RESEARCH ARTICLE

Bone density unveiled: Investigating the effects of beta-thalassemia major on growing children and adolescents

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Abstract

Objective: To evaluate bone mineral density in children and adolescents with beta-thalassemia major.

Method: The retrospective, cross-sectional, descriptive study was conducted from October 30 to November 15, 2024, at Peshawar General Hospital, Peshawar, Pakistan, and comprised data from January to August 2024 of paediatric beta-thalassemia major patients aged 2-18 years. Bone mineral density and Z-scores were evaluated using dual-energy X-ray absorptiometry scans of the lumbar spine, proximal femur and distal radius. Data was analysed using SPSS 25.

Results: Of the 281 patients with mean age 6.92±3.74 years, 176(62.6%) were boys and 105(37.4%) were girls. The mean bone mineral density for proximal femur was 0.59±0.14g/cm^2, for lumbar spine 0.53±0.14g/cm^{2}and for distal radius 0.35±0.09g/cm^2. Corresponding Z-scores were -0.41±1.81, -0.48±1.79 and -2.99±1.97 respectively. Low bone mass prevalence was 36(18.9%) at proximal femur, 43(16.4%) at lumbar spine, and 76(62.3%) at distal radius. Age negatively correlated with Z-scores at proximal femur (r=-0.27, p=0.001) and distal radius (r=-0.19, p=0.03). Male subjects had higher bone mineral density and Z-scores at the proximal femur than females(p=0.04).

Conclusion: The reduction was significant in bone mineral density, particularly at the distal radius, in paediatric patients with beta-thalassemia major. The negative correlation between age and bone mineral density underscored the importance of early and continuous bone health monitoring in such patients.

Keywords: Beta-thalassemia, Bone mineral density, Osteoporosis, Paediatric. (JPMA 76: 700; 2026)

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Introduction

Beta-thalassemia major (BTM) is a hereditary disorder characterised by impaired synthesis of the beta-globin chain of the haemoglobin (Hb) molecule. Patients with this condition suffer from ineffective erythropoiesis and peripheral haemolysis,[1] necessitating lifelong transfusion therapy. Advances in chelation therapy and periodic transfusions have increased the life expectancy of these patients significantly. Nonetheless, osteoporosis and osteopenia are common complications in individuals with BTM.[2]

Several factors lead to bone disease in thalassemia patients, with the predominant causes being bone marrow expansion, iron overload and endocrinological imbalances.[3,4] These factors give rise to increased bone resorption, which elevates the risk of fractures and bone deformities.[5] Early screening for bone health is essential in the management of BTM patients.

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One of the most common and widely used non-invasive methods for assessing bone mineral density (BMD) is dual-energy X-ray absorptiometry (DXA).This scan provides two fundamental scores: the T-score, which is the comparison of an individual BMD to the average BMD of a young adult with healthy bones; the Z-score compares BMD to the average BMD of individuals with the same age and gender group. Clinicians can use these scores to assess bone health and identify individuals at risk of osteoporosis and osteopenia.[6]

In Pakistan, where BTM management is advancing, there is still limited data on bone health of paediatric patients. The current study was planned to fill the gap in literature by evaluating BMD at the lumbar spine, proximal femur and distal radius using DXA scan.

Materials and Methods

The retrospective, cross-sectional, descriptive study was conducted from October 30 to November 15, 2024, at Peshawar General Hospital, Peshawar, Pakistan, and comprised data from January to August 2024 of diagnosed paediatric BTM patients aged 2-18 years who had been on a regular blood transfusion regimen. The patients had also been prescribed chelation therapy with deferasirox, and had regular visits with haematologists, and their compliance was monitored clinically. When available, serum ferritin levels were used as an indirect indicator of

therapy adherence. Data of patients who had incomplete DXA scans or demographic data, those who were not on regular transfusion or chelation therapy, and those who had comorbidities that could affect bone metabolism was excluded. The DXA scan reports and relevant clinical data was obtained from the hospital management information system. The scans were interpreted by a single radiologist experienced in paediatric DXA to ensure consistency. Patient data was carefully screened to ensure only one scan per patient was included.

BMD was assessed using a Hologic QDR 4500 C DXA scanner (Hologic Inc., Bedford, MA, USA). Measurements were taken at three sites: the lumbar spine (L1-L4), the proximal femur and the distal radius. Results were recorded as grams per centimetre-squared, and Z-scores were calculated by comparing the BMD to the average values of individuals in the same age and gender group. Since no validated Pakistani paediatric database is currently available, the Z scores were, therefore, generated using the manufacturer's default Caucasian reference database derived from the National Health and Nutrition Examination Survey (NHANES) densitometry data.[7] Since fracture history was not available in the study's dataset, The International Society for Clinical Densitometry (ISCD)-recommended terminology of 'low BMD' was used rather than osteoporosis. A BMD-Z score of <-2.0 was classified as indicative of "low bone density".[8] The DXA machine was routinely calibrated and maintained as per hospital protocols, ensuring scanner stability. Although only one DXA scan per patient was available, measurement error was minimised by ensuring a standardised scanning protocol for all participants.[9] All scans were done by trained radiology technicians.

Approval for the study was obtained from the institutional ethics review committee, which waived the requirement for individual consent due to the retrospective design of the study. The DXA scans used were fully anonymised.

Data was analysed using SPSS 25. Descriptive statistics were calculated for age, BMD at the proximal femur, lumbar spine and distal radius along with corresponding Z-scores. Continuous variables were expressed as means ± standard deviation. The gender distribution was summarised using frequencies and percentages. Normality of continuous variables was assessed using the Shapiro-Wilk test, and homogeneity of variances was checked by using Levene's test before performing t-tests and correlational analysis. Independent *t*-tests were used to compare BMD and Z-scores between male and female patients. Pearson correlation analysis was conducted to assess the relationship between age and BMD/Z-scores at the proximal femur, lumbar spine and distal radius. P≤0.05 was considered statistically significant. Regression analyses could not be conducted because complete data on confounding variables, such as pubertal status and biochemical markers, was unavailable.

Results

Of the 281 patients with mean age 6.92±3.74 years, 176(62.6%) were boys and 105(37.4%) were girls. The mean BMF was 0.59±0.14g/cm^2 for proximal femur, 0.53±0.14g/cm^2 for lumbar spine, and 0.35±0.09g/cm^2 for distal radius. Corresponding Z-scores were -0.41±1.81, -0.48±1.79, and -2.99±1.97 (Table 1).

Low bone mass prevalence was 36(18.9%) at proximal femur, 43(16.4%) at lumbar spine, and 76(62.3%) at distal radius (Figure 1). Age negatively correlated with Z-scores at proximal femur (*r*=-0.27, *p*=0.001) and distal radius (*r*=-0.19, *p*=0.03) (Table 2, Figure 2).

The mean proximal femur Z-score for males was -0.19±1.80 compared to -0.75±1.81 for females (95% confidence interval [CI]: 0.04-1.10, p=0.04), and the mean proximal femur BMD was 0.60±0.15g/cm^2 for males versus 0.56±0.13g/cm^2 for females (95% CI: 0.01-0.07, *p*=0.02) (Table 3).

Table-1: Bone mineral density (BMD) and Z-scores by skeletal site (Mean±SD).

Skeletal Site	BMD (g/cm^2)	Z-Score	n (%)
Proximal Femur	0.59±0.14	-0.41±1.81	190(67.6%)
Lumbar Spine	0.53±0.14	-0.48±1.79	262(93.2%)
Distal Radius	0.35±0.09	-2.99±1.97	122(43.4%)

SD: Standard deviation

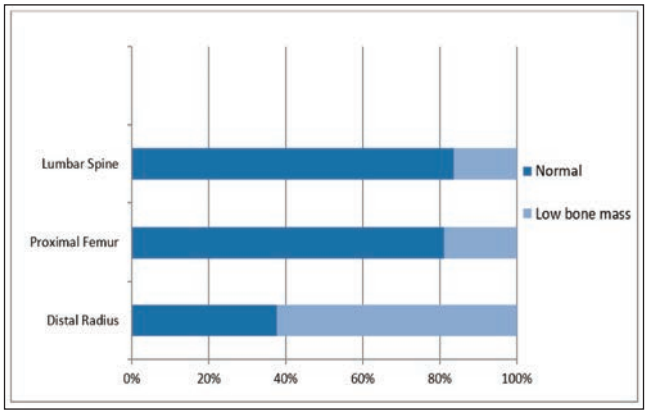

Figure:-1 Prevalence of low bone mass across different anatomical sites.

Table-2: Correlation of age with Z-scores across different anatomic sites.

Age		Proximal Femur Z-Score	Lumbar Spine Z-score	Distal radius Z-score
	Pearson Correlation	-0.27	-0.12	-0.19
	Sig (2-tailed)	0.00	0.06	0.03
	n	190	262	122

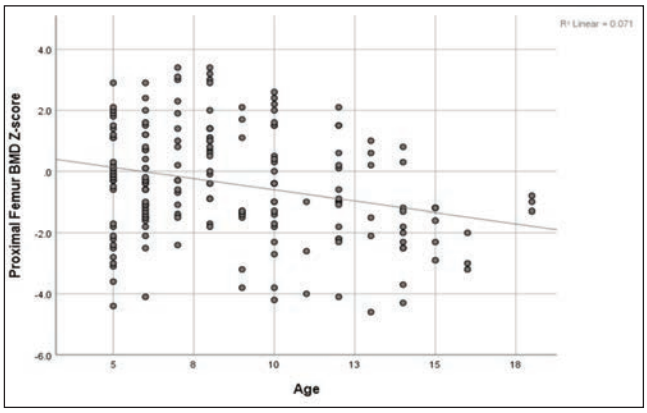

Figure:-2 Correlation of proximal femur bone mineral density (BMD) Z-score with age.

Table-3: Gender-based distribution of boe mineral density (BMD) and Z-scores (Mean±SD).

Gender	Skeletal Site	BMD (g/cm^2)	Z-Score	n (%)
Male	Proximal Femur	0.60±0.15	-0.19±1.80	176(62.6)
	Lumbar Spine	0.53±0.14	-0.37±1.81	
	Distal Radius	0.35±0.09	-2.89±2.14	
Female	Proximal Femur	0.56±0.13	-0.75±1.81	105(37.4)
	Lumbar Spine	0.53±0.13	-0.67±1.75	
	Distal Radius	0.35±0.08	-3.14±1.68	

Independent t-tests: Proximal femur BMD (p=0.02) and Z-score (p=0.04) were significantly higher in males; other sites showed no significant differences; SD: Standard deviation.

Discussion

The current study utilised DXA for evaluating BMD and to find the prevalence of low bone mass among paediatric BTM patients. The findings revealed several significant aspects of bone health in this vulnerable population. Consistent with previous studies,[8,10] the current data indicated that BTM children exhibited lower Z-scores. Notably, bone health varied considerably across different skeletal regions. The distal radius demonstrated the lowest mean Z-score (-2.99), indicating severe bone density reduction, whereas the proximal femur (-0.41) and lumbar spine (-0.48) showed relatively better, though compromised, bone density. The high prevalence of low bone mass at the distal radius (62.3%) compared to the proximal femur (18.9%) and lumbar spine (16.4%) suggested that the distal radius was particularly susceptible to bone density loss in this population.

In the current study, the radius exhibited the most pronounced reduction in bone density compared to other sites. This finding is consistent with results from previous studies,[11,12] which are among the few that have evaluated bone density at the radius. Existing literature predominantly focusses on the spine and femoral neck, often identifying the spine as the most affected site, and the current results also revealed significant bone density reduction in the spine relative to the femoral neck.[13,14]

The marked reduction in bone density observed at the distal radius can be attributed to early bone marrow expansion, and decreased thickness of the bone cortex. This expansion, a consequence of frequent blood transfusions and iron overload, contributes to the decreased bone density observed at this site. Importantly, the current study is the first research in Pakistan to include the distal radius in BTM assessment, highlighting an area often overlooked in similar studies.[10,15,16]

The significant negative correlations observed between age and Z-scores at the proximal femur and distal radius suggested that older paediatric patients tended to have lower bone density in these regions compared to younger patients. A decline in Z-scores with age has been reported by Christoforidis et al.[17] This trend may reflect the cumulative impact of chronic disease and its treatments on bone health over time.

The current study found significant gender-based differences in proximal femur BMD and Z-scores (Table 2). Male patients had higher mean proximal femur BMD and Z-scores compared to females. This observation aligns with earlier findings,[18,19] which noted higher proximal femur Z-scores in males, although the differences were not always statistically significant. Conversely, other studies reported that males were more affected in the lumbar region.[17] However, several studies found no significant differences in BMD between the genders.[11,12,20,21]

This finding is challenging to explain definitively, and warrants further investigation. However, one possible explanation could be hormonal differences and the additional impact of menstrual irregularities observed in females with BTM. These factors may contribute to the observed variations in bone density between the genders. Further research is needed to clarify these potential influences.

The current study has several limitations. The cross-sectional design prevented the researchers from assessing longitudinal changes in bone density. The lack of a control group with no pre-calculated sample size restricted the generalizability of the findings. The small number of distal radius scans (n=122) due to uncooperative children during scanning, along with variable sample sizes across skeletal sites, may have slightly affected site-specific comparisons. Bone age, Tanner staging, and adjustments for height or body size were unavailable, which could have improved interpretation of low BMD. Additionally, data on transfusion duration and frequency was in complete, precluding their inclusion in analysis. As a single-centre study, the findings may not fully represent the wider population, but they offer valuable baseline insight given the limited availability of paediatric DXA in Pakistan.

Conclusion

Significant reduction in bone density was noted in paediatric BTM patients, particularly at the distal radius. Males showed higher proximal femur BMD and Z-scores compared to females. The negative correlation between age and bone density highlighted the importance of early and sustained bone health monitoring. Preventive interventions are essential for improving bone health in these patients.

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Author Contribution:

SJA: Concept, methodology, investigation, writing, review and editing.
SA: Concept, methodology, formal analysis, investigation, writing-original draft preparation, review and editing.
US: Concept, writing-original draft preparation, review and editing.
MA & SKS: Methodology, investigation, writing, review and editing.
AK: Methodology, investigation, writing, review and editing.