Section: Miscellaneous

Original Research Article

OXIDATIVE STRESS MARKERS IN MALNOURISHED CHILDREN WITH BACTERIAL INFECTION

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ABSTRACT

Background: Malnutrition in children is a major public health problem and is often complicated by bacterial infections. Both conditions independently contribute to oxidative stress through excessive generation of reactive oxygen species (ROS) and depletion of antioxidant defenses. However, data on oxidative stress markers in malnourished children with bacterial infections are limited. The objective is to evaluate and compare oxidative stress markers and antioxidant status in malnourished children with bacterial infections and well-nourished infected controls. **Materials and Methods:** This hospital-based case–control study was conducted over one year (February 2024–January 2025) in the Departments of Pediatrics and Biochemistry at Maharishi Vishwamitra Autonomous State Medical College, Ghazipur, Uttar Pradesh, India. Fifty children aged 6 months–5 years with severe acute malnutrition (cases) and confirmed bacterial infections were compared with 50 age- and sex-matched well-nourished children with similar infections (controls). Serum malondialdehyde (MDA) and protein carbonyls were measured as oxidative stress markers. Antioxidant status was assessed by erythrocyte superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), reduced glutathione (GSH), vitamin C, and ceruloplasmin levels. Data were analyzed using Student's t-test and Pearson correlation, with $p<0.05$ considered statistically significant. **Result:** Cases had significantly higher MDA (5.42 ± 0.82 nmol/mL vs. 3.28 ± 0.69 nmol/mL, $p<0.001$) and protein carbonyls (3.15 ± 0.51 vs. 2.01 ± 0.38 nmol/mg protein, $p<0.001$) compared to controls. Antioxidant enzyme activities (SOD, catalase, GPx) and non-enzymatic antioxidants (GSH, vitamin C, ceruloplasmin) were markedly lower in cases (all $p<0.001$). MDA and protein carbonyls showed significant negative correlations with SOD and GSH levels. **Conclusion:** Malnourished children with bacterial infections experience heightened oxidative stress and diminished antioxidant defenses compared to well-nourished infected peers. These findings highlight the potential role of antioxidant support as part of comprehensive management in such cases.

INTRODUCTION

Malnutrition remains a major public health problem in developing countries, acting as both a cause and a consequence of impaired immunity and recurrent infections.[1] Undernutrition compromises almost every component of the immune system, especially in protein-energy malnutrition (PEM), which increases the susceptibility to and severity of infectious diseases.[2]

One of the important mechanisms linking malnutrition and infectious morbidity is oxidative stress—a condition in which the excessive production of reactive oxygen species (ROS) such as superoxide anions, hydroxyl radicals, and hydrogen peroxide overwhelms the antioxidant defense systems, leading to lipid, protein, and DNA damage.[3]

In severely malnourished children, oxidative stress has been reported to be higher than in well-nourished counterparts, with significant biochemical evidence of lipid peroxidation and depletion of antioxidant

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reserves. For instance, children with marasmus have been shown to exhibit elevated serum malondialdehyde (MDA) levels along with reduced glutathione (GSH), glutathione peroxidase (GPx), and selenium concentrations.[4] Similarly, studies in children with PEM (including both marasmus and kwashiorkor) have documented increased oxidative damage markers with a parallel decline in superoxide dismutase (SOD), GPx, ceruloplasmin, and vitamins A, C, and E.[5,6]

Hospital-based case–control studies from India further support this association, reporting significantly higher MDA levels and lower antioxidant parameters such as zinc and GSH in children with severe acute malnutrition (SAM) compared to healthy controls.[7,8] The oxidative imbalance appears to worsen in the presence of infection. In a comparative study of well-nourished infected children, moderately malnourished infected children, and severely malnourished infected children, the latter groups showed significantly higher lipid peroxidation, lower SOD and GPx activity, and increased genotoxicity as indicated by elevated micronuclei counts in reticulocytes.[9]

Taken together, these findings suggest that malnutrition particularly severe forms such as SAM creates a state of heightened oxidative stress and depleted antioxidant defenses, which may be further aggravated by bacterial infections. This interplay has important clinical implications for morbidity and recovery. The present study was undertaken to evaluate oxidative stress markers in malnourished children with bacterial infections, in comparison with well-nourished infected controls.[10,11]

Objectives

1. Compare oxidative damage (MDA, protein carbonyls) between malnourished infected and well-nourished infected children.
2. Measure and compare antioxidant defenses (GSH, SOD, catalase, vitamin C).
3. Assess relationships between nutritional status and oxidative imbalance.

MATERIALS AND METHODS

This hospital-based case–control study was conducted over a period of one year, from February 2024 to January 2025, in the Departments of Pediatrics and Biochemistry at Maharishi Vishwamitra Autonomous State Medical College, Ghazipur, Uttar Pradesh, India. The study included children aged 6 months to 5 years who were admitted to the pediatric ward with confirmed bacterial infections based on clinical features and laboratory investigations, including culture and sensitivity testing. Cases comprised children diagnosed with severe acute malnutrition (SAM) as per the World Health Organization (WHO) criteria, in addition to having a documented bacterial infection. Age- and sex-matched well-nourished children with similar bacterial infections, admitted during the same period, served as controls. Children with chronic systemic illnesses, congenital anomalies, metabolic disorders, or prior antioxidant supplementation within the past three months were excluded. After obtaining written informed consent from parents or guardians, 3–5 mL of venous blood was collected from each participant under aseptic conditions. Part of the sample was used for routine laboratory investigations, while the remainder was processed for oxidative stress marker analysis. Lipid peroxidation was estimated by measuring serum malondialdehyde (MDA) using the thiobarbituric acid reactive substances (TBARS) method. Protein oxidation was assessed through protein carbonyl content determination. Antioxidant status was evaluated by measuring erythrocyte superoxide dismutase (SOD) activity, catalase activity, and whole-blood glutathione peroxidase (GPx) activity, along with reduced glutathione (GSH), serum vitamin C, and ceruloplasmin levels, using standard spectrophotometric methods and commercially available assay kits with appropriate quality control. All biochemical analyses were performed in the Department of Biochemistry within four hours of sample collection to avoid degradation. Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), and comparisons between cases and controls were performed using the Student's t-test for normally distributed variables or the Mann–Whitney U-test for non-parametric data. Correlations between oxidative stress markers and nutritional parameters were assessed using Pearson's or Spearman's correlation coefficients, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 100 children were enrolled, comprising 50 malnourished children with bacterial infections (cases) and 50 well-nourished children with bacterial infections (controls). Both groups were comparable in terms of age and sex distribution [Table 1].

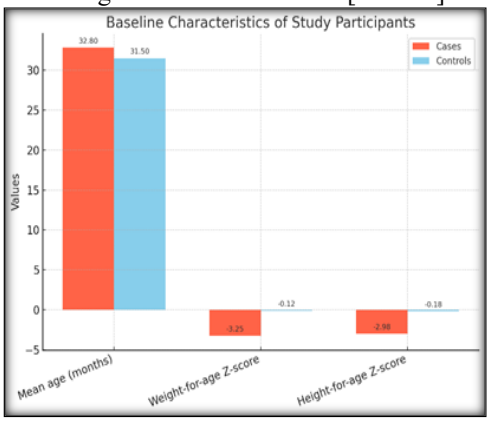

Figure 1: Comparison of baseline characteristics between malnourished children with bacterial infections (cases) and well-nourished infected controls. Data are presented as mean values for age, weight-for-age Z-score, and height-for-age Z-score.

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Table 1: Baseline characteristics of study participants

Parameter	Cases (n=50)	Controls (n=50)	p-value
Mean age (months)	32.8 ± 12.4	31.5 ± 11.8	0.61
Male: Female ratio	1.2: 1	1.3: 1	0.78
Weight-for-age Z-score	-3.25 ± 0.42	-0.12 ± 0.38	<0.001
Height-for-age Z-score	-2.98 ± 0.56	-0.18 ± 0.41	<0.001

Oxidative stress markers: The mean serum MDA and protein carbonyl levels were significantly higher in cases compared to controls, indicating greater lipid and protein oxidation in the malnourished group [Table 2].

Table 2: Comparison of oxidative stress markers between cases and controls

Marker	Cases (n=50)	Controls (n=50)	p-value
MDA (nmol/mL)	5.42 ± 0.82	3.28 ± 0.69	<0.001
Protein carbonyls (nmol/mg protein)	3.15 ± 0.51	2.01 ± 0.38	<0.001

Table 3: Antioxidant enzyme levels in cases and controls

Marker	Cases (n=50)	Controls (n=50)	p-value
SOD (U/mg Hb)	842 ± 95	1025 ± 112	<0.001
Catalase (U/mg protein)	28.6 ± 4.5	36.2 ± 5.1	<0.001
GPx (U/mg Hb)	19.4 ± 3.2	25.6 ± 3.9	<0.001

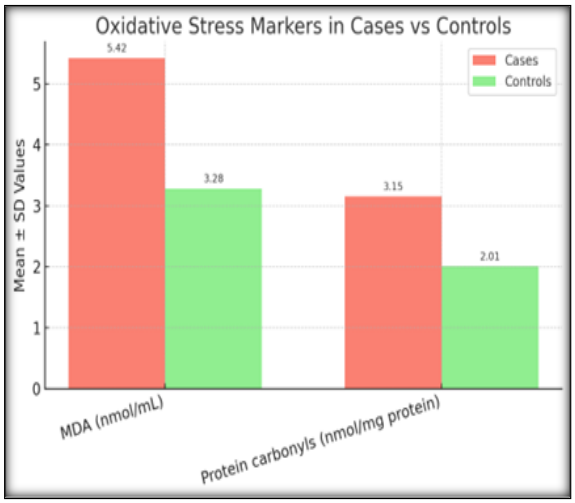

Figure 2: Comparison of oxidative stress markers between malnourished children with bacterial infections (cases) and well-nourished infected controls. Mean levels of malondialdehyde (MDA) and protein carbonyls were significantly higher in cases, indicating elevated oxidative stress.

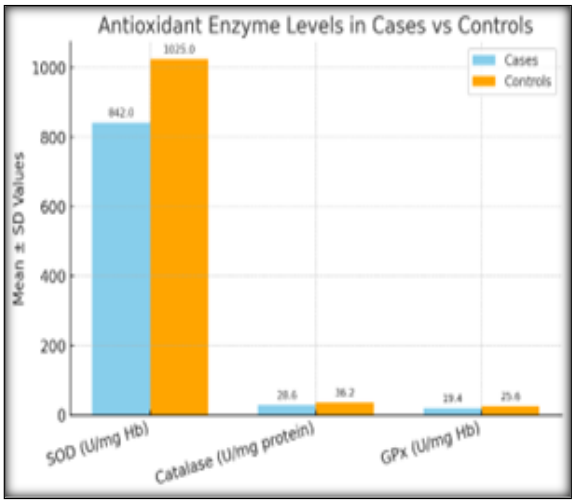

Figure 3: Comparison of antioxidant enzyme levels between malnourished children with bacterial infections (cases) and well-nourished infected controls. Superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) levels were significantly lower in cases, indicating compromised antioxidant defense.

Antioxidant enzyme activities

Malnourished children had significantly reduced activities of SOD, catalase, and GPx compared to controls [Table 3].

Non-enzymatic antioxidant status

Similarly, reduced GSH, vitamin C, and ceruloplasmin levels were found in cases compared to controls [Table 4].

Table 4: Non-enzymatic antioxidant levels in cases and controls

Marker	Cases (n=50)	Controls (n=50)	p-value
GSH (µmol/g Hb)	6.21 ± 1.15	9.42 ± 1.34	<0.001
Vitamin C (mg/dL)	0.48 ± 0.09	0.74 ± 0.11	<0.001
Ceruloplasmin (mg/dL)	18.6 ± 2.8	24.3 ± 3.1	<0.001

Table 5: Correlation between oxidative stress and antioxidant markers

Parameter 1	Parameter 2	Correlation coefficient (r)	p-value
MDA	SOD	-0.62	<0.001
MDA	GSH	-0.55	<0.001
Protein carbonyls	SOD	-0.49	<0.001
Protein carbonyls	GSH	-0.58	<0.001

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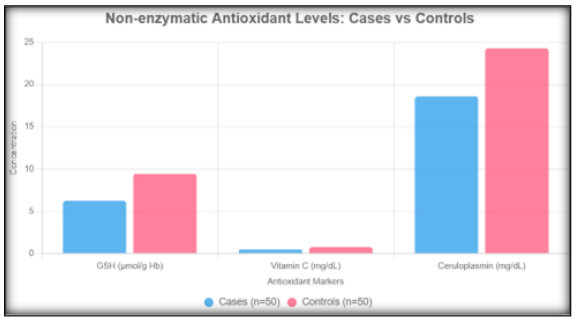

Figure 4: This chart visually compares the mean levels of GSH, Vitamin C, and Ceruloplasmin between cases and controls, with distinct colors for each group and appropriate labels. The y-axis represents the concentration, and the x-axis lists the antioxidant markers.

Correlation analysis

Pearson correlation analysis showed a strong negative correlation between MDA levels and SOD activity ($r = -0.62$, $p < 0.001$) and between protein carbonyl levels and GSH concentration ($r = -0.58$, $p < 0.001$) [Table 5].

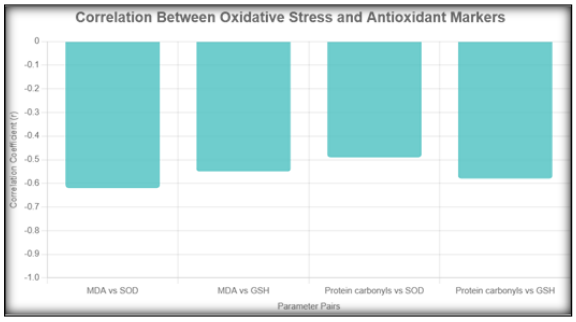

Figure 5: This chart shows the correlation coefficients for the specified parameter pairs, with the y-axis ranging from -1 to 0 to reflect the negative correlations. Each bar represents a parameter pair, and the height indicates the strength of the correlation.

Summary of key findings:

- Malnourished children with bacterial infections exhibited significantly higher oxidative stress markers (MDA, protein carbonyls).
- Both enzymatic (SOD, catalase, GPx) and non-enzymatic (GSH, vitamin C, ceruloplasmin) antioxidant defenses were markedly lower in cases.
- A strong inverse relationship existed between oxidative damage and antioxidant capacity.

DISCUSSION

This study demonstrated that malnourished children with bacterial infections exhibited significantly higher levels of oxidative stress markers malondialdehyde (MDA) and protein carbonyls along with markedly reduced enzymatic (SOD, catalase, GPx) and non-enzymatic (GSH, vitamin C, ceruloplasmin) antioxidant defenses compared to well-nourished infected controls. These findings are consistent with previous reports that malnutrition, particularly severe acute malnutrition (SAM), predisposes children to a pro-oxidant state and impaired antioxidant defense mechanisms.

In our cohort, mean MDA levels were significantly elevated in malnourished children, indicating enhanced lipid peroxidation. Similar results were observed by El-Kholy et al. (2016), who reported increased MDA in children with PEM, suggesting that oxidative damage to cell membranes is a hallmark of malnutrition-associated oxidative stress. MDA elevation has also been described by Awad et al. (2012) in marasmic and kwashiorkor patients, further supporting the role of malnutrition in promoting ROS-mediated lipid damage.

Protein carbonyl levels were also higher among cases, reflecting oxidative modification of proteins. This observation is in agreement with Bhat et al. (2014), who demonstrated increased protein carbonyl content in PEM children, correlating with severity of malnutrition. Oxidatively modified proteins can impair enzyme activities, alter signaling pathways, and contribute to tissue injury during infection.

The marked reduction in SOD, catalase, and GPx activities in our malnourished group aligns with findings by Ece et al. (2007) and Kumar et al. (2018), who reported decreased antioxidant enzyme activity in malnourished children due to reduced synthesis of enzyme proteins and depletion of essential cofactors like zinc, copper, and selenium. The low SOD and GPx activities observed in our study may further exacerbate the accumulation of superoxide anions and hydrogen peroxide, thereby amplifying oxidative damage.

Non-enzymatic antioxidants such as GSH, vitamin C, and ceruloplasmin were significantly lower in cases compared to controls. Similar results were reported by Rahman et al. (2010), who suggested that chronic undernutrition depletes intracellular glutathione reserves and impairs vitamin C recycling, while ceruloplasmin levels decline due to reduced hepatic protein synthesis. Since vitamin C directly scavenges ROS and regenerates vitamin E, its deficiency in malnourished children may leave cellular components more vulnerable to oxidative injury during infection.

The correlation analysis in our study revealed a strong inverse relationship between MDA and SOD as well as between protein carbonyls and GSH, suggesting that as oxidative damage intensifies, antioxidant defenses are proportionally weakened. This agrees with the observations of Das et al. (2014), who reported similar correlations in malnourished children with infectious diseases, indicating that oxidative imbalance may contribute to poor clinical outcomes.

The interplay between malnutrition and infection appears to be synergistic in generating oxidative stress. Malnutrition alone compromises immune function, reducing the ability to contain infections (Scrimshaw et al., 1997), while infection stimulates inflammatory cells to generate excess ROS as part of the immune response (Victor et al., 2009). In

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malnourished hosts, this ROS surge is inadequately neutralized, leading to cumulative oxidative damage. This vicious cycle may prolong illness, delay recovery, and increase morbidity.

Our findings highlight the need for a multifaceted approach in managing malnourished children with bacterial infections. In addition to nutritional rehabilitation and antimicrobial therapy, targeted antioxidant supplementation could be explored as an adjunctive strategy to mitigate oxidative injury. Trials by Manary et al. (2004) and Ndekha et al. (2009) have shown that antioxidant-enriched therapeutic foods may improve recovery rates in malnourished children, although results remain mixed and warrant further investigation.

Limitations of the present study include its single-center design, relatively small sample size, and lack of follow-up data to assess the impact of oxidative stress on long-term outcomes. Furthermore, dietary intake of antioxidants prior to admission was not quantified, which may have influenced baseline antioxidant status. Future research should involve larger multicenter studies with longitudinal follow-up and intervention arms assessing the efficacy of antioxidant supplementation in this population.

In summary, our results reinforce that malnourished children with bacterial infections are at a dual disadvantage heightened oxidative stress and weakened antioxidant defenses. This biochemical milieu may contribute significantly to disease severity and should be considered in both clinical management and public health strategies.

CONCLUSION

Malnourished children with bacterial infections exhibit a marked imbalance between oxidative stress and antioxidant defense, characterized by significantly elevated lipid and protein oxidation and reduced enzymatic and non-enzymatic antioxidants. This imbalance likely contributes to increased disease severity and delayed recovery. Addressing both nutritional deficits and oxidative stress, alongside appropriate antimicrobial therapy, may improve clinical outcomes in this vulnerable population. Incorporating antioxidant-rich interventions into nutritional rehabilitation programs could be a potential adjunct strategy, though further large-scale studies are needed to confirm their efficacy.

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