



Assessment of the Nutritional Status, Bone Mineralization, and Anthropometrics of Children with Thalassemia Major

Talasemi Majörlü Çocuklarda Nutrisyonel Durumun, Kemik Mineralizasyonu ve Antropometrik Ölçümlerin Değerlendirilmesi

© Serap Cevher BULGURCU¹, © Aylin CANBOLAT AYHAN², © Hamdi Cihan EMEKSİZ³, © Fahri OVALI¹

¹Istanbul Medeniyet University Faculty of Medicine, Department of Pediatrics, Istanbul, Turkey

²Istanbul Medeniyet University Faculty of Medicine, Department of Pediatric Hematology-Oncology, Istanbul, Turkey

³Istanbul Medeniyet University Faculty of Medicine, Department of Pediatric Endocrinology, Istanbul, Turkey

ABSTRACT

Objective: Children with thalassemia major (TM) are prone to growth failure and micronutrient deficiency. Thus, this study aimed to evaluate nutritional status, anthropometrics, and bone mineralization defects in patients with regular blood transfusion.

Methods: Data obtained were analyzed by evaluating laboratory tests, anthropometric measures, and bone mineral density.

Results: This study included 29 patients (62% male and 38% female) with a mean age of 12.26±4.74 years, mean pre-transfusion hemoglobin of 8.64±1.01 g/dL, and mean serum ferritin of 1158.6±556.8 ng/mL. Vitamin D (72.4%), selenium (72.4%), and folate (37.9%) deficiencies were most frequent. Hypocalcemia was observed in 17.2%, hypomagnesemia in 3.5%, and decreased ceruloplasmin in 10.3% of patients. Folate was higher between 2 and 6 years old (p=0.028). Ceruloplasmin was higher between 6 and 10 years old (p=0.018). Selenium was significantly higher in patients with a ferritin of ≥1500 (p=0.008). No significant ferritin-related differences were found in other micronutrients (p>0.05). Body mass index (BMI) were <5 percentile (p) in 31% of patient, whereas none was >95 p. Height in 24.5% and weight in 20.7% of patients were <3 p, whereas none with >97 p. BMI of patients aged 10-18 years was significantly higher (p=0.001). Anthropometric percentiles did not significantly differ in the mean serum ferritin and micronutrient levels. Hypoparathyroidism was observed in 13.8% and hypothyroidism in 3.5% of patients. Low bone density was detected in 14.8% (2 osteopenic and 2 osteoporotic) of patients. Bone mineral density did not significantly differ in the ferritin and micronutrient levels.

Conclusions: Nutritional support and deficiency prevention are important to minimize the burden of complications and increase the life expectancy and quality in patients with TM.

Keywords: Thalassemia, micronutrient, anthropometric, osteopenia, body mass index

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Corresponding Author

A. Canbolat Ayhan

Istanbul Medeniyet University

Faculty of Medicine, Department of

Pediatrics, Istanbul, Turkey

✉ canbolataylin@hotmail.com

ORCID: 0000-0001-6173-2350

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ÖZ

Amaç: Talasemi majör (TM) tanılı çocuklar büyüme geriliğine ve mikrobesein eksikliklerine yatkındırlar. Bu çalışmada, düzenli transfüzyon uygulanan hastalarda mikro besin seviyelerini, antropometrik ölçümleri, kemik mineralizasyon defektlerini değerlendirmeyi amaçladık.

Yöntemler: Laboratuvar testlerini, antropometrik ölçümleri ve kemik mineral yoğunluğunu değerlendirerek elde edilen verileri analiz ettik.

Bulgular: Çalışmaya ortalama yaşı 12.26±4.74 yıl, ortalama transfüzyon öncesi hemoglobin 8.64±1.01 g/dL, ortalama serum ferritin 1158.6±556.8 ng/mL olan 29 hasta (%62'si erkek, %38'i kız) alındı. En sık vitamin D (%72.4), selenyum (%72.4) ve folat (%37.9) eksikliği saptandı. Hastaların %17.2'de hipokalsemia, %3.5 hipomagnesemi, %10.3 seruloplazmin düşüklüğü saptandı. Folat 2≤ ile <6 yaş arasında, seruloplazmin 6≤ ile <10 yaş arasında daha yüksek saptandı (sırasıyla p=0.028, p=0.018). Selenyum, ferritin ≥1500 olan hastalarda anlamlı olarak yüksekti (p=0.008). Diğer mikrobesein düzeylerinde ferritin düzeyi ilişkili anlamlı farklılık

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saptanmadı ($p>0.05$). Hastaların %31'inin vücut kitle indeksi (VKİ) 5. Persentilin (p) altındaydı. VKİ 95. p'nin üzerinde olan hasta saptanmadı. Hastaların %24.5'inin boyu, %20.7'sinin vücut ağırlığı 3. p'nin altındaydı. Boy ve vücut ağırlığı açısından 97. p'nin üzerinde olan hasta saptanmadı.

Antropometrik ölçümlerin, hastaların kan mikrobesein ve ferritin düzeyleri ile anlamlı bir ilişkisi saptanmadı. On-18 yaş arasındaki hastaların VKİ anlamlı olarak daha yüksek bulundu ($p<0.001$). Antropometrik ölçümler, ortalama ferritin ve mikrobesein düzeyleri açısından anlamlı farklılık göstermedi. Hastaların %20.8'de endokrinolojik bozukluklar (hipoparatiroidi %13.8, hipotiroidi %3.5) gözlemlendi. Hastaların %14.8'inde (2 osteopenik, 2 osteoporotik) düşük kemik yoğunluğu saptandı. Kemik mineral yoğunluğunun mikrobesein ve ferritin düzeyleriyle anlamlı ilişkisi saptanmadı.

Sonuçlar: TM hastalarında nutrisyonel eksikliklerin önlenmesi ve beslenme desteğinin sağlanması kemik mineralizasyon bozuklukları ve büyüme geriliği gibi komplikasyonların gelişiminin en aza indirilmesi açısından önemlidir.

Anahtar kelimeler: Talasemi, mikrobesein, antropometrik, osteopeni, vücut kitle indeksi

INTRODUCTION

Thalassemia major (TM) is one of the chronic diseases in which nutritional deficiencies and endocrine complications are common. Increased iron overload, poor dietary intake, metabolic complications, and endocrinological disturbances are among the factors, which contribute to the nutritional status of these patients¹. Nutritional deficiency is related to multiple factors but hepatic iron overload is a significant cause of deficits in TM². Patients with thalassemia do not have a specific diet and supplementation has been demonstrated with a weak effect on the circulating nutrients^{1,2}. Thus, this study aimed to evaluate nutritional deficiencies, endocrinological dysfunctions, anthropometric measurements, and bone mineralization defects and assess their association with serum ferritin levels and age in children with TM.

MATERIALS and METHODS

This study included children with beta TM who have visited Istanbul Medeniyet University Goztepe Training and Research Hospital Pediatric Hematology-Oncology Department for regular blood transfusion. The study protocol was approved by the University of Health Sciences Turkey, Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee (decision no: 2019/0267, date: 22.05.2019) and written informed consent was obtained from the parents. Patients with known comorbidities, such as gastrointestinal, renal, or eating disorders, were excluded. The height and body weight were measured on the same day with blood sample collection. All measurements were taken by the same person. Height and weight percentiles (p) for age and sex were compared with reference data for Turkish children³. Body mass index (BMI) was calculated by dividing the weight in kilogram by the square of height in meters. Obesity was defined as BMI of ≥ 95 p, overweight as 85-95 p, normal weight as 5-85 p, and low weight was defined as BMI of <5 p. Height of <3 p was

defined as short stature and height >97 p was defined as tall³. All laboratory assessments and dual-energy X-ray absorptiometry (DXA) measurements were performed at our hospital. Laboratory evaluations included pre-transfusion hemoglobin, serum ferritin, vitamins C, E, D, and B12, folate, selenium, zinc, calcium, phosphorus, magnesium, albumin, total protein, ceruloplasmin, alkaline phosphatase, morning fasting glucose, glycated hemoglobin (HbA1c), insulin, thyroid-stimulating hormone, thyroxine, and parathyroid hormone (PTH). An average ferritin level was calculated by averaging serum ferritin values drawn in the last 6 months before the study to obtain a more accurate value. Vitamin D level of ≥ 30 ng/mL was defined as normal, <20 ng/mL was a deficiency, and 20-30 ng/mL was insufficiency⁴. Hyperglycemia was defined as fasting blood sugar of ≥ 100 mg/dL. All patients received iron chelation and prescribed folic acid but were not questioned for treatment compliance. Bone mineral density (BMD) was performed for 26 patients who were ≥ 6 years old and was measured by DXA (Lunar -DPXIQ, GE-Lunar corp. Madison, Wisconsin, USA). The lumbar spine (L1-L4) was scanned. Results were expressed as age and gender standardized Z-scores. BMD Z-score lower than -2 standard deviation (SD) indicated osteoporosis and between -2 and -1 SD indicated osteopenia. A Z-score higher than -1 SD indicated normal BMD. Data from the anthropometric measurements, laboratory results, and DXA were analyzed. Patients were evaluated in three age-related groups and three ferritin-level-related groups to evaluate the effects of age and ferritin levels on these parameters.

Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences version 17.0. The variable compliance to normal distribution was examined using histogram graphics and the Kolmogorov-Smirnov test. Mean, standard deviation, and median values were used for descriptive analyzes. Categorical variables were compared using the Pearson chi-square

test. The Mann-Whitney U test was used to evaluate nonparametric variables between the two groups, and the Kruskal-Wallis test was used when evaluating more than two groups. The Spearman correlation test was used to analyze the measurement data with each other. A p-value of <0.05 was considered statistically significant.

RESULTS

This study included 29 patients aged 2.33-18 (mean 12.26 ± 4.74) years, wherein 18 (62%) were male and 11 (38%) were female. The mean pre-transfusion hemoglobin level was 8.64 ± 1.01 g/dL (range: 5.8-10.6 g/dL). The mean serum ferritin was 1158.6 ± 556.8 ng/mL (range: 363-2,842). No significant difference was found between sex and ferritin concentration ($p > 0.05$). Vitamin D (72.4%), selenium (72.4%), and folate (37.9%) deficiencies were most frequent. Hypocalcemia was determined in 17.2%, hypomagnesemia in 3.5%, and decreased ceruloplasmin in 10.3 %. The prevalence of micronutrient deficiencies and biochemical and endocrine disturbances are shown in Table 1. None of our patients was overweight but 20.7% (7 patients) were with low weight. Height of >97 p and BMI >95 p was also not observed. The anthropometric measurements of patients are shown in Table 2. Anthropometric percentiles did not significantly differ in terms of mean serum ferritin concentration. Ferritin levels according to Anthropometrics are summarized in Table 3. Patient data were compared by dividing them into groups according to both age and serum ferritin levels. Accordingly, patients were divided into three age groups: 2-6, 6-10, and 10-18 years. Three (10.3%) patients were in the 2-6-year-old group; 7 (24.1%) in the 6-10-year-old group; 19 (65.5%) in the 10-18-year-old group. The comparison of results in the age-related groups is summarized in Table 4. A comparison between the age-related groups showed significantly higher folate levels in the 2-6-year-old group ($p = 0.028$) and higher ceruloplasmin level in the 6-10-year-old ($p = 0.018$) compared to the other groups.

BMI of patients 10-18 years old was significantly higher ($p = 0.001$). No significant differences were observed in the distribution of height, weight and BMI percentiles between age-related groups ($p > 0.05$, $p > 0.05$, and $p > 0.05$, respectively), as well as the mean serum ferritin level between age-related groups ($p > 0.05$).

Patients were divided into three groups according to their serum ferritin levels and their data were compared. The mean selenium level was significantly higher in patients with a ferritin of $\geq 1,500$ (66.6 ± 23.9 ug/L) than in

the group with 1,000-1,500 (40.1 ± 8.9 ug/L) ($p = 0.008$). A weak positive significant positive relationship was found between serum ferritin and vitamin C ($p = 0.035$, $r = 0.392$), whereas no significant ferritin-related differences in other nutrients ($p > 0.05$). A comparison of results in ferritin-related groups is summarized in Table 5. A low BMD was determined in 4 patients, osteopenia in 2, and osteoporosis in 2. No significant difference was found between genders in terms of DXA results ($p > 0.05$).

Table 1. The prevalence of clinical and laboratory disorders in patients with thalassemia major.

	Number of patients (n)	Frequency (%)
Anthropometrics		
Height of <3 p	7	24.1
Weight of <3 p	6	20.7
Weight of >97 p	0	0
BMI of <5 p	9	31.1
BMI of >95 p	0	0
Micronutrient deficiency/insufficiency: Vitamin B12	3	10.3
Vitamin C	3	10.3
Vitamin D	21	72.4
Vitamin E	1	3.5
Folate	11	37.9
Copper	1	3.5
Selenium	21	72.4
Zinc	2	6.9
Biochemical disorders		
Hypocalcemia	5	17.2
Hypophosphatemia	0	0
Hypomagnesemia	1	3.5
Increased ALP		
Hypoalbuminemia	0	0
Hypoproteinemia	0	0
Decreased ceruloplasmin	3	10.3
Increased HbA1c	18	62.1
Hyperglycemia	5	17.2
Endocrine disorders		
Hypoparathyroidism	4	13.8
Hypothyroidism	1	3.5
Hyperinsulinemia	1	3.5
Bone mineralization defects		
Osteopenia	2	7.4
Osteoporosis	2	7.4

BMI: Body mass index, ALP: Alkaline phosphatase

BMD did not significantly differ in terms of mean serum ferritin concentration and mean serum micronutrient levels ($p>0.05$). Characteristics, micronutrient levels, and comparison of patients according to DXA results are summarized in Table 6.

DISCUSSION

A significant prolongation was achieved with regular erythrocyte suspension transfusion and chelation therapy in patients with TM; however, complications due to iron accumulation in tissues still maintain their importance^{1,5,6}. Bone mineralization disorders, growth failure, and endocrinopathies are common complications associated

with an iron overload⁵⁻⁷. Chronic hypoxia due to anemia, chelation therapy side effects, low zinc levels, and endocrinopathies are some of the leading factors for short stature and growth failure^{8,9}. A significant proportion of short stature was observed, of which 24.1% of patients have <3% height but without a significant relationship between height and ferritin or other micronutrient elements. A previous study revealed that 49% of patients had short stature and 43% had low BMI¹⁰. Similarly, Hashemi's study revealed a 65.7% short stature¹¹. Contrary to ours, some prior reports revealed no significant differences between patients with thalassemia and control groups in terms of growth¹². In terms of body weight, 20.7% of our patients were <3 p. The BMI of 31% of patients was <5 p, between 5 and 50 p in 55.2% of patients, and between 50 and 95 p in 13.8% of patients, which are similar to previous studies. Hashemi et al.'s¹¹ study revealed that 45.1% of patients had low weight, whereas 18.6% had low BMI. Napoli et al.¹⁰ reported a decreased BMI at a rate of 47%. Hamed and El-Melegy¹² and Vogiatzi et al.⁷ revealed that height and BMI in thalassemic children are not different from control groups, unlike our results. Cunningham et al.'s¹³ study revealed the endocrinological complication in 48% of patients with TM between the ages of 16 and 24 years and reached 52% after 25 years. Our study revealed no significant difference between age-related groups in terms of growth and endocrine disorders. Osteopenia and osteoporosis can develop despite regular treatment^{5,6,8}. The most important way to prevent osteoporosis is the prevention of iron overload with effective chelation therapy. Contrarily, no significant relationship was determined between DXA and ferritin values, which we relate to the small number of our patients. The study conducted by Casale et al.¹⁴ revealed a 44.9% rate of osteoporosis, which decreased to 26.5% at the end of the

Table 2. The anthropometric measurements of the patients.

		n	%
Height	<3 p	7	24.1
	3-50 p	11	37.9
	50-97 p	11	37.9
	>97 p	0	0
Weight	<3 p	6	20.7
	3-50 p	19	65.5
	50-97 p	4	13.8
	>97 p	0	0
BMI	<5 p	9	31.01
	5-50 p	16	55.2
	50-95 p	4	13.8
	>95 p	0	0

BMI: Body mass index

Table 3. Ferritin levels according to anthropometrics.

Ferritin (ng/mL)				
		Mean $\pm$ SD	Range	p-values
Height	<3 p	1095.0 $\pm$ 540.9	475.0-2222.0	0.479
	3-50 p	1022.7 $\pm$ 449.2	363.0-1728.0	
	50-97 p	1335.0 $\pm$ 658.4	584.0-2842.0	
Weight	<3 p	984.2 $\pm$ 339.6	475.0-1510.0	0.147
	3-50 p	1136.2 $\pm$ 624.5	363.0-2842.0	
	50-97 p	1526.8 $\pm$ 341.9	1167.0-1988.0	
BMI	<5 p	1044.7 $\pm$ 536.2	554.0-2222.0	0.553
	5-50 p	1204.8 $\pm$ 567.6	475.0-2842.0	
	50-95 p	1230.5 $\pm$ 677.4	363.0-1988.0	

Kruskal-Wallis test, BMI: Body mass index, SD: Standard deviation

Table 4. Comparison of the age-related groups for the results.

	2-6 years mean $\pm$ SD	6-10 years mean $\pm$ SD	10-18 years mean $\pm$ SD	p-value
Ferritin	671.43 $\pm$ 320.29	1037.28 $\pm$ 676.92	1173.39 $\pm$ 550.77	0.326
Vitamin B12	472.0 $\pm$ 97.1	324.4 $\pm$ 133.4	376.7 $\pm$ 227.9	0.287
Vitamin C	23.8 $\pm$ 25.3	17.8 $\pm$ 9.4	10.66 $\pm$ 6.8	0.231
Vitamin E	0.7 $\pm$ 0.2	0.5 $\pm$ 0.1	0.6 $\pm$ 0.2	0.440
Vitamin D	20.0 $\pm$ 3.6	13.9 $\pm$ 5.9	13.3 $\pm$ 7.1	0.200
Folate	17.0 $\pm$ 0.9	8.1 $\pm$ 8.4	3.5 $\pm$ 2.5	0.028
Zinc	73.33 $\pm$ 11.9	77.3 $\pm$ 10.4	86.9 $\pm$ 15.6	0.140
Copper	68.7 $\pm$ 49.1	90.7 $\pm$ 17.7	72.0 $\pm$ 19.9	0.091
Selenium	55.2 $\pm$ 19.1	51.5 $\pm$ 18.7	54.4 $\pm$ 20.5	0.921
Ceruloplasmin	29.3 $\pm$ 3.2	31.0 $\pm$ 4.4	24.6 $\pm$ 8.8	0.018
Albumin	4.6 $\pm$ 0.6	4.4 $\pm$ 0.2	4.5 $\pm$ 0.3	0.284
Total protein	6.8 $\pm$ 0.9	6.9 $\pm$ 0.2	7.2 $\pm$ 0.6	0.235
Calcium	9.8 $\pm$ 0.9	9.3 $\pm$ 0.5	9.3 $\pm$ 0.6	0.492
Phosphorus	5.7 $\pm$ 1.1	4.6 $\pm$ 0.5	4.3 $\pm$ 0.7	0.051
Magnesium	2.1 $\pm$ 0.3	1.9 $\pm$ 0.12	1.9 $\pm$ 0.2	0.897
ALP (IU/L)	170.0 $\pm$ 43.9	143.9 $\pm$ 49.5	170.6 $\pm$ 104.1	0.808
TSH	2.9 $\pm$ 1.8	2.21 $\pm$ 0.52	2.1 $\pm$ 0.7	0.534
T4	1.0 $\pm$ 0.1	1.1 $\pm$ 0.1	1.0 $\pm$ 0.1	0.076
Glucose (mg/dL)	88.42 $\pm$ 5.72	91.42 $\pm$ 6.72	89.8 $\pm$ 6.48	0.771
HbA1c	6.12 $\pm$ 1.7	6.19 $\pm$ 1.66	6.23 $\pm$ 1.28	0.77
Insulin	3.9 $\pm$ 3.7	7.5 $\pm$ 5.9	8.6 $\pm$ 5.8	0.173
PTH (pg/mL)	28.6 $\pm$ 4.0	22.9 $\pm$ 5.2	30.2 $\pm$ 11.5	0.168
Kruskal-Wallis test, ALP: Alkaline phosphatase, TSH: Thyroid-stimulating hormone, PTH: Parathyroid hormone, SD: Standard deviation				

3-year follow-up period by making chelation treatments more effective¹⁴. Our study revealed that 6.9% of patients have osteopenia and 6.9% have osteoporosis. Vitamin D deficiency frequency was 72.41% and was similar to prior studies, which have reported as 54%, 69.8%, and 90%^{10,15,16}. Vitamin D deficiency is thought to be related to hepatic dysfunction and defective vitamin D hydroxylation due to iron overload¹⁷. No significant relationship or correlation was determined between vitamin D and ferritin. Yu et al.'s¹⁶ study revealed normal vitamin D levels in patients <5 years and that the deficiency progressively increased with age. Our study revealed no significant difference between the age groups. Bone metabolism defects have been demonstrated in many studies; however, their cause remains controversial¹⁵⁻¹⁷. The risk of developing endocrine disorders increases as ferritin increases¹⁶⁻¹⁹. The study conducted by Casale et al.¹⁴ revealed hypoparathyroidism in 2.3% of patients. Our study revealed hypoparathyroidism in 13.8% of patients, without a significant relationship or correlation between ferritin and PTH levels. Additionally,

no age-related difference was found. The most commonly used method for nutritional status evaluation of patients is the serum levels of minerals and vitamins. Increased loss, increased needs for micronutrients, and calcium deficiencies are common in TM due to poor dietary intake. Particularly, minerals, such as zinc, calcium, and albumin, with some transport proteins are excreted in the urine^{2,8}. The study conducted by Goldberg et al.² revealed that 40% of patients who were adequately fed were found to have low zinc, 20% copper, and 20% vitamin C. The increased iron load in the body in TM leads to the rapid oxidation of vitamin C, which ultimately leads to vitamin C deficiency in these patients. Our study revealed a weak positive correlation between vitamin C and ferritin levels in our patients ($p=0.035$).

Selenium deficiency was observed in 72.4% of patients and constitutes a very high rate. Calcium, magnesium, and other nutrient deficiencies were at lower rates and were similar to the literature²⁰. No significant relationship

Table 5. Comparison of the ferritin-related groups for the results.

	<1,000 ug/L mean ± SD	1,000-1,500 ug/L mean ± SD	≥1,500 ug/L mean ± SD	p-value
Age (years)	13.38±4.15	11.25±4.01	10.97±6.07	0.290
Vitamin B12 (pg/mL)	388.67±221.97	384.89±234.00	339.50±127.07	0.958
Vitamin C (mg/L)	11.73±13.47	13.81±7.85	16.42±9.30	0.137
Vitamin D (ng/mL)	15.68±6.92	11.89±5.51	14.39±7.68	0.463
Vitamin E (mg/dL)	0.56±0.19	0.56±0.20	0.63±0.23	0.716
Folat (ng/mL)	4.48±4.03	6.84±7.67	7.44±7.01	1.000
Zinc (ug/L)	87.17±18.82	81.33±13.71	79.25±7.48	0.657
Copper (ug/dL)	76.25±25.15	79.22±17.63	72.63±29.82	0.912
Selenium (ug/L)	55.45±15.90	40.13±8.99	66.57±23.86	0.008
Ceruloplasmin (mg/dL)	27.43±9.59	27.22±5.63	24.75±8.14	0.954
Albumin (g/L)	4.39±0.30	4.46±0.22	4.60±0.36	0.481
Total protein (g/L)	7.08±0.51	6.93±0.45	7.29±0.74	0.692
Ca (mg/dL)	9.27±0.51	9.30±0.68	9.55±0.49	0.475
P (mg/dL)	4.33±0.82	4.50±0.53	4.82±1.03	0.594
Mg (mg/dL)	1.94±0.19	1.99±0.18	1.98±0.21	0.851
ALP (iu/L)	188.33±116.78	163.33±59.30	128.63±56.20	0.400
TSH (uIU/mL)	2.26±0.74	1.82±0.47	2.65±1.06	0.055
T4 (ng/mL)	1.00±0.14	1.05±0.12	0.94±0.09	0.147
PTH (pg/mL)	31.91±10.47	25.63±10.12	25.66±8.70	0.267
Glukoz (mg/dL)	90.50±7.55	87.67±6.04	89.00±2.98	0.744
Insulin (uIU/mL)	8.54±6.43	7.17±6.05	7.45±4.56	0.801
HbA1c	5.82±1.30	6.47±1.22	6.25±1.32	0.344

Kruskal-Wallis test, Ca: Calcium, P: Phosphorus, Mg: Magnesium, ALP: Alkaline phosphatase, TSH: Thyroid-stimulating hormone, PTH: Parathyroid hormone, SD: Standard deviation

Table 6. Characteristics, micronutrient levels, and comparison of patients according to DXA results.

	Normal n-22 F: 9, M: 13	Osteopenia n-2 F: 1, M: 1	Osteoporosis n-2 F: 0, M: 2	p-value
Ferritin (ng/mL)	1149.92±587.62	1233.00±391.74	1193.00±475.18	0.905
Age (year)	12.74±4.24	10.50±9.19	7.96±7.95	0.523
Vitamin B12 (pg/mL)	373.68±208.12	418.00±229.10	333.00±83.44	0.926
Vitamin C (mg/lt)	14.41±11.28	10.75±4.60	7.30±3.25	0.657
Vitamin D (ng/mL)	14.29±6.63	13.55±13.36	12.95±4.31	0.980
Vitamin E (mg/dL)	0.57±0.21	0.60±0.21	0.61±0.13	0.813
Folate (ng/mL)	5.37±5.64	10.05±11.24	10.30±8.63	0.471
Zinc (ug/L)	81.40±13.96	93.00±14.14	95.50±26.16	0.356
Copper (ug/dL)	79.84±20.94	31.00±25.46	75.50±16.26	0.067
Selenium(ug/L)	53.29±20.23	61.02±21.76	52.35±3.75	0.705
Ca (mg/dL)	9.26±0.50	9.75±1.06	10.10±0.00	0.101
P (mg/dL)	4.37±0.68	5.70±1.27	5.25±1.06	0.136
Mg (mg/dL)	1.96±0.18	2.10±0.44	1.93±0.08	0.911

Kruskal-Wallis test, Ca: Calcium, P: Phosphorus, Mg: Magnesium, DXA: Dual-energy X-ray absorptiometry

or correlation was found between ferritin and nutrients in our results although increased iron accumulation plays an important role among the reasons for deficiencies, especially for vitamin C, E, and zinc levels in patients with an adequate nutritional history. Studies are yet to find the vitamin E needs in children with TM. Therefore, its routine use is not recommended. Patients with thalassemia do not have to follow a specific diet; however, they should have a balanced diet since nutritional deficiencies are closely associated with growth retardation and puberty delay²¹. Hypoproteinemia and hypoalbuminemia were not detected in any of our patients, and no significant correlation was found with ferritin levels but ceruloplasmin was under normal limits in 10.3% of patients. Food containing normal levels of fat and sugar is necessary to provide energy needs, especially for patients in the growing period; however, refined carbohydrates are not recommended to prevent the tendency of diabetes and glucose intolerance in adolescents^{2,8}, which are particularly closely related to high iron accumulation in patients with thalassemia. Regular and effective chelation therapy can improve glucose tolerance, especially in the early period and control blood sugar and insulin release^{8,22}. Our study revealed that the high fasting blood glucose ratio was 3.5% and the high insulin level ratio was also 3.5%. HbA1c is known as an unreliable diabetic index in thalassemia due to hemolysis and transfusions, thus our high rate of HbA1c is explained¹. Folate need increases with increased erythropoiesis, especially in patients who are infrequently transfused. Folate deficiency was observed at a high rate and was thought to be associated with supplementation compliance. Abnormal thyroid functions are often reversible with effective chelation^{8,23,24}. The rate of hypothyroidism in TM was 19.8% in the study conducted by Casale et al.¹⁴ and 10.8% in a multi-center study from Italy²⁵. Our rate was smaller than these reports and without a significant relationship with ferritin.

CONCLUSIONS

Our study highlights the importance of nutritional deficiencies in children with thalassemia. Despite regular transfusion and effective chelation treatment, short stature, endocrinological disorders, osteoporosis, vitamin D, and other nutritional deficiencies are common in these patients. Ensuring that they receive nutritional support when necessary is important. Preventing these complications and nutritional deficiencies and increasing the life expectancy and quality of patients is necessary. The small sample of our patients may affect this study, which needs to be further investigated in larger groups.

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Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Turkey, Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee (decision no: 2019/0267, date: 22.05.2019).

Informed Consent: Written informed consent was obtained from the parents.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Concept: S.C.B., A.C.A., H.C.E., F.O., Design: S.C.B., A.C.A., H.C.E., F.O., Data Collection and/or Processing: S.C.B., A.C.A., H.C.E., F.O., Analysis and/or Interpretation: S.C.B., A.C.A., H.C.E., F.O., Critical Revision: S.C.B., A.C.A., H.C.E., F.O., Writing: S.C.B., A.C.A., H.C.E., F.O.

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