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Evaluation of vitamin and mineral levels in children with poor appetite

Omer Okuyan[1], Sinem Durmus[2], Hafize Uzun[3]

[1]İstanbul Atlas University, Faculty of Medicine, Department of Pediatrics, İstanbul, Türkiye
[2]İzmir Katip Çelebi University, Faculty of Medicine, Department of Medical Biochemistry, İzmir, Türkiye
[3]İstanbul Atlas University, Faculty of Medicine, Department of Medical Biochemistry, İstanbul, Türkiye

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Abstract

Appetite disturbances in children may be linked to underlying micronutrient deficiencies, even in the absence of overt growth abnormalities. This study aimed to evaluate the association between caregiver-reported poor appetite and serum levels of select vitamins and minerals in children. A retrospective case-control study was conducted involving 200 children aged 2–16 years (100 with poor appetite and 100 age- and sex-matched controls). Serum levels of vitamin D, vitamin B12, folic acid, calcium, and phosphorus were compared between groups. There were no significant differences in age, sex distribution, or BMI between groups. However, children with poor appetite exhibited significantly lower serum concentrations of vitamin B12 (358.0 [244.25-465.25] vs. 440.0 [353.0-540.0] pg/mL, $p<0.001$), folic acid (8.0 [5.85-10.18] vs. 9.0 [7.08-11.53] ng/mL, $p=0.007$), and 25-hydroxyvitamin D [25(OH)D] (20.75 [14.15-26.13] vs. 25.0 [19.3-32.0] ng/mL, $p<0.001$). Levels of calcium ($p=0.022$), phosphorus ($p<0.001$), sodium, and potassium were also significantly reduced in the poor appetite group. BMI was negatively correlated with vitamin B12, folic acid, and vitamin D levels. Positive correlations were observed between calcium and both folic acid and vitamin B12, as well as between vitamin D and folic acid. Children with poor appetite may be at increased risk for multiple micronutrient deficiencies, particularly involving vitamin B12, folic acid, and vitamin D. Routine nutritional screening should be considered in pediatric patients presenting with appetite concerns, regardless of growth status.

Keywords: Calcium, children, folic acid, phosphorus, poor appetite, vitamin B12, vitamin D

Introduction

Appetite, defined as the desire for food, is a conscious desire that can be positively or negatively influenced by previous experiences with food and the appearance of the food [1]. Loss of appetite, on the other hand, is a common condition clinically characterized by decreased or absent appetite and reduced food intake. Although loss of appetite can be seen in children of all age groups, it is particularly common in children between the ages of 1 and 6 [2]. Loss of appetite may be observed in 30% of normally growing children and in 80% of children with growth and development problems [3,4].

Previous research has linked deficiencies in micronutrients such as iron, zinc, vitamin D, and B-complex vitamins to appetite loss, fatigue, and poor feeding behaviors in children [5-8]. Vitamin D has been implicated in appetite regulation via hormonal pathways, including leptin and ghrelin [9], while vitamin B12 and folic acid deficiencies may affect appetite through neurodevelopmental and gastrointestinal mechanisms [10,11]. However, most prior studies have focused on single-nutrient deficiencies or specific pediatric subgroups, such as children with chronic illnesses, growth failure, or malnutrition [12-15].

Despite this growing body of evidence, few studies have comprehensively evaluated multiple micronutrient levels in children who present with caregiver-reported poor appetite but otherwise have normal growth parameters and no underlying medical conditions. In clinical practice, such children are frequently encountered, yet their appetite concerns are often under-investigated in the absence of overt weight loss or growth delay.

Children with decreased appetite are commonly seen in pediatric practice, even when growth parameters are normal, leading to potential underrecognition during routine visits [5]. This study addresses that gap by comparing serum levels of vitamin D, B12, folic acid, calcium, and phosphorus, between children with poor appetite and healthy, age- and sex-matched controls. Unlike prior

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Corresponding Author: Omer Okuyan, İstanbul Atlas University, Faculty of Medicine, Department of Pediatrics, İstanbul, Türkiye
Email: omer.okuyan@atlas.edu.tr

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research focused on single deficiencies or specific conditions, it evaluates multiple micronutrients in a general pediatric population to explore whether subclinical imbalances may underlie appetite issues, supporting the role of nutritional screening in such cases.

Material and Methods

Study Design and Population

This retrospective observational study was conducted to evaluate serum levels of selected vitamins and minerals in children aged 2 to 16 years, who were reported by their parents to have reduced or absent appetite. The findings were compared with those of age-matched healthy children with a normal appetite. The study was designed as a single center. The study was carried out at the Department of Pediatrics, İstanbul Atlas University Hospital. Data collection commenced after receiving ethical approval and covered medical records between January 2024 and January 2025.

The required sample size was calculated using G*Power version 3.1, based on a two-tailed t-test comparing means between two independent groups (low appetite and control). Assuming an effect size of d=0.5 (medium effect), α=0.05, and power (1-β)=0.80, the minimum required sample size was determined to be 128 participants (64 per group). To increase statistical power and account for potential data loss, a total of 200 children were included: 100 in the low appetite group and 100 in the control group.

Inclusion Criteria

- Children between the ages of 2 and 16 years who were evaluated in the pediatric outpatient clinic and whose caregiver's reported concerns related to decreased appetite.
- Availability of complete biochemical test results, including serum levels of vitamin D, vitamin B12, folic acid, calcium, and phosphorus.
- Availability of growth parameters (height, weight, BMI) recorded during the same clinical visit.
- Children without any diagnosed chronic systemic disease or known metabolic disorder.

Exclusion Criteria

- Children with confirmed diagnosis of chronic illnesses such as renal failure, liver disease, endocrine disorders (e.g., hypothyroidism, diabetes mellitus), or malabsorption syndromes.
- Patients receiving vitamin or mineral supplementation within the past three months prior to the laboratory evaluation.
- Incomplete or missing medical records or laboratory results relevant to the study parameters.
- Children with diagnosed psychiatric or neurodevelopmental disorders that may independently affect appetite or feeding behavior.

Sampling Method

The study population included pediatric patients aged 2–16 years who presented to the outpatient pediatric clinic with complaints of decreased appetite between January 2024 and January 2025. Initially, 253 patients were screened for eligibility. Patients were excluded if their medical records lacked complete serum measurements of vitamin D, vitamin B12, folic acid, calcium, or phosphorus, or if they had chronic illnesses or conditions that could affect appetite or nutritional status. As a result, 153 patients were excluded, and 100 children meeting the criteria were included in the low appetite group.

The control group comprised healthy children attending routine pediatric check-ups during the same period, who had serum measurements for the same parameters. From an initial 177 healthy children screened, 77 were excluded due to incomplete data or other exclusion criteria, resulting in 100 children in the control group.

Data Collection

Data was obtained retrospectively from electronic medical records. Collected variables included demographic information, anthropometric data, clinical history related to appetite status, and laboratory test results. Hemogram and routine biochemical parameters, along with serum levels of vitamin D, vitamin B12, folic acid, calcium, and phosphorus, were recorded.

Biochemical Analysis

Serum levels of vitamin D, vitamin B12, and folic acid were measured using chemiluminescent immunoassay (CLIA) techniques. Mineral concentrations including calcium, and phosphorus were assessed using standard photometric methods as part of routine biochemistry panels, conducted in the hospital's central laboratory in accordance with manufacturer protocols and internal quality controls.

Ethical Considerations

Ethical approval for the use of patient data and the study protocol was granted by the Clinical Research Ethics Committee of İstanbul Atlas University, Atlas University Hospital (Approval Date: 17.02.2025; Document No: E-22686390-050.99-61872). The research was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki (1975), as revised in 2013. As this study was conducted retrospectively, informed consent was not obtained from participants.

Statistical Analysis

All statistical analyses were performed using JASP software (version 0.19.1). The normality of the data distribution was assessed using the Shapiro–Wilk test. For continuous variables with a normal distribution, results are presented as mean±standard deviation (SD), and group comparisons were performed using the independent samples Student's t-test. For non-normally distributed variables, data are presented as median (interquartile range [IQR]), and the Mann–Whitney U test was used for comparisons between groups. Pearson's correlation analysis was employed for normally distributed variables, and Spearman's rank correlation was used when assumptions of normality were not met. Categorical variables are presented as frequencies and percentages and compared using the chi-square test. A p-value <0.05 was considered statistically significant.

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Results

The study included a total of 200 participants, with 100 individuals in the control group and 100 individuals in the low appetite group. No statistically significant difference was observed between the groups in terms of gender distribution (49 females / 51 males in the control group vs. 53 females / 47 males in the low appetite group, p=0.572), age (6.5 [4.0-9.0] vs. 7.0 [5.0-9.25] years, p=0.089), body mass index (BMI) (17.47±4.14 vs. 18.48±5.04, p=0.121), hemoglobin (HGB) levels (12.20±1.05 vs. 12.39±1.12, p=0.218), or hematocrit (HCT) levels (36.50±3.10 vs. 37.06±3.15, p=0.211) (Table 1).

Table 1. Comparison of demographic and hematological parameters between control and low appetite groups

Parameters	Groups	Mean±SD/n/Median (IQR)	p-value
Gender (F/M)	**Control**	49/51	0.572
	Low appetite	53/47	
Age (years)[1]	**Control**	6.5 (4.0-9.0)	0.089
	Low appetite	7.0 (5.0-9.25)	
BMI (kg/m²)[2]	**Control**	17.47±4.14	0.121
	Low appetite	18.48±5.04	
Hemoglobin (g/dL)[2]	**Control**	12.20±1.05	0.218
	Low appetite	12.39±1.12	
Hematocrit (%)[2]	**Control**	36.50±3.10	0.211
	Low appetite	37.06±3.15	

[1]**Non-parametric test:** Mann-Whitney U test**;** [2]**Parametric test:** Independent samples t-test; *SD: standard deviation, IQR: interquartile range, n: number of subjects, F: female, M: male, BMI: body mass index

However, statistically significant differences were detected in several biochemical parameters between the groups (Table 2). Serum sodium (Na) levels were significantly lower in the low appetite group compared to the control group (137.50 [136.0-139.0] vs. 138.0 [137.0-139.0], p=0.003). Similarly, potassium (K) levels were also lower in the low appetite group (4.2 [3.98-4.30] vs. 4.2 [4.10-4.43], p=0.008).

Among the micronutrients, vitamin B12 levels were markedly lower in the low appetite group (358.0 [244.25-465.25] pg/mL) compared to the control group (440.0 [353.0-540.0] pg/mL), with a highly significant difference ($p=1.772\times10^{-5}$). Likewise, folic acid levels (8.0 [5.85-10.18] ng/mL vs. 9.0 [7.08-11.53] ng/mL, p=0.008) and 25-hydroxyvitamin D [25(OH)D] levels (20.75 [14.15-26.13] ng/mL vs. 25.0 [19.3-32.0] ng/mL, $p=9.668\times10^{-5}$) were significantly lower in the low appetite group.

Calcium (Ca) and phosphorus (P) levels were also significantly decreased in the low appetite group. The median calcium level was 9.82 (9.29-10.0) mg/dL in the low appetite group and 9.88 (9.56-10.0) mg/dL in the control group (p=0.032), while phosphorus levels were 4.90 (4.40-5.0) mg/dL and 5.0 (4.7-5.33) mg/dL, respectively ($p=7.469\times10^{-4}$).

Table 2. Comparison of biochemical parameters between control and low appetite groups

Parameters	Normal reference range	Groups	Mean±SD/Median (IQR)	p-value
Na (mmol/L)[1]	**135-145**	**Control**	138.0 (137.0-139.0)	0.003
		Low appetite	137.50 (136.0-139.0)	
K (mmol/L)[1]	**3.5-5.1**	**Control**	4.2 (4.10-4.43)	0.008
		Low appetite	4.2 (3.98-4.30)	
Vitamin B12 (pg/mL)[1]	**200-900**	**Control**	440.0 (353.0-540.0)	1.772×10^{-5}
		Low appetite	358.0 (244.25-465.25)	
Folic Acid (ng/mL)[1]	**3-17**	**Control**	9.0 (7.08-11.53)	0.008
		Low appetite	8.0 (5.85-10.18)	
Vitamin 25(OH)D (ng/mL)[1]	**20-50 (suffiecient), <20 (deficiency)**	**Control**	25.0 (19.3-32.0)	9.668×10^{-5}
		Low appetite	20.75 (14.15-26.13)	
Ca (mg/dL)[1]	**8.8-10.8**	**Control**	9.88 (9.56-10.0)	0.032
		Low appetite	9.82 (9.29-10.0)	
P (mg/dL)[1]	**4.0-6.5**	**Control**	5.0 (4.7-5.33)	7.469×10^{-4}
		Low appetite	4.90 (4.40-5.0)	

[1]**Non-parametric test:** Mann-Whitney U test; *SD: standard deviation, IQR: interquartile range, Na: sodium, K: potassium, Ca: calcium P: phosphorus

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In correlation analyses, several statistically significant relationships were observed. BMI was negatively correlated with vitamin B12 ($r=-0.278$, $p=0.005$), folic acid ($r=-0.216$, $p=0.031$), and vitamin 25(OH)D levels ($r=-0.214$, $p=0.033$) (Figure 1). Additionally, vitamin 25(OH)D levels were positively correlated with folic acid ($r=0.285$, $p=0.004$, Figure 2). Serum calcium levels were moderately and positively correlated with potassium ($r=0.471$, $p=7.52\times10^{-7}$), vitamin B12 ($r=0.252$, $p=0.012$), and folic acid levels ($r=0.198$, $p=0.049$). Furthermore, phosphorus levels were positively correlated with calcium ($r=0.244$, $p=0.015$) (Figure 3).

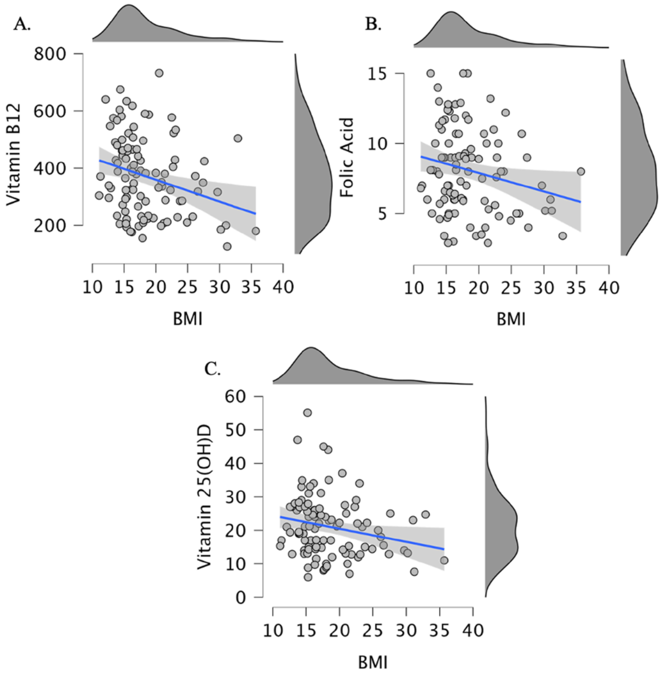

Figure 1. Correlation analysis between BMI and (**A**) Vitamin B12, (**B**) Folic Acid, and (**C**) Vitamin 25(OH)D levels

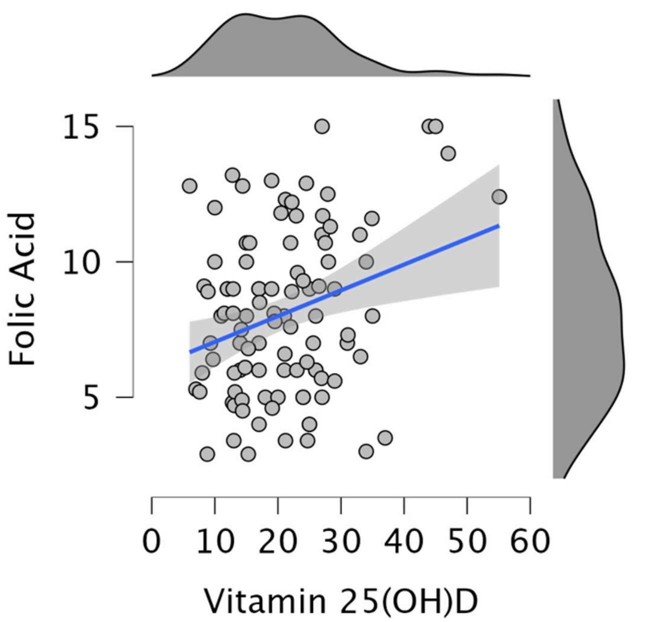

Figure 2. Correlation analysis between Vitamin 25(OH)D levels and folic acid levels

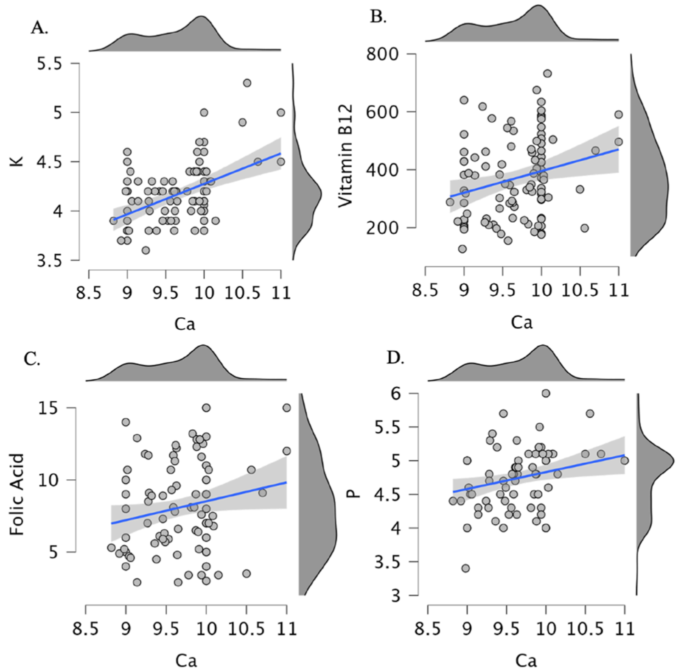

Figure 3. Correlation analysis between calcium levels and (**A**) potassium, (**B**) vitamin B12, (**C**) folic acid, and (**D**) phosphorus levels

Discussion

Appetite regulation in children is a complex process influenced by both physiological and nutritional factors. Deficiencies in micronutrients such as zinc, iron, vitamin B12, folic acid, and vitamin D may negatively affect appetite regulation in children by influencing metabolic, neurological, and gastrointestinal pathways [16-19]. In the present study, children with poor appetite had significantly lower serum levels of key micronutrients, including vitamin B12, folic acid, and 25-hydroxyvitamin D, compared to healthy controls. Additionally, essential minerals such as calcium and phosphorus were also significantly reduced in the low appetite group, indicating a potential link between appetite status and overall micronutrient balance. These findings suggest that poor appetite in children may be associated with underlying micronutrient deficiencies, highlighting the importance of routine nutritional assessment in pediatric patients presenting with feeding concerns, even in the absence of evident growth or developmental delays.

Loss of appetite, defined as the reduced perception of hunger, is a key factor affecting nutrition and food intake [20]. In this study, children with poor appetite showed significantly lower serum calcium and phosphorus levels compared to controls, indicating a potential link between mineral status and appetite regulation. Calcium and phosphorus are crucial for bone development and cellular functions, and their deficiencies may indirectly impair appetite through metabolic disruptions [21]. Foster et al. [22] highlight poor appetite as a common issue in pediatric chronic kidney disease, related to metabolic imbalances affecting calcium and phosphorus homeostasis, which impacts growth and nutrition. Similarly, ESPGHAN/ESPEN/ESPR/CSPEN guidelines [23]

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stress the importance of balanced calcium and phosphorus intake for bone mineralization and overall growth in children, recommending individualized monitoring and supplementation. These findings emphasize the complex relationship between micronutrient status and appetite, supporting the need for mineral assessment in children with feeding difficulties.

The findings of this study revealed significantly lower serum levels of vitamin B12, folic acid, and vitamin D in children with poor appetite compared to their healthy peers. Although differences like the 1 ng/mL folic acid may seem small, even mild micronutrient imbalances can affect appetite and development in children. Early detection is important to prevent progression to deficiency, supporting the value of routine screening in those with feeding issues. These results are consistent with previous research indicating that deficiencies in these vitamins may adversely affect appetite regulation and general nutritional status in pediatric populations. Vitamin B12 and folic acid are crucial for DNA synthesis, neurodevelopment, and erythropoiesis, and their deficiencies have been linked to fatigue, mood changes, and anorexia-like symptoms, which may contribute to reduced food intake [24,25]. Stabler [24] provides a comprehensive review of vitamin B12 deficiency, highlighting its role in DNA synthesis, neurodevelopment, and erythropoiesis. Deficiencies can lead to fatigue, mood changes, and anorexia-like symptoms, potentially reducing food intake. Allen [25] reviews the causes and consequences of folic acid deficiency, noting its critical role in DNA synthesis and cell division. Deficiency can lead to fatigue and poor appetite.

Vitamin B12 deficiency can impair gastrointestinal function, affecting gut motility and mucosal integrity, leading to reduced appetite [26]. It is also linked to low energy and feeding difficulties in children. Green [27] highlights the importance of vitamin B12 in pediatric nutrition, noting its deficiency may cause developmental delays and feeding problems. Hatamizadeh et al. [28] showed folic acid supplementation improved appetite in preschoolers, though further research on growth effects is needed. This finding aligns with our observation of lower folic acid levels in children with poor appetite and suggests that addressing folic acid deficiency may enhance feeding behavior. However, further studies are needed to clarify the effects of folic acid on growth outcomes. Bakırhan et al. [29] found that adherence to the Mediterranean diet in children with disabilities improved gastrointestinal health, reduced micronutrient deficiencies, and enhanced quality of life. These findings suggest that correcting micronutrient deficiencies and promoting nutrient-rich diets like the Mediterranean diet may improve appetite and overall health in pediatric populations.

Vitamin D, beyond its role in bone metabolism, has been increasingly linked to appetite regulation and energy balance, potentially through its effects on hormones like leptin and ghrelin and inflammatory pathways affecting hypothalamic function [30]. Pereira-Santos et al. [30] demonstrated a strong association between vitamin D deficiency and obesity, possibly due to sequestration in adipose tissue and reduced bioavailability. In our study, lower 25(OH)D levels in children with poor appetite may reflect not only insufficient intake or sun exposure but also a bidirectional relationship with feeding behavior. Our study did not include obese children; therefore, the obesity–vitamin D deficiency relationship is not directly relevant. The findings suggest vitamin D deficiency may affect appetite independently of obesity in this population. Park et al. [31] similarly reported high rates of vitamin D deficiency in children with nonspecific complaints, reinforcing the importance of micronutrient evaluation even in the absence of overt malnutrition. These findings highlight the relevance of routine nutritional screening, including vitamin and mineral assessments, in children with feeding difficulties. Addressing deficiencies—particularly in vitamin D, B12, and folic acid may improve appetite, support growth, and prevent longer-term health issues.

The present findings are consistent with prior literature showing associations between micronutrient deficiencies and poor appetite. In particular, the deficiencies in vitamin D, B12, and folic acid observed in our study align with their known roles in neurodevelopment, gastrointestinal health, and energy regulation. Supporting this, a regional study by Cansever Akay et al. [32] emphasized the widespread use of vitamin and mineral supplements among children in Turkey, suggesting a growing awareness of potential micronutrient insufficiencies in pediatric populations, even in the absence of clinical malnutrition. These findings underscore the importance of early nutritional screening and targeted supplementation as part of routine pediatric evaluations in children with feeding concerns.

The possibility of reverse causality should be considered, as micronutrient deficiencies may both contribute to and result from decreased appetite. Poor appetite can lead to inadequate nutrient intake, causing deficiencies, while existing deficiencies may impair appetite regulation. Prospective studies are needed to clarify the direction and causality of this relationship.

Limitations of the Study

This study has several limitations that should be acknowledged. First, due to its retrospective design, it relied on existing medical records, which may have resulted in incomplete or inconsistent data, particularly regarding dietary intake, socioeconomic status, or parental feeding practice factors known to influence appetite and nutritional status. Second, appetite assessment was based solely on caregiver reports rather than standardized appetite scoring tools, introducing potential subjective bias. Third, since the study was conducted in a single center, the findings may not be generalizable to broader populations with different nutritional habits or healthcare access. Fourth, appetite was assessed solely based on caregiver reports without using standardized tools, which may introduce subjectivity and bias. This limits the accuracy of the anorexia diagnosis in this retrospective study. Lastly, the cross-sectional nature of the data precludes establishing causality between micronutrient deficiencies and poor appetite.

Conclusion

This study found a significant association between reduced appetite in children and lower serum levels of vitamin B12, folic acid, vitamin D, calcium, and phosphorus. Appetite problems in children may warrant targeted micronutrient screening: vitamin B12 and folic acid levels for persistent poor appetite with gastrointestinal symptoms, and vitamin D, calcium, phosphorus for those with growth concerns. Such specific assessments could improve early detection and intervention. These subclinical deficiencies may both contribute to and result from poor appetite, impacting growth and health. Given appetite's multifactorial nature, micronutrient status is an important factor. Routine screening in children with appetite concerns may enable early intervention. However, due to the retrospective design, causality cannot be established. Prospective studies with standardized tools are needed to clarify these relationships.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

The protocol for sample collection was approved by the İstanbul Atlas University, Atlas University Hospital, Clinical Research Ethics Committee (Date: 17.02.2025; Document No: E-22686390-050.99-61872).

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