Original Article

Dual-Energy X-Ray Absorptiometry (DEXA) Scan and Biochemical Evaluation of Bone Mineral Density in Beta-Thalassemia Major

Huda Diaa Hussain and Affan E. Hasan

ABSTRACT

Objective: To assess whether or not BMD Z-score differs between children and older beta- thalassemia major patients as well as the relationship of serum ferritin, serum calcium, and vitamin D with bone mineral density.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Al-Karama Teaching Hospitals̓ Thalassemia Care Center Baghdad between 1st October 2024 to 31st May 2025.
Methods: This study was comprised 50 beta-thalassemia major patients equal or less than 15 years old, and 50 beta-thalassemia major patients over 15 years' old were enrolled. All patients underwent a medical examination, assessment of bone mineral density of lumbar spine by DEXA scan and a blood test to determine serum ferritin, serum calcium, and vitamin D levels.
Results: There were 24 (48%) patients normal, 18 (36%) patients had osteoporosis, and 8 (16%) patients had osteopenia in those under the age of 15 years while there were 22 (44%) patients with osteopenia followed by 14 (28%) patients with osteoporosis and 14 (28%) patients normal in patients over 15 years bone mineral density (BTM). The mean osteopathy score in those patients were 16.63, 24.43 and 16.97 as normal, osteopenia, and osteoporosis, respectively with significant difference between the two groups. There is no significant association between serum ferritin and BMD Z-score. Vitamin D levels exhibited substantial variations with BMD Z-score.
Conclusion: Osteopathy was prevalent among beta-thalassemia major patients. In this study, the most common causes of osteoporosis and osteopenia were ageing, poor nutrition, calcium and vitamin D inadequacy.

Key Words: Thalassemia**,** Dual energy x-ray absorptiometry, Bone mineral density, Lumber spine, Serum ferritin, Serum calcium ,Vitamin D

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INTRODUCTION

The name thalassemia comes from the Greek words thalassa (ocean) and haima (blood)]. Thalassemia is one of the most widespread hereditary disorders in the world.[1] The syndrome was originally detected in children of Mediterranean ethnicity, and it is most common in people from Mediterranean coastal area, Africa, Middle East, and South-East Asia.[2]
Thalassemias are autosomal recessive disorders characterized by diminished or absente formation of one or two polypeptide chains α or β in the adult human hemoglobin molecule (hemoglobin A, α_2/β_2]. This lead to low hemoglobin levels in red blood cells and anemia. Thalassemia syndromes are [classified depending on the globin chain affected or the abnormal hemoglobin involved; β-thalassemia is caused by β-globin gene abnormalities, whereas, α-thalassemia is caused by α-globin gene alterations.[3,4] Osteoporosis is [a major source cause of morbidity in these people, increasing the risk of fracture due to reduced bone density and decreased bone strength]. Currently, dual-energy X-ray absorptiometry (DEXA) is a common non-invasive and safe approach for evaluating bone density and assessing the severity of osteoporosis and osteopenia.[5]
Bone mineral density (BMD) is a critical component in assessing bone quality. Bone changes in thalassemia patients are largely caused by increased marrow erythropoiesis and considerable iron deposition, which causes bone marrow cavity expansion and reduced trabecular bone volume, resulting in reduced bone tissue and osteoporosis. Chelation and endocrinopathies, such as hypothyroidism,

Department of Physiology Department, College of Medicine, University of Baghdad.

Correspondence: Huda Diaa Hussain, Physiology Department, College of Medicine, University of Baghdad.
Contact No: 07740590171
Email: hudadhiaa11@gmail.com

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hypoparathyroidism, diabetes mellitus, and hypogonadism, all increase the risk of bone disease.[6,7]

According to the World Health Organization, osteoporosis is characterized by decreasing bone mass and microarchitectural degradation of bone tissue, resulting in greater bone fragility and a higher risk of fracture]. In osteoporosis, bone mineral density reduced, and bone microarchitecture is disrupted.[6]

Calcium is one of the most plentiful elements in the human body, and is mostly found in mineralized tissue (bone), which contains more than 99% of total body calcium in the form of calcium-phosphate complexes. It plays a key role in skeleton mineralization and is necessary for appropriate growth, development, and bone strength. Furthermore, it has a role in wide range of biological functions, including muscular contraction and nerve impulse transmission. In healthy individuals, calciotropic hormones such as parathyroid hormone (PTH), 1,25 dihydroxy vitamin D (1,25 OH-D), fibroblast growth factor 23 (FGF 23), and calcitonin keep serum ionized calcium levels within the physiological range of 1.10 to 1.35 mm.[8,9]

Vitamin D is critical for maintenance of bone mass through its act on multiple mechanisms. First, it promotes calcium absorption in the gut. Second, it promotes bone mineralization, by enhancing osteoblast differentiation and increasing phosphates absorption. Third, the action form of vitamin D (1,25 dihydroxy vitamin D) is required for both osteoblast and osteoclast activities. The traditional activities of vitamin D are caused by the active metabolite, calcitriol, that regulate serum calcium and phosphate homeostasis and, in turn, the development and maintenance of bone health.[10]

METHODS

This is a cross sectional study, that took place at the Thalassemia Care Center of Al-Karama Teaching Hospital from 1st October 2024 to 31st May 2025 vide letter No. 671 dated 7th May 2024. Patients aged 9 years and above were simply enrolled in this study while visiting the care facility. Verbal consent was obtained from the included patients or their guardians, and the study was approved by the ethical committee of Baghdad Medical University. A total 100 patients of both genders, split into two groups; 50 beta-thalassemia major patients with aged equal or less than 15 years and 50 beta-thalassemia major patients aged older than 15 years to compare them with the first group. Bone mineral density was measured for all participant at the area of lumbar spine using dual energy X-ray absorptiometry. All patients with thalassemia major, beta thalassemia, on iron lowering drugs (deferoxamine (desferal) or deferasirox (exjade), undergo splenectomy or not, patients aged 9 years and above and don't complain from other hematological disorders were included. All patients with alpha thalassemia, sickle cell anemia, beta thalassemia minor, beta thalassemia intermedia, pregnant women, age below 9 years, undergo bone marrow transplantation, receiving drug can affect BMD, such as antiepileptic drugs, or corticosteroids, fracture deformity in the measurement area, forging material or device in the measurement area and mental illness were excluded.

Sociodemographic and clinical data were collected during the patient's routine visits to the care center. All patients had a complete history taking, physical examination, and measurement of weight and height to determine body mass index (BMI) using Quetelets index.

Bone mineral density (BMD) was calculated as weight in kilograms divided by height in meters squared.[11]

Radiological and biochemical study: To assessed BMD of lumbar spine Hologic QRD DEXA scan system (OsteoSys SMART FAN-BEAM, OsteoSys Co. Ltd in South Korea) was used, which evaluated the results in form of T-score or Z-score. DXA scan was done. The patient's weight and height should measure in every scan. In our study the site for DXA measurements is the spine which was sensitive to early changes in bone density (mostly constituted of trabecular bone which has greater metabolic rate than cortical bone).[12]

T-score represents the standard deviation of BMD according to a person's young age group. While Z-score is the standard deviation of BMD according to the individuals age group, and use in diagnosis of secondary osteoporosis.

Z-score is recommended to be used for adult, in our study majority of the enrolled were children and adolescents; therefore, we adopted the BMD Z-score as the main parameter of bone density.[13,14]

WHO guidelines for diagnosing osteoporosis, a BMD Z-score of ≥1 was regarded normal, a Z-score between -1 and -2.5 was labeled osteopenia, and a Z-score of ≤-2.5 was considered osteoporosis.[14-16]

After taking aseptic precautions, total amount of 5-10ml of blood was obtained by venipuncture to ensure adequate serum is available for all tests and promptly submitted to the laboratory for estimation of serum ferritin, serum calcium, and vitamin D levels.

Statistical analysis was carried out using the SPSS-26. Independent sample t-test was used to compare variables between groups, and ANOVA was employed to evaluate differences between the means of three or more independent groups. Pearson's correlation was utilized to determine correlations between the Z-score of bone density with other factors. Statistical relationship or differences were considered significant if the $P<0.05$.

RESULTS

The mean age of patients was 19.08±9.564 years and the range was between 9-38 years. The mean, standard error of mean and standard deviation values were 44.04,

1.961 and 19.610 of weight factor, 144.52, 1.854 and 18.540 of height factor as well as 19.4219, 0.32961 and 3.29608 of BMI factor (Table 1)

One-way ANOVA test was used to divide 100 beta-thalassemia major patients in to three groups (normal, osteopenia, and osteoporosis). When assessing the statistical difference, there was a highly significant difference (P<0.001) between the osteoporosis and age (Table 2).

The diagnosis of osteoporosis is classified into three categories: normal, osteopenia and osteoporosis. The highest value 24 (48%) patients had normal, followed by 18 (36%) patients had osteoporosis, and 8 (16%) patients had osteopenia of G1 group while, the largest value 22 (44%) patients had osteopenia followed by 14 (28%) patients had normal and osteoporosis respectively in G2 group (Table 3).

Table No.1: The general demographic factors (n=100)

	Weight	Height	BMI
Mean	44.04	144.52	19.4219
Std. Error of Mean	1.961	1.854	.32961
Std. Deviation	19.610	18.540	3.29608

Table No. 2: General categorization of osteopathy (n=100)

Diagnosis of osteoporosis	N	Mean	Std. Deviation	Std. Error	P-value
Normal	38	16.63	9.054	1.469	0.001
Osteopenia	30	24.43	9.655	1.763	
Osteoporosis	32	16.97	8.209	1.451	
Total	100	19.08	9.564	.956	

Table No. 3: The diagnosis of osteoporosis distribution by age group

Age group		No.	%
≤ 15 years (n=50)	Normal	24	48.0
	Osteopenia	8	16.0
	Osteoporosis	18	36.0
15 years (n=50)	Normal	14	28.0
	Osteopenia	22	44.0
	Osteoporosis	14	28.0

The relationship between Z-score and S. ferritin: There was no significant difference (P-value=0.182) between Z-score and S. ferritin, however, there was a slight positive correlation (r= 0.135). This indicated that there is a modest and statistically insignificant positive correlation between Z-score and S. ferritin (Fig. 1).

The relationship between Z-score and vitamin D: Z-score and vitamin D showed a significant difference (P-value =0.019) and there was a strong positive connection(r=0.851). As the value close to +1 indicates that as the Z-score increases, vitamin D levels also tend to increase (Fig. 2).

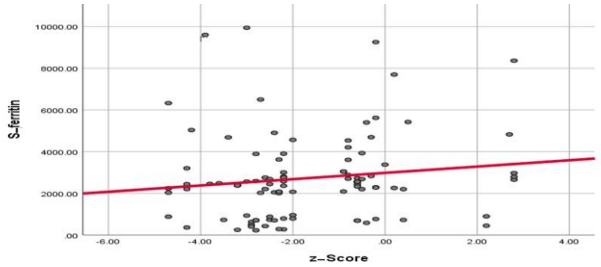

Figure No. 1: The correlation between Z-score and serum ferritin (P-value=0.182 r=0.135

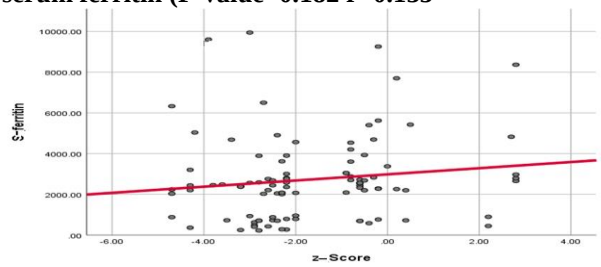

Figure No. 2: The scatter plot between Z-score and vitamin D (p-value=0.019 r=0.851)

DISCUSSION

In thalassemia, osteoporosis and osteopenia were known complication and can occur even in well-treated individuals. Bone pathology in thalassemia involves complex interactions of various factors affecting the bone growth.[17]

During the last decade, osteopenia and osteoporosis have been documented in around 30-50% of well treated thalassemia major patients and is a major source of morbidity in these individuals.[18]

In the present study, measuring BMD at lumbar spine with a DEXA scan, we discovered that 62 (62.00%) of 100 beta thalassemia major patients had low BMD. We found osteoporosis in thirty-two patients of the beta-thalassemia cases, osteopenia in thirty patients of the cases and normal BMD in thirty-eight of the cases. Mahmoodi and Farahanian obtained similar results in 2016[19], the finding reveled that BMD at LS was: 17.1% normal, 48.6% osteoporosis, and 34.3%osteopenia. Abbasi et al[20], observed that 82% of beta-thalassemia major patients had reduced BMD (osteoporosis and osteopenia), whereas 18% had normal BMD, which contradicted our findings. The discrepancies in the prevalence might be explained by diverse population surveyed, as well as the genotype of thalassemia differs internationally. Other possible factors included a small sample size of beta thalassemia major, random sampling of patients under the age of 15 years, with the

majority of participant aged 9-12 years, and increased awareness among most of their families about the importance of preventing or delaying the occurrence of bone changes in early age.

This study showed that there was a strong correlation between age and BMD Z-score, suggesting that low bone mineral density was more prevalent in younger patients. These findings matched to those reported by Ansaf et al.[21] The study discovered a constant decline in BMD as patients aged, with greatest substantial reduction occurring in those over 30 years old. This decrease in BMD with ageing caused by many factors: ineffective erythropoiesis leads to bone marrow expansion which causes bone deformities and cortical bone thinning which weakens the bone structure over the time; frequent blood transfusions cause iron deposition in bone, endocrine glands, and liver leading to disruption in bone metabolism; iron overload in endocrine glands particularly the pituitary gland (causing growth hormone deficiency), gonads (leading to hypogonadism), thyroid and parathyroid glands; vitamin D insufficiency, which is required for calcium absorption and bone strength.

Since patients with TM are dependent on transfusion, elevated ferritin levels promote iron deposition in several organs, most notably the bones. increased iron accumulation impairs bone mineralization and causes osteoporosis. In our study there was no association between BMD Z-score and S. ferritin. El-Nashar et al[22], found no association between S. ferritin and osteoporosis in patients with thalassemia. This finding was in consistent with our results.

This study found a high positive association between BMD Z-score and vitamin D, which was consistent with prior studies. Pirinççioğlu et al[23] found a positive association between vitamin D levels and BMD Z-score for lumbar spine while Wong et al[24], found no association between BMD and vitamin D levels.

CONCLUSION

Osteopathy (osteopenia and osteoporosis) has a high prevalence in patients with beta thalassemia major. The risk of osteopathy increases by increasing age, so regular monitoring of BMD by DEXA scan is essential to prevent the morbidity of osteoporosis in patients with beta thalassemia major. Ageing, poor nutrition, calcium, and vitamin D deficiency are the leading cause of osteopathy in this study sample.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Huda Diaa Hussain, Affan E. Hasan
Drafting or Revising Critically:	Huda Diaa Hussain, Affan E. Hasan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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