Zinc and iron levels in children with idiopathic short stature

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Background and aim

Short stature is a common problem in children globally, especially in developing countries. Several micronutrients, primarily zinc and iron, play important roles in linear growth, and their deficiencies result in stunting. The aim of this study was to assess the levels of zinc and iron in children with idiopathic short stature.

Patients and methods

A case–control study was conducted on 50 children, aged 2–15 years old, comprising 25 cases of idiopathic short stature (16 males and nine females) and 25 age-matched and sex-matched individuals as a control group. Patients were classified as having mild to moderate or severe short stature. All children were subjected to history taking, physical examination, and laboratory investigations, including complete blood count, urine analysis, stool analysis, and serum levels of zinc and iron.

Results

Mean hemoglobin concentration was significantly lower among cases when compared with control group (10.98 ± 1.2 vs 12.16 ± 0.96). Serum iron was lower in cases than control group, with insignificant difference (98.19 ± 34.7 vs 107.46 ± 46.23). According to zinc level, there is no significant difference between both groups (328.25 ± 280.95 vs 404.86 ± 411.02).

Keywords:

hemoglobin concentration, idiopathic short stature, serum iron, serum zinc

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Introduction

Short stature refers to a child whose height is 2 SD or more below the mean for children of that sex and chronologic age [1]. Most children with short stature are owing to variations of normal growth (99%), with 23% of them with familial short stature, 41% with constitutional delay of growth and maturation, and 36% with idiopathic short stature diagnosed after exclusion of endocrinal, metabolic, or other etiologies [2].

Short stature is common in developing countries and has been used as an indicator of a nation's general health condition. Nutritional factors that frequently cause stunting are low intake of protein or micronutrients such as iron, vitamin A, and zinc [3].

Essential trace elements are detected in small but not precisely known amounts in the living body of the human, such as zinc and iron, which account for only 0.02% of the total body weight [4].

Zinc is an essential trace element that is naturally present in some foods. More than 300 metalloenzymes require zinc as a catalyst as well as it plays a role in immune function, protein synthesis wound healing, DNA synthesis, and cell division [3]. It supports normal growth and development during pregnancy, childhood, and adolescence. A daily intake of zinc is required to maintain a steady state because the body has no specialized zinc storage system [5].

Zinc deficiency leads to anorexia and affects DNA and RNA synthesis, as well as replication of chondrocytes and osteoblasts [3]. It also affects growth hormone metabolism. It influences the growth hormone and insulin-like growth factor I systems that affects bone metabolism [6].

Iron is found in all living cells. Iron exists in two oxidation states, either ferrous form or ferric form. It has numerous vital roles in immune function, neurological function, cognitive development, and energy metabolism. Iron deficiency is one of the most common nutrition disorders, affecting large proportion of children and women in the developing world. [7]. Iron deficiency when growth is fast adversely affects both linear growth and weight gain [8]. It affects growth through insulin-like growth factor I-dependent mechanism. Children with iron deficiency anemia were shorter with markedly slower growth velocity [9]. Body growth, especially during infancy, requires relatively high energy supply and metabolism. Cellular energy metabolism is dependent on oxygen. Fe deficiency decreases oxygen-dependent cellular energy metabolism owing to decreased hemoglobin (Hb) synthesis and decreased red blood cells synthesis; consequently, iron deficiency leads to impaired cognitive abilities and defective linear growth [10].

Aim

The aim was to assess the level of zinc and iron in children with idiopathic short stature.

Patients and methods

This study was conducted on 50 children (25 were cases and 25 were control), aged 2–15 years old, comprising 25 cases of idiopathic short stature that presented to the endocrinology clinic at Assiut University Children Hospital complaining of short stature, and another 25 age-matched and sex-matched healthy children from their relatives, who were included as a control group.

Inclusion criteria

The inclusion criteria were as follows:
(1) Children of both sexes.
(2) Age 2–15 years.
(3) Initial height below the third percentile on Egyptian growth chart.

Exclusion criteria

The exclusion criteria were as follows:
(1) Skeletal dysplasias.
(2) Chromosomal diseases.
(3) Chronic diseases.

All cases and controls are subjected to full history taking, including family; socioeconomic status (seven items were assessed to categorize socioeconomic state into low, moderate and high; these items were mother's education, father's education, family income, family size, water supply, refuse disposal, and sewage disposal) [11]; history of taking food containing zinc such as chicken, dark meat, cereals, yogurt, milk, and peas [12]; history of taking food containing iron meat, green vegetables, liver, broccoli, lentils, and beans [13]; history of chronic diseases; and history of recurrent infections. They were also subjected to physical examination, including thyroid examination, signs of chronic diseases (chronic heart, pulmonary, endocrinal, hematological, and renal diseases), and dysmorphic features to exclude other causes of short stature. Moreover, we performed anthropometric measurements: weight (kg) was measured using scale to the nearest 100 g, height (cm) was measured using fixing stadiometer where subject was standing in erect position looking straight forward with his/her heels and back touching the wall. Weight and height were plotted to the age-appropriate and sex-appropriate Egyptian growth charts for determination of centile. Body mass index was calculated as weight in kilograms divided by the square of the height in meters (kg/m^2) and plotted on the age-appropriate and sex-appropriate Egyptian growth charts. Patients were classified as having mild to moderate (<-2SD) or severe (<-3SD) short stature [14]. Laboratory tests included complete blood count, urine analysis, stool analysis, and estimation of serum zinc and total iron.

Procedure

Blood samples were collected from patients, centrifuged, and then stored at −80°C. Iron concentration was determined as follows: the sample was collected in a tube with EDTA as anticoagulant. Iron reacted with chromazurol B and cetyltrimethylammonium bromide to form colored ternary complex and measured at 623 nm, then incubated for 5 min at 30°C. The intensity of the color produced was directly proportional to the concentration of iron in the sample. Zinc concentration was determined as follows: serum sample was mixed with the reagent, 2-(Brom-2-pyridylazo)-5-(*N*-pro pyl-*N*-sulfopropylamino)-phenol, and incubated for 10 min at 25°C. Zinc forms a red complex. The increase of absorbance was measured and was proportional to the concentration of total zinc in the sample.

Reference values were as follows:
(1) Serum iron (Fe): 50–120 μg/dl [15].
(2) Zinc concentration: 60–120 μg/dl [16].

Statistical analysis

The data were tested for normality using the Kolmogorov–Smirnov test and for homogeneity variances before further statistical analysis. Categorical variables were described by number and percentage, where continuous variables were described by mean and SD. χ^2-test used to compare between categorical variables, whereas comparison between continuous variables was done by independent-samples t-test. A two-tailed P less than 0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY).

Ethical consideration

The study was carried out at Assiut University Hospital after taking approval from Medical Ethics Committee of Faculty of Medicine with no: 17100104. Informed consent was taken from each child. Identifiable data were kept securely.

Results

The results of the studied cases showed that the percentage of male cases was more than females (64 vs 36%), and mean ± SD of age was 8.74 ± 4.07 years. Mean Hb concentration was significantly lower among cases when compared with control group ($P < 0.05$). Serum iron was lower in cases than control group with insignificant difference. Moreover, iron level in children with severe short stature was insignificantly lower than those with mild to moderate short stature (104.56 ± 48.2 vs 120.59 ± 45.86). According to zinc level, there is no significant difference between both groups, and according to severity, there is no significant difference between cases having mild to moderate short stature and those having severe type (450.13 ± 459.588 vs 261.5 ± 134.42).

Regarding the anthropometric measurements, the height and the weight were lower among cases compared with the controls, but with no significant difference between them. The controls were normal, with average height to age.

Discussion

Short stature refers to a child whose height is 2SD or more below the mean for children of that sex and chronologic age [17].

There is strong evidence that several micronutrients, primarily zinc and iron, play important roles in linear growth, and that deficiencies in these key nutrients may result in stunting [18].

When we stratified the cases according to the age, we found that most of them (76%) were of the age group 6–15 years. This result is in agreement with Rivera *et al.* [18], who carried out a study on 40 subjects, where 20 of them were stunted and the other 20 were normal, and showed that the mean age was 13.6 + 1.8 years. This study revealed that there is no statistically significant difference between the age groups of studied cases and severity of short stature, which is similar to the study conducted by El-Zanaty [19].

Regarding the sex of our studied cases, males constituted 64% of cases and females constituted 36% (Table 1). This is in contrast to the study by El Okda *et al.* [20], which showed no statistically significant difference in sex, as both males and females were equal, and also in contrast to the study done by Mesaed *et al.* [21], whose study was done on Egyptian children to determine probable causes of short stature and found that female percentage is slightly higher than male percentage (51.01 vs 48.09%). However, it is in agreement with Mardewi *et al.* [22], who showed a higher prevalence of short stature in males than in females. According to the relation of severity of short stature with sex, there was a significant difference ($P = 0.007$) (Table 2), as males with severe short stature were more than those with mild short stature, whereas females were equally distributed (50%).

Table 1 Demographic and clinical data of the studied cases with short stature

	n (%)
Sex	
Male	16 (64.0)
Female	9 (36.0)
Age (years)	
Mean±SD (range)	8.74±4.07 (2-15)
2<6 years	6 (24.0)
6-15 years	19 (76.0)
Socioeconomic status	
Low	13 (52.0)
Moderate	12 (48.0)
High	0
Food rich in zinc	
Good	5 (20.0)
Poor	20 (80.0)
Food rich in iron	
Good	3 (24.0)
Poor	22 (76.0)
Hx of recurrent infections	
No	14 (56.0)
Yes	11 (44.0)
Weight (years)	
2<6	11.58±1.36
6<15	23.37±8.43
Height (years)	
2<6	80.83±5.53
6<15	118.42±14.83
BMI (years)	
2<6	16.72±2.95
6<15	13.51±3.73

Recurrent infections: diarrhea, chest infections, and common cold. Hx, history.

The height and the weight of the studied cases were lower when compared with the controls (Ht: 109.4 ± 20.97 vs 112.82 ± 21.08), although there was no statistically significant differences. These findings are in agreement with a study done by Madan *et al.* [23] who found that weight and height in studied cases were lower than the control group.

Regarding the BMI of the studied cases (Table 1), the mean BMI of cases was 14.28 ± 3.77, whereas the mean BMI of the control group was 16.65 ± 3.17. This is in contrast to a study done by Ahmed *et al.* [24], who studied 40 children with short stature; their age ranged from 8 to 12 years and their mean BMI was 20.1 ± 1.36.

Concerning nutritional history, there was a higher percentage of children with severe short stature (66.7%) than those having moderate short stature in the group of breastfeeding children. On the contrary, 100% of children with artificial feeding had severe short stature (Table 2). This is in contrast to a study done by Mesaed *et al.* [21] who found that there was a higher significant percentage of children with severe short stature who had exclusive breastfeeding than those who were artificial feeding (53.6 vs 36.9%).

The percentage of children who were poor in taking food containing iron in studied cases was 76%, and the percentage of children who were poor in taking food containing zinc was 80%.

In this study, the percentage of children who had a parasitic infestation with severe short stature was 68.7% (Table 3). This in contrast to El Okda *et al.* [20], who found that 15% of their cases were positive regarding stool analysis (contain parasite), but it is near to Mesaed *et al.* [21], whose study showed that the percentage of children who had parasitic infection with severe short stature is higher than children who had normal stool analysis with moderate short stature (85.3 vs 25.3%).

Regarding Hb level in this study, the mean Hb level was 10.98 ± 1.2 (Table 4). According to the relation with severity of short stature (Table 4), children who had low Hb level with severe short stature were 78.9%, being more than children who had moderate short stature (21.1%). These findings were in agreement with a study by El Okda *et al.* [20], which showed that the Hb concentration was lower in short stature cases than in control group.

Regarding the zinc level in this study (Table 3), although there is no significant difference between the level of zinc and severity of short stature, children who had severe short stature had a lower level of zinc (261.5 ± 134.42) than those with moderate short stature (450.13 ± 459.588). This in agreement with the study done by Mardewi *et al.* [22] who found that the prevalence of low serum zinc level was 71%, and it appears to be associated with short stature.

Regarding the iron level in this study (Table 3), children with severe short stature had lower serum iron levels (104.56 ± 48.2), than those who had moderate short stature (120.59 ± 45.86). The study of Ahmed *et al.* [24], showed that there was a significant decrease in serum iron in children who were short stature (61.5 ± 3.65 μg/dl). The study by Sachdev *et al.* [25]reported a negative relationship between iron stores and growth, which did not document a positive effect of iron supplementation on the physical growth of children.

Table 2 Sociodemographic and clinical criteria of studied cases according to severity of short stature

	Mild to moderate <−2SD [*n* (%)]	Severe <−3SD [*n* (%)]	Total	*P*
Age (years)				
2<5	0	5 (100.0)	5	0.274
5-15	7 (35.0)	13 (65.0)	20	
Sex				
Male	0	11 (100.0)	11	0.007**
Female	7 (50.0)	7 (50.0)	14	
Residence				
Urban	3 (25.0)	9 (75.0)	12	0.989
Rural	4 (30.8)	9 (69.2)	13	
Type of feeding during first year of life				
Breast	6 (33.3)	12 (66.7)	18	0.137
Artificial	0	7 (100.0)	7	
Food rich in zinc				
Good	1 (33.3)	2 (66.7)	3	0.978
Poor	5 (22.7)	17 (77.3)	22	
Food rich in iron				
Good	1 (5.0)	0	1	<0.001**
Poor	5 (20.0)	19 (80.0)	24	

***Statistically significant (*P* value < 0.05).

Table 3 Laboratory data of the studied cases according to severity of short stature

	Mild to moderate [*n* (%)]	Severe [*n* (%)]	*P*
Hb level			
Normal	2 (33.3)	4 (66.7)	0.606
Below normal	4 (21.1)	15 (78.9)	
Urine analysis			
Normal	5 (22.7)	17 (77.3)	0.928
Pyuria	1 (33.3)	2 (66.7)	
Stool analysis			
Normal	1 (11.1)	8 (88.9)	0.364
Contain parasite	5 (31.3)	11 (68.7)	
Zinc level (mean±SD)	450.13±459.588	261.5±134.42	0.982
Iron level (mean±SD)	120.59±45.86	104.56±48.2	0.606

Hb, hemoglobin.

Conclusion

No definite relation is found between levels of serum zinc and iron and diagnosis of idiopathic short stature or its severity in children.

Limitation of this study

A small number of cases and controls were included in this study owing to financial issues. Further studies on a large number of cases are needed to elucidate the relation of trace elements and growth in children.

Table 4 Comparison between children with short stature vs controls

	Cases (n=25)		Control (n=25)		P
	Range	Mean±SD	Range	Mea±SD	
Weight (kg)	9.5-45	20.54±8.95	12.0-35.0	21.76±7.39	0.602
Height (cm)	74-145	109.4±20.97	85-150	112.82±21.08	0.568
BMI (kg/m^2)	6.8-19.2	14.28±3.77	9.5-24	16.65±3.17	0.020*
Hb (mg/dl)	8.2-13.5	10.98±1.2	10.5-14.1	12.16±0.96	<0.001**
Zinc (μg/dl)	0-1239	328.25±280.95	42-1832	404.86±411.02	0.445
Iron (mcg/dl)	47.4-175	98.19±34.7	36-207	107.46±46.23	0.426

Hb, hemoglobin, *Significance value below 0.05, **Statistically significant (P value < 0.05).

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Conflicts of interest

There are no conflicts of interest.

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