ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Cross-sectional Assessment of Physical Manifestations in Vietnamese Children with Thalassemia: A Single-Center Study

Talasemili Vietnamlı Çocuklarda Fiziksel Belirtilerin Kesitsel Değerlendirilmesi: Tek Merkezli Bir Çalışma

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Abstract

Introduction: This cross-sectional study intends to analyze the physical growth of children thalassemia patients and evaluate the factors linked to their physical features.

Materials and methods: This cross-sectional study tracked 44 pediatric thalassemia patients at a Central Vietnam Tertiary Pediatric Center from February to December 2023.

Results: The study participants had a mean age of 7.5 ± 4.3 years and an equal gender distribution. 64.5% of these individuals had thalassemia and required blood transfusions. 43.2% of subjects had serum ferritin levels above 1000 ng/ml, and the average hemoglobin content was 67.4 ± 16.1 g/L 31.8% of the children assessed had height-for-age measurements below -2 standard deviations, while 43.2% had weight-for-age measurements below -2 standard deviations. Significant correlations were found between height-for-age, weight-for-age, blood transfusion reliance, and serum ferritin levels ($p < 0.05$). No significant changes were seen between physical indices and disease type or hemoglobin concentration ($p > 0.05$). 31.8% of juvenile thalassemia patients were found to have stunting, whereas 43.2% exhibited wasting malnutrition in this study.

Conclusion: Blood transfusion reliance and serum ferritin concentration were found to be linked to a higher occurrence of stunting and wasting malnutrition in children with thalassemia

Keywords
Child, growth, beta-Thalassemia, alpha-Thalassemia

Öz

Giriş: Çalışmanın amacı, talasemili hastası çocukların fiziksel büyümesini analiz etmek ve fiziksel özellikleriyle ilişkili faktörleri değerlendirmektir.

Yöntem Ve Gereçler: Bu çalışmada Şubat-Aralık 2023 tarihleri arasında Orta Vietnam'daki Üçüncü Basamak Çocuk Sağlığı Merkezinde 44 talasemili çocuk hasta çapraz kesitsel olarak takip edildi.

Bulgular: Çalışmaya katılanların ortalama yaşı 7,5 ± 4,3 yıl olup cinsiyet dağılımları eşitti. Bu bireylerin %64,5'i talasemi hastasıydı ve kan transfüzyonuna ihtiyaç duyuyordu. Deneklerin %43,2'sinde serum ferritin düzeyleri 1000 ng/ml'nin üzerindeydi ve ortalama hemoglobin içeriği 67,4 ± 16,1 g/L idi. Değerlendirilen çocukların %31,8'inin boy/yaş ölçümleri -2 standart sapmanın altında, %43,2'sinin ise ağırlık/yaş ölçümleri -2 standart sapmanın altındaydı. Boy/yaş, ağırlık/yaş, kan transfüzyonuna bağımlılık ve serum ferritin düzeyleri arasında anlamlı korelasyonlar bulundu ($p < 0,05$). Fiziksel indeksler ile hastalık tipi veya hemoglobin konsantrasyonu arasında anlamlı bir değişiklik gözlenlenmedi ($p > 0,05$). Bu çalışmada juvenil talasemi hastalarının %31,8'inde bodurluk, %43,2'sinde ise israf hali malnutrition olduğu görüldü.

Anahtar kelimeler
Çocuk, büyüme, beta-Talasemi, alfa-Talasemi

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Sonuç: Kan transfüzyonuna bağımlılık ve serum ferritin düzeyinin, talasemili çocuklarda bodurluk ve israf hali malnutrisyonunun daha sık görülmesiyle ilişkili olduğu bulundu.

Introduction

Thalassemia is a group of inherited hemolytic blood disorders. It is one of the most common genetic diseases in the world. Thalassemia has a wide range of clinical presentations, from asymptomatic to severe cases requiring regular blood transfusions, which can lead to iron overload (1).

Children with thalassemia experience growth retardation due to several reasons such as chronic anemia, iron overload from blood transfusions, splenomegaly, and toxicity from iron chelation (2). Other factors that may also play a role include hypothyroidism, hypogonadism, growth hormone deficiency, zinc deficiency, chronic liver disease, malnutrition, and psychosocial stress (3,4).

The aforementioned consequences demonstrate that thalassemia is a societal problem, profoundly affecting patients, families, communities, and posing a social burden. Therefore, we conducted this study to analyze the physical growth of children thalassemia patients and evaluate the factors linked to their physical features.

Material and Methods

Study subjects

44 pediatric patients with thalassemia were included in this cross-sectional study, and they were monitored at a Tertiary Pediatric Center in Central Vietnam from February to December 2023.

The study group was classified into α-thalassemia and **β**-thalassemia groups based on the results of hemoglobin electrophoresis. The transfusion-dependent and non-transfusion-dependent types were classified according to the criteria of the International Thalassemia Federation (2), (5). In addition, patients were also classified into three groups based on hemoglobin concentration: Hb < 60 g/dL, 60 to < 90 g/dL, and ≥ 90 g/dL. Ferritin concentration was used to classify patients into two groups: ferritin ≤1000 ng/ml and >1000 ng/ml.

Assessment of physical parameters

A comprehensive clinical assessment was carried out during the exam. Height was measured using a stadiometer with an accuracy of 0.1 cm, while weight was measured using a minimal clothes scale with an accuracy of 0.1 kg.

The z-score of an observed value was calculated using the following formula:

$$z\text{-score} = [(\text{observed value} \div M)^{L} - 1]/L \times S.$$

M, L, and S denote the values of the reference population in this formula. The reference median, denoted as M, is an estimate of the population mean. L represents the power needed to standardize the data by removing skewness. The coefficient of variation is represented by S (or equivalent). Body mass index (BMI) for age, height for age, and weight for age Z-scores were calculated using the LMS methodology. The LMS values for age and sex were extracted from the World Health Organization's (WHO) 2007 growth reference enlarged tables and inputted into a data spreadsheet. The z-score formula was developed and used to calculate z-scores for each patient's parameters. Z-scores were used for multiple comparisons and statistical testing (6).

Statistical Analysis

The data was inputted, processed, and examined using SPSS Statistics 27 and Excel 2019. This study employed the Chi-square test and the t-test, revealing a statistically significant difference at a significance level of $p < 0.05$.

Results

Our study of 44 children with thalassemia found that the average age of children with Thalassemia was 7.5 ± 4.3 years. The age group 6-10 years old had the highest proportion (43.2%). The male/female ratio in the study was approximately 1/1, and the Kinh ethnic group accounted for the majority (95.5%). The proportion of cases with no family history was the highest (72.7%). β-thalassemia was the most common type, accounting for 63.6%, while α-thalassemia was found in 36.4% of children. The majority of children started blood transfusions before the age of 1 year. Almost all children will be treated with early blood transfusions after being diagnosed with the disease.

Clinical features

Pallor of the mucous membranes was the most common clinical feature, with a prevalence of 80.6%. Subsequently, symptoms included paleness of the palms (74.2%), paleness of the skin (67.7%), jaundice (38.7%), yellowing of the sclerae (48.4%), and increased pigmentation (38.7%). Craniofacial deformities were also common, with a prevalence of 45.2% for flat nose, 29% for prognathism, and 25.8% for parietal bossing. Hepatomegaly was present in 41.9% of patients, with grade IV splenomegaly being the most common (19.4%). The prevalence of hepatomegaly was 38.7%.

Of the 44 children studied, 29 were transfusion-dependent. The transfusion-dependent group was predominant in both α-thalassemia and β-thalassemia.

Paraclinical features

Most patients exhibited reduced levels of red blood cell (RBC) count, hemoglobin, mean corpuscular volume, and mean corpuscular hemoglobin. White blood cell count and platelet count were normal in the majority of individuals. The mean RBC count was 3.3 ± 1.3 T/L. The mean hemoglobin concentration was 65.3 ± 16.8 g/L. The proportion of patients with elevated serum ferritin was 71%, of which 48.8% had ferritin levels >1000 ng/ml.

Physical features

31.8% of children with thalassemia had height-for-age z-scores < -2SD, while 61.4% had normal height (-2SD < z-score < 2SD). 43.2% of children with thalassemia had weight-for-age z-scores < -2SD, and 9% had BMI-for-age z-scores < -2SD. The distribution of physical characteristics is shown in Table 1.

The relationship between physical indices and disease type is shown in Table 1. Children with α-thalassemia had lower height-for-age than children with β-thalassemia ($p < 0.05$). There was no difference in weight-for-age or BMI-for-age between the two disease types.

The relationship between physical indices and transfusion dependence is shown in Table 2. There was a relationship between height-for-age and weight-for-age and transfusion dependence. There was no relationship between BMI-for-age and transfusion dependence.

There was no relationship between physical characteristics and hemoglobin concentration ($p>0.05$).

There was a relationship between height-for-age, weight-for-age, and serum ferritin concentration, as shown in Table 3. Children with low height-for-age and weight-for-age had a higher proportion of serum ferritin levels >1000 ng/ml than children with normal height-for-age and weight-for-age. There was no relationship between BMI-for-age and serum ferritin concentration.

Discussion

Our study found that 31.8% of 44 children with thalassemia had height-for-age z-scores < -2SD, 43.2% had weight-for-age z-scores < -2SD, and 9% had BMI-for-age z-scores < -2SD.

Table 1. The relationship between physical features and disease phenotype

Physical features		All (n=44)		α-thalassemia (n=16)		β-thalassemia (n=28)		p-value
		n	(%)	n	(%)	n	(%)	
Height for age	< -2SD	14	31.8	6	37.5	8	28.6	<0.05
	-2SD ≤ Z-score ≤ 2SD	27	61.4	7	43.8	20	71.4	
	> 2SD	3	6.8	3	18.8	0	0.0	
Weight for age	< -2SD	19	43.2	7	43.8	12	42.9	>0.05
	-2SD ≤ Z-score ≤ 2SD	23	52.3	7	43.8	16	57.1	
	> 2SD	2	4.5	2	12.5	0	0.0	
BMI for age	< -2SD	4	9.1	3	18.8	1	3.6	>0.05
	-2SD ≤ Z-score ≤ 2SD	39	88.6	13	81.3	26	92.9	
	> 2SD	1	2.3	0	0.0	1	3.6	

SD: Standard Deviation; BMI: Body Mass Index

The Pamir Isik study reported a mean patient height SDS of -1.2 ± 1.34 (range: -4.64, 1.41), with 12 patients (25.5%) having a height below -2 SDS. The mean patient weight SDS was -1.07 ± 1.27 (range: -4.3, 1.32), with 11 participants (23.4%) having a weight below -2 SDS (4).

Our results are an improvement over previous studies, such as that of Dhouib et al. (7), which found that 57% of children had stunting.

In thalassemia, chronic anemia and iron overload can affect multiple organs, particularly the pituitary and endocrine glands. This can also reduce the absorption of nutrients and metabolism, leading to stunting, malnutrition, and low weight for age in children (4).

The majority of children in the study had a typical BMI for their age, indicating that thalassemia is a persistent condition that impacts both weight and height, resulting in a generally normal BMI. Children suffering from chronic malnutrition experience stunted growth.

According to our research results presented in Tables 2, 3, 4, and 5, the disease phenotype and hemoglobin concentration had little effect on height and weight. On the other hand, the degree of transfusion dependence and serum ferritin concentration were factors that increased the prevalence of undernutrition, stunting, and underweight in children with thalassemia.

A study by Harish Pemde et al. (8) of 154 patients with thalassemia also found no correlation between pre-transfusion hemoglobin level and physical characteristics, with $p > 0.05$.

Table 2: The relationship between physical features and transfusion dependence

Physical features		Transfusion-dependent (n=29)		Non-transfusion-dependent (n=15)		p-value
		n	(%)	n	(%)	
Height for age	< -2SD	13	44.8	1	6.7	*<0.05*
	-2SD ≤ Z-score ≤ 2SD	15	51.8	12	80.0	
	> 2SD	1	3.4	2	13.3	
Weight for age	< -2SD	17	58.6	2	13.3	*<0.05*
	-2SD ≤ Z-score ≤ 2SD	12	41.4	11	73.4	
	> 2SD	0	0.0	2	13.3	
BMI for age	< -2SD	2	6.9	2	13.3	*>0.05*
	-2SD ≤ Z-score ≤ 2SD	26	89.7	13	86.7	
	> 2SD	1	3.4	0	0.0	

SD: Standard Deviation; BMI: Body Mass Index

Table 3. The relationship between physical features and serum ferritin level

Physical features		Ferritin (ng/ml)				p- value
		≤1000		>1000		
		n	(%)	n	(%)	
Height for age	< -2SD	4	16.0	10	52.6	*<0.05*
	-2SD ≤ Z-score ≤ 2SD	18	72.0	9	47.4	
	> 2SD	3	12.0	0	0.0	
Weight for age	< -2SD	6	24.0	13	68.4	*<0.05*
	-2SD ≤ Z-score ≤ 2SD	17	68.0	6	31.6	
	> 2SD	2	8.0	0	0.0	
BMI for age	< -2SD	3	12.0	1	5.3	*>0.05*
	-2SD ≤ Z-score ≤ 2SD	22	88.0	17	89.4	
	> 2SD	0	0.0	1	5.3	

SD: Standard Deviation; BMI: Body Mass Index

Elalfy et al. (9) found that children with transfusion-dependent thalassemia had significantly lower average anthropometric measurements (weight, height, mid-upper arm circumference, skinfold thickness, and BMI) compared to those without, with a p-value of less than 0.001.

A study by Fung et al. (10) found that the proportion of patients with BMI < 5th percentile was lower in transfusion-dependent children (7.8%) than in non-transfusion-dependent children (11.8%)**.** A study by Elalfy et al. (9) also found that there was a correlation between BMI and transfusion status, with $p < 0.01$, and that children who were transfusion-dependent had lower mean BMI values.

A study by Hashemi et al. (3) found that mean serum ferritin levels were lower in children with height above the 5th percentile than in children with height below the 5th percentile. The study also found that mean serum ferritin levels were lower in children with weight above the 5th percentile than in children with weight below the 5th percentile. A study by Pemde et al. (8) also found a correlation between height and serum ferritin level, with higher mean serum ferritin levels in patients with short stature compared to patients with normal height.

Conclusion

In the thalassemia study group, the prevalence of stunting and underweight was 31.8% and 43.2%, respectively. Stunting and underweight were more common in children with thalassemia depending on serum ferritin levels and the degree of transfusion dependence.

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Ethics

Ethics Committee Approval: The study was initiated after obtaining approval from the Hue University of Medicine and Pharmacy Ethics Committee (18.01.2022 decision no: 57/NCKH-DHY). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of Interest: No conflict of interest was declared by the authors.

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