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Micronutrient Deficiencies and Thyroid Function in Children with Protein-energy Malnutrition

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Abstract

Protein-energy malnutrition (PEM) remains a significant public health problem in childhood and is frequently accompanied by multiple micronutrient deficiencies and metabolic alterations. This study aimed to simultaneously evaluate micronutrient status and thyroid function in children diagnosed with PEM. A retrospective analysis was conducted of the medical records of children aged 0-17 years who were admitted to Defne State Hospital between December 2023 and May 2025 with a diagnosis of PEM. Demographic characteristics, anthropometric measurements, and laboratory parameters, including hemoglobin, serum iron, ferritin, vitamin B12, vitamin D, blood urea nitrogen, creatinine, thyroid-stimulating hormone, and free T4 were recorded. Nutritional status was assessed using World Health Organization growth standards. A total of 65 children (32 males and 33 females) were included. Mild, moderate, and severe malnutrition were identified in 38.46%, 44.62%, and 16.92% of patients, respectively. Anemia and vitamin D deficiency were the most common abnormalities observed in 23.08% and 18.46% of patients, respectively. In contrast, vitamin B12 deficiency and abnormal thyroid function test results were detected at lower rates (3.08% and 4.62%, respectively). No significant differences were observed between genders in anthropometric measurements or malnutrition severity. The relatively low prevalence of thyroid dysfunction, compared with previous studies, may be attributable to the predominance of mild-to-moderate malnutrition in the study population. These findings suggest that the impact of PEM on micronutrient metabolism and endocrine function varies according to disease severity, and highlight the importance of a comprehensive clinical approach that includes assessment of both micronutrient and hormonal status in children with PEM.

Keywords: Anemia, micronutrient deficiency, protein-energy malnutrition, thyroid function, vitamin D

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Introduction

Malnutrition is a clinical condition resulting from inadequate intake of one or more nutrients, leading to impairment of growth, development, and metabolic balance[1]. Protein-energy malnutrition (PEM) remains a major health problem among children, particularly in low- and middle-income countries, and is associated with increased morbidity and mortality[2]. In our country, PEM continues to be an important public health concern within the pediatric population.

Iron deficiency anemia (IDA), thyroid dysfunction, and vitamin B12 deficiency are clinical conditions closely associated with childhood malnutrition. Recent evidence indicates that PEM is not a uniform disease entity but rather a heterogeneous condition comprising clinically variable subtypes related to different patterns of nutritional deficiency[3].

Childhood malnutrition and micronutrient deficiencies, especially IDA, constitute a major global health problem affecting millions of children. IDA is the most common nutritional disorder and the leading cause of anemia in children. If left untreated, it may lead to long-term adverse effects on neurodevelopment, immune function, and physical growth[4]. Recent comprehensive reviews have demonstrated that in children with acute malnutrition, anemia frequently coexists with other micronutrient deficiencies, thereby increasing disease severity[5].

Children diagnosed with severe acute malnutrition exhibit a markedly increased susceptibility to infections. Anemia, which is frequently observed in these patients, develops as a consequence of malnutrition and contributes to morbidity and mortality through both direct and indirect mechanisms[6,7]. This increased risk is thought to result from the combined effects of protein deficiency, micronutrient depletion, and impaired immune function[5].

Vitamin B12 is an essential micronutrient for motor, language, and cognitive development in children. In malnourished children, vitamin B12 deficiency may lead to developmental delay and severe anemia[8,9]. Emerging evidence suggests that vitamin B12 deficiency may persist despite nutritional rehabilitation and have lasting adverse effects on neurodevelopmental outcomes[5,8].

As the severity of malnutrition increases, serum levels of triiodothyronine (T3) and thyroxine (T4) may decline. This phenomenon is considered an adaptive response aimed at reducing energy expenditure. In PEM, decreased synthesis of carrier proteins such as albumin and T4-binding globulin contributes to lower circulating thyroid hormone levels. These hormonal changes resemble the non-thyroidal illness response observed in other severe conditions and may become clinically significant in prolonged or severe PEM[10].

Although numerous studies have examined PEM subtypes and micronutrient deficiencies, data integrating micronutrient status and thyroid function within the same pediatric PEM cohort remain limited[5,11].

Therefore, this study aimed to evaluate the levels of serum vitamin D, vitamin B12, blood urea nitrogen (BUN), creatinine, thyroid-stimulating hormone (TSH), and free T4 (fT4) in children diagnosed with PEM and determine the prevalence of anemia based on complete blood count data. By adopting an integrated approach, this study seeks to provide clinically relevant insights into the combined assessment of micronutrient deficiencies and thyroid function alterations in pediatric PEM.

Highlights

- Anemia (23.08%) and vitamin D deficiency (18.46%) were the most common micronutrient abnormalities observed in children with protein-energy malnutrition (PEM).
- Vitamin B12 deficiency (3.08%) and abnormal thyroid function test results (4.62%) were detected at relatively low frequencies.
- Moderate malnutrition accounted for the majority of cases, which may explain the low prevalence of thyroid dysfunction.
- Hematological parameters and vitamin D metabolism were affected more frequently than was thyroid function in pediatric PEM.
- These findings emphasize the importance of incorporating micronutrient and endocrine evaluations into the routine clinical assessment of children with PEM.

Materials and Methods

This retrospective study included children aged 0-17 years admitted to Defne State Hospital, located in the Hatay province, Türkiye, diagnosed with PEM between December 2023 and May 2025. Demographic characteristics, anthropometric measurements, and laboratory data were obtained from the hospital's electronic medical record system.

Anthropometric assessment included measurements of body weight and height, which were performed according to standardized clinical procedures. Nutritional status was evaluated in accordance with the World Health Organization (WHO) Child Growth Standards.

In children younger than five years of age (0-59 months), nutritional status was primarily assessed using weight-for-age Z-scores (WAZ), calculated based on the WHO Child Growth Standards (2006). Weight-for-age was preferred because it is the most stable and comparable indicator of overall nutritional status in children under five years of age[12]. Malnutrition severity was classified as follows: mild malnutrition, WAZ between -1 and -2 standard deviations (SDs) moderate malnutrition, WAZ between -2 and -3 SD; and severe malnutrition, WAZ below -3 SD.

In children and adolescents aged 5-19 years, nutritional status was assessed using body mass index (BMI)-for-age Z-scores (BAZ), in accordance with the WHO reference standard[13]. Accordingly, thinness was defined as a BAZ between -2 and -1 SD, moderate thinness as a BAZ between -3 and -2 SD, and severe thinness as a BAZ below -3 SD.

The study excluded children with the following conditions: metabolic disorders, urinary tract infections, malabsorption syndrome (e.g., celiac disease), protein-

losing enteropathy, nephrotic syndrome, chronic liver or kidney disease, and significant congenital anomalies.

Patients who had used medications known to affect thyroid function tests (e.g., amiodarone, corticosteroids, lithium, anticonvulsants, iodides) were excluded.

Patients with vitamin B12 levels below 200 pg/mL were designated as deficient, while those with levels between 200 and 300 pg/mL were classified as borderline[14].

Anemia was defined as a decrease in hemoglobin (Hb) concentration, hematocrit (Hct), or red blood cell count per cubic millimeter. The presence of anemia in patients was assessed as present if values were below the anemia threshold, which was defined as two SDs below the mean value for the age group[15].

In assessing thyroid function test results in patients, serum TSH and sT4 levels were evaluated according to patient age; TSH values were reported in µIU/mL and sT4 in ng/dL[16].

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hatay Mustafa Kemal University (approval number: 05, date: 18.06.2025). As this was a retrospective study based on existing medical records, informed consent was waived by the ethics committee.

Statistical Analysis

All statistical analyses were performed using SPSS v27.0 (IBM Corp., Armonk, NY, USA). The normality of the variables was assessed using the Shapiro-Wilk test. Descriptive statistics were reported using the mean, SD, median, minimum, and maximum values for continuous variables. Continuous variables with a normal distribution are presented as mean ± SD, whereas non-normally distributed variables are presented as median and interquartile range (IQR), according to normality testing. For variables that did not follow a normal distribution, comparisons between the two groups were performed using the Mann-Whitney U test. For variables that exhibited a normal distribution, comparisons between the two groups were conducted using the t-test. Categorical variables were presented as frequencies and percentages, and differences between groups were tested using the Pearson chi-square test. Statistical significance was set at $p<0.05$.

Results

The study comprised a total of 65 children diagnosed with PEM, of whom 32 (49.2%) were male and 33 (50.8%) were female. No statistically significant differences were observed between male and female patients in age, height, weight, or BMI; all $p>0.05$. The median age was 4.07 years (IQR: 6.41) in males and 4.42 years (IQR: 9.22) in females (p=0.990). Mean heights were 103.59±24.46 cm in males and 103.55±32.96 cm in females (p=0.995), while mean BMIs were 13.85±1.57 kg/m² in males and 13.61±1.27 kg/m² in females (p=0.496) (**Table 1**).

The severity of malnutrition was evaluated by gender. Mild malnutrition was observed in 25 patients (38.46%), moderate malnutrition in 29 patients (44.62%), and severe malnutrition in 11 patients (16.92%). Among male patients, 43.75% had mild malnutrition, 43.75% moderate malnutrition, and 12.50% severe malnutrition. In female patients, the corresponding rates were 33.33%, 45.46%, and 21.21%, respectively. No statistically significant difference was observed in the distribution of malnutrition severity between genders (p=0.549; **Table 2**).

The laboratory findings of the study population are summarised in **Table 3**. The mean Hb level was 12.19±1.02 g/dL, and the mean Hct value was 36.95±3.29%. The mean serum iron concentration was 68.59±30.93 µg/dL, while the median ferritin level was 34.49 ng/mL (IQR: 25.32 ng/mL). The median vitamin B12 and vitamin D levels were 463 pg/mL (IQR: 262) and 26 ng/mL (IQR: 17), respectively. Thyroid function parameters showed a median TSH level of 1.91 µIU/mL (IQR: 1.40 µIU/mL), with mean free T3 and fT4 levels of 4.18±0.69 ng/dL and 1.34±0.19 ng/dL, respectively. The mean blood urea nitrogen (BUN) and creatinine levels were 10.86±3.65 mg/dL and 0.38±0.11 mg/dL, respectively.

Evaluations of micronutrient deficiencies and abnormal thyroid function test results are presented in **Table 4**. Anemia was detected in 15 patients (23.08%), whereas 47 (72.31%) were not anemic. Serum iron deficiency and low ferritin levels were identified in 2 (3.08%) and 4 (6.15%) patients, respectively. The prevalence of vitamin B12 deficiency was 3.08% (2 patients), whereas that of vitamin D deficiency was 18.46% (12 patients). Abnormal thyroid function test results and low BUN levels were each present in 3 patients (4.62%).

Discussion

PEM is frequently associated with deficiencies of multiple micronutrients, such that a deficiency in one nutrient often coexists with deficiencies in others[17].

Table 1.
Demographic characteristics and anthropometric measurements of patients by gender

	Gender		p
	Male	Female	
n (%)	32 (49.20)	33 (50.80)	
Age (years)[a]	4.07; 6.41	4.42; 9.22	0.990*
Height (cm)[β]	103.59±24.46	103.55±32.96	0.995**
Weight (kg)[a]	12.75; 9.95	12.50; 14.40	0.689*
BMI[β]	13.85±1.57	13.61±1.27	0.496**

α Median; IQR
β Mean ± Standard deviation
*: p<0.05, Mann-Whitney U test
**: p<0.05, Independent samples t-test
BMI: Body mass index, IQR: Interquartile range

Table 2.
Degree of malnutrition according to gender

	Gender				Total		p
	Male		Female				
	n	%	n	%	n	%	
Mild	14	43.75	11	33.33	25	38.46	
Moderate	14	43.75	15	45.46	29	44.62	0.549*
Severe	4	12.50	7	21.21	11	16.92	
Total	32	100.00	33	100.00	65	100.00	

*: p<0.05, Pearson chi-square test

In our cohort, anemia and vitamin D deficiency were the most prominent abnormalities, a pattern that has also been reported in other settings. For example, research from India involving 104 children with PEM identified these two deficiencies as the most frequent findings[18]. Likewise, a Pakistani study of 150 malnourished children aged 6-60 months documented anemia in nearly 80% participants; most cases were attributable to iron deficiency. The study also reported rickets in more than a third of patients, vitamin A deficiency in 14% of patients, and zinc or B-complex vitamin deficiencies in more than a quarter of patients[19]. These results highlight the multifactorial nature of nutritional compromise in PEM. Similarly, among 428 children diagnosed with IDA

Table 3.
Laboratory findings of the patients

Hemoglobin (g/dL)[β]	12.19±1.02
Hematocrit (%)[β]	36.95±3.29
Serum iron (µg/dL)[β]	68.59±30.93
Ferritin (ng/mL)[α]	34.49; 25.32
Vitamin B12 (pg/mL)[α]	463; 262
Vitamin D (ng/mL)[α]	26; 17
TSH (µIU/mL)[α]	1.91; 1.40
Free T3 (ng/dL)[β]	4.18±0.69
Free T4 (ng/dL)[β]	1.34±0.19
Blood urea nitrogen (mg/dL)[β]	10.86±3.65
Creatinine (mg/dL)[β]	0.38±0.11

α Median ; IQR
β Mean ± Standard deviation
TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Thyroxine

Table 4.
Evaluation of micronutrient deficiencies and abnormal thyroid function test results

Parameter	Status	n	%
Anemia	Present	15	23.08
	Absent	47	72.30
	Not tested	3	4.62
Low serum iron	Present	2	3.08
	Absent	48	73.84
	Not tested	15	23.08
Low ferritin	Present	4	6.15
	Absent	46	70.77
	Not tested	15	23.08
Vitamin B12 deficiency	Present	2	3.08
	Absent	49	75.38
	Not tested	14	21.54
Vitamin D deficiency	Present	12	18.46
	Absent	35	53.85
	Not tested	18	27.69
Abnormal thyroid function tests	Present	3	4.62
	Absent	47	72.30
	Not tested	15	23.08
Low BUN levels	Present	3	4.62
	Absent	55	84.62
	Not tested	7	10.76
Total		65	100.0

BUN: Blood urea nitrogen

the combined prevalence of vitamin D insufficiency or deficiency was 62%. This finding corroborates evidence that micronutrient deficiencies are prevalent in the context of malnutrition[20].

Endocrine involvement, particularly disturbances in thyroid function, is another important consequence of PEM. Energy and protein deficiencies, limited production of transport proteins, altered peripheral conversion of hormones, and impaired iodine metabolism are among the proposed mechanisms. As nutritional status deteriorates, serum T3 and T4 concentrations fall while TSH levels tend to rise. Initially, the alterations reflect deficits in the binding protein, but with progression, hormone synthesis becomes impaired. Additional nutrient deficiencies, such as hypoalbuminemia, and micronutrient deficiencies (e.g., zinc and iodine) further compromise thyroid function. While this represents an adaptive attempt to conserve energy, the compensatory response may eventually fail in severe or prolonged cases[21-24].

Several studies corroborate this relationship. An Indian study of 60 malnourished children aged 1-5 years reported declines in T3 and T4 with increasing severity of malnutrition, accompanied by a parallel rise in TSH[23]. Another study in Türkiye compared malnourished children with healthy controls and found that T4 levels remained stable in mild-to-moderate PEM but were markedly reduced in severe PEM. T3 was suppressed across all PEM groups, whereas TSH levels remained relatively stable. These findings suggest a stepwise suppression of thyroid function, most evident for T3, with advancing malnutrition[22].

In contrast, abnormal results on thyroid function tests were detected in only three children (4.62%) in our study. When compared with previously reported rates, this proportion appears to be relatively low. The most plausible explanation for this finding is the predominance of mild and moderate, rather than severe, PEM in our study population. Mild and moderate forms of malnutrition may be insufficient to trigger marked hormonal disturbances, which may help explain the discrepancy between our findings and those reported in the existing literature.

In this context, another important consideration when interpreting thyroid function results in children with PEM is the euthyroid sick syndrome (ESS) characterized by alterations in thyroid hormone homeostasis in the absence of intrinsic thyroid disease. ESS has been described in various non-thyroidal conditions, including malnutrition, infections, renal and hepatic disorders, and other states of metabolic stress. The typical biochemical pattern of ESS includes reduced serum T3 levels, normal or low fT4 levels, and normal or mildly altered TSH levels. In the present study, thyroid function assessment was limited to TSH and fT4 measurements, as serum T3 levels were not available for a substantial proportion of patients. Therefore, the presence of ESS could not be reliably evaluated or excluded. This limitation should be considered when interpreting the relatively low prevalence of abnormal thyroid function observed in our cohort. However, the predominance of moderate rather than severe malnutrition in the study population

may partly explain the limited extent of thyroid hormone alterations detected.

Study Limitations

One of the main strengths of this study is that it is among the few studies to simultaneously assess micronutrient deficiencies and thyroid dysfunction in children with PEM. The inclusion of a broad age range enabled the analysis of age-related variations, while the use of retrospective data from the hospital's electronic medical records helped minimize measurement errors. Furthermore, the application of a standardized anthropometric classification based on the WHO criteria strengthened the methodological robustness of the study.

However, this study also has some limitations. It is a single-center, retrospective study, which limits the generalizability of the findings. The relatively small sample size may have reduced the statistical power, particularly in detecting low-frequency conditions such as thyroid dysfunction. Additionally, the prevalence of moderate malnutrition in the study population may have limited the ability to observe the full hormonal impact of severe malnutrition. Important micronutrients, such as vitamin A, zinc, and selenium, were not evaluated. The lack of T3 measurements in a substantial proportion of patients limited the full assessment of thyroid function. The lack of long-term follow-up data also prevented the assessment of the persistence of deficiencies and hormonal alterations.

Conclusion

The findings of this study indicate that, when micronutrient deficiencies and thyroid dysfunction are evaluated together in children diagnosed with PEM, anemia and vitamin D deficiency are relatively common, with prevalence rates of 23.08% and 18.46%, respectively. In contrast, vitamin B12 deficiency and abnormal thyroid function test results were observed at lower rates (3.08% and 4.62%, respectively). The lower frequency of thyroid dysfunction, compared with that reported in previous studies, may be attributable to the predominance of moderate malnutrition in the study population. These results suggest that the effects of PEM on micronutrient metabolism and the endocrine system vary according to the severity of malnutrition. Therefore, childhood malnutrition should be addressed through a comprehensive approach that includes not only assessment of macronutrient status but also evaluation of micronutrient and hormonal status.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hatay Mustafa Kemal University (approval number: 05, date: 18.06.2025).

Informed Consent: Because the study was designed retrospectively no written informed consent form was obtained from the patients.

Footnotes

Author Contributions: Dönger U: Medical Practices, Concept, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing; Çalışkan OF: Medical Practices, Analysis or Interpretation, Literature Search.

Conflict of Interest: The authors declare no conflicts of interest.

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