



EFFECT OF ZINC DEFICIENCY ON GROWTH HORMONE FUNCTION IN MALNOURISHED CHILDREN

Bibi Hajira Ishaq¹, Faheem Ullah^{*2}, Juneda Sarfraz³, Irshad Ahmed⁴, Irum Naz⁵, Farida Sherazi⁶

¹Assistant Professor, Department of Biochemistry, Khyber Medical College, Peshawar

^{*2}Assistant Professor, Endocrinology and Diabetes, KMU Hospital and Research Centre, Peshawar

³Associate Professor, Department of Public Health, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad

⁴Principal Medical Officer, DHQ Hospital, Lakki Marwat

^{5,6}Assistant Professor, Department of Paediatric Medicine, Naseer Teaching Hospital, Peshawar

***Corresponding Author:** Faheem Ullah,

Assistant Professor, Endocrinology and Diabetes, KMU Hospital and Research Centre, Peshawar

*Email: faheem_ullah41@yahoo.com

ABSTRACT

Background: Zinc is a vital micronutrient necessary in normal growth and in endocrine activity of children. Zinc deficiency is a frequent complication of malnourished children and could inhibit the activity of growth-related hormones. Growth hormone and insulin-like growth factor-1 (IGF-1) play a key role in physical growth and changes in these hormones can be a cause of the growth retardation observed in populations that are nutritionally deprived.

Objective: To determine the effect of zinc deficiency on growth hormone function in malnourished children.

Methods: This analytical cross-sectional study was conducted at Khyber Teaching Hospital, Peshawar from January 2023 to January 2024. Non-probability consecutive sampling was used to select 73 malnourished children between the ages of 2 and 12 years. They were measured in terms of demographic and anthropometric variables such as weight, height, body mass index, and mid-upper arm circumference. The venous blood samples were used to measure serum zinc, growth hormone, and insulin-like growth factor-1 (IGF-1). The enzyme-linked immunosorbent assay (ELISA) technique was used to determine hormonal levels. The SPSS version 25 was used to analyze the data. Independent sample t-tests and Pearson correlation analysis were used and the p-value of 0.05 was taken as significant.

Results: Out of 73 malnourished children, 42 (57.5%) were found to have zinc deficiency. Children with zinc deficiency showed significantly lower mean growth hormone levels (3.6 ± 1.3 ng/mL) compared with children having normal zinc levels (5.0 ± 1.5 ng/mL). Similarly, IGF-1 levels were reduced in the zinc-deficient group. A moderate positive correlation was observed between serum zinc levels and growth hormone ($r = 0.41$, $p = 0.001$) as well as IGF-1 levels ($r = 0.47$, $p < 0.001$).

Conclusion: Zinc deficiency was common among malnourished children and was associated with reduced growth hormone and IGF-1 levels. These findings suggest that inadequate zinc status may contribute to impaired growth hormone function and poor growth outcomes in malnourished children.

Keywords: Zinc deficiency, Growth hormone, IGF-1, Malnutrition, Children, Micronutrient deficiency, Pediatric growth.

INTRODUCTION

Childhood malnutrition is one of the major social issues in the world especially in developing nations where poverty, food insecurity, and inadequate access to healthcare are some of the underlying causes of poor nutritional conditions among children. Malnutrition is not only a problem in physical development but also on other metabolic, immunological, and endocrine activities which are critical in the normal development. Zinc deficiency is one of the most frequent and clinically important of all the micronutrient deficiencies related to malnutrition [1-3].

Zinc is a trace element that is vital in many biological functions such as cell division, protein synthesis, defense and hormonal activity. It is specifically crucial in childhood, when the growth and development are fast. Poor absorption or a lack of zinc could result in poor growth, sexual maturation, immunocompromised status and prone to infections. It has been observed that zinc deficiency is very common in malnourished groups of people and could be a major contributor to growth retardation in children [4-6].

One of the key endocrine systems that determine child growth is the growth hormone/insulin-like growth factor axis. The pituitary gland releases growth hormone that causes the secretion of insulin-like growth factor-1 (IGF-1) which is the one that mediates most of the growth-promoting action to the bone and tissues. Normal functioning of this hormonal system requires adequate nutritional status including adequate availability of micronutrients. Zinc has been reported to regulate the secretion and activity of growth hormone and can also regulate the IGF-1 synthesis [7-9].

Children with malnutrition often have disruptions in growth hormonal pathways, a fact that can further increase stunting and developmental delays. Nonetheless, the correlation between zinc deficiency and the role of growth hormone in the growth of malnourished children in most developing environments has not been widely studied. Knowing this association can give us an impression of what nutritional interventions might be done to help enhance the outcomes of growth. Therefore, the present study was conducted to evaluate the effect of zinc deficiency on growth hormone function among malnourished children. The study aimed to assess serum zinc levels and their association with growth hormone and IGF-1 concentrations in order to better understand the endocrine consequences of micronutrient deficiency in this vulnerable population.

METHODOLOGY

This analytical cross-sectional study was conducted to evaluate the effect of zinc deficiency on growth hormone function in malnourished children. The study was carried out at Khyber Teaching Hospital, Peshawar over a period of one year from January 2023 to January 2024. Prior to the commencement of the study. The study was conducted in accordance with the ethical principles of biomedical research involving human participants, and informed written consent was obtained from the parents or guardians of all participating children.

The sample size of 73 malnourished children was selected in the study through non-probability consecutive sampling method. Children who reported to the outpatient department of the pediatric ward or in the pediatric ward with clinical characteristics of malnutrition were screened to be eligible. The study involved children of age between 2 to 12 years of age who were found to be malnourished according to the anthropometric indicators. Children known to have endocrine disorders or chronic systemic disorders, congenital abnormalities or use of zinc supplementation or hormonal therapy were excluded to reduce the number of confounding factors.

The demographic and clinical data such as age, sex, place of residence, and socioeconomic status were collected using a structured data collection form. The anthropometric measurements (weight, height, BMI, and mid-upper arm circumference (MUAC)) were collected through the standardized methods. On the assessment of nutritional status, weight-age and height-age indices were used to establish the extent of malnutrition severity.

To conduct biochemical analysis, each of the participants was provided with venous blood samples in aseptic conditions. The concentration of serum zinc was determined through the routine laboratory techniques. The concentration of growth hormone and insulin-like growth factor-1 (IGF-1) was measured with the help of the Enzyme-Linked Immunosorbent Assay (ELISA) according to the requirements of the manufacturer. Each of the laboratory analyses was carried out in the hospital lab with calibrated equipment, which guaranteed reliability and accuracy of the outcomes.

Children were categorized into zinc-deficient and normal zinc groups based on standard reference values. The collected data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Descriptive statistics including mean, standard deviation, frequencies, and percentages were calculated for demographic, anthropometric, and biochemical variables. Independent sample t-tests were applied to compare hormonal levels between zinc-deficient and non-deficient groups, while Pearson correlation analysis was used to assess the relationship between serum zinc levels and growth hormone parameters. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 73 malnourished children were included in the study to evaluate the effect of zinc deficiency on growth hormone function. The demographic characteristics of the participants including age, gender, residence, and socioeconomic status were recorded to understand the baseline profile of the study population. Most of the children belonged to the younger age group and a slightly higher proportion were males.

Table 1. Demographic characteristics of study participants (n = 73)

Variable	Category	Frequency (n)	Percentage (%)
Age group	2–5 years	21	28.8
	6–9 years	27	37.0
	10–12 years	25	34.2
Gender	Male	40	54.8
	Female	33	45.2
Residence	Rural	44	60.3
	Urban	29	39.7
Socioeconomic status	Low	38	52.1
	Middle	28	38.4
	High	7	9.6

The nutritional status of children was evaluated on the basis of anthropometric measurements such as weight, height, body mass index and mid-upper arm circumference. The results revealed that a significant percentage of children had the signs of moderate to severe malnutrition.

Table 2. Nutritional status of malnourished children (n = 73)

Variable	Mean $\pm$ SD
Weight (kg)	18.4 $\pm$ 4.2
Height (cm)	110.3 $\pm$ 11.6
BMI (kg/m ²)	15.1 $\pm$ 1.8
MUAC (cm)	12.7 $\pm$ 1.3
Height-for-age Z score	-2.3 $\pm$ 0.6

Biochemical indicators such as serum zinc levels and growth hormone associated indicators were done to determine hormonal functionality amongst the participants. Zinc deficiency was observed in a significant proportion of children since the mean level of zinc in the serum was lower than normal.

Table 3. Biochemical parameters of study participants (n = 73)

Variable	Mean $\pm$ SD
Serum zinc ($\mu\text{g/dL}$)	61.8 $\pm$ 12.5
Growth hormone (ng/mL)	4.2 $\pm$ 1.6
IGF-1 (ng/mL)	138.7 $\pm$ 34.9
Hemoglobin (g/dL)	10.3 $\pm$ 1.4

Children have been divided further based on zinc status to analyze them. Among the entire respondents, it was found that over half of them had zinc deficiency. The comparison of the level of hormones in the zinc deficient and non-deficient groups showed that, children in zinc deficient group had lower growth hormone and IGF-1 levels than those in non-deficient group.

Table 4. Comparison of hormonal parameters according to zinc status

Variable	Zinc deficient (n=42) Mean $\pm$ SD	Normal zinc (n=31) Mean $\pm$ SD	p-value
Serum zinc ($\mu\text{g/dL}$)	52.4 $\pm$ 7.3	74.6 $\pm$ 8.1	<0.001
Growth hormone (ng/mL)	3.6 $\pm$ 1.3	5.0 $\pm$ 1.5	0.002
IGF-1 (ng/mL)	121.5 $\pm$ 29.7	161.8 $\pm$ 30.6	<0.001

To study the correlation between serum zinc and growth hormone functionalities, correlation analysis was conducted. There was a moderate positive relationship between serum zinc and growth hormone levels whereby lower levels of zinc indicated low levels of hormonal activity.

Table 5. Correlation between serum zinc level and growth hormone parameters

Variable	Correlation coefficient (r)	p-value
Zinc vs Growth hormone	0.41	0.001
Zinc vs IGF-1	0.47	<0.001

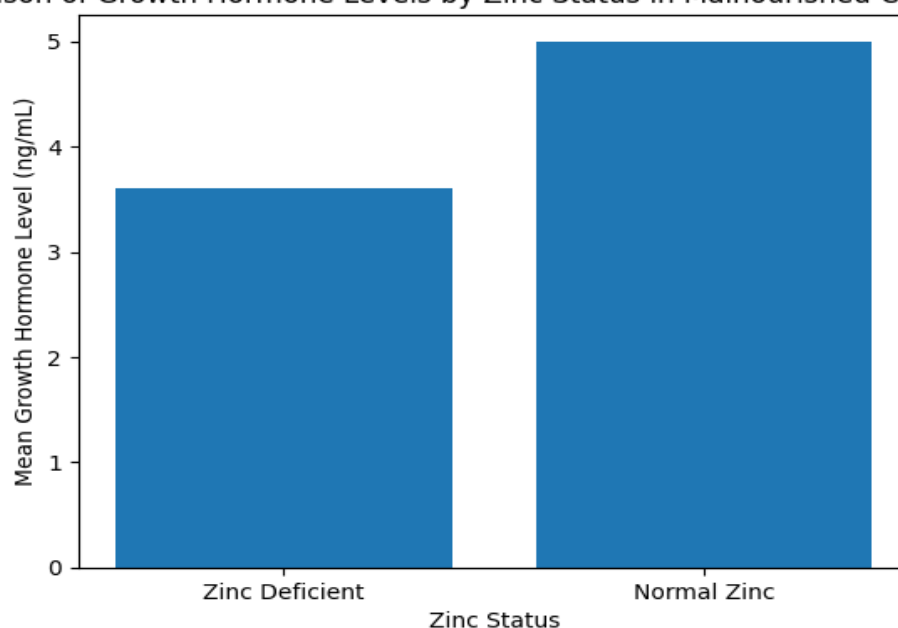
Comparison of Growth Hormone Levels by Zinc Status in Malnourished Children (n=73)

Figure 1. Comparison of mean growth hormone levels between zinc-deficient and normal zinc groups among malnourished children. Children with zinc deficiency showed lower mean growth hormone levels compared with those having normal zinc status.

DISCUSSION

The present study evaluated the effect of zinc deficiency on growth hormone function among malnourished children. The findings demonstrated that a substantial proportion of the participants had reduced serum zinc levels, and these children showed significantly lower growth hormone and IGF-1 levels compared with those who had normal zinc status. In addition, a positive correlation was observed between serum zinc concentration and growth hormone indicators, suggesting that zinc status plays an important role in regulating hormonal pathways related to growth [10-12].

Malnutrition is one of the significant issues affecting the general population of developing nations, especially in children where it leads to poor physical growth and developmental retardation. Malnourished populations have commonly been reported to have micronutrient deficiencies, particularly zinc deficiency. It has been established that zinc is part of various processes in the human body such as the synthesis of DNA, cell proliferation, immunity, and endocrine processes. The fact that zinc deficiency has been very common in malnourished children in the present study represents the nutritional fragility of the concerned population and the way micronutrient deficiencies may affect hormonal regulation [13-15].

It was also found that children who lacked zinc had low mean growth hormone and IGF-1 levels. The endocrine signaling and growth control of zinc is in line with this finding. Zinc plays a role in normal functioning of the hypothalamic-pituitary axis and is implicated in growth hormone secretion and activity as well as production of insulin-like growth factor-1 that mediate many of the growth-promoting actions of growth hormone. A lowered level of zinc perhaps may hinder these pathways thus leading to growth retardation in malnourished children [16, 17].

Moreover, serum zinc levels and growth hormone growth parameters have been found to have a positive relationship meaning that a better zinc status may possibly result in a better growth hormone activity. These results confirm the proposal that micronutrient deficiencies have not only an impact on nutritional status but can also impact endocrine processes that lead to normal growth and development. Dietary supplementation or dietary enhancement in zinc deficient children could thus contribute in the enhancement of the growth outcomes of malnourished children [18-20].

Despite the important findings, the study had certain limitations. The sample was relatively small and the research was performed in one of the tertiary care hospitals, which might restrict the applicability of the findings. Moreover, the cross-sectional design will not provide an opportunity to determine the cause and effect between the deficiency of zinc and the hormonal change. The current research has small sample sizes, cross-sectional, and intervention studies which may be considered as a limitation because future researchers may offer more concrete evidence on the impact of zinc on growth hormone regulation.

CONCLUSION

In conclusion, zinc deficiency was common among malnourished children and was associated with reduced growth hormone and IGF-1 levels. The study findings suggest that inadequate zinc status may contribute to impaired growth hormone function and growth retardation in malnourished pediatric populations. Early identification and correction of zinc deficiency may therefore help improve hormonal balance and support normal growth in affected children. Further research is recommended to explore the potential benefits of zinc supplementation in improving growth outcomes among malnourished children.

REFERENCES

1. Sari, Y.O., et al., *Malnutrition in children associated with low growth hormone (Gh) Levels*. 2021. **35**: p. S327-S329.
2. Allai, F.M., et al., *Malnutrition: impact of zinc on child development*, in *Microbial biofertilizers and micronutrient availability: The role of zinc in agriculture and human health*. 2021, Springer. p. 83-100.
3. Budzulak, J., et al., *Malnutrition as the cause of growth retardation among children in developed countries*. 2022. **29**(3).

4. Arfi, N., K. Khatoon, and F. Alim, *Zinc malnutrition in children and its consequences on health*, in *Microbial biofertilizers and micronutrient availability: the role of zinc in agriculture and human health*. 2021, Springer. p. 35-67.
5. Alaaraj, N., et al., *Growth of malnourished infants and children: how is inflammation involved?* 2021. **16**(5): p. 213-216.
6. Hussain, A., et al., *Mechanistic impact of zinc deficiency in human development*. 2022. **9**: p. 717064.
7. Das, S., et al., *Dietary magnesium, vitamin D, and animal protein intake and their association to the linear growth trajectory of children from birth to 24 months of age: Results from MAL-ED birth cohort study conducted in Dhaka, Bangladesh*. 2020. **41**(2): p. 200-210.
8. Cunha, T.A., et al., *Association between zinc and body composition: an integrative review*. 2022. **71**: p. 126940.
9. Monfared, V., et al., *The effect of zinc supplementation on anthropometric measurements in healthy children over two years: a systematic review and meta-analysis*. 2023. **23**(1): p. 414.
10. Vruwink, K.G., et al., *The effect of experimental zinc deficiency on development of the immune system*, in *Nutrient modulation of the immune response*. 2020, CRC Press. p. 263-280.
11. Abregú, F.M.G., et al., *Impact of zinc deficiency during prenatal and/or postnatal life on cardiovascular and metabolic diseases: experimental and clinical evidence*. 2022. **13**(3): p. 833-845.
12. Hassan, A., et al., *Role of zinc in mucosal health and disease: a review of physiological, biochemical, and molecular processes*. 2020. **12**(5).
13. Mohammadzadeh, A., et al., *Effect of Zinc Supplementation on Anthropometric Parameters of Male School Children*. 2023. **10**(4).
14. Ahmed, M.H., et al., *The impact of functional food in prevention of malnutrition*. 2022. **19**: p. 100288.
15. Nur, A., et al., *The Effect of Zinc Administration in Short Adolescent Mothers who Breastfeed on Zinc Level, Insulin-1 Growth Factors, and Infant Growth*. *Open Access Maced J Med Sci*. 2022 Jul 04; **10** (B): 1922-1926. 2022.
16. Hung, N.T., et al., *Effects of nutrient supplementation on micronutrient status and IGF-1 factor of the stunting children at 2 communes, Yen Son district, Tuyen Quang*.
17. Das, M., *Prevelence of Zinc Deficiency in Elementary School Children of Sagar District in Madhya Pradesh*.
18. Nuryanti, E. and A.T.J.S.R.i.P. Normawati, *The influence of zinc supplement in feeding patterns on the incidence of stunted in the toddler*. 2020. **11**(5): p. 680-2.
19. Robertson, R.C. *The gut microbiome in child malnutrition*. in *Nestle Nutr Inst Workshop Ser*. 2020.
20. Khan, S., *Managing Zinc Deficiencies Among Children*, in *Microbial Biofertilizers and Micronutrient Availability: The Role of Zinc in Agriculture and Human Health*. 2021, Springer. p. 407-429.