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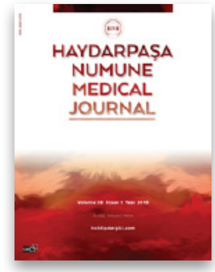

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ORIGINAL ARTICLE

The Relationship Between Serum Vitamin D Level, Anemia, and Iron Deficiency in Preschool Children

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Abstract

Introduction: Vitamin D deficiency and iron deficiency are the most common nutritional pandemic problems worldwide at all levels of society. In some studies, vitamin D has been shown to have an effect on erythropoiesis. The objective of this study was to investigate the relationship between serum vitamin D level, hemogram parameters, and serum iron level in preschool children.

Methods: The study group comprised 108 children aged between 2 and 5 years who visited a single pediatric hematology polyclinic between August 2014 and August 2017and whose serum vitamin D level and iron parameters were evaluated. The patients were divided into 3 groups according to the hemoglobin value, serum ferritin level, and transferrin saturation index calculation: iron deficiency, iron deficiency anemia, and a control group. Vitamin D deficiency, insufficiency, and normal categories were also used based on assessment of the serum vitamin D level.

Results: There were 41 children in the iron deficiency group, 32 classified as iron deficiency anemia, and 35 age- and sex-mated controls. The vitamin D level was statistically significant between the groups ($p<0.05$).

Discussion and Conclusion: According to our findings, vitamin D deficiency and insufficiency were prevalent, especially in children with iron deficiency anemia. It is recommended that the serum vitamin D level of children with iron deficiency anemia should be checked and vitamin D-fortified food consumption should be increased.

Keywords: Anemia; iron deficiency anemia; preschool; vitamin D.

Vitamin D insufficiency and iron deficiency are the most common nutritional pandemic problems worldwide at all levels of the population [1]. Vitamin D insufficiency affects approximately 1 billion people worldwide, and is an important nutritional problem, especially in preschool years [2]. The prevalence of iron deficiency in the world is 32.9%, consisting of mostly children under five years of age [3]. Vitamin D deficiency is associated with many diseases, such as cancer, diabetes mellitus and cardiovascular diseases, especially osteoporosis, rickets; iron deficiency has been implicated in relation to many problems, such as increased susceptibility to infections, growth retardation, decreased school success, and decreased exercise capacity [4, 5].

Vitamin D is a prohormone involved in the neuromuscular and skeletal system by regulating serum calcium/phosphorus balance [6]. Vitamin D is firstly hydroxylated to 25-hydroxy vitamin D in the liver and then converted to its active form of 1.25-dihydroxy vitamin D in the kidney, and its effect is mediated by cell cytoplasm and receptors in the nucleus [7]. Recent information shows that many organs, such as osteoblasts, lymphocytes, mononuclear cells, brain, pancreas, small intestine, colon, heart, skin, gonad,

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prostate and breast, commonly contain these receptors [5, 6]. Therefore, the effects of vitamin D are not limited to the musculoskeletal system.

In some studies, vitamin D has been shown to be effective on erythropoiesis by increasing the erythropoietin receptor level in erythroid precursor stem cells [7, 8]. Reduction of the need for erythrocyte stimulating agents and increased reticulocyte count in hemodialysis patients undergoing vitamin D replacement support this hypothesis [10]. Vitamin D increases the sensitivity to erythropoietin by decreasing proinflammatory cytokine and hepcidin secretion due to its anti-inflammatory properties. Activation of the vitamin D receptor also increases the release of interleukin-10, which has anti-inflammatory properties and positively contributes to erythropoiesis [11].

In the light of this remarkable information, serum vitamin D level is thought to be related to the hemoglobin level. However, clinical observational studies investigating this relationship are insufficient to make a definitive judgment. This study aims to investigate the relationship between serum vitamin D levels, hemogram parameters and serum iron levels in preschool children.

Materials and Methods

Hundred and eight children aged 2-5 years with measured serum vitamin D levels and iron parameters who were admitted to the pediatric hematology outpatient clinic between August 2014 and August 2017 were included in this study. The patients were divided into three groups according to hemoglobin, serum ferritin levels and transferrin saturation index (TSI) as iron deficiency, iron deficiency anemia and control groups.

Patients were evaluated according to their serum vitamin D levels as vitamin D deficiency, insufficiency and normal groups. The patients' files were retrospectively screened for serum vitamin D, hemoglobin (Hb), mean erythrocyte volume (MCV), mean erythrocyte hemoglobin (MCH), mean erythrocyte hemoglobin concentration (MCHC), erythrocyte distribution width (RDW), serum iron, total iron binding capacity (TDBK), serum ferritin, transferrin saturation index (TSI) levels, and the data obtained were recorded.

Patients with chronic disease, infection, inflammatory, hematological disease, unexplained hematological parameters and missing data were not included in this study. Patients' erythrocyte indexes were measured using automatic blood counting device LH 780 (Beckman Coulter, CA, USA), serum vitamin D levels with high performance liquid chromatography (Beckman Coulter, Gold HPLC System, USA), serum iron, total iron-binding capacity and serum ferritin levels with ADVIA® 1800 (Siemens, Erlangen, Germany) device. Patients with Hgb <11 g/dL were considered to have anemia; cases with serum ferritin levels <12ng/ml and transferrin saturation indexes <16% were considered to have an iron deficiency. Patients with anemia and iron deficiency were accepted as iron deficiency anemia. The transferrin saturation index was calculated based on the following formula:

Serum iron level/total iron-binding capacity x100

Vitamin D levels of <20 ng/mL was accepted as vitamin D deficiency, 20–30 ng/mL as vitamin D insufficiency, and >30 ng/mL as normal vitamin D level. The study protocol was approved by the local Ethics Committee (decision number-date: 19/147-2019) and conducted according to the Helsinki Declaration.

Statistical Analysis

SPSS 21.0 software was used for data analysis. Continuous variables were calculated as mean+standard deviation. Shapiro-Wilk and Levine tests were used for the normal distribution and homogeneity of the data. The correlation between the results was evaluated with Pearson correlation test. ANOVA test and the Turkey test were used for post-hoc analysis. Results were considered statistically significant if $p<0.05$.

Results

This study included 41 patients with iron deficiency, 32 patients with iron deficiency anemia and 35 age and sex-matched disease -free controls. The mean ages of iron deficiency, iron deficiency anemia and control groups were 40.2±10.1; 42.1±9.5; and 38±9.5 months, respectively ($p>0.05$), (Table 1). The male/female ratios of iron deficiency, iron deficiency anemia and control groups were 14/27; 18/14; 17/18, respectively ($p>0.05$) (Table 1).

The mean serum vitamin D levels of iron deficiency, iron deficiency anemia and control groups were 31.9±10.6 ng/mL; 27.3±13.8 ng/mL, and 35.9±15.4 ng/mL, respectively ($p<0.05$), (Table 1). The mean serum vitamin D level was higher in the control group than the other two groups. However, there was a statistically significant difference only between the control and iron deficiency anemia groups ($p<0.05$).

Patients were evaluated in three groups according to serum vitamin D levels in iron deficiency, iron deficiency anemia and control groups. In vitamin D deficiency group iron deficiency was detected in 4 (9.8%), iron deficiency anemia in 8 (25%) patients, while 3 (8.6%) patients had normal serum iron levels. In vitamin D insufficiency group iron deficiency was detected in 12 (29.3%), iron deficiency anemia in 6 (18.3%) patients, while 10 (28.6%) patients had normal serum iron levels. In the group with normal vitamin D levels iron deficiency was detected in 25 (61%), iron deficiency anemia in 18 (56.3%) patients while 22 (62.9%) patients had normal serum iron levels ($p<0.05$), (Table 2).

In the correlation analysis, a positive correlation was found between serum vitamin D level and hemogram and iron parameters ($p<0.05$) (Table 3).

Discussion

Vitamin D insufficiency is a major problem worldwide in children of all age groups [12]. The most important risk factors of vitamin D insufficiency are malnutrition, reduced sun exposure, sunscreen creams, skin pigmentation and geographic latitude [1].

Table 1. Comparison of demographic characteristics, and laboratory values of the patients according to groups

	DE (n=41)	DEA (n=32)	Control (n=35)	p
Age (month)	40.2±10.1	42.1±9.5	38±9.5	0.243
Gender, n				
Male	14	18	17	0.156
Female	27	14	18	
Vitamin D (ng/mL)	31.9±10.6	27.3±13.8	35.9±15.4	0.035
Hb (g/dl)	11.9±0.7	9.7±1	12.9±0.9	0.000
MCV	74.6±1.4	66.5±3.6	74.1±1.4	0.000
MCH	25.6±1.7	19.5±2	25.9±1.3	0.000
MCHC	32.7±0.9	29.3±1.2	33.4±1	0.001
RDW	12.9±0.9	17.8±2.5	12.54±0.8	0.000
Iron (mcg/dL)	31.4±9.3	28.4±9.5	70.6±19.6	0.000
Ferritin (ng/ml)	7.3±2.5	4.6±2.1	31±16.1	0.000
TSI (%)	9±2.83	6.4±2.3	19.7±5.2	0.000
TIBC (mcg/dL)	369.5±31.2	437.7±32.9	340.8±33.4	0.001

Hb: Hemoglobin; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin i; MCHC: Mean corpuscular hemoglobin concentration ; RDW: Red cell distribution width; TSİ: Transferrin saturation index; TIBC: Total iron binding capacity.

Table 2. Intergroup comparisons of patients' serum vitamin D levels

	DE (n=41)	DEA (n=32)	Control (n=35)	p
Vitamin D, n (%)				
<20 ng/mL	4 (9.8)	8 (25)	3 (8.6)	
20-30 ng/mL	12 (29.3)	6 (18.8)	10 (28.6)	0.035
>30 ng/mL	25 (61)	18 (56.3)	22(62.9)	

Table 3. Comparison between serum vitamin D levels with hemogram and iron parametres

	r	p
Hb (g/dl)	0.334	0.003
MCV	0.238	0.013
MCH	0.317	0.001
MCHC	0.325	0.001
RDW	-0.349	0.000
Iron (mcg/dL)	0.309	0.001
Ferritin (ng/ml)	0.346	0.002
TSİ (%)	0.307	0.001

r: Pearson correlation coefficient.

The different laboratory techniques and reference ranges used in the studies also make it difficult to estimate the true prevalence of vitamin D insufficiency [13]. In a study conducted by Doğan et al., [14] the mean vitamin D level was found to be 23.86±10.64 ng/ml in preschool children. When the limit value was taken as 30 ng/ml, vitamin D level was found to be insufficient in 69.9% of these children. In a study conducted by Jin et al. in children under 24 months of age, the mean vitamin D level was 32.7±24.3 ng/ml in healthy children and 18.1±11.4 ng/ml in children with iron deficiency anemia. Vitamin D levels were found to be insufficient in 20% of children with iron deficiency anemia [15].

In our study, the mean vitamin D level was found to be 35.9±15.4 ng/ml in healthy children and 27.3±13.8 ng/ml in children with iron deficiency anemia. Vitamin D levels were insufficient in 18.8% of children with iron deficiency. We think that the differences between these results are due to the risk factors varying between societies.

Vitamin D has a regulatory role in the immune system. Vitamin D shows its effect through vitamin D receptors. In addition to bone tissue, vitamin D receptors are found in hematopoietic cells, monocytes, lymphocytes and various precursor cells [16]. Activation of the vitamin D receptor leads to inhibition of inflammatory cytokines IL-1, IL-6, TNF-α and IFN- while increasing the release of IL-10 from lymphocytes [9]. Interleukin-10 has both anti-inflammatory effects and it also positively affects erythropoiesis [16]. Aucella et al. [17] reported that erythropoiesis is probably increased by the anti-inflammatory effect in patients with chronic kidney disease receiving calcitriol.

Hepcidin, a small polypeptide synthesized from the liver, is an important mediator in systemic iron hemostasis [12]. Excess hepcidin production leads to iron retention in macrophages and enterocytes, disrupting both syntheses necessary for erythropoiesis and leading to anemia [18]. In a study by Carvalho et al., low vitamin D levels were associated with increased hepcidin levels [19]. In our study, we found a positive correlation between serum vitamin D level and hemogram and iron parameters similar to these findings.

Conclusion

In conclusion, we think that vitamin D has an effect on iron metabolism and erythropoiesis based on the literature and the data we obtained. According to our findings, the prevalence of vitamin D deficiency and insufficiency is especially common in preschool children with iron deficiency anemia. Thus, we recommend that vitamin D levels should be checked and vitamin D-enriched food consumption should be increased in every child with iron deficiency anemia.

Ethics Committee Approval: Gülhane Training and Research Hospital Ethics Committee (decision number-date: 19/147-2019).

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Conflict of Interest: None declared.

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