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Role of Serum Zinc and Copper in Children with Gastroenteritis

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Abstract: *Gastroenteritis, also known as acute diarrhoeal diseases as the predominant symptom is diarrhoea. Diarrhoea is defined as the passage of loose, liquid or watery stools > 3 times a day lasting upto 10-14 days. Therefore children with marginal nutritional status are also at significant risk of developing micronutrients depletion such as zinc with an episode of diarrhoea. Zinc improves water and electrolyte, increases brush border enzymes activity and enhances the overall immune function. A study was conducted in the department of Biochemistry and Paediatrics, RIMS, Imphal over 70 children with Gastroenteritis cases and 70 healthy controls, in which serum Zinc and Copper levels were estimated and tried to find any correlation among children suffering from gastroenteritis and in healthy controls. The findings revealed reduced serum Zn level among gastroenteritis cases than healthy controls (70.30µg/dl Vs 102.24µg/dl) and increased Serum Cu level among gastroenteritis cases than healthy controls (170.91µg/dl Vs 118.56µg/dl) and the finding was statistically significant ($p<0.05$). And reduced serum Zn level in underweight (60.34±17.54µg/dl) than those with normal weight (70.21±20.23µg/dl) among the cases and controls. In conclusion gastroenteritis remains a leading cause of global childhood morbidity and mortality. The present study which revealed a significant decreased in Zinc level with increased in serum Copper level could be due to depletion of Zinc and an acute- phase response to infectious diarrhoeal diseases.*

Key words: *Zinc, Copper, Gastroenteritis, Diarrhoea, Infection.*

I. Introduction

Gastroenteritis also known as acute diarrhoeal diseases is defined as the passage of loose, liquid or watery stools > 3 times a day lasting up to 10-14 days [1]. It is the second leading cause of death under 5 yrs. and third of total paediatrics admission in hospitals and 760,000 death every year [2]. Gastroenteritis with diarrhoea is a common condition in children, potentially leading to dehydration, morbidity, and in some countries substantial mortality. Significant proportions of children who suffer from diarrhoea are malnourished with depleted micronutrient stores. Therefore children with marginal nutritional status are also at significant risk of developing micronutrients depletion such as zinc with an episode of diarrhoea [3].Zinc has a direct effect on intestinal villous, brush border enzymes activity and intestinal transport of water and electrolytes and also has a marked effect on T- cell function. Copper is present in cytosolic erythrocyte superoxide dismutase (Cu, Zn-SOD), which is an important scavenger of O_2^-, a free radical and in Ceruloplasmin which plays a role in acute-phase response to infectious diarrhoeal diseases [4].

II. Aims And Objects

1. To estimate serum zinc and copper levels in children suffering from gastroenteritis and in healthy controls
2. To find out any correlation between serum zinc and copper levels in children with gastroenteritis and in healthy controls
3. To establish any significant relationship between serum zinc levels and weight of children with gastroenteritis and healthy controls.

III. Materials And Methods

The study was a Case control study carried out in the Department of Biochemistry in collaboration with the Department of Paediatrics, Regional Institute of Medical Sciences, Imphal, Manipur during the period from November 2012 to October 2014. Seventy children with gastroenteritis in the age group 0-12 years attending Paediatric OPD and/or admitted in the ward, RIMS hospital were selected randomly as cases for the study and another 70 age and sex matched healthy children were taken as control group. Children with Congenital diseases, Malignancy, Systemic diseases, recurrent pneumonia, Malaria, Sickle cell anaemia or Leukaemia, on

micronutrients such as Zinc and Copper supplementation for the last 6 months were excluded from the study.

Approval for the study was taken from the Institutional ethical committee, RIMS, Imphal and informed consent was taken from all the participants' parents and guardians before the start of the study.

Detailed histories of all the participants were taken. Clinical examination including body temperature, signs of respiratory diseases, body height, body weight, tricep skinfold thickness, mid arm circumference for each participants were taken. Body height was estimated from total standing height. Body mass index (BMI) was calculated as weight (kg) divided by height meter squared (m^2). Triceps skin fold thickness was measured by Lange skinfold calliper (model 68902, USA) at the posterior midpoint between the acromion and the olecranon. Mid arm circumference was measured midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The mid arm circumference was measured with a flexible plastic tape and recorded to the nearest 0.1cm.

About 2 ml of venous blood was collected in the morning between 9-11 am by venepuncture from patient's antecubital vein and stored in a sterile plain vial for estimation of serum Zinc and Copper. It was processed within 1 hr of collection. Estimation of zinc and copper in the serum was done by colorimetric method using commercially available kit of Crest Biosystems, Goa, as described by Abe A and Yiamashita S [5] and Makino T [6]. Normal range: Zinc 60- 120 µg/dl; Copper 80-155 µg/dl.

IV. Statistical Analysis

All analyses were performed using statistical software SPSS version 16. All data were expressed in Mean ± Standard deviation. Frequency and percentage were used for categorical data. Pearson's correlation analysis and Student t-test was advocated wherever necessary. The p-value <0.05 was used as the cut off value for statistical significance.

V. Results And Observations

Table 1: Age distribution of study children

Age (years)	Gastroenteritis (cases)	Healthy (controls)	Total	Chi-square test	p=value
≤1	20 (28.6)	3 (4.3)	23 (16.4)	32.05	0.000
1.1-5	42 (60.0)	31 (44.3)	73 (52.1)		
5.1-10	6 (8.6)	26 (37.1)	32 (22.9)		
>10	2 (2.8)	10 (14.3)	12 (8.6)		
Total	70 (50.0)	70 (50.0)	140 (100.0)		
Mean± SD	2.7 ± 2.5	6.2 ± 3.4			

Table 1 shows that more than half of the children were in the age group 1.1-5 years which was same in both the gastroenteritis and healthy groups. Children with age >10 years was less (2.8%) in children with gastroenteritis but among healthy Controls, age ≤1 years was less (4.3%).

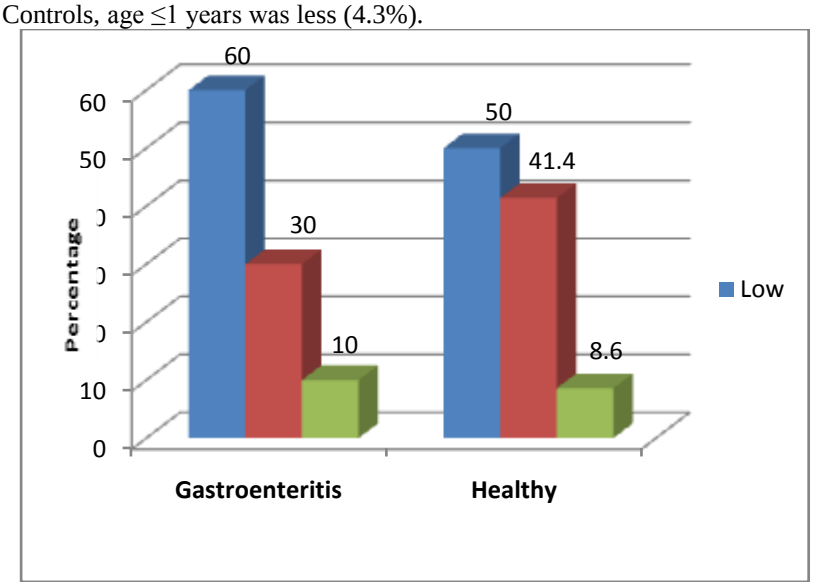

Figure 1: Distribution of study children by Socio – economic status.

Fig.1 shows that majority of cases and controls were from low socio-economic status (SES), followed by middle, and high socio-economic status had the least number of both cases and controls. The finding was statistically not significant.

Table 2: Comparison between Zinc and Copper among healthy children and gastroenteritis children

Parameter	Number	Mean ± SD	t-test	p-value
Zinc				
Gastroenteritis	70	70.3 ± 25.3	t-7.651	p=0.00
Healthy	70	102.2 ± 23.3		
Copper				
Gastroenteritis	70	170.9 ± 41.6	t- 7.617	p=0.000
Healthy	70	118.5 ± 39.6		

Table 2 shows that there was significantly lower Zinc level among gastroenteritis children than healthy (70.3 µg/dl Vs 102.2 µg/dl). Copper level was higher among gastroenteritis children than healthy children (170.9 µg/dl Vs 118.5 µg/dl) and the findings were statistically significant ($p<0.05$).

Table 3: Relation of serum zinc level among gastroenteritis and healthy children

Zinc level (µg/dl)	Gastroenteritis cases (%)	Healthy controls (%)	Total (%)	Chi-square test	p-value
≤60	28 (40.0)	3 (4.3)	31 (22.1)	25.89	0.000
>60	42 (60.0)	67 (95.7)	109 (77.9)		
Total	70 (100.0)	70 (100.0)	140 (100.0)		

Table 3 shows that 40% of Zn deficiency was in the gastroenteritis children whereas 4.3% of Zn deficiency was in healthy control children.

Table 4: Relation between serum zinc level and different group of children

	Normal weight Zn level (mean ± SD)	Underweight Zn level (mean ±SD)	t-test	p-value
Gastroenteritis	70.21 ± 20.23	60.34 ± 17.54	2.08	0.04
Healthy controls	109.42 ± 45.66	100.54 ± 43.22	0.674	0.50

Table 4 shows that among gastroenteritis children, underweight children had lower zinc level than normal weight children and the finding was found to be significant ($p<0.05$). The finding was same for healthy children but the finding was found to be insignificant.

Table 5: Relation between Zinc and Copper among gastroenteritis children

		Zinc	Copper
Zinc	Pearson Correlation	1	-0.331
	Sig. (2-tailed)		0.005
	N	70	70
Copper	Pearson Correlation	-0.331	1
	Sig. (2-tailed)	0.005	
	N	70	70

Table 5 shows that there was poor negative correlation between Zinc and Copper levels in gastroenteritis children ($r=-0.331$) and the finding was statistically insignificant.

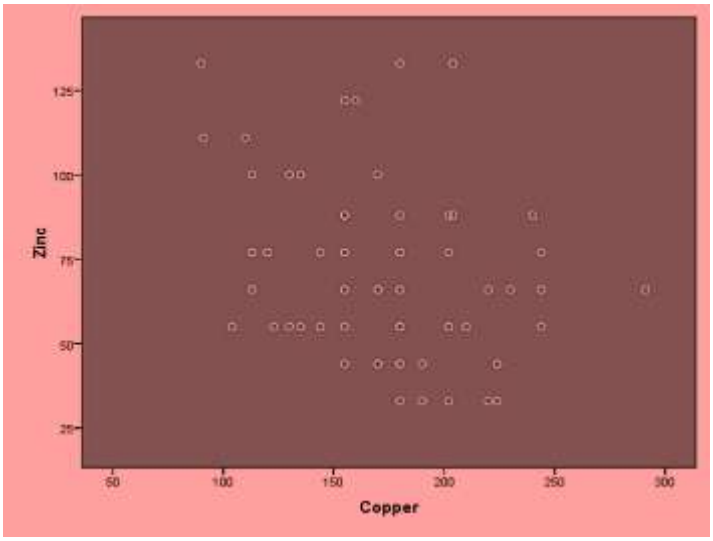

Figure 2: Scattered Diagram showing relation between Zinc and Copper among gastroenteritis children

Fig. 3 shows that there was poor correlation between Zinc and Copper levels in gastroenteritis children (r=-0.331) and the finding was statistically insignificant. This was shown in figure 6 (scattered diagram) as scattering of dots all around.

VI. Discussion

The age wise distribution (Table 1) shows that 60% of the cases belong to age group 1.1- 5yrs followed by 28.6 % in the age group ≤1yr but Children with >10yrs were least affected by gastroenteritis (2.9%). Similar findings were observed by Gupta S and Lalit U[7], Madhavan NK and Choudhary DR[8], Hotz C et al[9] and Cole RC et al[10]. They found the highest incidence in the age group < 5years. Hotz C et al[9] observed that the age was significantly associated with serum Zn concentrations. Serum Zn concentrations were lowest in young children and it steadily increase with age.

Madhavan NK and Choudhary DR[8] found that Zn deficiency among <5 yrs old children was a major cause of death due to morbidity and Zinc deficiency could account about 17% of the worlds population at risk and 4.4% under 5 years child death globally. Weaning with only cereal-based food, faulty feeding practice with inadequate intake of dietary Zn or diets high in phytate lead to low bioavailability of Zn resulting in low Zn absorption from the diet[11]. Distribution by socio-economic status (SES) (Fig. 1) reveal that 60% of cases belong to low SES, followed by 30% in middle SES and 10% in high SES. The trend was same for controls also. In developing countries, due to more general poverty and predominance of vegetarian diets which have high phytates content, lack of intake of animal foods and malnutrition coupled with the lack of knowledge about the importance of food group diversity for the health and growth of young children may contribute to reduce Zn level. Parasite infections like Malaria, helminthiasis, diarrhoea etc are common in poor and developing countries which can also lead to increased Zn losses [10,12].

Table 2 shows reduced serum Zn level among gastroenteritis cases than healthy controls (70.30µg/dl Vs 102.24µg/dl) and increased Serum Cu level among gastroenteritis cases than healthy controls (170.91µg/dl Vs 118.56µg/dl) and the finding was statistically significant ($p<0.05$). Similar findings were observed by Amare B et al [13] Krakas Z et al[14] and Erbagsi AB et al[15]. The lower concentrations of Zinc in cases than the controls could result from preceding deficiencies that might have enhanced susceptibility to infection, and/or from their high demands in overt infections causing diarrhoea. And higher serum Cu concentrations in cases than the controls could be an acute- phase response to infectious diarrhoeal diseases [16,17]. Plasma concentration of copper binding protein, ceruloplasmin and Cu are increased as an acute phase response in a variety of infection and inflammatory condition. Table 3 show that 40% of Zn deficiency was in the gastroenteritis children whereas 4.3% of Zn deficiency was in healthy control children. A low serum zinc concentration was shown to predict an increased risk of diarrhoea among children in India[18]. Underweight cases (Table 4) had lower serum Zn level (60.34±17.54µg/dl) than those with normal weight (70.21±20.23µg/dl). The same finding was also found in the controls. These findings were statistically significant for cases but not for controls group. Similar findings were observed by many workers.[18-21] The workers observed that serum Zn has a role in maintaining normal growth and function of the human body and Zn deficiency cause stunted growth, underweight and malnutrition. The low serum level of Zinc in underweight diarrheic patients can also be due to reduced dietary intake resulting from anorexia or decreased absorption or increased faecal loss. Furthermore, reduction in plasma Zinc that occurs during infection is attributable to redistribution within the body, or induced by pro inflammatory

cytokines which have been linked to specific host-defence mechanism [10, 12].The mechanism of action of zinc in the management of diarrhoea is not completely understood.[6] It is likely improving the absorption of fluids from the intestine, helping with clearance of organisms, and supporting regeneration and mucosal integrity, and is likely to have an immunity-related mechanism Table 5 and fig 2 show the relation between serum Zn and Cu among children with gastroenteritis. The present study showed a poor negative correlation between serum Zn and Cu in children with gastroenteritis (r=-0.331) and the finding was statistically insignificant. A concomitant increased in the serum Cu concentration is an expected finding in infectious/inflammatory conditions [15]. Zinc supplementation for diarrhoea in children is a safe and effective measure to shorten the illness and to reduce other complications including death. While the World Health Organization recommends a daily dose of 10 to 20 mg of zinc (based on age) for 10 to 14 days for management of acute diarrhoea.[20]

VII. Conclusion

Gastroenteritis remains a leading cause of global childhood morbidity and mortality. In developing countries like India, the scenario is worse due to infection, malnutrition and illiteracy thereby leading to excessive faecal loss of micronutrients such as Zinc.

The present study which was undertaken to estimate the serum Zinc and Copper levels and their correlation in children with gastroenteritis has revealed a significant decreased in Zinc level with increased in serum Copper level. From the previous and present studies, it is confirmed that Zinc plays a key role in gastroenteritis in children and its supplementation greatly helps in the prevention and treatment of childhood 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.

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