MARCADORES ÓSSEOS METABÓLICOS BIOQUÍMICOS E HORMÔNIO DA PARATIREOIDE EM PACIENTES COM β -TALASSEMIA MAIOR NA PROVÍNCIA DE MISAN / IRAQUE

PARATHYROID HORMONE AND BIOCHEMICAL METABOLIC BONE MARKERS IN PATIENTS WITH β -THALASSEMIA MAJOR IN MISAN PROVINCE / IRAQ

هرمون جار الدرقية وعلامات العظام الايضية الكيموحيوية عند مرضى بيتا فقر دم حوض البحر الأبيض المتوسط في محافظة ميسان/ العراق

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RESUMO

A beta-talassemia é um grupo heterogêneo de doenças hereditárias do sangue caracterizadas por defeitos na síntese das cadeias β da hemoglobina, resultando em fenótipos variáveis que variam de anemia grave a indivíduos clinicamente assintomáticos. Este estudo tem como objetivo avaliar os níveis séricos de PTH, vitamina D, cálcio, fósforo, fosfatase alcalina e magnésio nos principais pacientes com β -talassemia. Um total de 50 (30 homens e 20 mulheres) pacientes com β -talassemia maior com idades entre 11 e 16 anos e um número igual de adolescentes saudáveis pareados por sexo como grupo controle foram incluídos neste estudo. Um total de 52% dos pacientes residia em área urbana e não houve diferença significativa entre os pacientes e o grupo controle em relação à residência. Pacientes do sexo masculino apresentaram baixos níveis estatisticamente significativos ($P < 0,05$) de PTH sérico, vitamina D e níveis de cálcio, mas os níveis séricos médios de fósforo e fosfatase alcalina foram significativamente mais altos ($P < 0,05$) quando comparados ao grupo controle masculino. No entanto, as pacientes do sexo feminino apresentaram nível médio de PTH sérico baixo, mas sem significância estatística ($P > 0,05$), enquanto os níveis de vitamina D e cálcio foram altamente significativos ($P < 0,05$). Os níveis de fósforo e ALP aumentaram significativamente ($P < 0,05$) quando comparados aos controles femininos. Em relação ao grupo principal da β -talassemia, o presente estudo mostrou que pacientes do sexo masculino apresentaram níveis elevados não significativos ($P > 0,05$) de PTH, cálcio, fósforo e ALP. Por outro lado, o nível de vitamina D não foi significativamente ($P > 0,05$) baixo em pacientes do sexo masculino em comparação com pacientes do sexo feminino. O nível sérico médio de PTH teve uma correlação negativa com fósforo, mas teve uma associação positiva com vitamina D, cálcio, ALP e magnésio. Em conclusão, esse estudo demonstrou que os principais pacientes com β -talassemia têm um perfil ósseo metabólico bioquímico marcadamente perturbado. Também é recomendado o monitoramento regular do PTH e do perfil mineral bioquímico.

Palavras-chave: β -talassemia maior, PTH, marcadores ósseos metabólicos.

ABSTRACT

Beta-thalassemia is a heterogeneous group of hereditary blood disorders characterized by defects in the synthesis of the β - chains of hemoglobin, resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individuals. This study aims to assess the serum PTH, vitamin D, calcium, phosphorus, alkaline phosphatase, and magnesium levels in β -thalassemia major patients. A total of 50 (30 male and 20 female) patients with β -thalassemia major with ages range 11- 16 years and an equal number of sex-matched healthy adolescents as a control group were included in this study. A total of 52% of patients were lived in an urban area, and there was no significant difference between patients and the control group regarding residency. Male patients showed low statistically significant ($P < 0.05$) mean serum PTH, vitamin D, and calcium levels, but mean serum phosphorus and alkaline phosphatase levels were significantly higher ($P < 0.05$) as compared to the male control group. However, female patients had low, but without statistical significant ($P > 0.05$) mean serum PTH level, whereas vitamin D and calcium levels were highly significant ($P < 0.05$) reduced. The phosphorus and ALP levels were highly significantly ($P < 0.05$) increased as compared to female controls. Regarding β -thalassemia major group, the current study showed male patients had non-significant ($P > 0.05$) higher levels of PTH, calcium, phosphorus, and ALP. In contrast, vitamin D level was non-significantly ($P > 0.05$) low in male patients as compared

to female patients. Mean serum level of PTH had a negative correlation with phosphorus, but it had a positive association with vitamin D, calcium, ALP, and magnesium. In conclusion, this study demonstrated that β -thalassemia major patients have a markedly deranged biochemical metabolic bone profile. Regular monitoring of PTH and biochemical mineral profile is also recommended.

Keywords: β -thalassemia major, PTH, Metabolic Bone Markers.

المخلص

بيتا فقر دم البحر الابيض المتوسط (الثلاسيميا) هي مجموعة غير متجانسة من اضطرابات الدم الوراثية تتميز بخلل في تخليق سلاسل بيتا في الهيموغلوبين، مما يؤدي الى انماط ظاهرية متغيرة تتراوح بين فقر الدم الشديد الى بدون اعراض مرضية عند الافراد. تهدف الدراسة الى تقييم مستويات هرمون جار الدرقية، فيتامين D، الكالسيوم، الفسفور، أنزيم الفوسفاتيز القاعدي والمغنسيوم في مصل الدم لمرضى بيتا ثلاسيميا الكبرى. شملت الدراسة 50 مريضاً (30 ذكر و 20 أنثى) مصابين بمرض بيتا ثلاسيميا الكبرى والذين تراوحت اعمارهم من 11 – 16 سنة، وعدد متساو من المراهقين الاصحاء المطابقين للجنس كمجموعة ضابطة في هذه الدراسة. يسكن 52% من المرضى في المناطق الحضرية ولم يلاحظ اختلافات معنوية بين المرضى ومجموعة السيطرة فيما يتعلق بمنطقة الإقامة. المرضى الذكور لوحظ لديهم انخفاض معنوي ($p < 0.05$) في مستويات هرمون جار الدرقية، فيتامين D والكالسيوم، ولكن مستويات الفسفور وأنزيم الفوسفاتيز القاعدي مرتفعة معنويًا ($p < 0.05$) بالمقارنة مع المجموعة الضابطة من الذكور. ومع ذلك، هرمون جار الدرقية انخفض لدى المرضى من الإناث لكن لم يصل الى مستوى المعنوية ($p > 0.05$)، بينما مستوى فيتامين D والكالسيوم انخفض معنويًا ($P < 0.05$)، مستويات الفسفور وأنزيم الفوسفاتيز ارتفعت معنويًا ($p < 0.05$) بالمقارنة مع المجموعة الضابطة من الإناث. فيما يتعلق بمجموعة مرضى فقر دم البحر الابيض المتوسط (الثلاسيميا) الكبرى، بينت الدراسة الحالية ان المرضى من الذكور لديهم مستويات مرتفعة غير معنوية ($p > 0.05$) من هرمون جار الدرقية، الكالسيوم، الفسفور وأنزيم الفوسفاتيز القاعدي ومستوى منخفض غير معنوي ($p > 0.05$) من فيتامين D عند مقارنتهم مع المرضى من الإناث. أظهر هرمون جار الدرقية علاقة ارتباط سلبية مع الفسفور وعلاقة ارتباط موجبة مع فيتامين D، الكالسيوم، أنزيم الفوسفاتيز القاعدي والمغنسيوم. في الختام، أثبتت هذه الدراسة ان مرضى فقر دم البحر الابيض المتوسط (الثلاسيميا) الكبرى لديهم اضطراب بشكل ملحوظ في صورة العظام الايضية والكيموحيوية. توصي الدراسة الحالية بالمراقبة المنتظمة لمستوى هرمون جار الدرقية ومعايير العظام الكيوكيوية.

الكلمات المفتاحية: بيتا ثلاسيميا الكبرى، هرمون جار الدرقية، معايير العظم الايضية.

1. INTRODUCTION:

Beta-thalassemia is a heterogeneous group of hereditary blood disorders characterized by defects in the synthesis of the β - chains of hemoglobin, resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individuals. It has been estimated that about 1.5% of the global population (80 to 90 million people) are carriers of β - thalassemia, with about 60,000 symptomatic individuals born annually, the vast majority in the developing world (Galanello and Origa, 2010). In Iraq, the prevalence of thalassemia syndrome is 37.1/100.000 inhabitants, and β -thalassemia major represents 73.9% of all types of thalassemia (Kadhim *et al.*, 2017). β -thalassemia major is more severe transfusion-dependent anemia result from homozygosity or compound heterozygosity for a mutant β - globin gene and, occasionally, from heterozygosity for dominant mutations (Cao and Galanello, 2010; Olivieri, 1999).

The combination of transfusion and chelation therapy has dramatically extended the life expectancy of β -thalassemia major patients but is complicated by subsequent iron overload resulting in a high incidence of endocrine complication in children, adolescents, and young adults (Shamshirsaz *et al.*, 2003). Endocrine and metabolic bone disorders that are caused by repeated blood transfusions are of higher importance in β -thalassemia major patients. They are the second leading cause of mortality, after heart disorders, in these individuals (Chahkandi *et al.*, 2017).

Disturbance of calcium and phosphorus hemostasis due to parathyroid dysfunction, as well as metabolic bone diseases with various skeletal

complications including osteopenia, osteoporosis, scoliosis, rickets, spinal deformities, and spontaneous fractures, are a significant cause of morbidity and regularly reported in transfusion-dependent β -thalassemia major patients (Saboor *et al.*, 2017; Salama *et al.*, 2006). These complications are mainly due to repeated blood transfusion results in citrate toxicity and iron overload with deposition in parathyroid cells and tissue fibrosis, and chronic anemia (Galanello and Origa, 2010; Hamidi, 2016).

Bone turnover is assessed with several specific and sensitive serological markers, and serum PTH, calcium, phosphorous, alkaline phosphatase, vitamin D, and magnesium are characteristically altered with bone impairment in patients with thalassemia (Saboor *et al.*, 2017; Salama *et al.*, 2006; Khaleel, 2018).

This study aimed to assess the serum levels of PTH, vitamin D, calcium, phosphorus, alkaline phosphatase, and magnesium in β -thalassemia major patients.

2. MATERIALS AND METHODS:

Over six months, from 1st of December 2018 to the 31st of May 2019, a total 50 (30 male and 20 female) patients with β - thalassemia major with ages range between 11 to 16 years attended Misan Thalassemia Center along with 50 age and sex-matched healthy adolescents as control group were included in this case control study. Informed consent was obtained from parents or guardians of patients, and the Ethical Committee approved this study protocol at the College of Medicine, Misan University, Iraq. The diagnosis of β -thalassemia major was based on clinical history and examination in addition to the usual hematological data

(complete blood count, and Hb electrophoresis). The cases and control individuals were investigated for serum PTH, vitamin D, calcium, phosphorus, alkaline phosphatase, and magnesium levels. The assay principle for PTH based on competitive radioimmunoassay (RIA) (Cavalier *et al.*, 2015), combines an enzyme immunoassay sandwich method with a final fluorescent detection Enzyme Linked Fluorescent Assay (ELFA) was used for serum vitamin D measurement (Holick, 2007), serum calcium was determined by colorimetric method using methylmol blue indicator (Finley and Tietz, 1996), serum phosphorus level was determined by ammonium molybdate end point method (Drewes, 1972), ALP was also measured by colorimetric method using p-nitrophenylphosphate (Belfield and Goldberg, 1971), while spectrophotometric determination employing Calmagite was used to measured serum magnesium (Ingman and Ringbom, 1966).

Statistical analyses were reports as mean estimation $\pm$ standard error, t test, and correlation using Statistical Package for Social Science (SPSS) version 23 for windows. Comparison of categorical data was carried by Chi-square test. *P* value of <0.05 was considered as statistically significant.

3. RESULTS AND DISCUSSION:

A total 50 patients consisted of 30 (60%) male and 20 (40%) female β -thalassemia major patients and 50 healthy children matched for age and sex were studied as control group were enrolled in this study, see Table 1. In present study (52%, 26 patients) of thalassemia major patients lived in urban areas, while (38%, 19 patients) of control individuals were lived in rural area, and there was no significant difference between control and patients group regarding residency (*P* value 0.31), as shown in Table 2.

Regarding biochemical bone markers, data analysis showed that male patients have a highly significant ($p<0.05$) low serum PTH (35.01 ± 5.19 pg/ml), vitamin D (12.22 ± 0.67 ng/ml), and calcium (7.90 ± 0.19 mg/dL) levels in comparison to male control subjects (74.76 ± 7.30 pg/ml, 54.30 ± 4.69 ng/ml, and 9.84 ± 0.23 mg/dL respectively), but serum phosphorous (4.97 ± 0.32 mg/dL) and ALP (212.20 ± 19.40 U/L) were highly statistically significant ($p<0.05$) increased in male patients compared with male control (1.96 ± 0.14 mg/dL and 83.62 ± 7.11 U/L respectively), also serum magnesium (2.18 ± 0.38 mg/dL) was increased but without statistical significant (*P* value=0.386) in male patients compared with control (1.83 ± 0.09 mg/dL), see Table 3.

In comparison female patients with female control results revealed that serum PTH level (31.39 ± 5.69 pg/ml) decreased without statistical significant (*P* value=0.549), but vitamin D (12.70 ± 0.84 ng/ml) and calcium (7.55 ± 0.23 mg/dL) levels were highly significant ($p<0.05$) decreased in patients compared with control females (40.38 ± 4.66 ng/ml and 9.59 ± 0.24 mg/dL). Phosphorus (4.61 ± 0.52 mg/dL),

ALP (210.30 ± 33.54 U/L), and magnesium (2.04 ± 0.36 mg/dL) levels were measured higher. Still, only phosphorus level and ALP were highly significant ($P<0.05$) in female patients in comparison to the female control group (2.75 ± 0.21 mg/dL, 91.36 ± 4.55 U/L, and 1.76 ± 0.12 mg/dL respectively), as shown in Table 3.

Table 4, demonstrated that the serum levels of bone metabolic biochemical markers in male β -thalassemia major patients group including PTH (35.01 ± 5.19 pg/ml), calcium (7.90 ± 0.19 mg/dL), phosphorus (4.97 ± 0.32 mg/dL), ALP (212.20 ± 19.40 U/L), and magnesium (2.18 ± 0.38 mg/dL) were measured higher than in female patients (31.39 ± 5.69 pg/ml, 7.55 ± 0.23 mg/dL, 4.61 ± 0.52 mg/dL, 210.30 ± 33.54 U/L, and 2.04 ± 0.36 mg/dL respectively), but without significant difference, while vitamin D levels in male (12.22 ± 0.67 ng/ml) was lower without statistical significant difference than that in female patients (12.70 ± 0.84 ng/ml).

The results showed that the level of PTH had a negative correlation with phosphorus (-0.137), while it had a positive correlation with vitamin D (0.205), calcium (0.111), ALP (0.097) and magnesium (0.091). Vitamin D had an inverse correlation with phosphorus (-0.147) but is positively correlated with ALP (0.060), and magnesium (0.238), and significantly positive ($P<0.05$) with calcium (0.287). While calcium in our study results reported a negative correlation with ALP (-0.091) and a highly significant negative correlation with phosphorus (-0.583), but it had a highly significant positive ($P<0.01$) with magnesium (0.430). The level of phosphorus had an inverse correlation with magnesium level (-0.028), but it had a positive correlation with ALP (0.019) in our patient's results. Lastly, the level of serum ALP in our study showed a positive correlation with the level of serum magnesium (0.073) (Table 5).

In this study, 52% of β -thalassemia major patients lived in an urban area, and there was no significant difference between patients and the control group regarding residency. In agreement with our findings, Al-Ali and Faraj (2016) observed the incidence of β -thalassemia was significantly unchanged between the urban and rural populations, and so a study designed by Qurat-ul-Ain *et al.*, (2011) found the incidence of β -thalassemia was significantly higher in urban population than rural. In contrast, Tunç *et al.*, (2002) noticed the low frequency of β -thalassemia in the city center than in neighboring areas. The findings might be due to the same rate of consanguineous marriages among our population wherever they live, lack of effective prevention programs and poor legislation in our governorate.

Analysis of study results demonstrated that male patients in β -thalassemia major group have low statistically significant mean serum PTH, vitamin D, and calcium levels, but mean serum phosphorus and alkaline phosphatase levels significantly higher as compared to the male control group. However, in comparison to female β -thalassemia major patients with female control individuals, we observed low but without statistically significant ($P<0.05$) serum PTH

level. In contrast, vitamin D and calcium levels were highly significantly reduced, but phosphorus and ALP levels were highly significantly increased. Regarding β -thalassemia major group, the current study show male patients have non-significant higher levels of PTH, calcium, phosphorus, and ALP. In contrast, vitamin D level was non-significantly low in male patients as compared to female patients.

In agreement with our results, De Sanctis *et al.*, (1992) and Aleem *et al.* (2000) observed low PTH among β -thalassemia major patients. Low, PTH level among our patients is mainly due to the involvement of the parathyroid gland by iron overload, as well as its oxidative damage. Gutteridge and Halliwell (1998) and Goyal *et al.*, (2010) mentioned that parathyroid gland involvement by iron overload occurs particularly after ten years of age in β -thalassemia major patients, and a number of possible mechanisms have been described to be responsible for the damage of parathyroid glands through iron overload, which includes free radical formation and lipid peroxidation resulting in mitochondrial, lysosomal and sarcolemmal membrane damage. Also, Aleem *et al.*, (2000) found that parathyroid gland dysfunction in β -thalassemia major with iron overload is due to chelation therapy.

Parathyroid hormone is essential in calcium and phosphorus hemostasis and also plays a role in the conversion of vitamin D to its active form (1, 25 dihydroxycholecalciferol) in the kidney. A decrease in extracellular calcium concentrations or an increase in phosphorus concentrations leads to a PTH release from the parathyroid gland, which in turn increases renal reabsorption of calcium, renal activation of vitamin D, urinary phosphorus excretion, and bone resorption. In turn, vitamin D increases intestinal absorption and renal reabsorption of calcium and phosphorus (Penido and Alon, 2012; Kliegman, 2020). Documented abnormalities in PTH and biochemical metabolic bone markers values have been observed among β -thalassemia major (Hamidi, 2016; Dejkhamron *et al.*, 2018).

In agreement with our findings, Shetty and Shenoy, (2014), in their case-control study, found a significant decrease in serum PTH, and calcium, but significant increase in serum phosphorus and ALP in β -thalassemia major patients when compared to control. However, Goyal *et al.*, (2010) noticed serum PTH and serum calcium significantly reduced in β -thalassemia major patients that are similar to our results. Still, their serum ALP and phosphorus were not significantly altered when compared to the respective mean values for the control group. Also, Anju and Jain (2017) found serum calcium level was statistically significantly low, whereas serum phosphorus had no significant difference as compared β -thalassemia major patients to the control group. In contrast to our findings, Agrawal *et al.* (2016) observed that mean serum PTH was significantly higher and so calcium level but without significant difference, while phosphorus level was non-significantly lower in thalassemia patients compared to control. However, vitamin D value in their study is in agreement with our results was significantly lower in

patients compared to the control group. Still, there was no significant correlation found between vitamin D level and sex. In contrast, in our study, we found a significantly reduced level of vitamin D in male and female patients group compared to male and female control groups. However, in another study by Aggarwal *et al.*, (2018) found significant low vitamin D levels, despite serum PTH levels were not significantly different between cases and controls, while the serum level of calcium was found in the normal range in both groups, although the phosphorus and ALP levels were found to be significantly high in cases in comparison to controls.

The lower serum levels of vitamin D among β -thalassemia major patients can be due to decreased serum PTH level in our patients as a result of parathyroid gland involvement by iron overload. (Penido and Alon, 2012) documented PTH is one of the strongest stimulators of 1, 25 (OH)₂ D₃ production by increasing proximal tubular expression of 25(OH) D 1 α -hydroxylase, resulting in increased production of 1, 25(OH)₂ D₃. Moreover, Soliman *et al.*, (2013) mentioned that both defective synthesis of 25 (OH) vitamin D and/ or hypoparathyroidism had been described in β -thalassemia major patients.

Our results were consistent with that of (Khaleel *et al.*, 2018; Ridha *et al.*, 2018) when they observed serum magnesium level was significantly higher in patients than normal control. At variance with our findings, Arcasoy and Cavdar (1975) and Fahmy *et al.*, (2019) observed a normal serum magnesium level in β -thalassemia patients, while Al-Samarrai *et al.*, (2008) and Nafady *et al.*, (2018) in their study showed that serum magnesium level was significantly lower in patients than the healthy control group. Hyman *et al.*, (1980) had been speculated that hypomagnesemia could be due to chelation by citrate in chronically transfused patients, or could just be a consequence of the cellular iron overload, but, Genc *et al.*, (2016) observed that level of magnesium had no significant difference between controls and patients with β -thalassemia major regardless type of chelating therapies. The finding of serum magnesium in our thalassemia patients may result from diet, chelation therapies, bone involvement (as 50% of total body magnesium resides in the bone), an increased rate of hemolysis among our patients (as magnesium is one of the major intracellular ions). In our study PTH had no significant correlation with calcium and phosphorus; that's similar to El-Deen *et al.*, (2014) observation.

In agreement with our results (Ridha *et al.*, 2018) noticed vitamin D had a significant correlation with calcium and ALP, while no significant association between PTH with the vitamin D, calcium, phosphorus, ALP, and magnesium.

4. CONCLUSIONS:

There was no significant difference between control and β -thalassemia major patients groups regarding residency. β -thalassemia major patients

have markedly deranged biochemical metabolic bone markers. Male β -thalassemia major patients have highly significant decreased levels of serum PTH, vitamin D, and calcium. While serum phosphorous and ALP was a highly statistically significant increase in male patients compared with control. Female patients have highly significant decreased serum vitamin D and calcium levels, but phosphorus and ALP levels were highly significant in comparison to control. Regular monitoring of PTH and biochemical mineral profiles, as well as nutritional support and calcium/vitamin D supplementation, are highly recommended for these patients.

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Table 1. Number and percentage of control and β -thalassemia major patients according to gender

Gender	Control No. (%)	Patient No. (%)	Total No. (%)
Male	30 (60)	30 (60)	60 (60)
Female	20 (40)	20 (40)	40 (40)
Total	50 (100)	50 (100)	100 (100)

Table 2. Comparison between control and β -thalassemia major patients regarding residency

Residency	Control No. (%)	Patients No. (%)	Total	χ^2	P. value
Urban	31(62)	26 (52)	57	1.02	0.31
Rural	19 (38)	24(48)	43		
Total	50 (100)	50 (100)	100		

Table 3. Comparison of biochemical bone markers in control and β -thalassemia patients regarding gender

Variables	Gender	Control Group	Patients Group	P Value	T test
PTH (pg/ml)	Male	74.76 $\pm$ 7.30	35.01 $\pm$ 5.19	0.000	4.434
	Female	36.64 $\pm$ 6.57	31.39 $\pm$ 5.69	0.549	0.604
Vitamin D (ng/ml)	Male	54.30 $\pm$ 4.69	12.22 $\pm$ 0.67	0.000	8.867
	Female	40.38 $\pm$ 4.66	12.70 $\pm$ 0.84	0.000	5.842
Calcium (mg/dL)	Male	9.84 $\pm$ 0.23	7.90 $\pm$ 0.19	0.000	6.408
	Female	9.59 $\pm$ 0.24	7.55 $\pm$ 0.23	0.000	6.085
Phosphorus (mg/dL)	Male	1.96 $\pm$ 0.14	4.97 $\pm$ 0.32	0.000	8.730
	Female	2.75 $\pm$ 0.21	4.61 $\pm$ 0.52	0.002	3.300
ALP (U/L)	Male	83.62 $\pm$ 7.11	212.20 $\pm$ 19.40	0.000	6.223
	Female	91.36 $\pm$ 4.55	210.30 $\pm$ 33.54	0.001	3.515
Magnesium (mg/dL)	Male	1.83 $\pm$ 0.09	2.18 $\pm$ 0.38	0.386	0.874
	Female	1.76 $\pm$ 0.12	2.04 $\pm$ 0.36	0.486	0.704

Value represented mean $\pm$ SE.

Table 4. Biochemical bone markers according to gender and age groups in β -thalassemia patients

Variables	Male (30 patients)	Female (20 patients)	P Value	T test
PTH (pg/ml)	35.01 $\pm$ 5.19	31.39 $\pm$ 5.69	0.51	0.460
Vitamin D (ng/ml)	12.22 $\pm$ 0.67	12.70 $\pm$ 0.84	0.94	0.442
Calcium (mg/dL)	7.90 $\pm$ 0.19	7.55 $\pm$ 0.23	0.89	1.187
Phosphorus (mg/dL)	4.97 $\pm$ 0.32	4.61 $\pm$ 0.52	0.24	0.644
ALP (U/L)	212.20 $\pm$ 19.40	210.30 $\pm$ 33.54	0.34	0.052
Magnesium (mg/dL)	2.18 $\pm$ 0.38	2.04 $\pm$ 0.36	0.33	0.252

Value represented mean $\pm$ SE.

Table 5. Correlation between serum PTH and biochemical bone markers in β -thalassemia major patients

Variables	PTH	Vitamin D	Calcium	Phosphorus	ALP
PTH	1				
Vitamin D	.205	1			
Calcium	.111	.287*	1		
Phosphorus	-.137	-.147	-.583**	1	
ALP	.097	.060	-.091	.019	1
Magnesium	.091	.238	.430**	-.028	.073

* Correlation is significant at the 0.05 level (2-tailed), ** Correlation is significant at the 0.01 level (2-tailed).