CALCIUM HOMEOSTASIS IN CHILDREN WITH ß-THALASSEMIA MAJOR

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ABSTRACT

Objective: The aim of this meta analysis study is the change in calcium, phosphorus , 25-OH vitamin D_3 , alkaline phosphatase and parathyroid hormone level among children with B-thalassemia major.

Subject and Methods: The study group consisted of forty β-thalassemia patients , their ages ranged from 12-18 years and control group of forty healthy children. Inclusion criteria patients were diagnosed as β-thalassemia major depending on regular blood transfusions and blood samples were withdraw just pretansfusions. The results of serum total calcium , Ionized calcium , phosphorus ,alkaline phosphatase and serum parathyroid hormone were evaluated in both group.

Results: the mean serum total calcium (8.9 ± 1.3 mg/dl) was non significantly lower among β-thalassemia patients than control (9.1± 0.7 mg/dl). Phosphorus (6.6 ± 2mg/dl) and serum 25-OH vitamin D_3 (12.9 ± 4.5 ng/ml) were significantly lower among β-thalassemia patients than control (23.8± 10.5 ng/ml) .Serum parathyroid hormone (26.8 ± 6.5 pg/ml) was significantly lower among β-thalassemia patients than control (31.9± 5.2 pg/ml).

Conclusion: there were significant negative correlation between serum parathyroid hormone and both alkaline phosphatase and ferritin and a significant positive correlation between serum parathyroid hormone and 25-OH vitamin D_3

KEY WORDS: B-thalassemia , calcium , phosphorus , 25-OH vitamin D_3 , alkaline phosphatase and parathyroid hormone

INTRODUCTION

β-thalassemia syndromes are a group of hereditary blood disorders characterized by reduced or absent beta globin chain synthesis, resulting in reduced Hb in red blood cells (RBC), decreased RBC production and anemia. Most thalassemias are inherited as recessive traits ***(Galanello and Origa, 2010)***.

In most patients with ß-thalassemia major, hypopara-thyroidism is asymptomatic and hypocalcaemia

is detected only during routine laboratory exami-nations ***(Zafeiriou et al., 2001)***.

Calcium Homeostasis:

Calcium homeostasis is largely regulated through an integrated hormonal system that controls calcium transport in the gut, kidney, and bone. It involves two major calcium-regulating hormones and their receptors-PTH and the PTH receptor (PTHR) ***(Potts and Gardella, 2007)*** and $1,25(OH)_2D$ and the vitamin D receptor (VDR), as well as serum ionized calcium and the calcium-sensing receptor (CaR) ***(Jurutka et al., 2001).*** Serum calcium homeostasis has evolved to simultaneously maintain extracellular ionized calcium levels in the physiologic range while allowing the flow of calcium to and from essential stores. A decrease in serum calcium inactivates the CaR in the parathyroid glands to increase PTH secretion, which acts on the PTHR in kidney to increase tubular calcium reabsorption, and in bone to increase net bone resorption. The increased PTH also stimulates the kidney to increase secretion of $1,25(OH)_2D$, which activates the VDR in gut to increase calcium absorption, in the parathyroid glands to decrease PTH secretion, and in bone to increase resorption ***(Peacock, 2010)***.

Calcium - Phosphate Interactions:

Calcium and phosphate (inorganic phosphorus) interact in several fundamental processes. In the skeleton, calcium and phosphate metabolism work in cohort with osteoblasts, osteocytes, and extracellular matrix proteins to mineralize osteoid as it is deposited ***(Qin et al., 2004)***.

On the other hand, in non skeletal tissues, there is a less understood regulatory system that prevents the harmful deposition of calcium-phosphate complexes in soft tissue ***(Kirsch, 2006).***

The hormonal system regulating phosphate homeostasis involves two main hormones: fibroblast growth factor 23 (FGF-23) and the FGF/Klotho receptor complex and PTH and PTHR ***(Peacock, 2010).***

An increase in serum phosphate stimulates FGF-23 secretion from bone, which acts on the sodium-phosphate renal tubular transporters in proximal tubular cells of the kidney to decrease phosphate reabsorption. Concurrently, FGF-23 reduces renal secretion of $1,25(OH)_2D$, which decreases intestinal phosphate absorption ***(Quarles, 2008)***.

Serum PTH level, which is central to calcium homeostasis, also plays a key role in phosphate homeostasis. Increased serum PTH acting on renal co-transporters decreases renal phosphate reabsorption and serum phosphate, whereas decreased PTH increases renal phosphate reabsorption and serum phosphate (***Kronenberg, 2002)***.

Vitamin D Metabolites:

Vitamin D is an essential factor in the regulation of calcium and phosphorus balance. It is synthesized in the skin but is also present in the diet. The active form is 1,25 dihydroxy vitamin D. Its main action is to enhance the availability of calcium and phosphorus for new bone formation ***(Holick, 1987)***.

The steroid hormone 1,25(OH) $_2$ D_3 is the major biologically active metabolite of the vitamin D sterol family. The vitamin D precursor (previtamin D_3) is either ingested in the diet or synthesized in the skin from 7-dehydrocholesterol through exposure to sunlight ***(Webb and Holick, 1988).***

Recent studies have also shown important actions of vitamin D in many other tissues. Vitamin D enhances the intestinal absorption of calcium and phosphorus, increasing their serum levels.

- Along with PTH, vitamin D is a required factor in the bone resorption process.
- It also increases the reabsorption of urinary calcium and phosphorus in the renal tubules.

Through the vitamin D receptors it has a direct effect on the parathyroid glands to suppress PTH secretion ***(Holick, 1987)***.

PATIENTS AND METHODS

This cross sectional descriptive clinical study was carried out at the Hematology Unit of El-Hussein University Hospital during the period between March 2013 and January 2014.

The subject of the study comprised a group of 40 β-thalassemia patients, 22 (55%) were males and 18 (45%) were females. Their ages ranged from 12 years to 18 years with a mean age of 13.9 ± 1.8 years.

A Control group comprised of 40 healthy children, 21 (52.5%) were males and 19 (47.5%) were females. Their ages ranged from 12 years to 18 years with a mean age of 14.7 ± 1.8 years.

Inclusion Criteria:

Patients were diagnosed as β-thalassemia major depending on regular blood transfusions and blood samples were withdrawn just pretransfusion.

Exclusion Criteria:

Patients age below 12 years and or blood samples were withdrawn from patients after packed RBCs transfusion**.**

The study group was subjected to the following:

A standardized master sheet for all study subjects, and it provided the following:

I. Full history taking stressing on:

- History of pallor and jaundice.
- Blood transfusions: onset, regularity, and duration.
- Supplementation therapy.
- Iron chelation therapy.
- History of splenectomy.
- Family history of similar conditions.

II. Clinical examination stressing on:

- Pallor.
- Jaundice.
- Growth measurements.
- Vital signs.
- Systemic examination.

III. Laboratory investigations and methodology:

- **Sample collection:**

Five mL venous blood were collected by venipuncture, just pretransfusion, from each child.

Blood was allowed to clot. Serum was separated by centrifugation. Samples containing visible precipitate must be clarified prior to use. Samples were aliquoted and serum was kept frozen at -20°C till the time of assay. Repeated freeze - thaw cycles should be avoided. Hemolysed samples should be excluded.

Prior to assay, the frozen samples should be brought to room temperature slowly and mixed gently.

- **Serum Total Calcium, Ionized Calcium, Phosphorus and Alkaline Phosphatase** were measured using the autoanalyzer Olympus AU 400, Japan.
- **Serum Parathyroid Hormone:** Parathormone serum level was determined by the Enzyme-Linked Immunosorbent Assay (ELISA) using the hPTH-ELISA kit supplied from DIA Source (Belgium).

REAGENTS OF THE KITS:

1. Microtiter plate with 96 anti PTH (polyclonal antibodies) coated wells.
2. Conjugate: HRP labeled anti-PTH (monoclonal antibodies).
3. Zero calibrator in human serum and thymol.
4. Calibrator N = 1 to 5 in human serum and thymol.
5. Wash Solution (NaCl-Tween 20).
6. Controls - N = 1 or 2 in human serum with thymol.

7. Incubation Buffer with EDTA, Benzamidin and azide (<0.1%).
8. Chromogenic Solution (TMB: Tetramethylbenzydine).
9. Stopping reagent: HCl 1.0N.

REAGENT PREPARATION:

A. Calibrators: Reconstitute the zero calibrator with 3.0 mL distilled water and other calibrators with 1 mL distilled water.

B. Controls: Reconstitute the controls with 1 mL distilled water.

C. Working Wash Solution: Prepare an adequate volume of working wash solut- ion by adding 19 volumes of distilled water to 1 volume of Wash Solution (20x). Use a magnetic stirrer to homogenize.

PROCEDURE:

1. Select the required number of strips for the run.
2. Secure the strips into the holding frame.
3. Pipette 50 µL of Incubation Buffer into all wells.
4. Pipette 200 µL of each calibrator, control and sample into the appropriate wells.
5. Incubate for 2 hours at room temperature on a horizontal shaker set at 700 rpm ± 100 rpm.
6. Aspirate the liquid from each well.
7. Wash the plate 4 times by wash solution.
8. Pipette 100 µL of anti-PTH-HRP conjugate into all the wells.
9. Incubate for 1 hour at room temperature on a horizontal shaker.
10. Aspirate the liquid from each well.
11. Empty and wash the plate 4 times with wash solution.
12. Pipette 100 µL of the chromogenic solution into each well within 15 minutes.
13. Incubate the microtiterplate for 30 minutes at room temperature on a horizontal shaker set at 700 rpm ± 100 rpm, avoid direct sunlight.
14. Pipette 200 µL of stop solution into each well.

CALCULATION OF RESULTS:

1. Read the plate at 450 nm against a reference filter set at 630 nm.
2. Calculate the mean of duplicate determinations.
3. Calculate the average absorbance values for each set of duplicate standard and samples. Create a standard curve by plotting the mean absorbance for each standard concentration on the ordinate

against the PTH concentration on the abscissa. Draw a calibration curve through the calibrator points

4. Read the concentration for each control and sample by interpolation on the calibration curve.

The normal serum PTH level is 15 – 65 pg/ml ***(Fischbach and Dunning, 2009)***.

Statistical Analysis of Data:

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 18.0.

Descriptive statistics were done for quantitative parametric data as mean±SD (standard deviation) and minimum and maximum of the range, while they were done for qualitative data as number and percentage.

Inferential analyses were done for quantitative variables using independent t-test in cases of two independent groups with parametric data and for qualitative data, inferential analyses for independent variables were done using Chi square test for differences between proportions. Correlations were done using Pearson Correlation. Linear regression model was used to find out independent factors affecting PTH.

The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant. The P value is a statistical measure for the probability that the results observed in a study could have occurred by chance.

RESULTS

Table (1): Comparison between Patients and Controls as Regards Serum Total Calcium.

Serum Total Calcium (mg/dL)	Patients	Controls	P
Mean ± SD	8.9±1.3	9.1±0.7	#0.336
Range	5.2–12.1	7.6–10.2	
<8.1 mg/dL : n (%)	6 (15.0%)	4 (10.0%)	^0.499
≥8.1 mg/dL : n (%)	34 (85.0%)	36 (90.0%)	

#Independent t-test, ^Chi square test.

Table (2): Comparison between Patients and Controls as Regards Serum Phosphorus.

Serum PO_4 (mg/dL)	Patients	Controls	P
Mean ± SD	6.6±2.0	5.4±1.1	**#0.002***
Range	3.2–12.7	3.2–7.7	
>5.9 mg/dL : n (%)	21 (52.5%)	10 (25.0%)	**^0.012***
≤5.9 mg/dL : n (%)	19 (47.5%)	30 (75.0%)	

#Independent t-test, ^Chi square test

Table (3): Comparison between Patients and controls as Regards Serum 25-OH Vitamin D_3

Serum 25-OH D_3 (ng/mL)	Patients	Controls	P
Mean ± SD	12.9±4.5	23.8±10.5	**#<0.001***
Range	7.3–20.8	10.4–55.0	
<10.0 ng/dL : n (%)	15 (37.5%)	0 (0.0%)	**^<0.001***
≥10.0 ng/dL : n (%)	25 (62.5%)	40 (100.0%)	

#Independent t-test, ^Chi square test, *Significant

Table (4): Comparison between Patients and Controls as Regards Serum Parathyroid Hormone.

Serum PTH (pg/mL)	Patients	Controls	P
Mean±SD	26.8±6.5	31.9±5.2	**#<0.001***
Range	9.5–40.0	24.3–46.0	
<15.0 pg/mL : n (%)	2 (5.0%)	0 (0.0%)	^0.152
≥15.0 pg/mL : n (%)	38 (95.0%)	40 (100.0%)	

#Independent t-test, ^Chi square test, *Significant

Table (5): Correlation between Serum Parathyroid Hormone and the Other Factors among Patients.

	r	P
Age	0.053	0.747
Duration of Illness	0.160	0.323
Total Calcium	0.008	0.962
Ionizing Calcium	0.009	0.954
Phosphorus	0.226	0.161
Alkaline Phosphatase	-0.322	**0.043***
25-OH D_3	0.319	**0.045***
Ferritin	-0.884	**<0.001***

#Pearson correlation, *Significant

- There were significant negative correlations between serum PTH and both serum alkaline phosphatase and ferritin, and a significant positive correlation between serum PTH and 25-OH vitamin D_3.

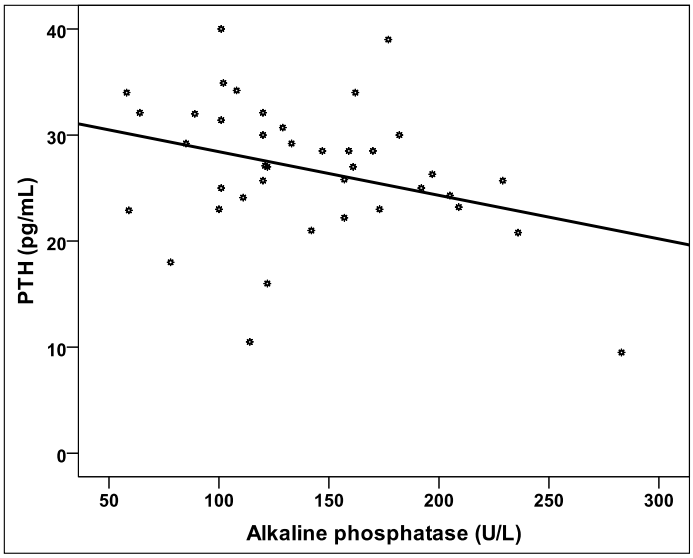

Figure (1): Correlation between serum PTH and serum ALP among Patients.

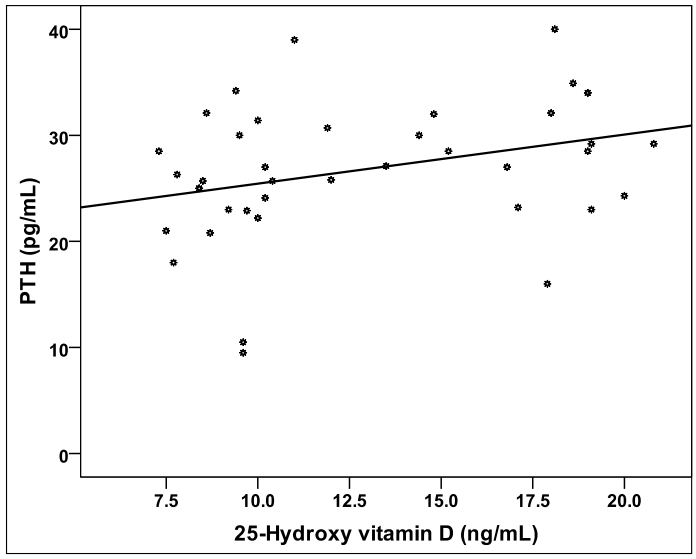

Figure (2): Correlation between serum PTH and serum 25-OH vitamin D_3 among Patients.

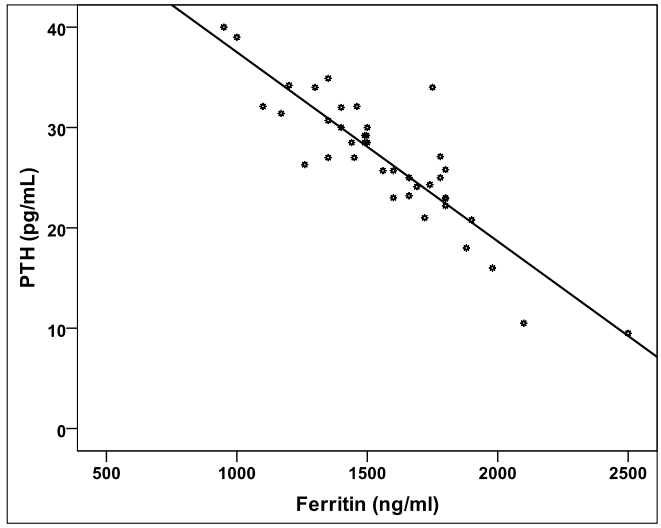

Figure (3): Correlation between serum PTH and serum ferritin among Patients.

- Using linear regression age (=duration of illness), serum total calcium and 25-OH vitamin D_3 were significant factors rising PTH level while serum ferritin was a significant factor supressing PTH level **(increasing serum ferritin by 100 ng/mL leads to reduction of PTH by 1.4 pg/mL)**.

Table (6): Comparison between Patients and Controls as Regards Tanner Maturity Rating.

Variable	Stage	Patients n (%)	Controls n (%)	P
Tanner stage (n, %)	I	24 (60.0%)	0 (0.0%)	^ <0.001*
	II	15 (37.5%)	0 (0.0%)	
	III	1 (2.5%)	1 (2.5%)	
	IV	0 (0.0%)	25 (62.5%)	
	V	0 (0.0%)	14 (35.0%)	

#Independent t-test, ^Chi square test, *Significant

- 24 patients, accounting for 60%, had Tanner Maturity stage 1, and 15 patients, accounting for 37.5%, had stage 2 while only 1 patient, accounting 2.5%, had stage 3. Also frequencies of higher Tanner stages were significantly lower among patients than controls.

DISCUSSION

Thalassemia is one of the commonest single gene disorder prevalent all over the world. It is estimated that (1.5%) of the world population are carries of β-thalassemia. Until the last few decades, thalassemia was regarded as a uniformly fatal disease and death was expected during the second decade of life. However, better understanding of molecular biology and prenatal diagnosis, better laboratory techniques for diagnosing complications, availability of blood components and provision of comprehensive care have resulted into better and prolonged survival ***(Latehony et al., 2006)***.

The aim of this study was to detect changes in serum Calcium, Phosphorus, ALP, 25-OH Vitamin D_3 and PTH levels among children with β-thalassemia major.

In the current study, the results showed that serum total and ionized calcium were non-significantly lower among patients than controls. As regards serum PO_4 was significantly higher among patients than controls while serum PTH and serum ALP were significantly lower among patients than controls. There were significant negative correlations between serum PTH, serum alkaline phosphatase and serum ferritin, while there were signifi-

cant positive correlation between serum PTH and 25-OH vitamin D_3.

In our study, the results showed that there is no statistically significant difference between patients (8.9±1.3 mg/dL) and controls (9.1±0.7 mg /dL) as regard serum total calcium level (P value = 0.336). Only 6 patients (15%) had serum total calcium < 8.1 mg/dL Table (1).

This may be explained by regular calcium supplementation for (5.1±1.2 year) as described by protocol of management of thalassemic patients in our Hematology Clinc. As well as the relative increase in serum ca by increased bone resorption in adolescent thalassemic patients.

This is in agreement with the study done, in India by ***(Goyal et al., 2010)*** who found normal calcium levels (9.78±0.13 mg/dL) among β-thalassemia patients and this reflects the adequate supplementation of calcium.

Also, our cases had a long history of thalassemia i.e. oeteopenia /osteoporpsis as complication of bone demineralization and expansion due to endocrine complications hypoparathyroidism and mainly hypogonadism leads to increase of serum calcium in peripheral blood.

On the other hand, in the study done by ***(Dhouib et al., 2011)***, in Tunisie, serum calcium level was low (6.24 mg/dL) and also in the study done by ***(Basha et al., 2014)*** in India, serum calcium level was low (5.534±1.11 mg/dL). probably because the thalassemic patient were young in age not adolescent children.

Autio and Mait, in 2005, observed that 61% of their patients with β-thalassemia had hypocalcemia. They further observed that these patients did benefit from vitamin D_3 and calcium supplementations.

In the present study, the results show that there was a statistically significant difference between patients (12.9±4.5 ng/mL) and controls (23.8±10.5 ng/mL) as regard serum 25-Hydroxy vitamin D_3 level (P value was 0.001) (meaning that 25-OH vitamin D_3 levels were significantly lower in thalassemic patients than in controls of similar age). This is may be explained by inadequate vitamin D_3 supplementation for thalassemic patients in our studied group Table (3).

This is in concordance with the results recorded by ***(Napoli et al., 2006),*** in Italy, that showed a statistically significant difference between patients (20.3±0.7 ng/mL) and controls (25.2 ± 1 ng/mL) as

regards serum 25-hydroxy vitamin D_3 level (P value was 0.01), meaning that all patients had vitamin D_3 deficiency ***(Rioja et al., 1990) and (de Vernejoul et al., 1982)***.

This agree with our result as vitamin D deficiency is also implicated in the pathogenesis of osteopenia in thalassemia major.

In the present study, results showed that there was a statistically significant high level of serum phosphorus among patients (6.6±2.0 mg/dL) than controls (5.4±1.1 mg/dL) (P value was 0.002)Table (2). This is in concordance with the results recorded by ***(Dhouib et al., 2011)***, in Tunisie, serum phosphorus was (8.16±1.32 mg/dL) and ***(Basha et al., 2014)***, in India, serum phosphorus was (5.748 ± 0.95 mg/dL).

High phosphorous levels stimulate the release of PTH ***(Jensen et al., 1997)*** and reduce the 1α-hydroxylase, thus regulating PTH and 1,25 vitamin D_3 levels ***(Portale et al., 1986).***

Hypoparathyroidism (HPT) secondary to siderosis in thalassemia patients was first described by Gabriele ***(Gabriele, 1971)***. Due to the significant increase in the lifespan of these patients, many endocrine abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hypoparathyroidism develop due to an iron overload ***(Jensen et al., 1997)***.The incidence of hypoparathyroid dysfunction varies from 0% up to almost 22.5% of patients ***(Perignon and Brauner, 1993)***.

In our study, the results showed statistically significant lower serum levels of parathormone among patients (26.8±6.5 pg/mL) than controls (31.9±5.2 pg/mL) (P value was 0.001) and this may be explained by the iron deposition in the parathyroid gland in thalassemic patients.

This is in agreement with the results recorded by ***(Goyal et al., 2010),*** in India (serum PTH was 33.4±2.07 pg/mL), ***(Basha et al., 2014),*** in India (serum PTH was 5.748±1.89 ng/L) and ***(Dhouib et al., 2011),*** in Tunisie (serum PTH was 2±1.21 ng/L).

Since the concentration of ferritin is not a valuable tool in the prediction of the development of hypopathyroidism, parathyroid function should be tested periodically, particularly when iron-overload complications occurs ***(Dhouib and Turki, 2011).***

There are two possible explanations for the occurrence of hypoparathyroidism in thalassemia major patients. The first and

possibly the most important factor is the deposition of iron in parathyroid gland leading to gland dysfunction. Another factor may be suppression of parathyroid secretion induced by bone resorption resulting from increase calcium in peripheral blood.

Endocrine commplications: hypothyroidism, hypoparathyroidism and mainly hypogonadism are considered as a major cause of osteopenia/osteoporosis in thalassemia. Even after restoring hemoglobin levels ,adequate hormone replacement and effective iron chelation with normalization of iron status. thalassemia patients continue to show imbalanced bone remodeling (**Chatterjee R., 2011)** with an increased resorption phase resulting in seriously diminished bone mineral density .This give us a hand to explain the normal calcium level of our patient as most of them have prolonged course of the disease. Prevention of hypogonadism seems to be very an effective way for preventing osteoporosis in thalassemic patients. Continous hormonal replacement therapy improve bone density parameters. Thus decrease calcium in peripheral blood decrease resorption. thus decrease hypoparathyroidism.

In our study, Increasing ferritin by 100 ng/mL leads to reduction of PTH by 1.4 pg/mL due to iron deposition in the tissue and causes hemosidrosis Table (4), fig.(3).

In other study, it was observed that there is no clear relationship between hypothyroidism and serum ferritin levels. In an Italian study conducted by the department of pediatrics, observed 24 patients of HPT in β-thalassemia major ***(De Satictis et al, 1992)***. HPT is thought to be mainly the consequence of iron deposition in the parathyroid glands. The age of their patients when HPT was diagnosed ranged from (11 to 24 years) (mean 16.5±5.9 years). Their serum ferritin levels ranged from (810 to 15,200 ng/mL) (mean 3,772±955 ng/mL).

The severity of hypoparathyroidism varied widely. The onset of hypoparathyroidism was preceded or followed in most patients by other endocrine and/or cardiac complications ***(Dhouib et al., 2011)***.

Olivieri and Nathan, in 1994, found no clear relationship between hypoparathyroidism and serum ferritin levels in their patients, suggesting either an individual sensitivity to iron toxicity or early damage of the parathyroid gland before chelation had reduced the iron overload. It has been shown that prognosis for survival is best for those

thalassemia patients in whom serum ferritin levels can be maintained below 2,500 µg/L, but at the same time some patients who receive ideal management in terms of present standards do develop significant endocrine damage. A multicenter study found that 22% of their thalassemia patients had endocrine complications, with a serum ferritin level below 2,000 µg/L. From the preceding discussion, it is quite obvious that although optimal chelation therapy does reduce the incidence of HPT and other endocrine complications, nonetheless some patients will continue to develop HPT ***(Olivieri and Nathan, 1994).***

Serum ferritin may not have been a reliable indicator of iron overload.

It was recently demonstrated that the degree of iron overload, at least reflected by ferritin levels, was not associated with the development of other endocrine complications ***(Cario et al., 2003) and (Angelopoulos et al., 2006).***This indicates that long-term iron balance rather than current iron status is related to the development of hypoparathyroidism ***(Dhouib et al, 2011)***.

In the current study, the results showed that serum total calcium and serum ionized calcium were non-significantly lower among patients than controls. As regards serum PO_4 was significantly higher among patients than controls while serum hypoparathyroidism and serum ALP were significantly lower among patients than controls. There were significant negative correlations between serum hypoparathyroidism, serum alkaline phosphatase and serum ferritin, while there were significant positive correlation between serum hypoparathyroidism hand 25-OH vitamin D_3.

Using linear regression age (=duration of illness), serum total calcium and 25-OH vitamin D_3 were significant factors rising PTH level while serum ferritin was a significant factor supressing PTH level (increasing serum ferritin by 100 ng/mL leads to reduction of PTH by 1.4 pg/mL) fig (2) ,fig (3).

CONCLUSIONS

- Patients had significantly more frequent weight, height and BMI $<5^{th}$ percentile than controls.
- Frequencies of higher Tanner stages were significantly lower among patients than controls.
- There were significant negative correlations between serum

PTH and both serum alkaline phosphatase and ferritin, and a significant positive correlation between serum PTH and 25-OH vitamin D_3.

- Using linear regression age (=duration of illness), serum total calcium and 25-OH vitamin D_3 were significant factors rising PTH level while serum ferritin was a significant factor supressing PTH level (increasing serum ferritin by 100 ng/mL leads to reduction of PTH by 1.4 pg/mL).

RECOMMENDATIONS

- We recommend that all children with β-thalassemia in all centers all over the country should be funded to be maintained on good iron chelation.
- All children with β-thalassemia should receive adequate supply of calcium and 25-OH vitamin D_3.
- Further studies with larger sample size and longer duration of follow-up should be required.
- All children with β-thalassemia should be regularly investigated for:
  1. Serum total calcium to avoid hypocalcemia
  2. PTH to avoid hypoparathyroidism
  3. 25-OH Vitamin D_3
  4. hormonal replacement where it needed.

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الملخص العربى

يعد مرض أنيميا البحر المتوسط من أهم أمراض الدم الوراثية الانحلالية (التي تسبب تكسر كريات الدم الحمراء) الشائعة على مستوى العالم بشكل عام وعلى مستوى منطقة البحر الأبيض المتوسط بشكل خاص ومن الأمراض التى تعتمد بصورة أساسية فى علاجها على نقل الدم بصفة مستمرة ولذا فإن الأطفال المصابين بهذا المرض يصبحون عرضة لحدوث مضاعفات نتيجة تراكم الحديد في أعضاء مختلفة من الجسم إن لم ينتظم المريض باستعمال أدوية تعمل على سحب الحديد الزائد من الدم والتخلص منه عن طريق البول، وتتمثل هذه المضاعفات في تشحم الكبد واسوداد لون الجلد وخلل هرموني (مرض السكري) وانخفاض في هرمون الغدة الدرقية وهرمون الغدة الجار درقية وهرمونات الغدة النخامية.

وقد أجريت هذه الدراسة على عدد (40) طفلا من هؤلاء الأطفال وقد تم أخذ التاريخ المرضى لهم كاملا وعمل فحص اكلينيكي وعدد من التحاليل الطبية تتضمن نسبة الكالسيوم والفسفور وفيتامين (د) وهرمون الغدة الجار درقية في الدم.

وقت إجراء هذه الدراسة كانت أعمار هؤلاء الأطفال تتراوح بين (12) سنة إلى (18) سنة بمتوسط (13.9) سنة ± (1,8) سنة بينما كانت أعمارهم وقت تشخيص المرض لأول مرة تتراوح بين (6) أشهر إلى (12) شهراً بمتوسط (9,2) شهر ± (2). (29) طفلا يمثلون (72,5)% من العدد الكلي كانت أوزانهم أقل من المستوى الخامس و(30) طفلاً يمثلون (75)% كانت أطوالهم أقل من المستوى الخامس.

وباستخدام "مقياس تنر" للنمو ظهر أن (24) طفلا يمثلون (60)% من العدد الكلى كانوا ضمن المرحلة الأولى، بينما كان (15) طفلا يمثلون (37,5)% ضمن المرحلة الثانية، بينما كانت المرحلة الثالثة بها طفل واحد ويمثل (2,5)%، وأما المرحلتين الرابعة والخامسة فقد كانتا خاليتين من الأطفال.

وبالتحاليل المعملية تبين أن المستوى الكلي للكالسيوم بالدم بالميليجرام/ ديسيليتر كانت تتراوح بين (5,2) الى (12,1) بمتوسط (8,9) ± (1,3) ميليجرام/ ديسيليتر، بينما كان مستوى الفسفور بالدم بالميليجرام/ ديسيليتر كانت تتراوح بين (3.2) الى (12.7) بمتوسط (8.9) ± (1.3) مجم/ديسيليتر، أما مستوى هرمون الغدة الجار درقية بالدم بالبيكوجرام/ ملليليتر كانت تتراوح بين (9,5) الى (40) بمتوسط (26,8) ± (6,5) بيكوجرام/ ملليتر .

وكذلك تبين أن مستوى فيتامين (د) بالدم بالنانوجرام/ ملليتر كانت تتراوح بين (7,3) الى (20,8) بمتوسط (12,9) ± (4,5) نانوجرام/ ملليتر ، ومستوى إنزيم الفوسفاتيز القلوي بالدم باليونت/لتر كانت تتراوح بين (58) الى (283) بمتوسط

(139,9) ± (50,8) يونت/لتر ، أما مستوى الحديد فى الدم (فريتين) بالميكروجرام / ليتر بين هؤلاء الأطفال كان يتراوح بين (950) الى (2500) بمتوسط (1583,5) ± (293,5) ميكروجرام / ليتر.

وقد أظهرت النتائج المعملية والدراسات الإحصائية أن نسبة هرمون الغدة الجار درقية وفيتامين (د) ومستوى إنزيم الفوسفاتيز القلوي في الأطفال المصابين بأنيميا البحر المتوسط أقل من الأطفال الأصحاء بينما كان مستوى الفسفور بالدم أعلى عن نظائرهم من الأصحاء وكذلك أظهرت الدراسات عدم وجود اختلاف ملحوظ في نسبة الكالسيوم بين هؤلاء الأطفال وأقرانهم من الأصحاء.

وكذلك أظهرت الدراسات والنتائج أن الكالسيوم وفيتامين (د) عوامل لارتفاع مستوى هرمون الغدة الجار درقية بينما الحديد (الفيريتين) من عوامل خفض مستوى الهرمون بالدم.

فقد لوحظ أن زيادة نسبة الحديد (الفيريتين) 100 نانوجرام/مليميتر في الدم يؤدي إلى انخفاض مستوى هرمون الغدة الجار درقية بنسبة (1,4) بيكوجرام/ميلليتر.