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ORIGINAL RESEARCH

Micronutrient Deficiencies and Diarrheal Diseases: Evaluating Zinc and Copper Levels in Children

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ABSTRACT
Diarrhea is a leading cause of child mortality in developing countries, responsible for an estimated 2.5 million deaths annually. In India, it accounts for 13% of all deaths in children under five, with approximately 300,000 fatalities each year. This study aimed to evaluate the serum levels of zinc and copper in children suffering from diarrhea and explore their roles in the condition's severity and duration. Zinc, known for enhancing immune response and intestinal health, and copper, an important element in various enzymatic processes, were measured in 25 children aged 6 months to 5 years with acute, persistent, or chronic diarrhea, and compared to 25 healthy controls.
The study found significantly lower serum zinc (39.26 ± 12.18 µg/dl) and copper levels (68.60 ± 14.34 µg/dl) in children with diarrhea compared to healthy controls (zinc: 78.60 ± 11.63 µg/dl; copper: 99.26 ± 15.62 µg/dl), with p-values < 0.001 for both. These deficiencies correlated with longer diarrhea duration and higher stool frequency, particularly in male patients. Zinc supplementation showed substantial benefits, reducing the severity and duration of diarrhea and the likelihood of future episodes. These findings underscore the importance of zinc in diarrhea management and support its use in treatment protocols.
Further studies with larger sample sizes and additional micronutrient assessments are recommended to enhance understanding and develop comprehensive strategies to combat pediatric diarrhea, ultimately reducing the global health and economic burden, particularly in developing nations like India.
Keywords: Diarrhea, Zinc, Copper, Children, Deficiency, Supplementation

INTRODUCTION

Diarrhea causes an estimated 2.5 million child deaths in developing countries each year. It is the third leading killer of children in India today and is responsible for 13% of all deaths in children less than five years of age and kills an estimated 300,000 children in India each year. Clinically, diarrhea is defined as passage of 3 or more loose or watery stools in 24 hours. For exclusively breastfed infants, a change in consistency of stool with increased frequency is regarded as diarrhea. When there are three diarrhea-free days between two episodes, they are considered as two separate episodes.[1]Types of diarrhea: Acute diarrhea- Diarrhea lasting < 2 weeks.Persistent diarrhea- lasting 2- 4 weeks. Persistent diarrhea is usually seen in infancy with more than 60% episodes occurring in infants < 6 months age and 90% before 1year of age.Chronic diarrhea- Diarrhea lasting > 4 weeks.[2]

Micronutrients are nature's wonder drugs, playing a central role in metabolism and in the maintenance of various homeostatic functions. By definition, those nutrients whose daily requirements is <100 mg are called micronutrients, e.g. iron, zinc, copper, manganese, and fluoride. There is a highly integrated system to control the flux of micronutrients in illness, and this demonstrates just how important the body perceives the micronutrients to be. An adequate intake therefore is necessary to sustain metabolism and tissue function, but provision of excess supplements to

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individuals who do not need them may be harmful. Clinical benefit is most likely in those individuals who are severely depleted and at risk of complications, and is unlikely if this is not the case.[3] Zinc improves the absorption of water and electrolytes, improves regeneration of the intestinal epithelium, increases the levels of brush border enzymes, and enhances the immune response, allowing for a better clearance of the pathogens. Another report has recently provided evidence that zinc inhibits toxin-induced cholera, in cultured Caco-2 cells. Thus, Zinc plays an important role in modulating the host resistance to infectious agents and reduces the risk, severity, and duration of diarrheal diseases. There is a close association between diarrhea and zinc deficiency particularly with co-existing malnutrition (Fig. 1& 2).[4]

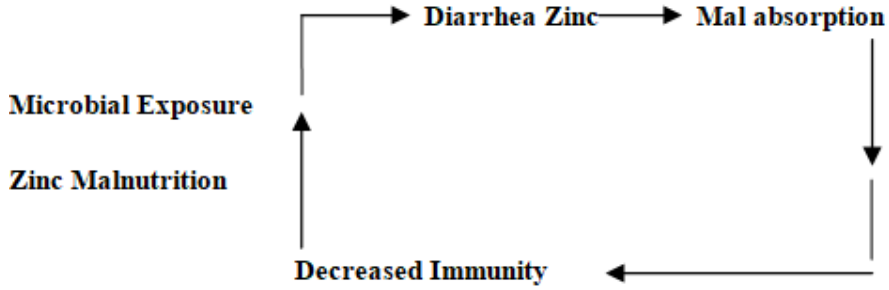

Figure 1: A plausible link between malnutrition, diarrhea and zinc deficiency.[4]

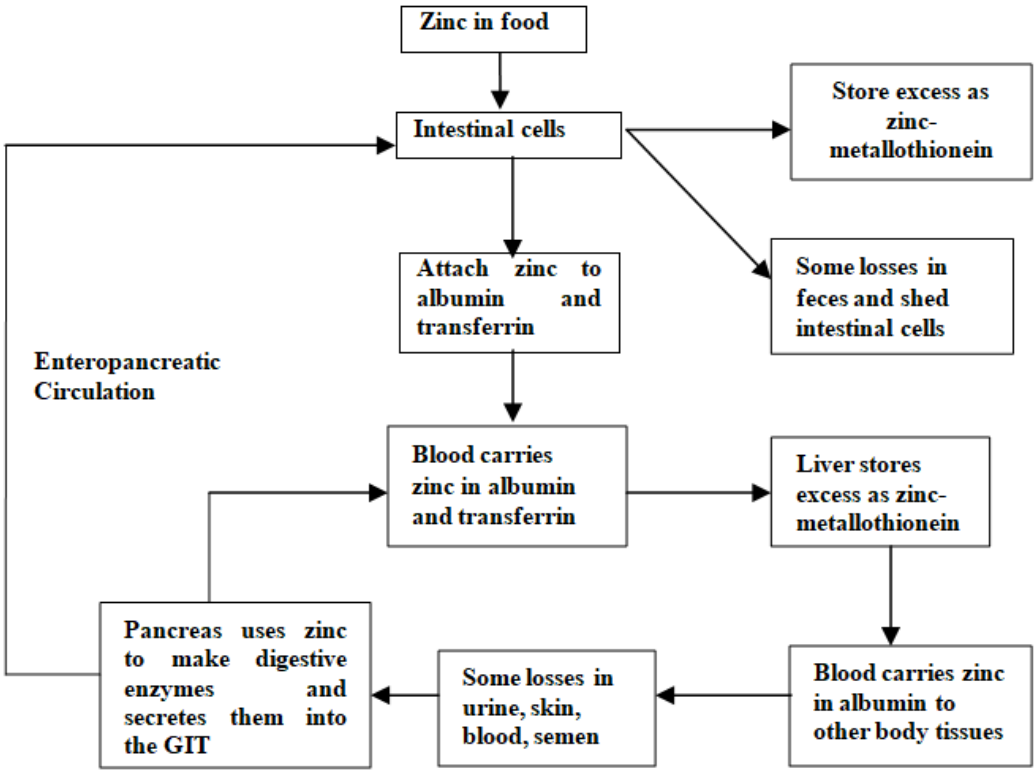

Figure 2: Zinc metabolism.

Copper is present in cytosolic erythrocyte superoxide dismutase (Cu, Zn-SOD), which is an important scavenger of O2-, a free radical and in Ceruloplasmin which plays a role in acute-phase response to infectious diarrhoeal diseases.[5]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. Zinc has a fundamental role in cellular metabolism, with profound effects on the immune system and the intestinal mucosa. Zinc supplementation has shown significant benefits in prevention and treatment of diarrhea.[6] In recent years, a number of other studies have corroborated these preliminary findings in children with both acute and persistent diarrhea. One of the first of these studies, in India, found that children with acute diarrhea got better faster when they received a zinc supplement. This trial in New Delhi compared vitamin supplements with and without 20 mg elemental zinc administered daily to 937 children with acute diarrhea. The children who received zinc recovered more quickly and they had 23% less chance of continuing diarrhea on any day after starting the zinc supplement. The children receiving zinc also had fewer loose stools so that in this study the zinc

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reduced the severity of the diarrhea as well as hastening recovery. Other trials from different parts of the world from Papua New Guinea to Peru have shown similar benefits. The data from these studies has been pooled and the results demonstrate a consistent, significant and clinically important benefit of supplements containing oral zinc in children aged less than five years who have acute diarrhea. Children had a 15% faster recovery with zinc.[7]

Routine zinc supplementation given to low-birth-weight babies for a year has resulted in substantial reduction in mortality. WHO Task Force, 2001, and the National Task Force of Indian Academy of Pediatrics (IAP) have recommended use of zinc in the treatment of diarrhea. Improved dietary quality and intake, food fortification and cultivation of zinc dense plants are some ways of mitigating zinc deficiency.[8-11] Keeping in view the importance of copper and zinc and its association with diarrhea, the study was planned to evaluate serum copper and zinc levels in children suffering from diarrhea.

MATERIALS AND METHODS

Study Area: The study was conducted in the Department of Biochemistry in collaboration with the Department of Pediatrics, RDJM Medical college, Turki, Muzaffarpur.

Study period: Study was conducted from February 2023 to April 2024.

Study Population: 25 subjects in the age group of 6 months- 5 years who are admitted in Paediatric ward and emergency in medical collage of RDJM was selected for the study. Those children having Acute, Persistant and chronic diarrhea was included in the study.

25 healthy age-matched children were taken as control.

Exclusion criteria

1. Congenitaldiseases, Malignancy, Systemic diseases, recurrent pneumonia, Malaria, Sickle cell anaemia or Leukaemia.
2. Children more than five years of age
3. Children less than 6 months of age.
4. Children with bloody diarrhea.
5. Children put on I/V drip containing copper or zinc or on any copper zinc preparationfor the last 6 month
6. Children having single episode of watery stool.

Sample collection and estimation of serum zinc

2 ml of venous blood was aseptically collected from cubital vein/femoral vein, centrifuged and serum was separated. Serum zinc and copper levels were estimated by colorimetric kit method described by M. Saito (1982)[12] and Makino.[13]

Normal range: Zinc 60- 120 µg/dl; Copper 80-155 µg/dl.

RESULTS AND DISCUSSION

Table 1 Comparison of serum zinc levels in healthy controls and the diseased (cases)

S. No	Group	No. of cases	Mean(µg/dl)	SD±	SE
1	Healthy control	25	78.60	11.63	0.46
2	Diseased(cases)	25	39.26	12.18	0.48
t-value = 11.68; p-value = 0.0001*					
*p value < 0.05 have been considered to be significant SD=Standard deviation, SE=Standard error					

Table 1shows that out of 50 children enrolled in the study, a total of 25 children were healthy whose mean serum zinc levels were 78.60± ±11.63 µg/dl. The remaining 25 diseased children had mean serum zinc levels of 39.26±12.18 µg/dl. The statistical analysis showed that the association between serum zinc levels of healthy controls and diseased was highly significant (t-value = 11.68 and p-value = 0.0001).

Table 2 Correlation Analysis of Factors with Copper and Zinc Concentrations in Diarrheal Patients

Factors	Correlation with Copper Concentration	p-value	Correlation with Zinc Concentration	p-value
Diarrheal Duration after Entrance	-0.52	0.031	-0.45	0.067
Stool Excrement in Male Patientsonly	-0.63	0.012	-0.58	0.021
Total Diarrheal Duration (Pre andPost)	-0.48	0.046	-0.52	0.037

Our analysis described a remarkable correlation between diarrheal duration after the entrance, stool excrement in male patients only and total (both pre and post) diarrheal duration with the concentration of copper and zinc at the entrance time. Those children get suffered from diarrhoea more severely and of longer duration, who were having low concentrations of copper and zinc in the plasma (table 2).

In the present study, it was observed that the serum Zinc and Copper levels were significantly lower in children suffering from diarrhea (39.26 ± 12.18 vs.

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78.60 ± 11.63 µg/dl, p<0.001) and (99.26 ± 15.62 vs. 68.60 ± 14.34µg/dl, p<0.001). The serum zinc levels as per age subgroups in healthy and diseased children are comprehensively represented in Figure3.Zinc supplementation is a new addition to the diarrhea treatment strategy and one that promises to greatly improve diarrhea management. Two recent advances in managing diarrheal disease that can drastically reduce the number of child deaths include: 1) Newly formulated oral rehydration solution (ORS), containing lower concentrations of glucose and salts, to prevent dehydration and the need for intravenous therapy; and 2) Zinc supplementation to decrease the duration and severity of diarrhea and the likelihood of future diarrhea episodes in the 2-3 months following supplementation [11].

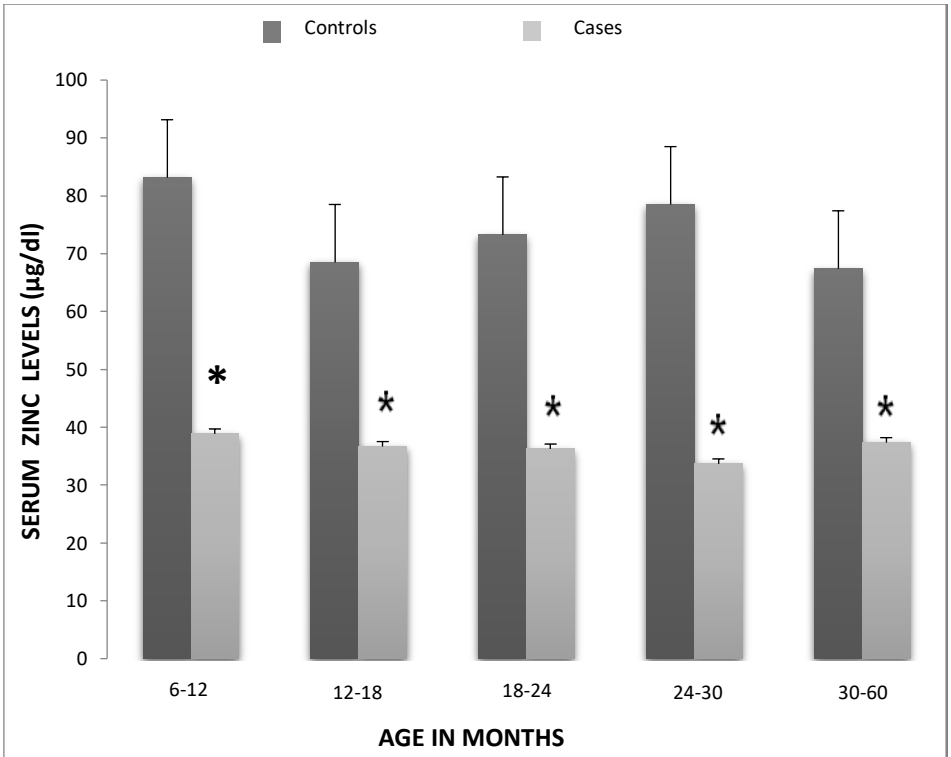

Figure 3. Comparison of serum zinc levels in different age groups in healthy (control) and diseased (cases) children. *p<0.05.

CONCLUSIONS AND FUTURE PERSPECTIVES

The present study which was undertaken to estimate the serum Zinc and Copper levels and theircorrelation in children with Diarrhea has revealed a significant decreased in Zinc and Copper level. From the previous and present studies, it is confirmed that Zinc plays a key role in diarrhea in children and its supplementation greatly helps in the prevention and treatment of diarrhoea. Further studies with different micronutrients and biomarkers with newer methods are encouraged for easy understanding and assessment so as to control diarrhoeal diseases in children. Thus, the study may help in solving the global economic burden on the health services in particular and societies/communities as a whole and make this world a better place especially for the developing countries like India.

Certain limitations of the present study merit attention. The population size, i.e. the number of children should have been more in order to acquire more comprehensive data for analysis. Along with zinc and copper, other nutrients such as vitamin A should also be estimated to assess its impact on diarrhea. Lastly, zinc supplements to the diarrheal children and re-evaluation in terms of recurrence and morbidity could provide more confirmatory evidence on the impact of zinc on diarrhea.

REFERENCES

1. Ibrahim KA, Omale S, Dayom DW, Onyebuchi OB. Assessment of knowledge and practice of zinc sulphate supplementation in the treatment of diarrhoea among under-five children in Primary Health Care centres in Keffi, Nigeria. Journal of Pharmacy & Bioresources. 2023 Oct 19;20(3):107-16.
2. Camilleri M, Murray JA, Diarrhea and constipation. In:Fauci AS, Braumwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. editors. Harrison`s principles of internal medicine. 17th ed. United States of America: Mc Graw Hill Company, Inc. 2008. p. 245- 254.

DOI: 10.69605/ijlbpr_13.6.2024.87

3. Alan S A (2006) The key role of micronutrients. Clin Nutr 25: 1-13.
4. Bajait C and Thawani V(2011) Role of zinc in pediatric diarrhea. Indian J Pharmacol 43(3): 232–235.
5. Sajid A, Ahmad M, Sajid S. Therapeutic role of Zinc; Evaluation in patients with diarrhoeal illnesses. Professional Med J 2010;17(3) 472-478.
6. Cho YE, Choi SH, Kwun IS. The Micronutrient Zinc in Human Health and Disease. InEmerging Solutions in Sustainable Food and Nutrition Security 2023 Oct 29 (pp. 289-304). Cham: Springer International Publishing.
7. Penny M. The role of zinc in child health. Instituto de Investigacion Nutricional, Peru. Available from: http://www.interzinc.org/pdf/ZP_TheRoleOfZincInChildHealth.pdf Accessed on: 5th May 2012.
8. Jiang Y, Mandal K, Lu H. Serum Zinc Levels and Immune Status of Children with Persistent Diarrhea Following Oral Zinc Supplementation. Yangtze Medicine. 2021 Jan 7;5(1):33-42.
9. Penny M (2011) The role of zinc in child health. Peru: IZA. Available from: http://www.interzinc.org/pdf/ZP_TheRoleOfZincInChildHealth.pdf. Retrieved 02-05-2013.
10. USAID (2005) Diarrhoea Treatment Guidelines: 1- 46. Available from: http://www.a2zproject.org/pdf/USAID_DiarrENGL.pdf. Retrieved 02-05-2013.
11. Bajait C and Thawani V (2011) Role of zinc in pediatric diarrhea. Indian J Pharmacol 43(3): 232–235.
12. Makino T, Saito M, Horiguchi D and Kina K (1982) Estimation of serum zinc levels. Clin Chim Acta 20: 127-135.
13. Abe A, Yiamashita S. Colorimetric method for the estimation of Zinc and Copper. Clin Chem Acta 1989; 35(4): 552-54.