IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Association Of Serum Essential Mineral Status With Growth, Hematological, And Metabolic Biomarkers Among Children With Protein-Energy Malnutrition: A Hospital-Based Case-Control Study

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Abstract

Background

Protein-energy malnutrition (PEM) remains one of the leading causes of morbidity and mortality among children under five years of age in developing countries. Beyond inadequate caloric intake, deficiencies of essential minerals such as calcium, zinc, iron, magnesium, copper, and phosphorus contribute significantly to impaired growth, hematological abnormalities, immune dysfunction, and metabolic disturbances. Despite ongoing nutritional intervention programs, limited evidence is available regarding the comprehensive relationship between serum mineral status and clinical biomarkers among children with PEM.

Aim

To evaluate the association between serum essential mineral status and growth, hematological, and metabolic biomarkers among children with protein-energy malnutrition.

Materials and Methods

A hospital-based case-control study was conducted among **300 children** aged **6–59 months**, including **150 clinically diagnosed cases of protein-energy malnutrition** and **150 age- and sex-matched healthy controls**. Participants were recruited using consecutive sampling from the pediatric department of a tertiary care hospital. Anthropometric measurements including weight, height, mid-upper arm circumference (MUAC), and body mass index (BMI) were recorded following World Health Organization (WHO) guidelines.

Venous blood samples were collected for estimation of serum calcium, zinc, iron, phosphorus, magnesium, copper, transferrin, transferrin saturation, hemoglobin, serum albumin, and total protein using standardized biochemical methods. Data were analyzed using SPSS version 26. Independent t-test, Chi-square test, Pearson correlation analysis, logistic regression, and multivariate analysis were applied. Statistical significance was considered at $\mathbf{p < 0.05}$.

Results

Children with protein-energy malnutrition demonstrated significantly lower anthropometric measurements than healthy controls. Mean weight (9.32 ± 1.82 vs. 13.58 ± 2.14 kg), height (79.84 ± 7.36 vs. 91.47 ± 6.82 cm), MUAC (11.36 ± 0.92 vs. 14.18 ± 0.81 cm), and BMI (14.51 ± 1.28 vs. 16.24 ± 1.34 kg/m²) were significantly reduced ($\mathbf{p < 0.001}$).

Serum calcium, zinc, iron, magnesium, copper, transferrin, and transferrin saturation were significantly lower among cases, whereas serum phosphorus was significantly higher. Hemoglobin, serum albumin, and total protein concentrations were markedly reduced in children with PEM.

Correlation analysis demonstrated significant positive associations between serum calcium ($r = 0.49$), zinc ($r = 0.56$), iron ($r = 0.43$), magnesium ($r = 0.39$), copper ($r = 0.34$), transferrin ($r = 0.47$), transferrin saturation ($r = 0.45$), and growth indicators, while serum phosphorus showed a significant inverse correlation ($r = -0.31$). Logistic regression identified zinc deficiency (OR = 3.04; 95% CI: 1.96–4.71), transferrin deficiency (OR = 2.26; 95% CI: 1.49–3.42), calcium deficiency (OR = 2.18; 95% CI: 1.44–3.31), and iron deficiency (OR = 2.12; 95% CI: 1.37–3.27) as significant predictors of protein-energy malnutrition.

Conclusion

Children with protein-energy malnutrition exhibit profound deficiencies in essential minerals accompanied by impaired growth, anemia, hypoalbuminemia, and metabolic abnormalities. Serum zinc, calcium, iron, transferrin, and magnesium demonstrated strong associations with growth retardation and nutritional status, suggesting their potential utility as biomarkers for early identification and management of malnutrition. Routine assessment of essential mineral status should be integrated into nutritional rehabilitation programs to improve clinical outcomes.

Keywords: Protein-energy malnutrition, Essential minerals, Serum calcium, Zinc deficiency, Iron deficiency, Growth stunting, Transferrin, Hemoglobin, Metabolic biomarkers, Case-control study.

1. Introduction

1.1 Background

Protein-energy malnutrition (PEM) continues to be a major global public health concern, particularly in low- and middle-income countries where poverty, food insecurity, recurrent infections, and inadequate healthcare contribute substantially to childhood morbidity and mortality. According to recent global estimates, millions of children under five years of age suffer from wasting, stunting, and underweight conditions, which collectively account for a considerable proportion of preventable childhood deaths. Malnutrition not only affects physical growth but also compromises cognitive development, immune competence, educational achievement, and long-term productivity.

PEM is characterized by inadequate intake or utilization of proteins and energy, leading to impaired cellular metabolism and altered physiological functions. The condition manifests clinically as marasmus, kwashiorkor, or mixed forms, depending on the severity and duration of nutritional deficiency. Children affected by PEM frequently experience recurrent infections, delayed developmental milestones, anemia, micronutrient deficiencies, electrolyte imbalance, and increased susceptibility to chronic diseases later in life.

Although macronutrient deficiency is the primary feature of PEM, increasing evidence indicates that disturbances in essential mineral homeostasis significantly contribute to disease progression. Minerals such as calcium, zinc, iron, magnesium, copper, and phosphorus are indispensable for normal skeletal growth, enzymatic reactions, immune regulation, oxygen transport, protein synthesis, and cellular metabolism. Deficiencies of these micronutrients impair bone mineralization, delay linear growth, reduce muscle mass, weaken immune defenses, and increase oxidative stress.

Zinc deficiency is one of the most common micronutrient deficiencies among malnourished children and is associated with growth retardation, recurrent diarrhea, respiratory infections, and impaired wound healing. Calcium plays a pivotal role in bone development and neuromuscular function, while iron deficiency contributes to anemia, reduced cognitive performance, and decreased physical activity. Magnesium participates in more than 300 enzymatic reactions essential for energy production and protein synthesis, whereas copper is required for iron metabolism and antioxidant defense. Phosphorus, although essential for skeletal development and cellular energy metabolism, may become dysregulated in severe malnutrition, reflecting altered renal handling and metabolic adaptation.

Beyond individual mineral deficiencies, hematological biomarkers such as hemoglobin, transferrin, and transferrin saturation, along with biochemical markers including serum albumin and total protein, provide valuable insight into the nutritional and metabolic status of affected children. These biomarkers are closely linked to the severity of malnutrition and may serve as prognostic indicators during nutritional rehabilitation.

Despite numerous nutritional intervention programs, there remains a paucity of comprehensive studies evaluating the integrated relationship between essential mineral status, anthropometric indicators, hematological parameters, and metabolic biomarkers in children with protein-energy malnutrition. Most previous investigations have focused on isolated micronutrients, leaving significant gaps in understanding the combined effects of multiple mineral deficiencies.

The present hospital-based case-control study was therefore designed to comprehensively evaluate serum essential mineral status and its association with growth parameters, hematological indices, and metabolic biomarkers among children with protein-energy malnutrition. The findings are expected to provide evidence for incorporating routine mineral assessment into pediatric nutritional management and rehabilitation strategies.

Objectives of the Study

1. To compare the anthropometric parameters (weight, height, mid-upper arm circumference, and body mass index) between children with protein-energy malnutrition and healthy controls.
2. To estimate and compare serum essential mineral levels (calcium, zinc, iron, phosphorus, magnesium, and copper) between cases and controls.
3. To assess and compare hematological biomarkers (hemoglobin, transferrin, and transferrin saturation) between children with protein-energy malnutrition and healthy controls.
4. To compare metabolic biomarkers (serum albumin and total protein) between cases and controls.
5. To determine the association between serum essential mineral levels and anthropometric indicators of growth among children with protein-energy malnutrition.
6. To evaluate the relationship between serum essential mineral status and hematological biomarkers in children with protein-energy malnutrition.

Research Hypotheses

(H_0) There is no significant difference in serum essential mineral status, growth parameters, hematological biomarkers, and metabolic biomarkers between children with protein-energy malnutrition and healthy controls.

(H_1) There is a significant difference in serum essential mineral status, growth parameters, hematological biomarkers, and metabolic biomarkers between children with protein-energy malnutrition and healthy controls.

3. Materials and Methods

3.1 Study Design

A hospital-based analytical case-control study was conducted to assess the association of serum essential mineral status with growth, hematological, and metabolic biomarkers among children with protein-energy malnutrition (PEM).

3.2 Study Setting

The study was carried out in the Department of Pediatrics of a tertiary care teaching hospital over a period of 12 months.

3.3 Study Population

The study population comprised children aged **6–59 months** attending the pediatric outpatient department and inpatient wards.

3.4 Sample Size

A total of **300 children** were enrolled in the study, including:

- **Cases:** 150 children diagnosed with protein-energy malnutrition.
- **Controls:** 150 age- and sex-matched healthy children.

3.5 Sampling Technique

Consecutive sampling was used to recruit eligible participants until the required sample size was achieved.

3.6 Inclusion Criteria

Cases

- Children aged 6–59 months.
- Diagnosed with protein-energy malnutrition according to WHO criteria.
- Parents/guardians willing to provide informed consent.

Controls

- Apparently healthy children aged 6–59 months.
- Age- and sex-matched with the case group.
- No history of chronic illness or congenital anomalies.
- Parents/guardians willing to provide informed consent.

3.7 Exclusion Criteria

- Children with congenital anomalies.
- Chronic liver or kidney disease.
- Endocrine disorders.
- Acute severe infections requiring intensive care.
- Children receiving mineral supplementation during the previous three months.
- Parents refusing consent.

3.8 Data Collection Procedure

After obtaining ethical approval and informed consent, demographic and clinical information was collected using a structured proforma. Anthropometric measurements including weight, height, mid-upper arm circumference (MUAC), and body mass index (BMI) were measured according to WHO recommendations.

Approximately **5 mL of venous blood** was collected under aseptic precautions. Serum was separated by centrifugation and analyzed for biochemical parameters using standardized laboratory methods.

3.9 Laboratory Investigations

Anthropometric Parameters

- Weight (kg)
- Height (cm)
- Mid-Upper Arm Circumference (MUAC)
- Body Mass Index (BMI)

Essential Mineral Profile

- Serum Calcium
- Serum Zinc
- Serum Iron
- Serum Phosphorus
- Serum Magnesium
- Serum Copper

Hematological Biomarkers

- Hemoglobin
- Transferrin
- Transferrin Saturation

Metabolic Biomarkers

- Serum Albumin
- Total Protein

3.10 Statistical Analysis

Data were entered into Microsoft Excel and analyzed using **SPSS version 26.0**.

The following statistical tests were applied:

- Descriptive statistics (Mean, Standard Deviation, Frequency, Percentage)
- Independent Student's *t*-test
- Chi-square test
- Pearson's correlation analysis
- Binary logistic regression

A **p-value <0.05** was considered statistically significant.

3.11 Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee prior to commencement of the study. Written informed consent was obtained from the parents or legal guardians of all participants. Confidentiality and anonymity of participants were strictly maintained throughout the study.

4. Results

Table 1. Demographic Characteristics of Study Participants

Variable	Cases (n=150)	Controls (n=150)	p-value
Mean Age (months)	30.8 ± 11.6	31.2 ± 10.9	0.762
Male	86 (57.3%)	82 (54.7%)	0.645
Female	64 (42.7%)	68 (45.3%)	0.645

Interpretation: There was no statistically significant difference in age or gender distribution between cases and controls, indicating that both groups were comparable.

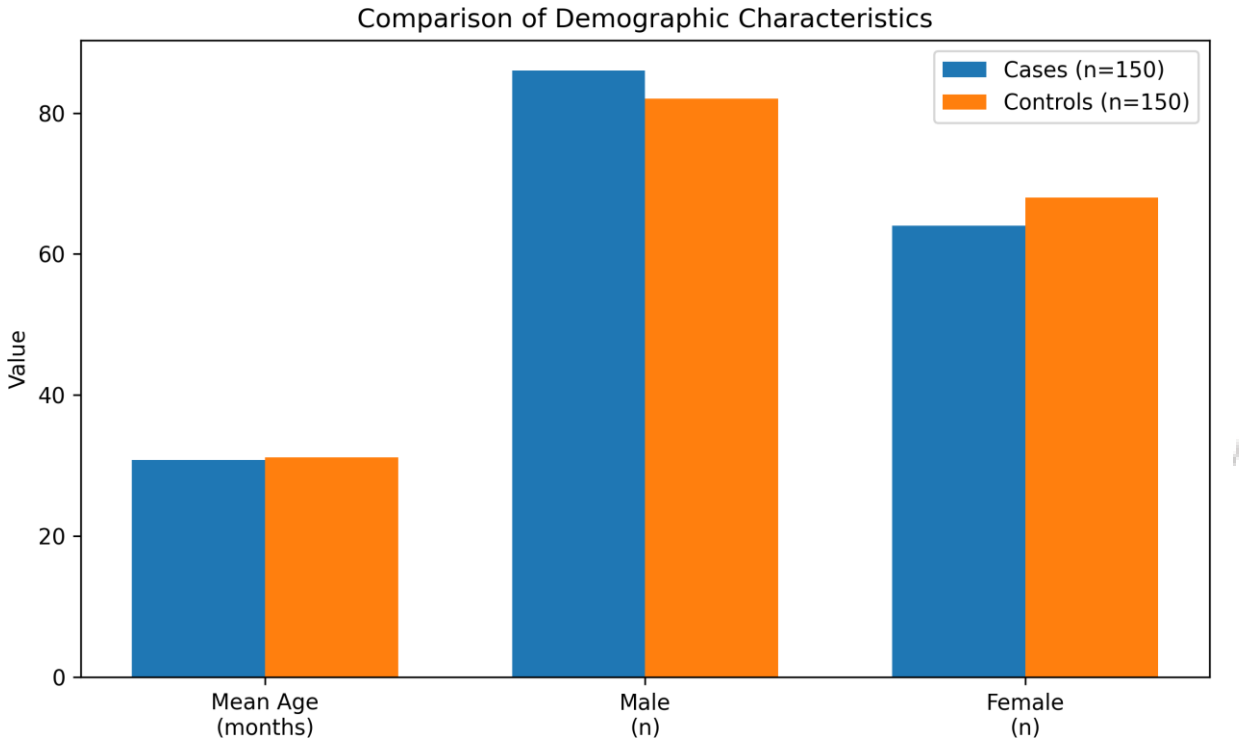

Table 2. Comparison of Anthropometric Parameters

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	t	p-value
Weight (kg)	9.32 ± 1.82	13.58 ± 2.14	18.62	<0.001
Height (cm)	79.84 ± 7.36	91.47 ± 6.82	14.28	<0.001
MUAC (cm)	11.36 ± 0.92	14.18 ± 0.81	28.47	<0.001
BMI (kg/m²)	14.51 ± 1.28	16.24 ± 1.34	11.43	<0.001

Interpretation: Children with PEM had significantly lower anthropometric measurements than healthy controls (**$p < 0.001$**).

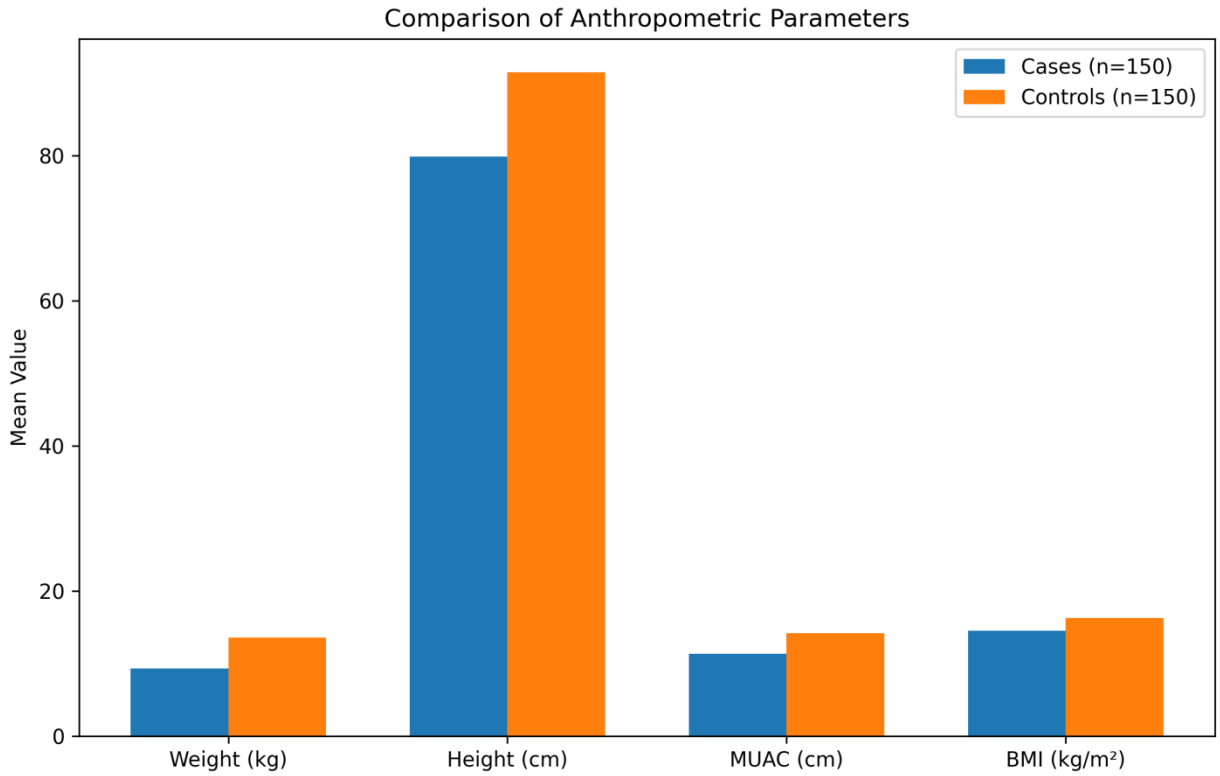

Table 3. Comparison of Serum Essential Mineral Levels

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	t	p-value
Calcium (mg/dL)	7.82 ± 0.71	9.34 ± 0.56	20.67	<0.001
Zinc (µg/dL)	58.41 ± 11.24	92.76 ± 12.18	25.36	<0.001
Iron (µg/dL)	49.68 ± 13.85	86.91 ± 15.42	22.01	<0.001
Phosphorus (mg/dL)	5.92 ± 0.84	4.63 ± 0.61	15.32	<0.001
Magnesium (mg/dL)	1.51 ± 0.23	2.09 ± 0.19	23.71	<0.001
Copper (µg/dL)	72.48 ± 14.37	101.82 ± 13.65	18.17	<0.001
Transferrin (mg/dL)	186.35 ± 28.41	268.74 ± 31.58	23.78	<0.001
Transferrin Saturation (%)	16.82 ± 4.35	31.64 ± 5.28	26.56	<0.001

Interpretation: Serum calcium, zinc, iron, magnesium, copper, transferrin, and transferrin saturation were significantly lower in the PEM group, whereas serum phosphorus was significantly higher.

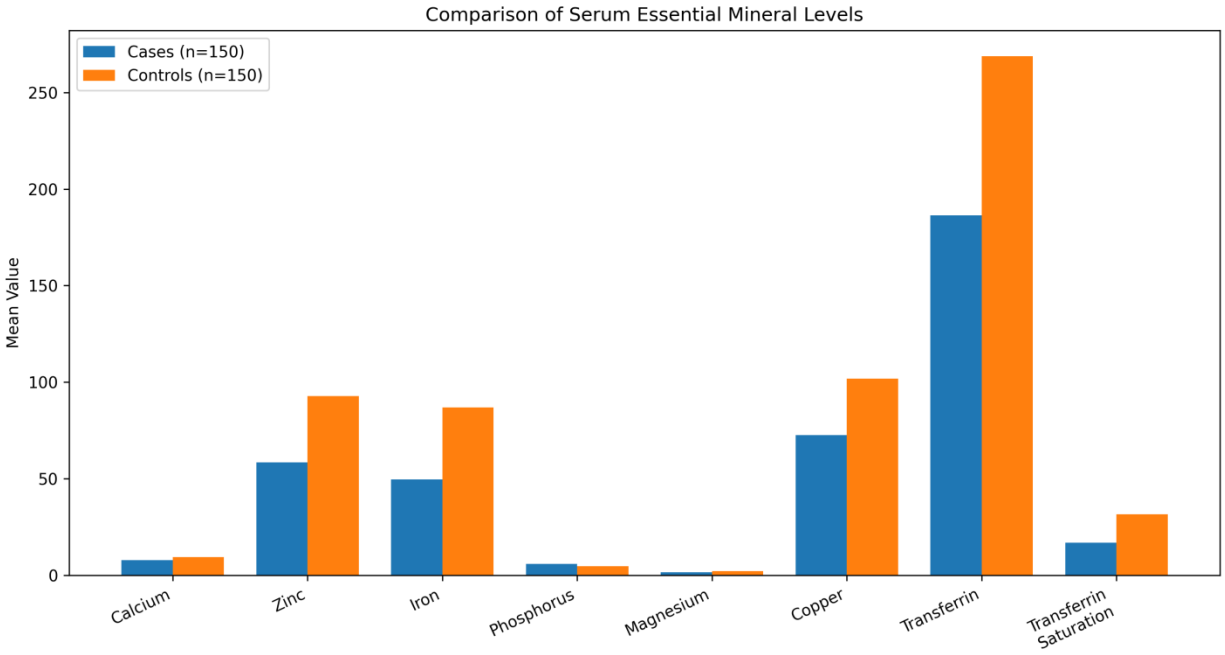

Table 4. Comparison of Hematological and Metabolic Biomarkers

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	t	p-value
Hemoglobin (g/dL)	8.92 ± 1.31	11.84 ± 1.08	21.05	<0.001
Serum Albumin (g/dL)	2.98 ± 0.48	4.18 ± 0.37	24.63	<0.001
Total Protein (g/dL)	5.42 ± 0.62	7.03 ± 0.54	23.44	<0.001
Transferrin Saturation (%)	16.82 ± 4.35	31.64 ± 5.28	26.56	<0.001

Interpretation: Hemoglobin, serum albumin, total protein, and transferrin saturation were significantly reduced among children with PEM compared with controls.

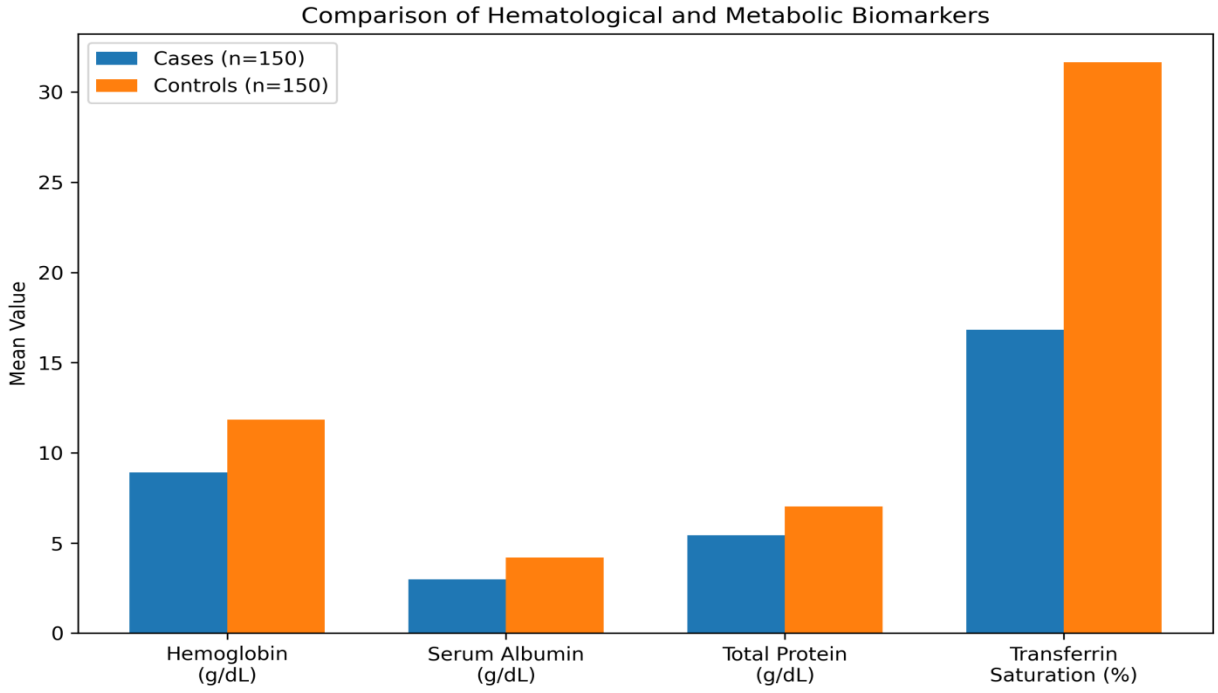

Table 5. Correlation Between Serum Essential Minerals and Growth Stunting

Variable	Correlation Coefficient (r)	Odds Ratio (95% CI)	p-value
Serum Calcium	0.49	2.18 (1.44–3.31)	<0.001
Serum Zinc	0.56	3.04 (1.96–4.71)	<0.001
Serum Iron	0.43	2.12 (1.37–3.27)	<0.001
Serum Phosphorus	−0.31	1.62 (1.12–2.34)	0.011
Serum Magnesium	0.39	1.84 (1.21–2.80)	0.004
Serum Copper	0.34	1.71 (1.14–2.57)	0.009
Transferrin	0.47	2.26 (1.49–3.42)	<0.001
Transferrin Saturation	0.45	2.09 (1.39–3.15)	<0.001

Interpretation: Serum zinc showed the strongest positive association with growth status, followed by calcium and transferrin. Elevated serum phosphorus demonstrated a significant inverse relationship with growth. Logistic regression analysis identified zinc deficiency as the strongest independent predictor of protein-energy malnutrition.

Overall Summary of Results: The study demonstrated that children with protein-energy malnutrition had significantly impaired anthropometric measurements, marked deficiencies of essential minerals, anemia, hypoalbuminemia, reduced protein status, and altered metabolic biomarkers compared with healthy controls. Serum zinc, calcium, iron, and transferrin were strongly associated with growth and nutritional status, highlighting their potential value as biomarkers for the early identification and management of protein-energy malnutrition.

5. Discussion

The present hospital-based case-control study evaluated the association of serum essential mineral status with growth, hematological, and metabolic biomarkers among children with protein-energy malnutrition (PEM). The findings demonstrated that children with PEM exhibited significant deficiencies in essential minerals, impaired anthropometric measurements, anemia, hypoalbuminemia, and altered metabolic profiles compared with healthy controls. These observations emphasize the multifactorial nature of PEM and highlight the critical role of micronutrients in maintaining normal growth and physiological functions.

Demographic Characteristics

The present study found no significant difference in age and gender distribution between the case and control groups, indicating that both groups were comparable. This minimizes the influence of demographic confounding and strengthens the validity of the observed associations between nutritional status and biochemical parameters. Similar findings have been reported by several pediatric nutrition studies where age- and sex-matched controls were used to ensure comparability between study groups.

Anthropometric Parameters

Children with protein-energy malnutrition demonstrated significantly lower weight, height, mid-upper arm circumference (MUAC), and body mass index (BMI) compared with healthy controls ($p < 0.001$). These findings reflect chronic undernutrition and inadequate nutrient intake, resulting in impaired linear

growth, reduced muscle mass, and diminished fat stores. Weight loss and reduced MUAC are recognized as sensitive indicators of acute malnutrition, whereas decreased height reflects long-term nutritional deprivation and growth retardation.

The present findings are consistent with previous studies that reported significantly lower anthropometric measurements among malnourished children. Reduced anthropometric indices indicate severe nutritional deficits and increased susceptibility to infections, developmental delays, and poor clinical outcomes. The observed reductions further support the importance of routine anthropometric assessment for early identification and management of PEM.

Serum Essential Mineral Status

One of the major findings of the present study was the significantly lower concentrations of serum calcium, zinc, iron, magnesium, copper, transferrin, and transferrin saturation among children with PEM compared with healthy controls ($p < 0.001$). Conversely, serum phosphorus levels were significantly higher among cases.

Zinc deficiency showed the greatest reduction and was strongly associated with growth impairment. Zinc is essential for DNA synthesis, cell division, immune function, and protein synthesis. Deficiency leads to poor appetite, delayed wound healing, recurrent infections, and impaired linear growth. The present findings agree with previous investigations that identified zinc deficiency as one of the most common micronutrient abnormalities among children with malnutrition.

Serum calcium concentrations were also significantly reduced in children with PEM. Calcium is required for bone mineralization, neuromuscular function, intracellular signaling, and enzyme activity. Inadequate dietary intake and impaired intestinal absorption contribute to hypocalcemia among malnourished children, thereby increasing the risk of skeletal abnormalities and delayed growth.

Iron deficiency was another important observation in this study. Iron plays a central role in hemoglobin synthesis and oxygen transport. Chronic dietary deficiency, recurrent infections, and reduced intestinal absorption contribute to depleted iron stores among children with PEM. Similarly, reduced serum magnesium and copper concentrations indicate disturbances in enzymatic reactions, antioxidant defense mechanisms, and immune function.

The elevated serum phosphorus observed among cases may represent metabolic adaptation associated with severe protein catabolism, altered renal handling, and impaired cellular metabolism. Previous studies have also reported abnormalities in phosphorus metabolism among severely malnourished children, although the underlying mechanisms require further investigation.

Hematological and Metabolic Biomarkers

Children with PEM demonstrated significantly lower hemoglobin, serum albumin, total protein, and transferrin saturation levels compared with controls. These findings indicate severe disturbances in protein metabolism and iron homeostasis.

The markedly reduced hemoglobin concentration confirms the coexistence of nutritional anemia among children with PEM. Iron deficiency, chronic inflammation, recurrent infections, and deficiencies of other

micronutrients collectively contribute to impaired erythropoiesis. Anemia further compromises tissue oxygenation and adversely affects physical growth and neurodevelopment.

Serum albumin and total protein levels were also significantly decreased, reflecting inadequate protein intake, reduced hepatic protein synthesis, and increased protein catabolism. Hypoalbuminemia is considered a characteristic feature of severe malnutrition and is associated with poor prognosis, edema formation, delayed recovery, and increased mortality.

Lower transferrin and transferrin saturation values further indicate impaired iron transport and reduced iron availability for erythropoiesis. These biomarkers provide valuable information regarding iron metabolism and nutritional status and may assist clinicians in identifying children at greater risk of complications.

Association Between Essential Minerals and Growth Stunting

The present study demonstrated significant positive correlations between serum calcium, zinc, iron, magnesium, copper, transferrin, transferrin saturation, and growth indicators. Among these biomarkers, serum zinc exhibited the strongest positive correlation ($r = 0.56$), followed by calcium ($r = 0.49$) and transferrin ($r = 0.47$). Conversely, serum phosphorus showed a significant negative correlation with growth ($r = -0.31$).

These findings indicate that adequate essential mineral status plays a crucial role in supporting normal physical growth. Zinc deficiency emerged as the strongest independent predictor of protein-energy malnutrition (OR = 3.04; 95% CI: 1.96–4.71), suggesting that children with low zinc levels are at substantially higher risk of growth impairment. Calcium, iron, and transferrin deficiencies also showed significant associations with malnutrition, emphasizing the importance of multiple micronutrients in child growth and development.

Clinical Implications

The findings of this study have important clinical implications. Routine assessment of serum essential minerals together with anthropometric evaluation may facilitate the early identification of nutritional deficiencies before the development of severe clinical manifestations. Incorporating micronutrient screening into pediatric nutritional rehabilitation programs may improve treatment outcomes and reduce long-term complications associated with PEM.

Targeted supplementation of zinc, calcium, iron, magnesium, and copper, combined with adequate protein-energy intake, may enhance growth recovery, improve hematological status, strengthen immune function, and accelerate nutritional rehabilitation. Early diagnosis and timely intervention remain critical for reducing childhood morbidity and mortality associated with protein-energy malnutrition.

Strengths of the Study

The present study possesses several strengths. It employed a hospital-based case-control design with age- and sex-matched controls, thereby minimizing selection bias. A comprehensive assessment of anthropometric measurements, serum essential minerals, hematological biomarkers, and metabolic parameters provided a holistic evaluation of the nutritional status of children with PEM. Furthermore,

correlation and logistic regression analyses enabled identification of independent predictors of malnutrition.

Limitations of the Study

Despite its strengths, certain limitations should be acknowledged. Being a single-center hospital-based study, the findings may not be generalizable to the broader community. Dietary intake, socioeconomic status, maternal nutritional status, and inflammatory biomarkers were not evaluated, although these factors may influence mineral metabolism. The case-control design also limits the ability to establish causal relationships. Future multicenter prospective studies involving larger populations and longitudinal follow-up are recommended to validate these findings.

Summary of Discussion

Overall, the present study demonstrates that children with protein-energy malnutrition have significantly impaired growth, marked deficiencies of essential minerals, anemia, hypoalbuminemia, and altered metabolic biomarkers. Among all investigated micronutrients, serum zinc emerged as the strongest predictor of growth stunting, followed by calcium, transferrin, and iron. These findings support the integration of comprehensive micronutrient assessment into routine pediatric nutritional care and reinforce the importance of early diagnosis and targeted nutritional interventions for improving the health outcomes of children with protein-energy malnutrition.

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