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Osteoporosis in B-Thalassemia Major Patients in Mosul Iraq

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Abstract
Background: Thalassemia is defined as a complete absence of one or more of the four globins in the red blood cells due to the deletion of or nonfunctioning of one or more genes. Osteoporosis is a universal medical problem, affecting both genders.
Objective: To find out any relationship between osteoporosis and thalassemia in our community
Materials and Methods: In the current study, 74 thalassemic major patients (36 male and 38 female) between 1 to 30 years (mean 12y) were included at AL Salaam General Teaching Hospital and in Ibn AL Atheer Pediatric Teaching Hospital, (Thalassemia center) in Iraq/ Mosul city from 1st June 2010 to 1 July 2011. Assessment was done by one rheumatology research physician and one radiologist for the bone densitometry examination.
Results: The frequency of osteoporosis in thalassemic Iraqi patients Daul X- Ray absorptiometry scans (DEXA) has been found to be 67.5%, while osteopenia has been found in 9.4% and normal Bon Mass Density (BMD) in 22.9%.
Conclusions: Osteoporosis in thalassemic Iraqi patients was too high and even more in those patients with poor compliance regarding their attendance to the thalassemia center.

Keywords: osteoporosis, b-thalassemia, major

Introduction
Thalassemia is defined as a complete absence of one or more of the four globins in the red blood cells due to the deletion of or nonfunctioning of one or more genes [1] Osteoporosis is a universal medical problem, affecting both genders [2]. It is generally accepted that its main causes are aging, genetic disorders of osteogenesis, lack of certain nutritional elements or physical activity and endocrine disorders mainly estrogen deficiency [3]. Other causes include neoplastic disorders, gastrointestinal disorders causing malabsorption, liver diseases, inflammatory conditions, and drugs [4].

Materials and Methods
In the current study, 74 thalassemic major patients (36 male and 38 female) aged I to 30 years (mean 12y) were included at AL Salaam General Teaching Hospital and in Ibn AL Atheer Pediatric Teaching Hospital, (Thalassemia center) in Iraq / Mosul city from 1 June 2010 to 1st July 2011. Assessment was done by one rheumatology research physician and one radiologist for the bone densitometry examination.
The study was a clinical cross-sectional for both genders with B-thalassemia major. Investigation conducted included a chest X ray, serum iron, total iron binding capacity (TIBC), serum ferritin level, transferrin saturation, serum calcium, serum phosphorus, serum alkaline phosphatase, blood urea, serum creatinine, hepatitis B and C, fasting blood sugar, Echo for heart, tanner staging and serum testosterone for delay puberty and Daul-X- Ray absorptiometry scans (DEXA) bone scan. For this purpose, hollogic type from GE American origin was used by the researchers. We depended on Z score in measuring the osteoporosis (more than -1.5) osteopenia (-1 to -1.5) and normal (up to -1) sever osteoporosis were more than -2.5.
The using of Z score and not the T score because the Z score compare between the same age while the T score compare with post-menopausal woman.
We divided the patients into three types according to their compliance (it is defined as the extend to which a patients behavior coincides with the doctors prescription) in case of thalassemia this is more specifically defined as the extent to which the patient adheres to R the number of days per week, number of hours per day, and number of grams of desferrioxamine per infusion prescribed by the physician, the first time they visited the thalassemic center and the first date of diagnosis, first date of blood transfusion, first date of chelating therapy received, and the blood transfusion per week or delay in attendance and toke the therapy (blood transfusion, chelating therapy One suggest approach is the used of a compliance index (Cohen, Cappellini *et al* 1999):-
Compliance index = No. of days of treatment/year
No. of days for which treatment is prescribed

Statistical analysis
P-value‒S.P.S.S.—Chi-square have been used for the analysis our data.

Results
The analysis shows that the bony disorder in B thalassemic major patients increased with age (bone pain, carpopedal spasm, osteoporosis) [figure1], and with low serum iron and low T.I.B.C. and with increased transferrin saturation. we have found that we have good,fair and bad compliance with gender [table 2], The compliance of patients with treatment was rated as in 24 good, in 36 fair and in14 bad.

We have found that the bad compliance of patients is good with younger age group while the fair and bad compliance was more with older age [figure 2], also good compliance has been found with those early diagnosed cases and earlier administration of chelating therapy and blood transfusion, also good compliance was more in patients with normal serum iron, high serum ferritin level and normal T.I.B.C [table 3]. Also, we have found that a normal BMD has been found more in patients with good compliance [figure3], we also found that three thalassemic patients two female one male where have had another types of blood disorders like chronic hemolytic anemia(G6PD), sidroblastic anemia and sickle cell anemia which diagnosed in our hospital lab. We found nine patients with thalassemia have had cardiac dysfunction (mitral valve regurgitation whiçh lead to heart failure), five patients with hepatitis type -C, six patients had delayer puberty according to Tanner staging and serum testosterone level, and six patients with diabetes mellitus, and eleven patients with bone problems [table 4]. The prevalence of osteoporosis in thalassemic Iraqi patients Daul -X- Ray The absorptiometry scans (DEXA) has been found to be 67.5%, while osteopenia has been found in 9.4% and normal Bon Mass Density (BMD) in 22.9% [table1].

Discussion

The modern radiologist is unlikely to encounter the classic radiographic features of B thalassaemia other than in teaching files [5]. The main pathological change that leads to radiological skeletal changes in beta thalassemia major is extensive marrow proliferation [6]. The severity of the skeletal responses is related to the type of thalassemia, the extent and duration of the disease, the type of treatment and the volume of blood transfusions given to the patient, as well as the side effects of transfusion-chelating therapy, and the bone involved [7]. The radiographic features can be divided into those affecting the skeleton (axial and appendicular) and those occurring extra-medullary. Axial skeletal changes mainly include skull and facial bones, para nasal sinuses, vertebral bodies and in weight-bearing bones, while appendicular skeleton manifestations are more pronounced in peripheral bones, mainly hands and feet as well as ribs. Patients on repeated blood transfusion and iron-chelating therapy may demonstrate variable range of manifestations than in the scope of untreated patients. We found that osteoporosis in thalassemic patients increased in males more than females which may be due to good compliance in females (44.7%) than in males (19.4%) and bad compliance of males (27.8%) Compared to bad compliance of females (10.5%). We found that severe osteoporosis in males is more than in female which was associated with bad complains, We found that osteoporosis was associated with the complication in thalassemic patients (abnormal cardiac function, hepatitis, diabetes mellitus and bone problem (50.1%). This is due to the effects of these diseases on the function of the bone marrow in addition to the effect of disease itself. We found that serum calcium was low in 13.5% and serum alkaline phosphates high in (9.5%) of patients and these patients-have Osteoporosis which is normally because the osteomalasia and osteoporosis. Normally one affects the other. Renal functions were normal in these patients because the main cause of osteoporosis was hereditary due to deletion of globulin (thalassemia major) not because secondary reasons The other investigations explained the normal occurrence in the sequence of the disease like the value of T.I.B.C (low (60.8%) or normal(39.2%). and the serum transferrin saturation was normal (21.7%) and high (78.3%). We found that osteoporosis was moving in one line with bad compliance, the normal BMD was moving with good compliance. Also, the age of the patients was associated with compliance inversely because of the chronicity of the disease with age and the effect of the drug itself in the bone marrow and the effect of the iron itself on the body with age in these patients. During the last decade, the presence of osteopenia and osteoporosis in well-treated thalassemic was described in different studies with high prevalence up to 50% [8].

The pathogenesis of osteoporosis in thalassemia major is complicated and differed from the pathogenesis of bone deformities characteristically found in non-transfused patients who develop bone distortion mainly due to ineffective haemopoiesis and progressive marrow expansion [8]. Several factors are implicated in reduction of bone mass in thalassemia major. Delayed sexual maturation, growth hormone (GH) and insulin growth factor-(IGF)-1 deficiency, parathyroid gland dysfunction, diabetes, hypothyroidism, ineffective haemopoiesis with progressive marrow expansion, direct iron toxicity on osteoblasts, as well as liver disease have been indicated as possible etiological factors for thalassemia- induced osteoporosis [9, 10]. Furthermore, iron chelating has correlated with growth failure and bone abnormalities, and high desferrioxamine dosage has been associated with cartilage alterations [11].

Conclusion

Osteoporosis in thalassemic Iraqi patients was too high and even more in those patients with bad compliance regarding their attendance to the thalassemia center.

Recommendations

We need to inform the thalassemic patients about the risk of osteoporosis and the need for their awareness regarding such complication and the importance of their compliance with therapy.

Table 1: D.X.A. study in thalassemic patients with gender

Gender	normal	osteopenia	osteoporosis	sever osteoporosis	total
Male	8	2	8	18	36
Female	9	5	12	12	38
Total	17(23.0%)	7(9.5%)	20(27.0%)	30(40.5%)	74

Table 2: Compliance according to gender

Gender	good	Fair	Bad	total
Male	7(19.4%)	19(52.8%)	10(27.8%)	36
Female	17(44.7%)	17(44.7%)	4(10.5%)	38
Total	24	26	14	74

Table 3: Frequencies of investigations

Type of inestigation normal rang normal high low total
Serum calcium (9.6-10.6) mg/dl 64(86.5%) 0 10(13.5) 74
Serum alk. Phos. (149-222) u/L 67(90.5%) 7(9.5) 0 74
Serum phosphates (3.1-4.7) mg/dl 67(90.5%) 0 7(9.5) 74
Blood urea (6-21) mg/dl 74(100%) 0 0 74
Serum creatinine (0.8-1.3) mg/dl 74(100%) 0 0 74
Total I.B.C. (45-72) micro mol/L 29(39.2%) 0 45(60.8%) 74
Serum ferritin level male (20-250) ng/ml
famal (10-120) ng/ml 0 74(100%) 0 74
Serum transferring (30-50) % 16(21.3%) 58(78.7) 0 74

Table 4: Frequencies of complication associated with thalassemia

Type of complain number (%) male female
Cardiac function 9(12.2%) 6 3
(heart failure, mitral value regurgitation)
Hepatitis –C- 5(6.8%) 2 3
Delay puberty 6(8.1%) 4 2
(according to tanner staging and serum testosterone level)
Diabetes 6(8.1%) 3 3
(F.B.S. were from 160-230mg/dl)
Bon problem; -
Bon pain 7(9.5%) 4 3
Carpopedal spasm 4(5.4%) 3 1

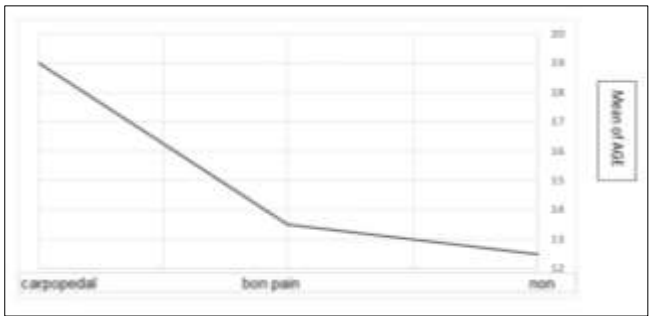

Fig 1: Relation between bone problems and age of patients (year)

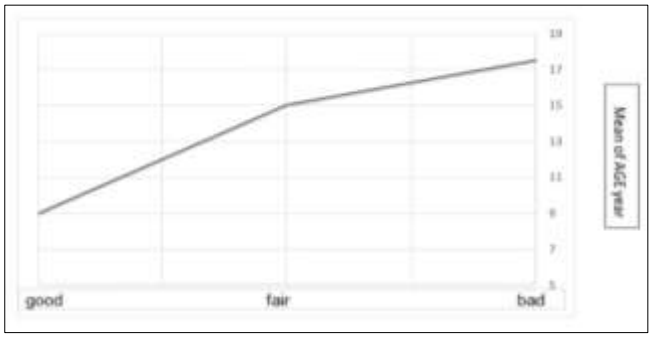

Fig 2: Relation between compliance and age of pateints (year)

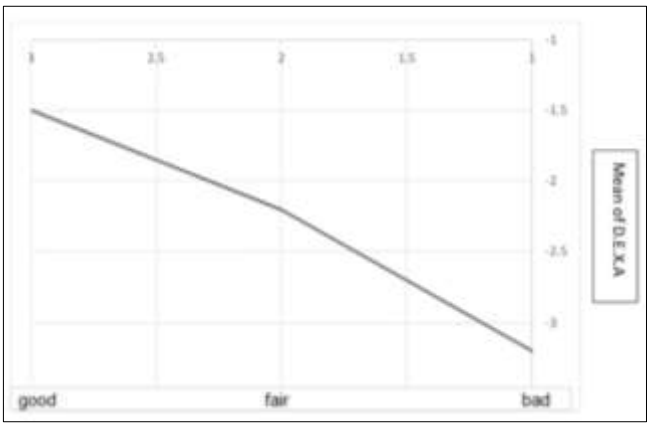

Fig 3: Relation between compliance and D.E.X.A. of patients

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