

## Bone Mineral Density in Beta-Thalassemia Major and Intermedia

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**Objectives:** This study was conducted to assess bone mineral density (BMD) and bone mineral content (BMC) in patients with  $\beta$ -thalassemia major and intermedia, and to correlate them with biochemical and hematological profile. **Design:** 106 thalassemic patients (49 major and 57 intermedia) were scanned by dual energy x-ray absorptiometry technique for BMD and BMC at lumbar spine and femoral neck. The effects of sex, transfusion/chelation program as well as hemoglobin, calcium, phosphorus, alkaline phosphatase and serum ferritin level were also evaluated on BMD and BMC. **Results:** Patients with thalassemia major and intermedia, younger than 20 yr, showed lower BMD and BMC in the lumbar region ( $p < 0.05$ ). Both parameters correlated significantly with hemoglobin level; other biochemical and hematological parameters did not influence BMD and BMC values. **Conclusion:** Bone marrow density is a good index of bone status in patients with Thalassemia and should be done in these patients annually.

**Keywords:** Bone mineral density, Osteoporosis, Thalassemia.

Thalassemic patients show a variety of bone disorders including bone pain, bone deformity, bone age delay, growth failure, rickets, scoliosis, spinal deformities, nerve compression, pathologic fracture, osteopenia and osteoporosis(1,2). Osteoporosis is characterized by low bone mass and disruption of bone architecture, resulting in reduced bone strength and increased risk of fractures(3). Thalassemia used to be a potentially lethal condition in childhood, but treatment with optimized transfusion programs and chelating therapy has substantially improved patients' life expectancy and quality of life(2,4). Thus, as thalassemic patients age, osteoporosis is emerging as an important cause of morbidity(5).

Bone mineral density (BMD) is a good index of bone status and the most important predictor of fracture risk(5,6). Dual energy X-ray absorptiometry (DEXA) is an excellent non-invasive choice for repeated measurements of any temporal changes of BMD because of 1% precision rate and low radiation exposure(6).

There are more than 20,000 thalassemic patients

in Iran, but there are no data reflecting their bone health status(7). In this study, we determined the Bone Mineral Density (BMD) and Bone Mineral Content (BMC) of patients with thalassemia major and intermedia and correlated these with biochemical and hematological profiles to identify potential risk factors.

### Subjects and Methods

A total of 106 Iranian patients affected by thalassemia (49 thalassemia major, 57 thalassemia intermedia) were enrolled in this study, from February 2002 to October 2004. These subjects were categorized into two groups: children ( $< 20$  y) and adults ( $\geq 20$  y). As the normal data of bone mass for children group was not available, we also selected 85 sex and age matched controls. Adults were stratified based on BMD expressed as T-score, *i.e.*, normal, osteopenic (between  $-1$  to  $-2.5$  SD) and osteoporotic patients (below  $-2.5$  SD)(7,8). An informed consent was obtained from participants, their parents or legal guardians.

Enrolled subjects were scanned for bone mineral

density (BMD) and bone mineral content (BMC) at anteroposterior lumbar spine (L1-L4) and femoral neck, using dual energy X-ray absorptiometry (LUNAR DPXMD#7164), which was daily calibrated according to manufacturer's instructions. The BMD and BMC results were respectively expressed as mean values ( $\text{g}/\text{cm}^2$ )  $\pm$  SD and ( $\text{g}$ )  $\pm$  SD, and as T-score (difference in SD from healthy age matched subjects).

Venous blood samples were obtained for serum calcium, phosphorus, alkaline phosphatase, and hematological parameters; hemoglobin and ferritin. Biochemical and hematological parameters, packed cell transfusion/deferoxamine injection programs and incidence of bone fractures were followed and recorded during the whole of study period when patients had continuous periodical referrals to Cooley's center.

Data were analyzed using SPSS software (version 11.5; SPSS Inc., Chicago, Ill, USA). Students' t-test was applied to compare the means. Association between variables was compared using Pearson's Chi-Square test.  $p < 0.05$  was considered significant.

## Results

The study included 49 patients with thalassemia major (26 males and 23 females; mean age:  $13.2 \pm 5.8$  yr) and 57 cases with thalassemia intermedia (29 males and 28 females; mean age:  $14.2 \pm 6.9$  yr).

Mean lumbar BMD and BMC values of patients (age  $< 20$  yr) with thalassemia major were not significantly different from ones with thalassemia

intermedia. However, thalassemic patients showed significant lower lumbar BMD and BMC values comparing normal controls (Table I). The incidence of pathologic fractures was similar in thalassemia major (5/49, 10.27) and thalassemia intermedia (5/57, 8.7%) ( $p = 0.5$ ).

The mean BMD and BMC values were significantly higher in patients with thalassemia major whose Hb level was greater than 10 g/dL ( $0.72 \text{ g}/\text{cm}^2$  vs.  $0.63 \text{ g}/\text{cm}^2$ ,  $p = 0.013$  and  $21.1 \text{ g}$  vs.  $17.23 \text{ g}$ ,  $p = 0.004$ , respectively). Other biochemical and hematological parameters as well as sex, blood transfusion and chelation programs did not influence BMD and BMC values.

Nine major thalassemic patients and 12 intermedia thalassemic patients were older than 20 years. The number of patients with BMD values more than  $-1$  SD below the mean was more frequent at both regions [15 (71.4%) at lumbar and 21 (100%) at femoral], but the number of cases was not enough to permit statistical analysis.

## Discussion

Data regarding bone density in thalassemia intermedia are limited(9). In our study, the bone mineral values and incidence of pathological fracture did not differ between patients with thalassemia intermedia and thalassemia major even if their treatment programs were different. This may suggest the similarity in bone status between these patients. Previous studies have shown a remarkable decrease in BMD values either at both femoral and lumbar(7,8,10) or only at lumbar(6,11) regions. Our findings are in agreement with latter suggesting that

**TABLE I**– BMD and BMC Values of Patients (age  $< 20$  yr) and Controls.

Group	n	BMD* L1-L4	BMD Femoral neck	BMC* L1-L4	BMC Femoral neck
Thalassemia major	40	$0.60 \pm 0.08$	$1.13 \pm 0.05$	$9.18 \pm 2.10$	$5.05 \pm 0.85$
Thalassemia intermedia	45	$0.62 \pm 0.04$	$1.27 \pm 0.05$	$9.24 \pm 1.90$	$3.42 \pm 0.80$
p value		0.6	0.6	0.4	0.7
Thalassemia	85	$0.61 \pm 0.10$	$1.20 \pm 0.09$	$15.83 \pm 3.50$	$3.05 \pm 0.90$
Normal controls	85	$0.76 \pm 0.05$	$1.04 \pm 0.11$	$23.10 \pm 2.85$	$4.25 \pm 1.10$
p value		0.00	0.3	0.00	0.2

\* BMD = Bone Mineral Density ( $\text{g}/\text{cm}^2$ ), BMC = Bone Mineral Content (g).

### What this Study Adds

- Patients with thalassemia intermedia have bone mass diminution similar to those with Thalassemia major.

the lumbar spine may be more affected in thalassemia.

We similarly observed a significant correlation between low bone mass and low Hb level in major thalassemic patients and not intermedia(1). It might be due to an acceptable level of hemoglobin in patients with thalassemia intermedia.

No correlation was observed between treatment details and bone mass values. One may again argue that the low bone mass in thalassemia is more the reflection of endocrine abnormalities rather than the hematological problems(12).

There was no significant difference between genders regarding bone mineral values contrary to other groups indicating more bone changes in males than in females(13). Shamshirsaz, *et al.* and others have similarly showed no significant difference in prevalence of osteoporosis between boys and girls(7,9).

Since Iranian thalassemic patients have shown a considerable decrease in bone mass according to our study and the others(7); annual evaluation of bone mineral status is recommended.

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## Effect of Feeding Type on the Efficacy of Phototherapy

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**Objectives:** The objective of this study was to assess the efficacy of phototherapy for nonhemolytic hyperbilirubinemia and rebound bilirubin levels in breast-fed newborns as compared with mixed-fed (breast milk and formula) newborns. **Study Design/Setting:** Prospective study of effects of feeding type on response to phototherapy in newborns. **Methods:** The subjects were 53 full-term healthy newborns with nonhemolytic hyperbilirubinemia [defined as total serum bilirubin 12 mg/dL ( $^3$  205.2  $\mu$ mol/L) in the first 48 hours of life or 15 mg/dl ( $^3$  256.5  $\mu$ mol/L), on subsequent days]. Groups were formed according to type of feeding. Group 1 consisted of 28 breast-fed newborns and group 2 consisted of 25 mixed-fed newborns. Phototherapy was terminated when total serum bilirubin concentration fell to 14 mg/dL (<239.4  $\mu$ mol/L). Rebound bilirubin measurements were obtained 24 hours after phototherapy ended. **Results:** The groups were comparable with respect to age at the start of phototherapy. The amount of weight loss (relative to birth weight) recorded at the start of phototherapy was significantly greater in group 1 than in group 2 ( $8.1 \pm 3.9\%$  vs.  $5.4 \pm 2.6\%$ ;  $p = 0.004$ ). The duration of phototherapy was significantly longer in group 1 than in group 2 ( $38.6 \pm 12.6$  h vs.  $26.8 \pm 9.4$  h;  $P < 0.001$ ). The 24-hour rate of decrease in bilirubin concentration in group 2 was significantly higher than that in group 1 [ $5.4 \pm 2.2$  mg/dL/d ( $92.3 \pm 37.6$   $\mu$ mol/L/d) vs.  $4 \pm 1.3$  mg/dL/d ( $68.4 \pm 22.2$   $\mu$ mol/L/d);  $p = 0.01$ ]. The overall rate of decrease in bilirubin concentration in group 1 was significantly lower than that in group 2 [ $0.16 \pm 0.05$  mg/dL/h ( $2.73 \pm 0.85$   $\mu$ mol/L/h) vs.  $0.22 \pm 0.09$  mg/dL/h ( $3.76 \pm 1.53$   $\mu$ mol/L/h);  $p = 0.01$ ]. There was no significant difference between the two groups with respect to rebound bilirubin concentration ( $P = 0.184$ ). **Conclusion:** Phototherapy effectively reduced bilirubin levels in breastfed newborns with hyperbilirubinemia, but these patients show significantly slower response to this treatment than mixed-fed newborns.

**Key words:** Breast-feeding, Hyperbilirubinemia, Newborn, Phototherapy.

Breastfed newborns have a higher incidence of hyperbilirubinemia and exhibit earlier onset and often longer duration of this condition than formula-fed newborns(1-3). Phototherapy is effective and widely used for treating neonatal hyper-bilirubinemia and breast-fed newborns

respond well(4,5). To date, only one objective study has examined the link between breast-feeding and efficacy of phototherapy in healthy full-term newborns with hyperbilirubinemia(6).

The aim of this investigation was to determine