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Original Research Article

Oxidative stress in children with severe acute malnutrition between 6 months to 5 years of age

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ABSTRACT

Background: Severe acute malnutrition (SAM) constitutes one of the major nutritional and health problems in children under five years of age in developing countries. It has a significant contribution to the mortality and morbidity in this age group of children. So, there is a need to look for the pathophysiology identifying events at cellular level to formulate better management strategies. The oxidative stress and a possible consequential accelerated apoptosis may contribute to pathophysiology in malnutrition. Markers of oxidative stress are Malondialdehyde levels (MDA), a byproduct of lipid peroxidation and antioxidants like Zinc and Glutathione (GSH). So the objective of study is to measure oxidative stress in hospitalized children with severe acute malnutrition (SAM) between 6 months to 5 years of age through serum levels of Zinc, glutathione and MDA.
Methods: This was a hospital based prospective case control study where 100 hospitalised children from 6 months to 5 years of age with severe acute malnutrition were selected along with 100, sex and age matched healthy controls from outpatient department. Oxidative Stress was analysed by measuring serum levels of Zinc, GSH and MDA. Control group was simultaneously analysed for similar parameters of oxidative stress.
Results: Serum GSH and Zinc levels were found to be significantly lower while serum MDA level was found to be significantly higher in cases as compared to controls.
Conclusions: Severe acute malnourished children had an increased oxidative stress and decreased antioxidant defence compared with healthy controls.

Keywords: Glutathione, Malnutrition, Malondialdehyde oxidative stress, Zinc

INTRODUCTION

Under nutrition is one of the most concerning health and developmental issues in India as in other parts of the world. World Health Organization (WHO) defines malnutrition as 'the cellular imbalance between supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions'.[1] According to WHO guidelines malnutrition is a significant factor in approximately one third of the nearly 8 million deaths in children who are under 5 years of age worldwide.[2] It has been estimated that in India 65 %, i.e. nearly 80 million children under 5 year of age suffer from varying degrees of malnutrition. According to NFHS 3 data 23 percent of total under 5-year children are wasted in which 6.4% are severely wasted.[3] The prevalence of malnutrition varies across states, with Madhya Pradesh recording the highest rate (55 percent) and Kerala among the lowest (27 percent). Out of these 6 million malnourished children, 1.3 million have SAM It said that 60 out of 100 children in Madhya Pradesh suffer from malnutrition while the national average is a mere 42.[4] It has been seen that there is high mortality, treatment failure or short-term improvement even after so many

awareness programmes and training regarding this burning issue. One of the reason behind this is the little knowledge regarding changes at cellular level in SAM children. It is evident that free radical reactions have been implicated in many diseases, including atherosclerosis, cancer, diabetes mellitus, etc.[5,6] Earlier studies have shown that in malnutrition, there is excess production of reactive oxygen intermediates such as superoxide anion (O2–), hydroxyl radical (OH-), singlet oxygen and hydrogen peroxide (H_2O_2) within the erythrocytes. All these events lead to oxidative stress.[7,8,9] It is worth noting that the free radicals are very short lived and unstable, so they are difficult to measure. However, their detrimental effects can be measured by estimating their byproducts. Capacity of body to defend itself from free radicals can be measured by assessing the blood levels of antioxidant micronutrients like Zinc and endogenous antioxidants like Glutathione. Hence, there is need to understand the nature of antioxidants and their resultant benefits in the larger interest of the deprived population of developing countries.[10] Preliminary research correlated Zinc levels with poor growth in children with malnutrition. With this background knowledge, the study aspired to evaluate oxidative stress in malnourished children.

METHODS

This was a prospective case control study conducted in the department of Pediatrics of a tertiary level Medical college hospital in Madhya Pradesh. Children of age 6 months to 5 years with severe acute malnutrition as per WHO criteria were included while Patients having failure to thrive due to any organic cause, refusal of consent from parents were excluded. Written informed consent was taken from parents of all the children included in the study. Ethical approval was obtained from Institutional ethical committee. All anthropometric measurements including weight, height, mid upper arm circumference of the child with SAM were taken. All baseline investigations as prescribed in management of SAM were taken and 5 ml blood sample was drawn on admission using aseptic precautions and serum was separated by centrifugation at 3000 rpm for 10 minutes at room temperature and levels of GSH, Zinc and MDA were measured from serum using Ellman method (1959) Atomic Absorption Spectrophotometry method and Jean CD et al (1983) method respectively as markers of oxidative stress. Simultaneously samples were taken from age and sex matched healthy control group for comparison. Conclusion was drawn statistically to correlate outcome. Statistical analysis was done using SPSS IBM Version 20 software and Microsoft Excel. The results were expressed as mean SD. P value (<0.00%1) and (<0.05%) were considered to be highly and significant respectively.

RESULTS

A total of 200 children were enrolled in this study, out of which 100 cases and 100 controls were taken. Among these 100 cases, 28 cases dropped out at follow up. Baseline characteristics of these groups were comparable. Serum GSH level (mean+SD) was found to be significantly lower in cases (33.12+12.17µmol/ml) as compared to controls (78.60+14.22 µmol/ml) (p value<0.001). Similarly serum Zinc level (mean+SD) was found to be significantly lower in cases(63.87+16.17 µg/dl) as compared to controls (79.81+20.09 µg/dl) (p value<0.001).while Serum MDA level (mean+SD) was found to be significantly higher in cases(7.89+1.23 nmol/ml) as compared to controls (4.79+1.87 nmol/ml) (p value<0.001).

Table 1: Indices of oxidative stress and antioxidants among cases and control.

Parameters	Cases (SAM) N=100 (Mean±SD)	Controls N=100 (Mean±SD)	P value
MDA (nmol/ml)	7.89±1.23	4.79±1.87	<0.001 (HS*)
Zinc (µg/dl)	63.87±16.17	79.81±20.09	<0.001 (HS*)
GSH (µmol/ml)	33.12±12.17	78.60±14.22	<0.001 (HS*)

*HS- Highly significant

Oedematous SAM were associated with higher oxidative stress as compared to Non-oedematous SAM as there is significantly higher level of serum MDA(p=0.029) and lower level of serum Zinc(p=0.042) and serum GSH(p=0.031) as compared to Non-oedematous SAM.

Table 2: Indices of oxidative stress and antioxidant among Non-edematous and edematous SAM.

Para-meters	Non-oedematous SAM N=73 (Mean±SD)	Oedematous SAM N=27 (Mean±SD)	P value
MDA (nmol/ml)	8.0±1.3	8.9±1.3	0.029(S*)
Zinc (µg/dl)	68.9±16.0	61.5±15.7	0.042(S*)
GSH (µmol/ml)	33.8±11.8	27.4±13.2	0.031(S*)

DISCUSSION

In the present study, we analyzed the markers of oxidative stress in children with severe acute malnutrition that is found to be increased with decreased antioxidant defence compared with healthy controls. Malondialdehyde, product of lipid peroxidation is generated in excess amount and significant increase in level of MDA in malnourished compared to healthy controls indicates occurrence of lipid peroxidation.

Lipid peroxidation lead to loss of membrane fluidity and integrity which lead to decrease efficiency with which

ATP are generated in mitochondria, thus further aggravating the adverse effect of already reduced energy intake in malnourished children. Antioxidants break the chain of lipid peroxidation and trap free radicals thus preventing oxidative damage. The body has several endogenous antioxidant defense systems which include enzymes, compounds, minerals and vitamins. In the present study it was found that serum Zinc and Glutathione was found to be significantly low in malnourished children.

This was found to be in accordance with previous studies done by Ghone AR et al in which Sixty severe acute malnutrition patients were studied before and after supplementation of antioxidants for one month, and their status were compared with those of 60 age and sex matched healthy controls.[11]

The levels of serum MDA, serum Vitamin E, serum zinc, erythrocyte superoxide dismutase was analyzed. Significantly increased levels of serum MDA were found in the patients as compared to those in controls, and significant depletions were found in the levels of serum vitamin E, zinc and Erythrocyte Superoxide Dismutase in patients with Severe Acute Malnutrition as compared to those in controls. Recently a study was conducted in Bhopal People's medical college by Sharma A et al.[10] They have taken 60 severe acute malnourished children age 6 months 5 years and 60 age and sex matched healthy controls and evaluate the effect of oxidative stress in them.

Mean serum MDA was found to be significantly raised while vitamin C and Zinc were significantly decreased in malnourished children as compared to healthy controls. From these observations it is evident that stress is created as a result of deficiency of nutrients in severe acute malnourished children. This stress lead to production of excess reactive oxygen species (ROS) that lead to lipid peroxidation and consequent formation of MDA in blood.

In another study of Jain A et al serum Zinc and Malondialdehyde concentrations and their relation to Total Antioxidant Capacity(TAC) in Protein Energy Malnutrition.[12] The significant increase in serum MDA concentration associated with the decrease in serum TAC, Zinc and Alkaline phosphatase in malnourished children suggest that these children were potentially susceptible to high oxidative stress.

Thus, significantly lower level of antioxidant and increased oxidative stress suggests that failure of antioxidant defense mechanism against oxidative stress may be an important factor in the pathogenesis of SAM.

CONCLUSION

Severe Acute Malnutrition is a condition threatened with increased oxidative stress and decreased antioxidant defence mechanism. Oedematous SAM has more oxidative stress than non-oedematous SAM, explaining more morbidity and mortality associated with oedematous SAM.

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