Estimation of Serum Zinc Levels in Children with Short Stature

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ABSTRACT
Background: Factors affecting malnutrition in toddlers include genetics, hormones, gender, infectious diseases, and chronic diseases. Nutritional factors that cause stunting include low intake of energy, protein, and micronutrients such as iron, vitamin A, and zinc.
Objective: the aim of this study was to estimate the relation between serum zinc levels and short stature among children. **Patients and methods:** our study included 50 children with short stature (Group I), and 30 children with normal stature as a control group (Group II). Any children with possible genetic, endocrinological cause of short stature, severe nutritional insufficiency, age beyond the 2-10 years range or having any chronic illness or infections were excluded from the study. **Results:** we found non-significant relations between serum zinc and demographic characteristics among group I cases. Also, we found non-significant relations between serum zinc and anthropometric measures (weight, BMI and head circumference) among group I cases. On the other hand, we found a positive and significant relation between serum zinc level and both of height and height percentile. Also, pallor was associated with significantly lower levels of serum zinc. We found non-significant relations between serum zinc and laboratory investigations among group I cases. The only exception was the moderate positive highly significant correlation between HB and serum zinc level. **Conclusion:** our study concluded that lower serum zinc level is associated with short stature among preschool children, and is also associated with more anemia, and lower WBCs count.
Keywords: Zinc, Children, Short stature.

INTRODUCTION
Zinc is a metal with great nutritional importance and is particularly necessary in cellular replication and the development of the immune response [(1)]. Zinc plays an important role in growth; it has a recognized action on more than 300 enzymes by participating in their structure or in their catalytic and regulatory action [(2)]. Zinc also enhances vitamin D effects on bone metabolism through the stimulation of DNA synthesis in bone cells [(2)]. Also zinc plays a critical role in many biochemical pathways and physiological processes in the body including cell growth, cell differentiation and metabolism and reproduction [(3)].

Zinc deficiency is characterized by growth retardation, loss of appetite, and impaired immune function. In severe cases, zinc deficiency can result in hair loss, diarrhea and eye and skin lesions [(4)].

Short stature is a condition in which the height of the individual is more than 2 standard deviations (SD) below the corresponding mean height for a given age, sex and population, in whom no identifiable disorder is present. It can be subcategorized into familial and non-familial short stature, and according to pubertal delay. It should be differentiated from dysmorphic syndromes, skeletal dysplasias, short stature secondary to small birth size (small for gestational age, SGA), and systemic and endocrine diseases [(5)].

AIM OF THE WORK
The aim of this study was to estimate the relation between serum zinc levels and short stature among children.

PATIENTS AND METHODS
Study design: A cross sectional controlled study.
Subjects: A total of 80 children aged 2-10 years were included in this study, and divided according to stature into two groups:

- 50 children with short stature were included as the "case" group (Group I).
- 30 age and sex matched children with normal stature were included as the "control" group (Group II).

All of the cases and controls were recruited from the pediatric outpatient clinic of Al-Azhar University Hospitals, Assiut during the period from June 2018 to April 2019.

Sampling:

- For sampling procedure, we used special software "PS Power and Sample Size Calculation" version 3.1.2.
- Based on previous studies' data, the PS software calculated the sample size to be 50 cases and at least 25 controls.

Methods:
All of the participants were subjected to the following:

- Full history.
  - Personal history (age, sex, residence).
  - Complaint and its duration.
  - History suggesting of zinc deficiency
  - Nutritional history
  - Developmental history.
  - Family history.
- Examination including:
  - Vital signs and general look
  - General examination

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- Anthropometric measures according to the WHO growth charts for weight, age, head circumference upper to lower segment ratio and BMI.

- Investigations:
- Serum zinc level.
- CBC.
- Stool analysis.
- X ray of the wrist joints.

Ethical considerations:

- **The study was approved by the Scientific Ethical Committee of Faculty of Medicine, Al-Azhar University.**
- An informed written consent was taken from the patients of all of the participants in the study.

Statistical analysis

- Statistical package for social sciences (IBM-SPSS), version 24 (May 2016); IBM- Chicago, USA; was used for statistical data analysis.
- Mean and standard deviation were used as descriptive value for quantitative data.
- Student t test was used to compare the means between two groups.
- Qualitative data were expressed as numbers and percentages and Pearson Chi square test was used to compare them.
- Pearson correlation test was used estimate the correlation coefficient between two quantitative variables.
- For all these tests, the level of significance (P-value) was explained as significant if p<0.05 and highly significant if p<0.001.

RESULTS

Table (1): Comparison between the two study groups regarding demographic characteristics and history findings

Item		Group I: Short stature	Group II: Control	P value
Number of cases		50	30	-
Age (years)	Mean±SD	5.74±2.67	4.97±2.30	0.419 (NS)
Sex	Male	27 (54%)	14 (46.7%)	0.525 (NS)
	Female	23 (46%)	16 (53.3%)	
Residence	Urban	26 (52%)	14 (46.7%)	0.644 (NS)
	Rural	24 (48%)	16 (53.3%)	
Feeding	Normal	9 (18%)	23 (76.7%)	**<0.001 (HS)**
	Anorexia	41 (82%)	7 (23.3%)	
Family history	Positive	10 (20%)	0	**0.009 (S)**
	Negative	40 (80%)	100%	

NS: Non-significant, S: Significant, HS: Highly significant

This table shows that age, sex and residence showed non-significant difference between the two groups. On the other hand, anorexia was significantly higher among short stature group (Group I) compared to normal height group (Group II), family history was present in one fifth of group I cases, compared to zero among group II.

Table (2): Comparison between the two study groups regarding biochemical results

Item		Group I: Short stature	Group II: Control	P value
Serum Zinc (mg/dl)	Mean±SD	42.4±1.6	117.1±5.1	**<0.001 (HS)**
HB (gm/dl)	Mean±SD	10.43±1.5	12.89±1.13	**<0.001 (HS)**
RBCs (mcl)	Mean±SD	4.16±0.57	4.44±0.58	**0.038 (S)**
WBCs ($\times 10^9$/l)	Mean±SD	7.51±1.11	8.49±1.04	**0.044 (S)**
PLTs ($\times 10^3$/ml)	Mean±SD	262±6	250±7	0.452 (NS)
ESR (mm/hr)	Mean±SD	8.44±1.67	8.63±1.59	0.819 (NS)
CRP (mg/l)	Positive	18(36%)	4(13.3%)	**0.028 (S)**
	Negative	32(64%)	26(86.7%)	
SGOT (u/l)	Mean±SD	17.7±2.19	16.9±2.34	0.633 (NS)
SGPT (u/l)	Mean±SD	19.5±1.3	17.5±2.07	0.297 (NS)
Urea (mg/dl)	Mean±SD	12.4±2.8	10.7±2.8	0.085 (NS)
Creatinine (mg/dl)	Mean±SD	0.99±0.16	0.95±0.12	0.205 (NS)

NS: Non-significant, S: Significant, HS: Highly significant, mcl: million cells per microliter

This table shows that serum zinc showed major drop among group I compared to group II, with a highly significant difference. Also, HB, RBCs and WBCs showed significant drop among group I cases. The percentage of group I cases with positive CRP was significantly higher than group II. On the other hand, ESR, liver and renal functions showed non-significant difference between the two groups.

Table (3): Comparison between males and females in short stature group regarding demographic characteristics and history findings

Item		Males	Females	P value
Number of cases		27	23	-
Age	Mean±SD	5.04±.35	6.57±2.84	**0.043 (S)**
Residence	Urban	14 (51.9%)	12 (52.2%)	0.982 (NS)
	Rural	13 (48.1%)	11 (47.8%)	
Feeding	Normal	5 (18.5%)	4 (17.4%)	0.918 (NS)
	Anorexia	22 (81.5%)	19 (82.6%)	
Family history	Positive	4 (14.8%)	6 (26.1%)	0.321 (NS)
	Negative	23 (85.2%)	17 (73.9%)	

NS: Non-significant, S: Significant

This table shows that males were younger than females among group I cases, with significant difference. All other demographic characteristics showed non-significant differences between males and females.

Table (4): Comparison between male and female children in short stature group regarding biochemical results

Item		Males	Females	P value
Serum Zinc(mg/dl)	Mean±SD	40.0±2.1	45.1±1.2	0.416 (NS)
HB (gm/dl)	Mean±SD	10.4±1.72	10.5±1.31	0.944 (NS)
RBCs (mcl)	Mean±SD	4.25±0.54	4.05±0.61	0.235 (NS)
WBCs ($\times 10^9$/l)	Mean±SD	7.2±1.04	7.87±1.04	0.268 (NS)
PLTs ($\times 10^3$/ml)	Mean±SD	320±8	324±7	0.835 (NS)
ESR (mm/hr)	Mean±SD	9.33±2.65	7.39±1.47	0.061 (NS)
CRP (mg/l)	Positive	8 (29.6%)	10 (43.5%)	0.309 (NS)
	Negative	19 (70.4%)	13 (56.5%)	
SGOT (u/l)	Mean±SD	16.8±2.2	18.8±1.1	0.441 (NS)
SGPT (u/l)	Mean±SD	18.7±2.7	20.5±1.0	0.557 (NS)
Urea (mg/dl)	Mean±SD	12.5±2.8	12.2±2.8	0.779 (NS)
Creatinine (mg/dl)	Mean±SD	0.99±0.18	1.0±0.14	0.719 (NS)

NS: Non-significant, mcl: million cells per microliter

This table shows that all of the laboratory investigations showed non-significant differences between males and females.

Table (5): Serum zinc level in relation to demographic characteristics and history findings in short stature group

Item		Mean±SD of serum zinc*/ Pearson Correlation**	P value
Age (y)		0.075**	0.604 (NS)
Sex	Male	40.04±22.08*	0.199 (NS)
	Female	45.09±21.24*	
Residence	Urban	42.08±20.53*	0.928 (NS)
	Rural	42.64±23.10*	
Feeding	Normal	40.11±21.49*	0.734 (NS)
	Anorexia	42.85±21.89*	
Family history	Positive	46.97±21.87*	0.077 (NS)
	Negative	36.00±20.09*	

NS: Non-significant, Y: years

This table shows that there are non-significant relations between serum zinc and demographic characteristics among group I cases.

Table (6): Correlation between serum zinc level and biochemical results in short stature group

Item		Mean±SD of serum zinc*/ Pearson Correlation**	P value
HB (gm/dl)		0.505**	**<0.001 (HS)**
RBCs (mcl)		-0.127**	0.381 (NS)
WBCs (×10^9/l)		0.024**	0.870 (NS)
PLTs (×10^3/ml)		-0.249**	0.081 (NS)
ESR (mm/hr)		-0.011**	0.938 (NS)
CRP	Positive	44.33±2.55*	0.632 (NS)
	Negative	41.25±2.94*	
SGOT (u/l)		-0.127**	0.380 (NS)
SGPT (u/l)		-0.079**	0.585 (NS)
Urea (mg/dl)		0.020**	0.893 (NS)
Creatinine (mg/dl)		0.053**	0.717 (NS)

NS: Non-significant, HS: Highly significant, mcl: million cells per microliter

This table shows that there are non-significant relations between serum zinc and laboratory investigations among group I cases. The only exception is the positive highly significant correlation between HB and serum zinc level.

DISCUSSION

The mean age of our study population was around 5 years. Around half of them were males and the other half were females. Also, half of the cases had a rural residence and the other came from urban areas. Age, sex and residence showed non-significant difference between the two groups. Our study population were older than those of **Mardewi *et al.*** [6], where the mean age was around 38-42 months. On the other hand, our cases were younger than those of the Egyptian study done by **El-Okda *et al.*** [7] where the mean age of their children was 13 years.

We found no sex difference between the two study groups, which was agreed by many studies [7, 8]. On the other hand, our results were somewhat different from that of **Mushtaq *et al.*** [9] who found that short stature was more prevalent among males compared to females. The cause of this difference may be because they studied older children and adolescents (with a range from 3-18 years).

Anorexia was significantly higher among short stature group (82%) compared to normal height group (23.3%); with a significant difference. The study of **Mardewi *et al.*** [6] found that feeding was better among normal stature children compared to short stature ones. The study done by **El-Okda *et al.*** [7] showed that cases with short stature showed poor intake of cereals, red meat, egg, dairy products, bread, fresh vegetables, chips and similar snakes; compared with those with normal stature.

Family history was present in one fifth of group I cases, compared to zero among group II. The difference was statistically significant. Pallor was positive in the majority of group I cases (76%) which was opposite to group II (10%) with significant difference. Serum zinc showed major drop among group I (with a mean of 42.4±21.6) compared to group II (117.1±25.1), with a highly significant difference. This was similar to the results of the study done by **El-Okda *et al.*** [7].

The study done by **Mardewi *et al.*** [6] showed that impaired serum zinc was significantly higher among short stature children compared to normal stature ones. Using multivariate analysis, they found that low caloric intake and low serum zinc level were the two independent risk factors for short stature among their cases. However, a recent Ethiopian study done on preschool children by **Tessema *et al.*** [10] showed that serum zinc had non-significant relation with stature or weight among their study cases.

Another older study showed also that serum zinc was not associated with short stature [11]. They explained this results by the possible low number of cases and the borderline serum zinc deficiency among many of their cases.

HB, RBCs and WBCs showed significant drop among group I cases; with mild but significant anemia, low RBCs count and leucopenia among group I cases compared to group II. The study done by **Gadallah *et al.*** [12] found that short stature children had significantly lower HB and iron levels, along with lower serum ferritin level. Also, they found that serum iron and serum zinc showed positive and significant relation among short stature children. Similar results were reported by **El-Okda *et al.*** [7].

The percentage of group I cases with positive CRP (36%) was significantly higher than group II (13.3%). In our study, ESR, liver and renal functions showed non-significant difference between the two groups. Among group I cases, we found that males were younger than females (mean age was 5 versus 6.6 respectively), with significant difference. All other demographic characteristics showed non-significant differences between males and females.

All of the anthropometric measures showed non-significant differences between males and females. Also, all of the laboratory investigations showed non-significant differences between males and females. Our results were similar to those of **Gao *et al.*** [13] who found no significant difference between males and females regarding zinc level. However, these results were somewhat different from that found by **Ibeanu *et al.*** [14] who found that zinc deficiency was more common among males compared to females. This may be because the zinc level in muscle is higher than in fat. As such, males need more zinc than females because their growth rate is higher and their proportion of muscle per kilogram body weight is larger. The study done by **El-Okda *et al.*** [7] reported that HB and RBCs were significantly higher among males compared to females.

In our study, we found non-significant relations between serum zinc and demographic characteristics among group I cases. This was similar to the study done by **Gao *et al.*** [13]. In our study, we found non-significant relations between serum zinc and anthropometric measures (weight, BMI and head circumference) among group I cases. On the other hand, we found a positive and significant relation between serum zinc level and both of height and height percentile. Also, pallor was associated with significantly lower levels of serum zinc. The study of **Gao *et al.*** [13] found that serum zinc showed non-significant relation to anthropometric measures (weight, height, BMI and head circumference) and also IQ level.

We found non-significant relations between serum zinc and laboratory investigations among group I cases. The only exception is the moderate positive highly significant correlation between HB and serum zinc level. These results were somewhat similar to the results of the study done by **El-Okda *et al.*** [7] who found that serum zinc was significantly associated with HB and WBCs level.

CONCLUSION

- Our study concluded that lower serum zinc level is associated with short stature among preschool children, and is also associated with more anemia, and lower WBCs count.
- There was significant drop of all anthropometric measures in short stature group.
- Anorexia and pallor were significantly higher among short stature group.
- One fifth of short stature group showed positive family history.

RECOMMENDATIONS

- Zinc supplementation should be advised for all children with short stature.
- Further studies with larger number of cases should be done to prove this association between serum zinc and height among preschool children; especially because some researches denied this association.
- All essential nutrients should be advised for all children to enhance healthy growth.

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