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Relationship Of Plasma Zinc Levels With Severe Acute Malnutrition Among Children Under Five Years In Nowshera, Khyber Pakhtunkhwa

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Abstract

Background: *Zinc (Zn) is regarded as a trace element/mineral but forms an integral part of several enzymes (metallo-enzymes) in the body including carbonic anhydrase, lactate dehydrogenase, alkaline phosphatase, carboxypeptidase & superoxide dismutase. Predisposing factors for Zn deficiency include malabsorption and intake of high phytates. Zn supplementation improves the condition dramatically. Apart from the deficiencies of other trace elements, Zn deficiency is highly prevalent in undernourished children. However, the prevalence & relationship of Zn deficiency with severe acute malnutrition (SAM) in children has not been studied in this part of the province. The objective was to determine plasma zinc level in severely malnourished children belonging to Nowshera, Khyber Pakhtunkhwa and to find its relationship with three forms of SAM.*

Methods: *Ninety children with SAM of both sexes, in the age range of 6 months to 59 months, categorized in three groups, 30 in each (Marasmus, Group I, Marasmic Kwashiorkor, Group II & Kwashiorkor, Group III) were randomly selected in a cross-sectional study. Anthropometric parameters like weight & height (or length) were recorded. Blood samples were taken for determination of plasma Zn levels.*

Results: *Plasma Zn levels of all 90 severely malnourished children were below normal. Using the independent "student-t test", Zn levels of children among all the three groups were compared***:** *In Group I children with marasmus, Zn level was 64.71±2.05, in Group II children with marasmic-kwashiorkor, the level was 64.05±4.24 and in group III children with kwashiorkor, it was 57.85±3.90 irrespective of age and sex. Plasma zinc levels were significantly low in kwashiorkor, followed by marasmic kwashiorkor and marasmus. Children in different age groups revealed no significant difference in Plasma zinc levels. Zinc deficiency was equally prevalent in both sexes.*

Conclusion: *Plasma Zn concentration is decreased in children with all three types of SAM. It also concludes that out of all the three, marked Hypozincemia is the feature of kwashiorkor.*

KEY WORDS: *Zinc, Malnutrition, Kwashiorkor, Marasmus.*

INTRODUCTION

Since its discovery in 1869 by Raulin [1], Zinc is known to be one of the "essential minerals" needed by the human body. Total zinc content of body is about 2 g, out of which 60% is in skeletal muscles and 30% in bones. More than 300 enzymes in the biological systems have been identified to be Zn dependent in the biochemical pathways. Some important ones are carboxypeptidase, carbonic anhydrase, alkaline phosphatase, lactate dehydrogenase, ethanol dehydrogenase and glutamate dehydrogenase. RNA polymerase contains zinc and hence, Zn is required for DNA & protein biosynthesis. Zn is a constituent of zinc-finger proteins, which regulate gene transcription. Extracellular superoxide dismutase is zinc dependent and so, zinc is an anti-oxidant. Zinc containing protein, Gusten, in saliva is important for taste sensation [2, 3].

The normal plasma zinc level in children generally ranges from 0.7 to 1.2 ppm (parts per million), which translates to 70-120 µg/dL or 10.7-18.4 µmol/L. Plasma zinc concentrations can fluctuate based on various factors, including age, nutritional status, and health conditions[4].

The World Health Organization (WHO) defines malnutrition as "the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions." [5] Severe acute malnutrition is defined as severe wasting (extreme thinness diagnosed by a weight-for-length or weight for height below −3 SD of the WHO Child Growth Standards) and/or bilateral nutritional edema. Other terms are *marasmus* (severe wasting), *kwashiorkor* (characterized by edema), and *marasmic kwashiorkor* (severe wasting + edema) [3, 6].

Childhood malnutrition affects more than 180 million children under the age of 5 years. Malnourished children are at high risk of increased mortality and morbidity. They are deficient in both macronutrients (protein, fats and carbohydrates) and micronutrients, including vitamins and trace elements[3, 5].

Apart from other trace elements, Zinc deficiency is quite common in the developing world and is often associated with malnutrition or other micronutrient deficiencies (iron). 1.7% of total global deaths in less than 5 yrs children are attributed to Zn deficiency [3, 7, 8].

Chronic zinc deficiency is associated with a spectrum of clinical manifestations ranging from mild to severe degree and characterized by dwarfism (stunting), poor weight gain, increased rates of diarrhea, pneumonia, malaria, poor wound healing, hypogonadism, acrodermatitis enteropathica, behavioral and mental changes, dermatitis, and T-cell immunodeficiency. Diets rich in phytates bind zinc, impairing its absorption. Malabsorption, sickle cell anemia, chronic renal disease, and chronically debilitating diseases are also known to be predisposing factors for Zn deficiency. Zinc supplementation in at-risk children reduces the incidence and severity of diarrhea, pneumonia, and possibly malaria. In developing countries, children who have diarrhea may benefit from zinc supplementation, especially if there is underlying malnutrition [3, 7, 8]. Zinc supplementation also benefited the developmental quotients in stimulated children, improved the hand and eye co-ordination and reduced the recurrent bacterial, viral, fungal and protozoal infections [9].

Natural sources of zinc include lean beef, egg yolks, meat, fish, lamb, milk, oysters, pork, sesame, sunflower seeds, soybeans, turkey, wheat bran and germ, and whole-grain products. Improved dietary quality & intake, food fortification and cultivation of zinc dense plants are some ways of mitigating zinc deficiency[2, 3, 10].

MATERIALS & METHODS:

This study was a hospital based descriptive cross-sectional study.

Operational Definition

Children whose weight for height is below −3SD or less than 70% of the median or having edema is termed as severely malnourished. If the weight for height is less than 70% of median, or less than −3 SD in the absence of edema is termed as "marasmus". If weight for height is between 70 to 90% of median in the presence of edema, it is called as kwashiorkor and when the weight for height is below 70% of the median or −3SD in the presence of edema, is labeled as marasmic- kwashiorkor [6].

Normal plasma concentration of Zn is 70-120 µg/dL (or 0.7 to 1.2 parts per million) [4].

Inclusion/Exclusion Criteria: Patients of both sex and age ranging between 6 months and 59 months who were marasmic, kwashiorkor or marasmic-kwashiorkor (30 from each group) with severe malnutrition (according to NCHS / WHO reference values) were included in the study. Patients with 1st and 2nd degree protein calorie malnutrition and those with secondary malnutrition were excluded from the study. Infections, loose motions and dehydration which are the factors having impact on serum zinc levels were either excluded or treated before the determination of Zn.

Equal number of patients meeting the inclusion and exclusion criteria after informed consent from parents were chosen from all three groups of malnutrition for the sake of comparison. Blood samples were taken for determination of Zn that was done by colorimetric method.

2 ml of blood was taken in heparinized tube which was centrifuged at 3000 rpm for 10-15 minutes to separate plasma from blood cells. The plasma was transferred into a clean test tube to which an equal volume of 10 % trichloroacetic acid (TCA) was added. After thorough mixing, the mixture was centrifuged to separate the protein precipitate. To 1 ml of supernatant, 1 ml of zinc reagent & 1 ml of Ammonium acetate buffer were added. After waiting for 15 minutes, a pink colored complex was formed. The absorbance of the test sample was measured against the Zn standard in UV-Visible spectrophotometer at 560 nm. Finally, a calibration curve was created by plotting absorbance values versus the concentration of the Zn standards. Based on the absorbance readings, Zn concentration was measured

Means and medians were calculated for zinc levels in all three groups (marasmus, kwashiorkor and marasmic kwashiorkor). To test the significance of the difference between the three different groups of severely malnourished children, "Student t Test" was applied. P values were calculated at the level of significance chosen as 0.05. The degree of freedom was determined and the tabulated values at the specified degrees of freedom were noted. The "calculated t test value" was compared to the "tabulated t value".

RESULTS:

Ninety severely malnourished patients meeting the inclusion criteria were analyzed for serum zinc levels. It included kwashiorkor, marasmic and marasmic-kwashiorkor patients, thirty (30) from each group. Distribution of severely malnourished children according to sex with their mean serum zinc values are given (Table I).

Plasma zinc mean value for kwashiorkor 57.85±3.90 µg/dL, for marasmus 64.71±2.05 µg/dL and for marasmic-kwashiorkor 64.05±4.24 µg/dL, were all well below the normal zinc level in plasma (N=70-120 µg/dL).

All 30 (100%) kwashiorkor patients showed their serum zinc values significantly reduced when compared to the normal in all four groups divided age wise (Table II).

Plasma levels were reduced in all of the marasmic kwashiorkor patients except in five (16.6%) patients (in whom the levels were found above 70 µg/dL. The mean values of Plasma zinc in all four groups divided according to age were however even then below the normal (Table III).

Twenty-eight (93.3%) marasmic patients had their serum zinc values below normal. While two patients (6.6%) showed values just above normal, the mean value for all 30 patients was below normal (Table IV).

Table 1: Severely malnourished children (n=90) according to sex with their mean plasma Zn values (µg/dL)

Group	Sex	Number of Cases (%age)	Mean Zn Values (µg/dL)
Kwashiorkor	Male	13 (43.3 %)	58.4
	Female	17 (56.6 %)	57.3
Marasmic – Kwashiorkor	Male	11 (36.6 %)	64.4
	Female	19 (63.3 %)	63.7
Marasmus	Male	18 (60.0 %)	65.1
	Female	12 (40.0 %)	64.3

Table: II Plasma Zinc levels (µg/dL) in Group III Children (N=30) with Kwashiorkor by Age Groups

Age Combined		6 mo – 1 Y		1 – 2 Y		2 – 3 Y		3Y – 59 mo	
No of Pts (%)	Mean ± SD	No of Pt's (%)	Mean ± SD	No of Pt's (%)	Mean ± SD	No of Pt's (%)	Mean ± SD	No of Pt's (%)	Mean ± SD
30 (33.33%)	57.85 ± 3.90	2 (2.22%)	58.5 ± 0.177	17 (18.88%)	59.5 ± 0.165	8 (8.88%)	59.7 ± 0.245	3 (3.33%)	53.7 ± 0.085

Table III: Plasma Zinc levels (µg/dL) in Group II Children (N=30) with Marasmic-Kwashiorkor by Age Groups

Age Combined		6 mo – 1 Y		1 – 2 Y		2 – 3 Y		3Y – 59 mo	
No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD
30 (33.33%)	64.05 ± 4.24	2 (2.22%)	62.5 ± 4.17	17 (18.88%)	64.1 ± 1.85	8 (8.88%)	66.1 ±5.07	3 (3.33%)	63.5 ± 2.72

Table IV: Plasma Zinc levels (µg/dL) in Marasmic Group I Children (N=30) by Age Groups

Age Combined		6 mo – 1 Y		1 – 2 Y		2 – 3 Y		3Y – 59 mo	
No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD	No of Pts (%)	Mean ± SD	No of Pt's (%)	Mean ± SD	No of Pt's (%)	Mean ± SD
30 (33.33%)	64.71 ± 2.05	2 (2.22%)	65.24 ± 4.95	17 ± (18.88%)	67.1 ± 1.79	6 ± (6.66%)	63.3 ± 1.19	5 (5.55%)	63.2 ± 2.28

The mean zinc values of both the males and females in each group of malnutrition showed similar results indicating the similar prevalence of zinc deficiency in both sexes.

Using the independent "Student t Test" serum zinc levels of patients in kwashiorkor group were compared to marasmic group and to the marasmic kwashiorkor group and then marasmic group to the marasmic kwashiorkor group.

No statistically significant difference ($P > 0.05$) was observed between the serum zinc levels of "kwashiorkor and marasmic kwashiorkor", and between marasmic and marasmic kwashiorkor, while statistically significant difference ($P < 0.05$) was found between the values in kwashiorkor and marasmic children.

DISCUSSION:

Zinc deficiency is common in children from developing countries due to lack of intake of animal foods, high dietary phytate content, inadequate food intake and increased fecal losses during diarrhea [10], predisposing them to increased risk of illness and death from infectious diseases. Randomized controlled trials of zinc supplementation provide the best estimate of this risk through demonstrated preventive benefits.[11]

A working group meeting was convened by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), the International Atomic Energy Agency (IAEA), and the International Zinc Nutrition Consultative Group (IZiNCG) to review methods of assessing population zinc status and provide standard recommendations for the use of specific biochemical, dietary, and functional indicators of zinc status in populations. The recommended biochemical indicator is the prevalence of serum zinc concentration less than the age/sex/time of day-specific cutoffs [12].

Although Plasma zinc concentration, represent <1% of the body zinc pool [2], still it can be considered a useful biomarker of a population's risk of zinc deficiency and response to zinc interventions [13].

Our study revealed lower mean serum zinc values in all three groups of severely malnourished children. Atino T and Johnson A[14], Kandzierska D [15], Singla PN [16] et al after comparison stated that the plasma zinc levels were low in the malnourished and that decrease of plasma zinc levels related to increase of the degree of malnutrition and a significantly positive correlation between serum zinc and height-for-age ($r=0.8809$, $p<0.001$). Infections exacerbate the zinc deficiency [17] not only in severe malnutrition but grade I and II (mild to moderate) are affected as well in accordance to study conducted by Khalidi F [18] et al. Mean serum zinc values were lowest in kwashiorkor, followed by marasmic kwashiorkor and then by marasmic group as stated by Atalay Y et al [19] after analyzing 37 patients' serum and by BE and Golden MH [20] after 42 patients' analysis. Mean serum zinc concentration (0.682) in kwashiorkor children in our study is comparable to the mean value (0.66ppm) by Subotzky EF et al [21], and to (0.71ppm) by Jalil A [22].

According to Atalay Y et al [19] the serum zinc levels were significantly lower in patients with marasmic kwashiorkor than in the control group. The mean serum zinc values in kwashiorkor and marasmic kwashiorkor in our study also matches that of De Souza [23]. The serum zinc levels were significantly lower for these patients than those with good nutritional status. Zinc mean value 0.824+/-0.205 ppm in our children with marasmus was also similar to 0.869 ppm by Golden MH et al [20] noticed that in the absence of edema there was a strong correlation of serum zinc status, stunting and severe wasting. Serum zinc levels in our study were found above the normal value (1.2ppm) in 2 marasmic and 5 kwashiorkor pts. Inquiry revealed 3 patients were already receiving zinc supplements prescribed by doctors and the actual reasons in rest of the 4 pts could not be identified. Zinc deficiency has got drastic effects on the children's defense mechanisms and growth. According to one of the studies [19], zinc supplemented children had a better rate of weight gain and recovery of the immune system, as assessed by skin-test response, T-cell blastic proliferation, immunoglobulins, and marked reduction in frequency of infections.

All of the above studies indicate that severely malnourished children are zinc deficient and zinc supplementation is mandatory during rehabilitation phase [24, 25].

CONCLUSIONS

Since patients in all the three groups of malnutrition are zinc deficient irrespective of the age and sex, particularly in severe form, all the malnourished children need zinc supplementation during nutritional rehabilitation.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES:

1. Raulin J. Chemical studies on vegetation. Ann. Des. Sci. Nat. 1869; 11:93–99. (*Originally in French*: Raulin J. Etudes cliniques sur la vegetation. Ann Sci Natl Botan Biol Vegetale.1869; 11: 93-99)
2. Vasudevan DM, Sreekumari S, Vaidyanathan K. Textbook of Biochemistry. 7th ed. Philadelphia: Jaypee Brothers Medical Publishers; 2013. Chapter 39. Mineral Metabolism and Abnormalities (Zinc); 522
3. Kliegman RM, St Geme III JW, Blum NJ, Tasker RC, Shah SS, Wilson KM. Severe Acute Malnutrition. In: Behrman RE. ed. Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier, 2020. 300
4. King JC, Cousins RJ. Zinc. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR (Eds.), Modern Nutrition in Health and Disease. 11th ed. Philadelphia: Lippincott Williams & Wilkins, 2014. 189-202
5. Ashworth A, Khanum S, Jackson A, et al: Guidelines for the inpatient treatment of severely malnourished children. 2003; World Health Organization.
6. WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children: A Joint Statement by the World Health Organization and the United Nations Children's Fund. Geneva: World Health Organization; 2009. Available from: https://www.ncbi.nlm.nih.gov/books/NBK200775/
7. Prasad AS. Discovery of human zinc deficiency: 50 years later. Journal of Trace Elements in Medicine and Biology. 2013; 26(2-3): 66-69
8. Brown KH, Wuehler SE, Peerson JM. The importance of zinc in human nutrition and estimation of the global prevalence of zinc deficiency. Food and Nutrition Bulletin. 2001; 22(2): 113-125.
9. Gardner JMM, Powel CA. Zinc supplementation and psychosocial stimulation: effects on the development of undernourished Jamaican children. Am J Clin Nutr 2005; 82:399-405.
10. Bhatnagar S, Natchu UC. Zinc in child health and disease. Indian J Pediatr. 2004 Nov;71(11):991-5
11. Black RE. Zinc deficiency, infectious disease and mortality in the developing world. J Nutr. 2003; 133(5 Suppl 1):1485S-9S
12. de Benoist B, Darnton-Hill I, Davidson L, Fontaine O, Hotz C. Conclusions of the Joint WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators. Food Nutr Bull. 2007; 28(3 Suppl): S480-4

13. Hess SY, Peerson JM, King JC, Brown KH. Use of serum zinc concentration as an indicator of population zinc status. Food Nutr Bull. 2007; 28 (3 Suppl): S403-29.

14. Atino T, Johnson A, Mbofung C, Tindimebwa G. Plasma zinc status of protein energy malnourished children Acta Trop 1982 Sep; 39(3):265-74.

15. Kandzierska D. Zinc and copper levels in the blood serum of infants with chronic nutrition disorders Pediatr Pol. 1989 Apr; 64(4): 241-7

16. Singla PN, Chand P, Kumar A, Kachawaha JS. Serum, zinc and copper levels in children with protein energy malnutrition. Indian J Pediatr. 1996 Mar-Apr; 63(2):199-203.

17. Brown KH. Effect of infections on plasma zinc concentration and implications for zinc status assessment in low-income countries. Am J Clin Nutr. 1998; 68 (2 Suppl):425S-429S

18. Khaldi F, Ben Mansoor A, Hedhili A, Kaabachi N, Gueddana N, Mebazaa A, Ben Naceur B. Zincemia, cupremia and infection in malnourished children Arch Pediatr. 1995; 2(9): 854-7.

19. Atalay Y, Arcasoy A, Kurkcuoglu M. Oral plasma zinc tolerance test in patients with protein energy malnutrition. Arch Dis Child. 1989 Nov; 64(11):1608-11

20. Golden MH, Harland PS, Golden BE, Jackson AA. Zinc and immunocompetence in protein-energy malnutrition. Lancet. 1978; 1(8076): 1226-8

21. Subotzky EF, Heese HD, Sive AA, Dempster WS, Sacks R, Malon H. Plasma zinc, copper, selenium, ferritin and whole blood manganese concentrations in children with kwashiorkor in the acute stage and during refeeding. Ann Trop Paediatr. 1992;12(1):13-22

22. Jalil A. Management and effect of different levels of protein on the recovery of kwashiorkor and marasmic-kwashiorkor children. Thesis 2000; 53-9

23. De Souza NM, Shuhama T, Brasil Mdo R, Collares EF, Tone LG. Zinc in protein-calorie malnutrition. I. Concentration in serum of children with the clinical types, kwashiorkor and marasmic kwashiorkor. Arq Gastroenterol. 1981; 18(2):77-80.

24. Lazzerini M, Ronfani L. Oral zinc for treating diarrhoea in children, Cochrane Database Syst Rev. 2013: (1); CD005436

25. Walker CLF, Black RE. Zinc treatment for serious infections in young infants, Lancet. 2012: 379;2013–2033