CORRESPONDENCE

Fractures and Low Bone Mineral Density in Patients with Beta Thalassemia Major

Rahul Naithani^{1,4} · Tulika Seth¹ · Nikhil Tandon² · Jagdish Chandra³ · H. Pati¹ · Renu Saxena¹ · V. P. Choudhry¹

Received: 25 January 2017 / Accepted: 19 April 2017 / Published online: 22 April 2017
© Indian Society of Haematology & Transfusion Medicine 2017

To the Editor,

Low bone mineral density (BMD) is emerging as an important cause of morbidity and disability in the adults with transfusion dependent thalassemia [1]. There is lack of data in patients from India [2, 3]. We assessed bone mineral density in patients attending our thalassemia day care center.

Forty patients largely from lower and middle income groups were recruited, of which 26 were male. The median age of the study cohort was 19.5 years (15–38 years). The mean weight was 44 ± 10.3 kg and mean height was 152.5 ± 12 cm. Pain was evaluated using a Quadruple visual analog scale. BMD was measured in all patients by a dual energy X-ray absorptiometry (DXA) densitometer (Hologic, Bedford, MA, USA) at the lumbar spine (L1–L4), left hip and left forearm. Adults were stratified based on BMD expressed as T-score, i.e., normal, osteopenic (between -1 and -2.5 SD) and osteoporotic patients (below -2.5 SD). Z score less than -2 were used to classify low BMD in patients less than 20 years.

Hormonal levels were assessed in 32 patients and 12 (37.5%) patients showed evidence of hypogonadism. Eight

patients (25%) were hypothyroid. Three patients (7.5%) were HbsAg positive. Twenty-three (57.5%) patients had anti HCV antibody positive and 3 patients (7.5%) were HIV positive. HCV RNA was not measured. All patients were receiving iron chelation in the form of deferiprone. Six patients were also receiving desferrioxamine infusion. The iron chelation was irregular in most patients as reflected by the mean serum ferritin levels of 4141 ± 2275 ng/ml. Mean serum calcium, phosphate and alkaline phosphatase levels were 8.7 ± 0.8 mg/dl, 5.4 ± 1.8 mg/dl and 257 ± 183 IU respectively.

Seven (17.5%) patients complained of bone pain. Pain scores of 1, 3, 4 and 5 were reported by 1, 2, 3 and 1 patient respectively. The Pain score did not correlate with any of the evaluated study variables. There were ten fractures in 7 patients (17.5%) at different sites on review of their history. Six patients had history of fractures while one patient developed a fracture during the study period. Fractures in most of the patients were associated with some form of trauma. Moreover, three patients had 2 episodes of fractures. Six patients with fracture had osteoporosis. No study parameter correlated with the fracture risk. Table 1 shows the fracture sites in the study patients.

In children less than 20 years age, fifteen patients (75%) had low bone mineral density (Table 2). The BMD at forearm was significantly lower in patients with hypogonadism ($p = 0.022$), smaller height ($p = 0.028$) and weight ($p = 0.025$). Hypogonadism was negatively associated with low BMD at hip ($p = 0.093$).

Mean age in patients more than 20 years is 22.8 ± 4.5 years. There were 11 females. Five (25%) patients had hypogonadism. Twelve patients (60%) were seropositive for hepatitis C. Seventeen patients (85%) had osteoporosis and 3 patients (15%) had osteopenia. The BMD at lumbar region ($p = 0.039$) and hip region

✉ Rahul Naithani
dr_rahul6@hotmail.com

¹ Department of Hematology, All India Institute of Medical Science, New Delhi, India

² Department of Endocrinology and Metabolism, All India Institute of Medical Science, New Delhi, India

³ Division of Pediatric Hematology-Oncology, Department of Pediatrics, Lady Hardinge Medical College and Kalawati Saran Children's Hospital, New Delhi, India

⁴ Division of Hematology and Bone Marrow Transplantation, Max Super Speciality Hospital, New Delhi, India

Table 1 Fracture sites in the patients on history

Patient	Age ^a /gender	Site	Trauma	Comment	Pain score	BMD
1	19/M	Radius and ulna	Fell while running	3 year back	3	Osteoporosis
2	20/M	Tibia	Fell while running	11 year back	0	Osteoporosis
	20/M	Hand	Put hand under head while sleeping	2 year back	0	
3	16/F	Ankle-right	RTA-hairline fracture	2 year back	3	Osteoporosis
4	32/F	First metatarsal	Twisting of foot	7 year back	2	Osteopenia
	32/F	First metatarsal	Twisting of foot	1 month back	2	
5	17/M	Ankle-right	Fell from first floor balcony	14 years back	0	Osteoporosis
	17/M	Tibia-right	Rickshaw injury	8 years back	0	Osteoporosis
6	16/M	Radius	Playing	10 years back	0	Osteoporosis
7	22/M	Femur shaft	Playing	During study	0	Osteoporosis

^a Age at the time of study**Table 2** Bone mineral density in patients

Patients <20 years (n = 20)			Patients >20 years (n = 20)		
Site	Bone mineral density (g/cm ²)	Z score	Bone mineral density (g/cm ²)	Z score	T score
L1	0.696 ± 0.158		0.855 ± 0.177		
L2	0.730 ± 0.189		0.873 ± 0.138		
L3	0.768 ± 0.173		0.856 ± 0.119		
L4	0.787 ± 0.164		0.877 ± 0.124		
Total lumbar	0.7485 ± 0.165	−2.6 ± 1.5	0.867 ± 0.125	−1.7 ± 1.2	−1.8 ± 1.2
Femoral neck	0.733 ± 0.152		0.694 ± 0.126		
Trochanter	0.6374 ± 0.140		0.587 ± 0.102		
Intertrochanteric area	0.895 ± 0.178		0.844 ± 0.147		
Total hip	0.782 ± 0.157	NA	0.740 ± 0.117	1.7 ± 0.8	1.7 ± 0.8
Upper 1/3 forearm	0.364 ± 0.083		0.356 ± 0.077		
Mid	0.427 ± 0.076		0.435 ± 0.073		
Lower 1/3	0.502 ± 0.094		0.477 ± 0.114		
Total	0.426 ± 0.074	NA	0.426 ± 0.071	NA	−3.6 ± 1.6

NA not available

($p = 0.043$) was lower in hypogonad patients. Hepatitis C infection was associated with lower z scores at hip ($p = 0.029$) and lower T scores at forearm ($p = 0.047$). There were no differences in BMD between men and women, and did not correlate with iron overload.

During the last decade, the presence of osteopenia or osteoporosis in well-treated thalassemia major (TM) patients has been described in different studies with a frequency of approximately 40–50% in the studied populations [1, 2]. Young age in our cohort suggests that bone health starts to suffer early in life. Merchant et al. [3] have documented an incidence of 81% osteoporosis in children from western Indian center.

We did not observe a correlation between low bone mass and low Hb level in our thalassemic patients. We have not measured vitamin D levels and it is known that vitamin D deficiency can result in low bone mineral

density. Hypogonadism is a well-recognized cause of osteoporosis and osteopenia. However, despite hormonal replacement, calcium and vitamin D administration, effective iron chelation, and normalization of hemoglobin levels, patients with TM continue to lose bone mass [4, 5].

The North American Thalassemia Clinical Research Network database registry noted an overall fracture prevalence amongst all thalassemia syndromes of 12.1%. Prevalence increased with age and with use of sex hormone replacement therapy. Presence of endocrinopathies anthropometric parameters, heart disease or hepatitis C was not significant independent predictors of fractures [5].

It would have been ideal if we could perform proper hormonal assessment in all children and everyone was chelated properly. Nonetheless, this study points out poor bone health and fracture risk in Indian patients with transfusion dependent thalassemia.

Acknowledgements We sincerely thank Dr. Ankush Desai for editorial comments on this paper.

Funding Financial support was obtained from Shantha Biotech for DXA scans of these children.

Compliance with Ethical Standards

Conflict of interest Rahul Naithani, Tulika Seth, Nikhil Tandon, Jagdish Chandra, H. Pati, Renu Saxena and V. P. Choudhry declare that they have no conflict of interest.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Voskaridou E, Terpos E (2004) New insights into the pathophysiology and management of osteoporosis in patients with beta thalassaemia. *Br J Haematol* 127(2):127–139
2. Bansal D, Venkateshwaran S, Khandelwal N, Marwaha RK (2011) Quantitative computed tomography is unreliable for measurement of bone mineral density in inadequately chelated adolescent patients with β -thalassemia major: a case-control study. *Pediatr Blood Cancer* 56(3):409–412
3. Merchant R, Udani A, Puri V, D’cruz V, Patkar D, Karkera A (2010) Evaluation of osteopathy in thalassemia by bone mineral densitometry and biochemical indices. *Indian J Pediatr* 77(9):987–991
4. Morabito N, Lasco A, Gaudio A, Crisafulli A, Di Pietro C, Meo A, Frisina N (2002) Bisphosphonates in the treatment of thalassemia-induced osteoporosis. *Osteoporos Int* 13:644–649
5. Vogiatzi MG, Autio KA, Mait JE, Schneider R, Lesser M, Giardina PJ (2005) Low bone mineral density in adolescents with beta thalassemia. *Ann N Y Acad Sci* 1054:462–466