ORIGINAL RESEARCH

Study of serum calcium, zinc and iron in severe acute malnourished children of low economic group

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ABSTRACT

Background: Malnutrition is a broad and encompassing phrase. Malnutrition often pertains to the condition of under nutrition, which arises due to insufficient intake, inadequate absorption, or excessive nutrient loss. However, this word also incorporates over nutrition, which occurs as a consequence of excessive ingestion of certain nutrients. Severe acute malnutrition (SAM) is correlated with heightened severity of prevalent infectious illnesses, and mortality in children afflicted with SAM is predominantly attributable to infections AM is associated with Ca deficiency and increases the risks of rickets and hypocalcemia. Zinc deficiency is common world-wide but is seen with greater frequency in developing countries. Zinc deficiency can be inherited or acquired and typically presents with infectious, inflammatory, gastrointestinal, or coetaneous involvement. Iron is an essential micronutrient for human beings due to its pivotal involvement in several physiological processes, including but not limited to oxygen transportation, oxidative metabolism, cellular proliferation, and numerouscatalytic events⁵. Nutritional anaemia is one of the major causes of growth retardation, decreased physical activities and cognitive function in children. **Aim:** Aim of our study is to study of serum calcium, zinc and iron in severe acute malnourished children of low economic group. In our study, mean calcium was 5.93 ± 1.17 mg/dl in case, and mean calcium was 7.87 ± 0.42 mg/dl in Control. Mean calcium was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean calcium between case and control. In our study, mean iron was $46.12 \pm$ 9.33 μ g/dlin case, and mean iron was 63.21 \pm 13.46 mcg/dl in control. Mean iron was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean iron between case and control. In our study, the mean zinc was 0.41 ± 0.23 µg/dl in case, and the mean zinc was 0.88 ± 0.17 µg/dl in control. Mean zinc was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean zinc between case and control. According to above graph calcium iron and zinc is positively correlated with MUAC. **Material and methods**: After institutional ethics committee approval, research authors would commence. Participants gave informed consent before in this study, a total of 200 cases ≤.5 year of either gender, diagnosed as sever malnourished were enrolled from Paediatric Department. The study included 100 SAM patients and 100 healthy controls from Indore's Index Medical College & Research Centre (IMCRC) departments of paediatrics OPD. This prospective observational study follows Indore IMCHRC rules & regulations. However, the study's limitations, including its cross-sectional design, call for longitudinal investigations to establish causality between macronutrient deficiencies and levels in SAM-affected children. Additionally, the research primarily focused on a specific geographical region. **Conclusion:** A healthy diet in children is important to provide nutrients that support optimum physical growth and cognitive development and to also establish healthy eating behaviours that lower risk of chronic diseases in adulthood. Although it is generally advised that micronutrients should be obtained from food, many children do not reach daily intake recommendations for select micronutrients, including vitamins A, C, D, and E, and some minerals, such as calcium and magnesium. Therefore, with our study we found that there is significant difference in calcium, iron, and zinc level between cases and control. So, there is significant need for assessment of calcium, iron, and zinc level, which further helps in decreasing complications associated with calcium, iron, and zinc level and there is strict need for maintaining it, which further helps in decreasing morbidities and mortalities among children's.

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INTRODUCTION

Malnutrition can occur when an individual fails to ingest the necessary quantity or quality of nutrients that constitute a balanced and nutritious diet over a prolonged duration. In the following discourse, the terms malnutrition and under nutrition are utilized synonymously. The prevalence of malnutrition among children is widespread in developing nations, such as India. A significant proportion exceeding 33% of mortality cases among children aged 0-5 years can be attributed to the presence of malnutrition^[1]. Severe acute malnutrition (SAM) is correlated with heightened severity of prevalent infectious illnesses, and mortality in children afflicted with SAM is predominantly attributable to infection. There are notable differences in the diagnosis and therapy of infection between children who are malnourished and those who are well-nourished. The purpose of this brief is to provide an overview of the empirical basis supporting significant practical inquiries concerning the treatment of infectious illnesses in children with severe acute malnutrition (SAM), as well as to identify areas in need of further investigation[**2]** .SAM is associated with Ca deficiency and increases the risks of rickets and hypocalcemia. A study found that 26% had hypocalcemia(<2·12mmol/l), 65·3% had vitamin D deficiency (serum 25-(OH)D< 30 mol/l) and 42% had clinical rickets. Importantly, hypocalcaemia occurred more commonly in patients with clinical rickets, suggesting an increased vulnerability in patients already displaying signs of decreased Ca and/or vitamin D reserve. Rickets is clinically significant as it is associated with skeletal deformities, dental abnormalities, bone pain, muscle weakness, failure to thrive, developmental delay,

hypocalcaemia seizures and, sometimes, even death from complications of hypocalcaemia[**3]** . Zinc is an integral part of more than 200 enzymes and has significant task in nucleic acid metabolism, cell replication, tissue repair and growth. Inadequate Zn intake may limit the growth of these children during recovery from malnutrition thru clinical features of Zn deficiency like poor appetite, growth failure, skin lesion, diarrhea, poor wound healing and poor immunity. Zinc deficiency is a major health problem worldwide, especially in developing countries; hence it is designated by the World Health Organization as a major disease contributing factor^[4]. Iron is an essential micronutrient for human beings due to its pivotal involvement in several physiological processes, including but not limited to oxygen
transportation, oxidative metabolism, cellular transportation, oxidative metabolism, cellular proliferation, and numerous catalytic events. Inorder to confer advantageous effects, it is important to sustain the concentration of iron inside the human body with in the optimal threshold[**5]** . The process of iron metabolismis highly intricate; including severs all organs and tissues, with their interplay playing a crucial role in maintaining iron homeostasis. There is currently no known active mechanism for the excretion of iron. Consequently, the intestinal absorption of iron is rigorously regulated in order to maintain equilibrium with the daily excretion^[6]. The bone marrow serves as the primary consumer of iron inside the human body, as it is the location where erythropoietin occurs. Conversely, the reticule endothelial system is responsible for the recycling of iron through the process of erythrocytephagocytises^[7]. So this study we performed to evaluate calcium, iron and zinc among SAM patients.

RESULTS

Table 1: Age Distribution

In our study, 39% of cases were in the age group of ≤ 1 year in Group 1 (case), 27% of cases were in the age group of 1 year, 11% of cases were in the age group of 2 year, 11% of cases were in the age group of 3 year, 11% of cases were in the age group of 4 year, and 1% of cases were in the age group of 5 year. In Group 2 (control), 36% of cases were in the age group of 1 year, 19% of cases were in the age group of 2 year, 19% of cases were in the age group of 3 year, 13% of cases were in the age group of 4 year, and 1% of cases were in the age group of 5 year and when we compared the mean age between cases and control there is not much significant difference between cases and control.

Table 2: Gender Distribution

In our study, 74% of cases were male and 26% were female in Group 1 (case), and 70% of cases were male and 30% were female in Group 2 control and there is not much significant difference between males and females in cases and control.

Table 3: Descriptive Table

Table 4: Comparison Of Mean Calcium In Case & Control Group.

In our study, mean calcium was 5.93 ± 1.17 mg/dl in Group 1 (case), and mean calcium was 7.87 ± 0.42 mg/dl in Group 2 (Control).Mean calcium was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean calcium between Group 1 (case) and Group 2 (control).

Table 5: Comparison of mean iron µg/dl in case & control group.

In our study, mean iron was 46.12 ± 9.33 µg/dl in Group 1 (case), and mean iron was 63.21 ± 13.46 mcg/dl in Group 2 (control). Mean iron was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean iron between Group 1 (case) and Group 2 (control).

In our study, the mean zinc was 0.41 ± 0.23 µg/dl in Group 1 (case), and the mean zinc was 0.88 ± 0.17 µg/dlin Group 2 (control). Mean zinc was higher in the control group as compared to the malnutrition group, and there was a significant difference in mean zinc between Group 1 (case) and Group 2 (control).

Correlation between MUAC and calcium

Were, X= MUAC Y= CALCIUM According to above graph calcium is positively correlated with MUAC The value of r is 0.0475

Correlation between MUAC and IRON

The value of r is 0.0463 Were,

X= MUAC $Y = IRON$

According to above graph iron is positively correlated with MUAC

Correlation between MUAC and ZINC

The value of r is 0.0227 Were, $X=$ MUAC $Y = ZINC$

According to above graph zinc is positively correlated with MUAC

DISCUSSION & OUTCOME

About 99% of calcium in the body is found in bones and teeth. Adequate intake of calcium throughout childhood and adolescence is important for proper mineralization of growing bones, attainment of peak bone mass, and reduction of risk for osteoporosis in adulthood. Thus, dietary intake recommendations for calcium in children are established based on the calcium intake needed to support bone accretion and overall calcium retention (i.e., the dietary intake needed to achieve positive calcium balance). The RDA is 1,000 mg/day for children ages 4 to 8 years and 1,300 mg/day for boys and girls ages 9 to 13 years. Calcium intake recommendations are higher in children ages 9 to 13 to account for increased needs of the mineral during puberty[**8]** . Iron is an essential component of hundreds of proteins and enzymes involved in various aspects of metabolism, including oxygen transport and storage, electron transport and energy metabolism, antioxidant and beneficial prooxidant functions, oxygen sensing, and DNA synthesis^[9]. Iron is stored in the body as ferreting, and serum level of ferritin is a good clinical indicator of iron status in children. Iron deficiency, which is the most common nutritional deficiency in the world, is a major public health problem, especially in developing nations, but it is also prevalent in industrialized nations. Severe iron deficiency leads to irondeficiency anaemia, which affects more than 30% of the global population $(2 \text{ billion people})^{[10]}$. Irondeficiency anaemia results when there is inadequate iron to support normal red blood cell formation. The anaemia of iron deficiency is characterized as Microcytic and hypo chromic, meaning red blood

cells are measurably smaller than normal and their haemoglobin content is decreased. At this most severe stage of iron deficiency, symptoms maybe a result of inadequate oxygen delivery due to anaemia and/or sub-optimal function of iron-dependent enzymes^[11]. Low red cell count, low Haematocrit, and low haemoglobin concentrations are all used in the clinical diagnosis of iron-deficiency anaemia. Most observational studies have found relationships between iron-deficiency anaemia in children and poor cognitive development, poor school achievement, and behaviour problems. However, itis difficult to separate the effects of iron-deficiency anaemia from other types of deprivation in such studies, and confounding factors may contribute to the association between iron deficiency and cognitive deficits. Iron has an important role in the development of the cells that produce myelin; as noted above, the myelin sheath is the insulating layer of tissue comprised of lipids and proteins that surrounds nerve fibres. This sheath acts as a conduit in an electrical system, allowing for rapid and efficient transmission of nerve impulses. Iron is also important for enzymes involved in the synthesis of certain neurotransmitters and for DNA synthesis. The mineral zinc is essential for growth and development, immune function, neurological function, and reproduction. Zinc plays a number of catalytic, structural, and regulatory roles in cellular metabolism. Zinc deficiency is a major public health concern and has been estimated to affect more than 2 billion people in less developed nations. Children are at increased risk for zinc deficiency, which can lead to delayed physical growth, impaired immunity, and possibly to delayed mental development. Mild forms

of this mineral deficiency, which are common in both developing and developed nations, appear to have negative effects on growth and development. Mild zinc deficiency contributes to impaired physical growth in children. Significant delays in linear growth and weight gain, known as growth retardation or failure to thrive, are common features of mild zinc deficiency in children. Modest zinc supplementation (5.7 mg/day) resulted in increased growth rates compared to placebo. More recently, a number of larger studies in developing countries observed similar results with modest zinc supplementation. A meta-analysis of growth data from zinc intervention trials recently confirmed the widespread occurrence of growth-limiting zinc deficiency in young children, especially in developing countries. Although the exact mechanism for the growth-limiting effects of zinc deficiency is not known, recent research indicates that zinc availability affects cell-signalling systems that coordinate the response to the growth-regulating hormone, insulin-like growth factor-1 (IGF-1). Adequate zinc intake in children is essential in maintaining the integrity of the immune system, and zinc deficiency is associated with increased susceptibility to a variety of infectious agents. The adverse effects of zinc deficiency on immune system function are likely to increase the susceptibility of children to infectious diarrhoea, and persistent diarrhoea contributes to zinc deficiency and malnutrition. Zinc supplementation in combination with oral rehydration therapy has been shown to significantly reduce the duration and severity of acute and persistent childhood diarrhoea and to increase survival in a number of randomized controlled trials. Recently, a meta-analysis of randomized controlled trials concluded that zinc supplementation reduces the frequency, severity, and duration of diarrheal episodes in children under five years of age. The World Health Organization and the United Nations Children's Fund currently recommend zinc supplementation as part of the treatment for diarrheal diseases in young children. Zinc supplementation may also reduce the incidence of lower respiratory infections, such as pneumonia. A pooled analysis of a number of studies in developing countries demonstrated a substantial reduction in the prevalence of pneumonia in children supplemented with zinc. A recent meta-analysis found that zinc supplementation reduced the incidence but not duration of pneumonia or respiratory tract illnesses in children under five years of age. Due to conflicting reports, it is not yet clear whether zinc supplementation has utility in treating childhood malaria.

From table 3 to table 6 we observed and analyzed that mean calcium was 5.93 ± 1.17 mg/dl in Case and mean calcium was 7.87 ± 0.42 mg/dl in Control. Mean calcium was higher in the control group as compared to the malnutrition group and there was a significant difference in mean calcium between case and control. Similar to our study, frank S et al in 2000 also observed that total calcium, total protein, albumin, and inorganic phosphate concentrations were decreased in a variable degree according to the clinical type of PEM, ascending to normal levels during recovery from PEM**[12] .** In another study by Smileet al. (2020) determine the prevalence of hypocalcaemia among children hospitalized with SAM. Serum Ca and 25-hydroxycholecalciferol (25- (OH) D) were estimated. Conducted a cross sectional study to determine the prevalence and predictors of hypocalcaemia in under-five children (1–59 months) hospitalized with SAM in a tertiary care hospital in Delhi, between November 2017 and April 2019. A logistic regression model was constructed taking hypocalcaemia as a dependent variable, and sociodemographic and clinical variables as independent variables. Hypocalcaemia was documented in thirty-nine (26 %) children hospitalized with SAM, the prevalence being comparable between children aged <6 months (11/41, 26·8 %) and those between 6 and 59 months (28/109, 25.7 %) ($P = 0.887$). Vitamin D deficiency (serum 25-(OH) D<30 nmol/l) and clinical rickets were observed in ninety-eight (65.3%) and sixty-three (42%) children, respectively. Rickets and hypocalcaemia are common in children with SAM. They suggested that routine supplementation of vitamin D should be considered for severely malnourished children and Calcium may be empirically prescribed to severely malnourished children with clinical rickets, abdominal distension and/or sepsis^[13]. In our study mean Copper was 1.27 ± 0.23 g/l in case and the mean Copper was 1.28 ± 0.23 g/l in control. Mean Copper was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Copper between case and control. In one study by Chowdhury et al. (2016)in my men Singh Medical College Hospital from 1st October 2009 to 31st May 2011. They analyzed children aged 1-5 years with presence of one or more criteria WHM <70%, WHZscore <-3SD, Bipedal edema & Mid upper arm circumference <110mm were taken as study group and children aged 1-5 years with normal growth allowable normal range of variation is between 3rd and 97th centile curve or median (50th centile) ±2SD of weight for age growth chart (CDC growth chart, USA, 2000) were taken as reference group. Persistent diarrhoea, Patients taking medications containing zinc, copper, magnesium, phosphorus & calcium, PEM with shock were excluded from study group. After analysis of total 120 study populations, they include 90 Out of 120 were taken as a study group (SAM) & 30 were reference group. In reference group serum Zn, Cu, Mg, P value was $103.80\pm8.86\mu g/dl$, 135.92±13.57μg/dl, 2.31±0.18mg/dl, 3.96±0.22mg/dl respectively. In study group serum Zn, Cu, Mg, P value was 60.33±11.08μg/dl, 80.60±15.46μg/dl, 1.47±0.22mg/dl, 2.00±0.52mg/dl respectively. All these results show that there is significant difference between study group & reference group. They

suggested that, decreased level of these parameters, close biochemical monitoring and follow up should be emphasized for the children with SAM[**14]** . In another study by Gautam B al. (2008)in the department of Biochemistry, Mymensingh Medical College in cooperation with the Paediatric wards of Mymensingh Medical College Hospital and Ganadhakshya Nagar Hospital, Dhaka during the period from July 2005 to June 2006. They explore the status of serum zinc and copper level in Bangladeshi children with Protein Energy Malnutrition (PEM) as a means to monitor the possibility of management of these children as each of these mineral deficiencies produce typical deficiency syndromes. A total of 68 children aging from five months to five years were included in this study. Subjects were divided into two groups-Group I (Control; n=20)-children with normal growth, weight for age between 3rd and 97th centile curve, Centres for Disease Control (CDC) growth chart, USA, 2000 and group II-(children with PEM; n=48)-children with retarded growth, weight for age below 3rd centile of CDC growth chart, USA, 2000. Group II was again divided into three subgroups according to Wellcome classification of PEM and clinical features. These were Group IIA: Marasmus (n=19), Group IIB: Kwashiorkor (n=14) and Group IIC: Marasmic Kwashiorkor (n=15). Among the different groups of children mean+/-SD (Standard Deviation) of serum zinc in PEM (59.85+/-11.18 microg/dl), Marasmus (66.73+/-8.23 microg/dl), Kwashiorkor (49.69+/- 10.35 microg/dl) and Marasmic Kwashiorkor (60.63+/-8.04 microg/dl) were all significantly lower (p<0.001) than in control group (106.16+/-13.36 microg/dl). Similarly mean+/-SD of serum copper in PEM (82.73+/-16.35 microg/dl), Marasmus (93.72+/- 9.77 microg/dl), Kwashiorkor (63.75+/-13.12 microg/dl) and Marasmic Kwashiorkor (86.52+/-8.68 microg/dl) were all also significantly lower (p<0.001) than in control group (135.88+/-11.88 microg/dl). It is evident from the study that serum zinc and copper level significantly decrease in children with PEM which is similar to our study findings**[15] .**In our study mean Phosphorus was 2.28 ± 0.43 mg/dl in case and the mean Phosphorus was 2.28 ± 0.44 mg/dl in control. Mean Phosphorus was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Phosphorus between case and control.In our study mean Magnesium was 2.27 ± 0.39 mg/dl in case and the mean Magnesium was 1.90 ± 0.30 mg/dl in Group 2 (Control). Mean Magnesium was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Magnesium between case and control. In our study mean Iron was 46.12 ± 9.33 µg/dl in case and mean Iron was 63.21 \pm 13.46 µg /dl in control. Mean Iron was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Iron between case and control. In our study mean Zinc was 0.41 ± 0.23 µg /dl in case and the mean Zinc was 0.88

 \pm 0.17 mcg/dl in control. Mean Zinc was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Zinc between case and control. In our study mean Serum Albumin was 2.26 ± 0.60 g/dl in case and mean Serum Albumin was 4.20 ± 0.78 g/dl in control. Mean Serum Albumin was higher in the control group as compared to the malnutrition group and there was a significant difference in mean Serum Albumin in between case and control. Similar to our study another research work done by Kang-Sheng et al, (2015)they included minerals such as zinc, copper, selenium, calcium, and magnesium. They evaluated the distribution and correlation of nonessential (lead) and essential elements in whole blood from 1- to 72 month-old children. Levels of copper and magnesium were 18.09 ± 4.42 µmol/L and 1.42 ± 0.12 mmol/L, respectively. 6.04% of all children showed copper levels below the normal threshold, the levels of Magnesium were stable in different age groups. Though the overall mean blood zinc and iron concentrations (61.19 \pm 11.30 µmol/L and 8.24 \pm 0.59 mmol/L, respectively) gradually increased with age and the overall deficiency levels (24.1% and 36.0%, respectively) decreased with age, zinc and iron deficiencies were still very stable. Controlling for gender and age, significant positive correlations were found when comparing copper to zinc, calcium, magnesium, and iron ((r = 0.333, 0.241, 0.417, 0.314, $p < 0.01$); zinc to magnesium and iron ($r = 0.440$, $0.497p < 0.01$; and magnesium to Calcium and iron $(r = 0.349, 0.645, p < 0.01)$. The overall mean blood lead levels (41.16 ± 16.10) were relatively unstable among different age groups. The prevalence of lead intoxication in all children was 1.3%. Calcium levels decreased gradually with age, with an overall concentration of 1.78 ± 0.13 mmol/L. In another study by Raza M et al. (2020) conducted acrosssectional study aimed to determine the frequency of electrolyte imbalance in children with SAM admitted at a tertiary care hospital. This cross-sectional study includes 184 patients with SAM aged between 6 and 60 months, who were admitted at the inpatient Department of Paediatrics, Civil Hospital, Karachi, Pakistan, from January to July, 2017. Out of 184 children, 62% (n = 114) were males and 38% (n = 70) were females and 172 (93.5%) patients had electrolyte imbalance. Hypokalaemia was present in 79.9%, whereas hypocalcaemia, hyponatremia, and hypomagnesemia were present in 71.7%, 48.9%, and 13.6%, respectively. They found that electrolyte disturbances are common in SAM. Serum electrolytes of every malnourished child admitted should be assessed and corrected to avoid fatal outcomes. Study concluded that hypokalaemia followed by hypocalcaemia as the common electrolyte abnormalities in children with SAM. They suggested that, serum electrolytes of every malnourished child admitted should be evaluated and corrected at the earliest to avoid any life-threatening outcomes^[17]. In

another study by Ha F al. (2022) effects of malnutrition in the optimal growth, development, and health of infants, and the reference intervals (RIs) from these trace elements in the blood are very important for an accurate assessment of the status of the elements. In their study, blood samples from a total of 13,446 infants (7206 boys and 6240 girls) were used, and the copper (Cu), zinc (Zn), calcium (Ca), magnesium (Mg), and iron (Fe) in their blood were determined using atomic absorption spectrometry. In their multivariable analysis, after making the relevant adjustments for the confounding factors, the age of the infants showed a significant positive correlation with the concentrations of Zn, Ca, Mg, and Fe found in the blood $(p<0.01)$. Furthermore, there were obvious differences in the Cu, Zn, and Ca levels in the blood according to the gender of the infants $(p<0.01)$. similar to this study we also found that there is positive correlation of MUAC with calcium, magnesium, phosphorous, copper, zinc and albumin levels**[18]** . So, with our study we also suggested that same that there is strong need for assessment of macronutrients for proper development of children to achieve their milestones in times and to further decrease mortality, morbidity and complications associated with deficiency of this minerals included in our study.

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