Evaluation of some essential element levels in thalassemia major patients in Mosul district, Iraq

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ABSTRACT

الأهداف: يوجد فقر الدم البحري الشديد نوع بيتا في جميع أنحاء العالم ويعتبر من أحد أهم المشاكل الصحية في المناطق الاستيطانية. إن توفر المعلومات خاصة المتعلقة بقيم الهيموكلوبين والعناصر الأساسية يمكن اعتبارها من العوامل المحددة الأساسية للشفاء من المرض. أجريت الدراسة الحالية لتقييم مستويات بعض العناصر الأساسية في مرضى فقر الدم البحري في منطقة الموصل .

الطريقة: أجريت الدراسة على ١٠٥ من الأطفال المصابين بمرض فقر الدم البحري الشديد والمعتمدين على نقل الدم وبأعمار ٢,٥ إلى ١٨ سنة من مراجعي مستشفى ابن الأثير التعليمي في مدينة الموصل(خلال عام ٢٠٠٥) إضافة إلى ٥٤ من الأطفال الأصحاء كمجموعة سيطرة. تم اختيار المرضى بطريقة منتظمة وبدراسة معتمدة من قبل المستشفى. استخرجت قيم العناصر الأساسية في المصل. استخدم المعدل والإنحراف المعياري ومعامل العلاقات وفحص زت للاختبارات الإحصائية واعتبرت القيم أقل من ٠,٠٥ معنوية إحصائيا.

النتائج: وجد انخفاض في مستويات الزنك والمغنيسيوم وارتفاع في مستويات النحاس والبوتاسيوم في مرضى فقر الدم البحري (١٠٥) مقارنة مع مجموعة السيطرة (٥٤) , بينما اتضح بان مستويات الكالسيوم والفوسفور والصوديوم هي ضمن قيمها الطبيعية.

خاتمة: يبدو بان التغييرات في مستويات العناصر الأساسية مرتبطة مع الاضطرابات المختلفة المرافقة للمرض. فانخفاض الزنك قد يكون نتيجة لارتفاع نسبته في الإدرار الناتج من إطلاق الزنك من كريات الدم الحمراء المتحللة بينما ارتفاع النحاس قد يكون نتيجة للالتهابات الحادة والمزمنة وتحلل صبغة الدم والذي يعتبر من الاضطرابات المرافقة لفقر الدم البحري. قد تكون الزيادة في مستويات الصوديوم نتيجة للتلف الكلوي. أما انخفاض مستويات المغنيسيوم قد يكون نتيجة لانخفاض إفراز الغدة جار الدرقية.

Objectives: To evaluate the levels of some essential elements in thalassemic patients in Mosul, Iraq.

Methods: One hundred and five thalassemic blood transfusion dependent children, 2.5-18 years of age attending Ibn-Al-Atheer teaching hospital in Mosul City, Iraq, during 2005, were used in this study. Fifty-four healthy subjects served as a control group. Patients were allocated in a non-randomized prospective cross-sectional hospital based study. Essential elements levels were estimated. The mean, standard deviation, correlation coefficient, and z-test were used. *P*-values <0.05 were considered statistically significant.

Results: Low serum zinc, and magnesium, and high serum copper, and potassium levels were found among the 105 thalassemic patients compared to the 54 controls. Levels of calcium, phosphate, and sodium were within normal limits.

Conclusion: Fluctuations in the essential elements levels seem to be related to the different complications associated with the disease. Zinc deficiency may be attributed to hyperzincuria resulted from the release of Zn from hemolyzed red cells. Hypercupremia occurs in acute and chronic infections and hemochromatosis, which is a principal complication of thalassemia. Increased Na levels may be due to renal damage. Hypomagnesemia may occur due to hypoparathyroidism.

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Thalassemia occurs throughout the world and is one of the major public health problems in the endemic regions, such as the Mediterranean countries, Middle East, North Africa, and Asia.[1,2] Thalassemia syndrome is a series of genetic disorders

in the hemoglobin (Hb) synthesis characterized by a reduced rate of production of one or more of the globin chains of hemoglobin. Some complications reported to be associated with this disease include growth retardation,[3-5] diabetes mellitus,[6,7] endocrine dysfunction,[8,9] hypothyroidism,[10,11] progressive liver failure,[12] and cardiac complications.[13,14] The disease still hides some important secrets, therefore, the provision of information especially the values that are concerned with Hb and those of essential elements, can be considered as a profitable tool in the cure of the disease. Low serum and plasma zinc (Zn) levels clinically resemble homozygous β-thalassemia.[15,16] Some studies showed that the serum Zn concentration in thalassemic patients tended to be below normal, and an elevated level of serum copper (Cu) in thalassemic patients was also reported.[17] Hypocalcemia in β-thalassemia patients was described by some investigators.[18,19] Associated with hypocalcemia is an increased level of serum phosphate (P).[18,20,21] Aldudak et al[22] reported increased levels of serum sodium (Na) and potassium (K) in thalassemic patients, and decreased levels in serum magnesium (Mg) was found by other workers.[16,23] The present study was conducted to evaluate the levels of some essential elements in thalassemic patients in Mosul, Iraq.

Methods. One hundred and five thalassemic blood transfusion dependent children with the age of 2.5-18 years (62 males and 43 females) attending Ibn-Al-Atheer teaching hospital in Mosul city, in the northern part of Iraq, during the year 2005 were included in this study. Fifty-four healthy subjects, aged 4-17 years served as the control group. All pediatric age patients were included, only those with diseases other than thalassemia were excluded. Patients were recruited when they came to the hospital to receive blood transfusion. The local ethical committee approved the study. An informed consent was gathered from the patients. Five milliliters of venous blood were drawn from the cubital vein using disposable needles and syringes without using tourniquet. All samples were collected in the morning. The blood sample was divided into 2 parts: part one was added to a tube containing ethylenediamine tetraacetic acid for the hematological studies. Part 2 was used for estimation of serum electrolytes, and minerals by centrifuging the blood after clotting. Serum Zn, Cu, and Mg levels were estimated using a Pye Unicam model atomic absorption spectrophotometer (Pye Unicam Ltd, England), which was adjusted according to the Pye Unicam instruction.[24] Serum Ca and P levels were measured using a BioMérieux kit according to O-cresolphthalein complex one method.[25] Serum Na and K levels were estimated using a flame photometer method.[26]

The mean, standard deviation, correlation coefficient, and Z-test were used. The differences were considered significant when $p<0.05$. Statistical analysis was applied using SPSS 10 computer program.

Results. Serum Zn and Cu levels are shown in **Table 1**. The mean serum Zn levels in thalassemic patients are significantly lower than in the control group, whereas the mean serum Cu levels in the patients group are significantly higher than that of the control group. The mean Cu:Zn ratio in thalassemics is significantly higher than in the control group, however, the correlation between serum Cu and Zn levels was not significant. Serum Ca and P levels were within normal limits in 83 cases, while low value (7.18 ± 0.64 mg/dl) serum Ca and high value (7.84 ± 1.98 mg/dl) serum P were found in 22 cases. The mean serum Ca level in all patients was lower than in the control group. Serum P level in the thalassemics was higher than the controls. The mean patient Ca:P ratio was lower than that in the

Table 1 - Serum zinc (Zn) and copper (Cu) levels

Group	Serum Zn µg/dl	Serum Cu µg/dl	Cu:Zn ratio
Patients			
Male	39.74 ± 21.98	164.10 ± 48.92	5.35 ± 4.54
Female	37.37 ± 18.45	159.74 ± 52.38	4.41 ± 1.04
Total	**38.65 ± 20.25***	**162.10 ± 50.92***	**4.74 ± 2.73***
Control			
Male	98.33 ± 23.63	105.11 ± 27.66	1.14 ± 0.45
Female	94.23 ± 32.06	97.83 ± 23.86	1.15 ± 0.43
Total	**96.44 ± 27.63**	**101.75 ± 25.98**	**1.14 ± 0.44**

*$p<0.001$ compared to controls.
Data are expressed as mean ± SD

Table 2 - Serum calcium (Ca) and phosphorus (P) levels.

Group	Serum Ca mg/dl	Serum P mg/dl	Ca:P ratio
Patients			
Male	8.51 ± 1.07	6.12 ± 1.56	1.26 ± 0.49
Female	8.51 ± 0.90	5.92 ± 1.57	1.32 ± 0.61
Total	**8.55 ± 1.00**	**6.01 ± 1.56**	**1.27 ± 0.57**
Control			
Male	9.01 ± 0.68	5.35 ± 0.97	1.76 ± 0.45
Female	8.99 ± 0.68	5.17 ± 0.98	1.81 ± 0.45
Total	**9.01 ± 0.68**	**5.27 ± 0.97**	**1.78 ± 0.44**

Data are expressed as mean ± SD

Table 3 - Serum potassium (K) and sodium (Na) levels

Group	Serum K mEq/L	Serum Na mEq/L	Na:K ratio
Patients			
Male	4.94 ± 0.54	136.80 ± 3.4	29.33 ± 3.28
Female	4.95 ± 0.41	136.00 ± 3.34	28.68 ± 2.26
Total	**4.49 ± 0.49***	**136.92 ± 3.39**	**29.03 ± 2.84†**
Control			
Male	4.68 ± 0.51	135.96 ± 4.30	27.85 ± 3.18
Female	4.67 ± 0.33	135.16 ± 3.67	27.58 ± 2.07
Total	**4.71 ± 0.44**	**135.59 ± 3.98**	**27.74 ± 2.79**

*p<0.05 compared to controls, †p<0.01 compared to controls.
Data are expressed as mean ± SD

Table 4 - Serum magnesium level.

Gender	Patients (mg/dl)	Control (mg/dl)
Male	1.91 ± 0.39	2.02 ± 0.43
Female	1.89 ± 0.35	1.96 ± 0.39
Total	**1.91 ± 0.38**	**1.99 ± 0.42**

Data are expressed as mean ± SD

control group (**Table 2**). The results of serum K and Na levels are summarized in **Table 3**. The mean K level in the thalassemics was significantly higher than in the controls. No significant difference was found between the mean serum Na level in thalassemics and the control group. The mean Na:K ratio in the patients group was significantly higher than the control group. **Table 4** shows the mean serum Mg, which was slightly less in the patients group than that in the control group.

Discussion. Beta-thalassemia major seems to be more prevalent in Mosul district as compared to other regions of Iraq, which is obviously due mainly to the high rate of consanguineous marriage among the rural population. This study was limited to one center, and it was difficult to recruit patients from the other centers in other Iraqi cities. Essential trace elements are required by both humans and animals for normal growth, protein synthesis, and most of them are components of certain enzymes. In this study, the thalassemic patients showed low levels of serum Zn and high levels of Cu in comparison with the control group. These findings are comparable to the results reported by other studies.[15,16,27] Depression of serum Zn levels in our young patients is more pronounced than older thalassemic patients. The etiologic factor of Zn deficiency in thalassemic patients is reduced Zn intake and chelation therapy.[28] Urinary loss of Zn is another factor that may contribute to the Zn deficiency, and an increase of glomerular filtration rate of Zn can also be responsible for hyperzincuria resulting from the release of Zn from hemolyzed red cells.[15,28] Hypercupremia in thalassemic patients remains unclear.[28] Iron absorption needs Cu containing enzymes and cofactors, and it affects the release of iron in Hb synthesis.[15,28] Hypercupremia occurs in acute and chronic infections and hemochromatosis, which is a principal complication of thalassemia,[29] since the frequent blood transfusion increases iron absorption and excess deposition of iron in the tissues causing visceral hemochromatosis.[16]

Low serum Ca levels and high P levels were found in 20.9% of the patients, above 10 years of age in comparison with the controls, whereas, in all patients, the mean values of the 2 elements were within normal limits. These results are in agreement with the findings of other studies,[30,31] but disagrees with those obtained by Kontesis et al.[32] Hypocalcemia and hyperphosphatemia in these patients seem to be related to hypoparathyroidism (HPT) which is a well-known syndrome associated with thalassemia major.[10,33,30] The cause of HPT is assumed to be due to iron deposition in parathyroid glands.[19]

Determination of Na and K levels in thalassemic patients reveals higher Na and K levels compared to the controls. An increased Na level in β-thalassemia major may be due to renal damage resulting from iron overload in such patients,[29] whereas an increased K level occurs in patients with red blood cell (RBC) hemolysis, which may occur in stored blood that is transfused to the patient since K tends to leak from RBC to the plasma in the stored blood.[34] Serum Mg in thalassemic patients was comparable to the control group, which is in agreement with the findings reported by other studies.[16,23] Hypomagnesemia may occur due to HPT resulting from iron overload.[23] It was obvious from this study, that patients with β-thalassemia have low serum Zn and high serum iron compared to the controls.

From previous studies,[20,34] it was shown that low serum Zn is a cause of growth retardation. It is suggested that other studies involving the addition of Zn to the diet of thalassemic patients is needed to clarify this issue. The high serum iron may be the cause behind hepato-splenomegaly, which is a known clinical feature associated with thalassemia.

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