchitecture. The 2D BMD measurements fail to visualize the 3D spatial distribution of bone mass, which is an important element of bone strength.[4] Improved clinical metrics of bone strength are required that can demonstrate skeletal resistance to fracture more adequately as compared to BMD.

Recent developments suggest that micro computed tomography (microCT), which enables 3D imaging, might be a better alternative. For instance, microCT imaging can be used to assess bone volume fraction (BVF, the volumetric distribution of bone mass), which is a strong determinant of bone strength, but the *in vivo* use of microCT imaging is hampered by radiation hazards.[3] Nonetheless, with technological advancements in CT technology minimizing radiation dosage, microCT based measures have the potential to accurately diagnose osteopenia or osteoporosis and predict the risk of fracture.[5] The dire QoL issues necessitate the need for future research to employ novel improved metrics of bone strength instead of BMD for ascertaining the impact of diseases such as hemoglobinopathies themselves or their treatments on the skeletal health of the patients.

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Reply from the Author

Thank you for your correspondence. Your queries may be answered by a very simple explanation. The quantitative ultrasound was used as an initial screening method due to an abundance of reasons, some of which are due to its ease of use, portability, cost-effectiveness, convenience, and relatively no radiation exposure. Those who were screened positive were followed up later on with further radiological and biochemical investigations for confirmation of diagnosis as well as management. This way, we have reasonably facilitated the screening of a large number of children from the starting point with minimal consequences than what would have been practically and logically possible using any of the options you referenced.

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