

# Folate, Vitamin B12 and Serum Ferritin Levels by Age and Gender in Children Presenting with Protein and Energy Insufficiency: A Retrospective Review

## Protein ve Enerji Yetersizliği ile Başvuran Çocuklarda Yaş ve Cinsiyete Göre Folat, Vitamin B12 ve Serum Ferritin Düzeyleri: Retrospektif Bir İnceleme

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### ABSTRACT

**Objectives:** The aim of this study is to determine the levels of folate, vitamin B12, and ferritin according to gender and age groups in children who visited the hospital with the complaint of protein and energy deficiency.

**Methods:** Folate levels of 74 patients with protein and energy deficiency complaints, vitamin B12 levels of 184 patients, and ferritin levels of 187 people who were admitted to the hospital were included in the study. The hospital reference ranges for children were used to diagnose folate, vitamin B12, and ferritin levels and to determine their normal ranges.

**Results:** When the folate levels were examined in the study, it was determined that approximately 2% of the children in the 0-6 age group were below <3.89 ng/mL, and all of the children in the 7-18 age group were within the normal range. When the vitamin B12 levels are examined, it was determined that 3.3% of the children had a vitamin B12 level below 191 ng/L, and 14.3% of the 7-18 age group were below 191 ng/L. Considering the ferritin levels, it was determined that 51.6% of the children were below 30 µg/L. When evaluated according to gender, the majority of folate and B12 levels in both men and women were within the normal range, while 47.1% of women and 41% of men had ferritin levels below the normal range.

**Conclusion:** It was observed that the folate, vitamin B12, and ferritin levels of the patients could vary according to geographical regions. For this reason, we think that it should be focused on the 0-6 age range, where the incidence of micronutrient deficiencies and infectious diseases is the highest.

**Keywords:** Protein Insufficiency, Child, Folate, B12, Ferritin

### ÖZ

**Amaç:** Bu çalışmada protein ve enerji yetersizliği şikayetiyle başvuran çocuklarda cinsiyet ve yaş gruplarına göre folat, B12 vitamini ve ferritin düzeylerini belirlenmesi amaçlanmaktadır.

**Gereç ve Yöntem:** Hastaneye başvuran ve şikayeti protein ve enerji yetersizliği olan 74 kişinin folat düzeyi, 184 kişinin vitamin B12 düzeyi ve 187 kişinin ferritin düzeyi çalışmaya dahil edildi. Folat B12 vitamini ve ferritin düzeylerini teşhis etmek ve normal aralıklarını belirlemek için hastanenin çocuklar için belirlediği referans aralıkları kullanıldı.

**Bulgular:** Çalışmada folat düzeyleri incelendiğinde; 0-6 yaş grubundaki çocukların yaklaşık %2'sinin <3,89 ng/mL'nin altında olduğu, 7-18 yaş grubundaki çocukların tamamının normal aralıkta olduğu belirlendi. B12 vitamini düzeyleri incelendiğinde; Çocukların %3,3'ünün B12 vitamini düzeyinin 191 ng/L'nin altında olduğu, 7-18 yaş grubundakilerin ise %14,3'ünün 191 ng/L'nin altında olduğu belirlendi. Ferritin seviyelerine bakıldığında; Çocukların %51,6'sının 30 µg/L'nin altında olduğu belirlendi. Cinsiyete göre değerlendirildiğinde hem erkeklerde hem de kadınlarda folat ve B12 düzeylerinin büyük çoğunluğu normal aralıkta bulunurken, kadınların %47,1'i ve erkeklerin %41'i ferritin düzeylerinin normal aralığın altında olduğu tespit edildi.

**Sonuç:** Hastaların folat, vitamin B12, ve ferritin düzeylerinin coğrafi bölgelere göre değişebildiği görüldü. Bu nedenle mikrobesein eksikliklerinin ve bulaşıcı hastalıkların görülme sıklığının en yüksek olduğu 0-6 yaş aralığına odaklanılması gerektiğini düşünüyoruz.

**Anahtar Kelimeler:** Protein Yetersizliği, Çocuk, Folat, B12, Ferritin

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## INTRODUCTION

It is defined as protein-energy deficiency in the clinical-pathological picture that occurs when one or more nutrients are taken in a way that disrupts the body's adjustment (1). Childhood malnutrition accounts for approximately half (45%) of all deaths among children under the age of 5 worldwide (2). Growth in children; it is the increase in the ratio of body volume and mass with the increase in cell number and size. Development, on the other hand, is known to mean bodily maturation by changing the content of cells, tissues, and structures (3). Malnutrition rate continues to be a problem in developing countries (4). Malnutrition affects one in nine people worldwide, and this rate seems to increase even more in low-income countries, especially among children younger than five years old. Malnutrition in early childhood can have harmful neurodevelopmental effects, with significant increases in lifelong cognitive, neurological, and mental health problems, and its consequences may spread to future generations (5). Vitamin B12 deficiency in childhood is a rare disease that shows nonspecific symptoms. It was stated that many cases were exclusively breastfed and were children of mothers with low cobalamin levels. The development of the patients is normal in the early period. It has been reported that symptoms and signs such as megaloblastic anemia, loss of acquired motor abilities, and growth and development retardation can be seen around 3-8 months (6). Ferritin protein is found in body cells and especially in cells known as hepatocytes, which make up approximately 75% of the liver, bone marrow, and immune system cells. Ferritin, which is responsible for the storage of iron taken through food and its release, when necessary, is also defined as the body's iron store (7). Folate deficiencies are one of the most common vitamin deficiencies affecting children around the world (8). Folate, formerly defined as a treatment for megaloblastic anemia during pregnancy, is now seen as an essential vitamin for child growth (9). Unlike plants

and humans, they do not have a metabolic system to synthesize folate and therefore must be obtained entirely from dietary sources (10). This study aimed to determine the levels of folate, vitamin B12, and ferritin according to gender and age groups in children who visited the hospital with the complaint of protein and energy deficiency.

## MATERIALS AND METHODS

The study was approved by the Ethics Committee of a State University (decision no: 2022/104, date: 21.09.2022). The results of folate, vitamin B12, and serum ferritin levels requested from patients who visited Şırnak State Hospital between July 2020 and June 2022 were retrospectively analyzed. The reference range used by the hospital for children was taken as a sample to diagnose folate, Vitamin B12, and ferritin levels and to determine their normal ranges. Results were grouped as low, normal, and high based on the reference ranges of 3.89-26.8 ng/mL for Folate, 191-663pg/mL for Vitamin B12, and 30-400 ng/mL for Ferritin. The data of the patients were obtained from electronic health records in the hospital database. Therefore, an informed consent form was not obtained from the patients. B12 levels of 184 people, folate levels of 74 people, and ferritin levels of 187 people who visited the hospital were included in the study. Ferritin, B12, and folate levels were determined according to the age and gender of the patients. In the analysis of the data, patient names and private information were kept confidential and ethical rules were followed. The ages of the children included in the study were evaluated by dividing them into two groups, 0-6 and 7-18. Folate, Serum B12, and ferritin levels were analyzed and recorded in the laboratory as an immunoassay on the Roche Cobas device using the electrochemiluminescence method.

**Table 1: Folate, vitamin B12 and ferritin levels of the patients by age and gender**

	Age				Gender			
	0-6 year		7-18 year		Female		Male	
	n	(%)	n	(%)	n	(%)	n	(%)
<b>Folat</b>								
<3,89 ng/mL	1	2	0	0	0	0	1	3.1
3,89-26,8 ng/mL	48	98	25	100	42	100	31	96.9
>26,8ng/mL	0	0	0	0	0	0	0	0
<b>Vitamin B12</b>								
<191ng/L	4	3.3	9	14.3	7	7.1	6	7.1
191-663 ng/L	98	81	53	84.1	85	85.8	66	77.6
>663 ng/L	19	15.7	1	1.6	7	7.1	13	15.3
<b>Ferritin</b>								
<30 µg/L	64	51.6	19	30.2	49	47.1	34	41
30-400 µg/L	60	48.4	44	69.8	55	52.9	49	59
>400 µg/L	0	0	0	0	0	0	0	0

## Statistical analysis

The statistical analysis was performed using the SPSS 21.0 package program (SPSS, Version 21.0. Armonk, NY: IBM USA). The conformity of the data to the normal distribution was examined with the Kolmogorov-Smirnov test. Nonparametric tests were applied because it did not fit the normal distribution. The Mann-Whitney test was used to determine whether there was a significant difference between the folate, vitamin B12, and ferritin levels of the children according to gender and age. Frequency distributions, number, percentage, and median, minimum, and maximum values were given in descriptive statistics. A value of  $P < 0.05$  was considered significant.

## RESULTS

Folate, Vitamin B12, and Ferritin levels were grouped according to the reference ranges used by the hospital for children, and frequency distributions of low, normal, and high-level results by age and gender were given (Table 1). When evaluated according to age, 2% of the patients aged 0-6 years had Folate levels below 3.89 ng/mL, while the rest of this group was found to be within the normal range. Folate levels of the patients aged 7-18 years were found to be within the normal range. It was found that the vitamin B12 levels of the patients aged 0-6 years were below the normal range in 3.3%, <191ng/L, 81% were in the normal range, and 15.7% were above the normal range >663 ng/L. Vitamin B12 levels of patients aged 7-18 years were found to be below the normal range in 14.3%, 84.1% were at normal levels, and 1.6% were above normal levels. It was determined that ferritin levels of patients aged 0-6 years were below the 51.6% normal range, ie <30 µg/L, and 48.4% had normal levels, ie 30-400 µg/L. It was determined that 30.2% of the ferritin levels in the 7-18 age range were below the normal levels, and 69.8% of them were within the normal range (Table 1).

When evaluated according to gender, it was found that all of the folate levels of female patients were in the normal range, while it was below the normal level of 3.1% in men, and 96.9% of them were at normal levels. It was determined that the vitamin B12 levels of the female patients were below the normal range in 7.1%, 85.8% were at the normal level, and 7.1% were above the normal levels. Vitamin B12 levels of male patients were found to be below normal levels in 7.1%, 77.6% at normal levels, and 15.3% above normal levels. Ferritin levels of female patients were found to be below the normal range in 47.1% and 52.9% in the normal range (Table 1).

## DISCUSSION

Protein and energy deficiency is one of the most common health problems in developing countries, and it is reported that it mostly affects children between the ages of six months and five years (11). This problem is seen at a rate of 11% to 69.5% in children aged 0-6, depending on different regions and settlement characteristics, and emerges as an important health problem (12,13). The problem of protein and energy deficiency causes the death of approximately 5 million children every year. In developing countries, 1-5% of

children under the age of five die from severe malnutrition (14). It is also common in developing countries and poor areas of developed countries. In this case, the most affected age group is infants (15,16). Adequate nutrition in children; It is only possible to take and use the calories, protein, vitamins, minerals, and trace elements necessary for the maintenance of life and adequate growth (17-18). Vitamin B12 deficiency in childhood is a rare disease with nonspecific symptoms. It has been reported that many cases are exclusively breastfed and children of mothers with low cobalamin levels (6). Studies have been published reporting that malnutrition in the population may differ between genders. In a study by Şensoy et al., the malnutrition rate of women was found to be higher than that of men (19). In this study, it was observed that folate levels and vitamin B12 levels of malnourished female patients were better than in males, while ferritin levels were found to be better in males than females. This may be due to the difference in the number of patients and population in the study. In a study on micronutrient deficiency among children in China, it was reported that there was no significant difference in B12 between genders (20). In a study conducted in India between the ages of 6-59 months, it was reported that B12 deficiency is more pronounced in children under 24 months (21). In this study, it was observed that 3.3% of children aged 0-6 were below the normal range, and 14.8% of children aged 7-18 years were below the normal range. The reason for this may be that the 0-6 age group receives enough vitamin B12 both externally and with the intense consumption of red meat by breastfeeding mothers. Saka et al. reported that ferritin levels were higher in women (22). In our study, it was observed that the ferritin levels according to gender were below normal compared to 47.1% of women and 41% of men. The reason for this difference in our study may have been caused by the population included in the study and the effect of geographical conditions. In a study conducted by Wang et al. on children under the age of three, it was reported that the prevalence of anemic was higher in children under the age of two (23). In our study, when ferritin levels were evaluated according to age, it was observed that 51.6% of the 0-6 age group was below normal, and 30.2% of the 7-18-year old children were below the normal levels. It can be said that the child does not take adequate supplementary food supplements, but if the child is between the ages of 7-18, it can be said that the ferritin level of the child increases depending on the supplementary foods and nutrients he receives in his diet. A study by Anwer et al. reported that most malnourished children, especially females, had more folic acid deficiency (24). In this study, it was determined that all of the women were within normal ranges. The reason for this can be said that more common folic acid-containing foods are consumed in the region. In a study conducted in Norway, 5.8% of the two-year-olds and 13.2% of the four- to six-year-olds reported levels below the normal value. In this study, it was determined that 2% of children aged 0-6 years were in the normal range (25-26).

## Limitations of the Study

The most important limitation of our study is that it is a retrospective study, and the height and weight of the patients

are not included in the system. In addition, information such as subjects' living conditions, dietary characteristics, and whether they used folate, vitamin B12, and serum ferritin supplements could not be obtained. On the other hand, the single-centered nature of the study prevents the generalizability of the results.

## CONCLUSION

In conclusion, the Folate, vitamin B12, and ferritin levels of patients may differ according to geographical regions, depending on their regional dietary habits. Complementary nutrition interventions usually focus on the 0-6 age range where there is growth stagnation, micronutrient deficiencies, and the highest incidence of infectious diseases in developing countries, and also take into account gender situations. Therefore, interventions that are effective in reducing malnutrition should be a high priority. It has been observed that the 0-6 age range is an important period in general. For example, we think that micronutrient supplementation, a food-based comprehensive approach, and programs that target individual nutritional deficiencies will be more effective.

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