Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2021; 43(3):202-210

Research Article / Araştırma Makalesi

Vitamin D Level in Pediatric Patients with Severe Iron Deficiency Anemia

Ağır Demir Eksikliği olan Çocuk Hastalarda Vitamin D Düzeyi

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Abstract

This study aimedto determine the frequency of Vitamin D deficiency in children with severe iron deficiency anemia. This study included 60 patients with severe iron deficiency anemia between 6 and 72 months and 60 healthy children with similar age and sex. Patients diagnosed with severe iron deficiency anemia with blood hemoglobin level below 7 g/dl were included in the patient group. Regarding the etiology of anemia, a blood sample was taken from the patient group for hemogram, reticulocyte count, biochemical analyses, serum iron and iron binding capacity, transferrin saturation, ferritin, vitamin B12, folic acid and serum Vit D levels. Vitamin D deficiency (<20 ng/mL) was present in 75% (n=45) of the patient group, while 1.7% (n=1) of the control group ($p<0.001$). Vitamin D level of the patient group (16.2±13.3 ng/ml) was significantly lower than the control group (36.3±15.1 ng/ml) ($p<0.05$). While there were no children with retardation in the control group, 16.7% of the patient group had developmental retardation ($p<0.001$). Vitamin D deficiency has very high prevalence and Vitamin D level was found to be significantly low in patients with severe iron deficiency anemia. Consequently, patients with severe iron deficiency anemia should be evaluated and treated for Vitamin D deficiency.

Keywords: Severe iron deficiency anemia; Vitamin D deficiency; Childhood; Developmental retardation; Transfusion

Özet

Bu çalışmada ağır demir eksikliği anemisi olan çocuklarda Vitamin D eksikliği sıklığının belirlenmesi amaçlanmıştır. Bu çalışmaya 6-72 ay arasında ağır demir eksikliği anemisi olan 60 hasta ile benzer yaş ve cinsiyette 60 sağlıklı çocuk dahil edildi. Hasta grubuna kan hemoglobin düzeyi 7 g/dl'nin altında ağır demir eksikliği anemisi tanısı alan hastalar dahil edildi. Aneminin etiyolojisi ile ilgili olarak hasta grubundan hemogram, retikülosit sayımı, biyokimyasal analizler, serum demir ve demir bağlama kapasitesi, transferrin satürasyonu, ferritin, vitamin B12, folik asit ve serum Vitamin D düzeyleri için kan örneği alındı. Vitamin D eksikliği (<20 ng/mL) hasta grubunun %75'inde (n=45), kontrol grubunun %1.7'sinde (n=1) mevcuttu ($p<0.001$). Hasta grubunun Vitamin D düzeyi (16.2±13.3 ng/ml), kontrol grubuna (36.3±15.1 ng/ml) göre anlamlı olarak düşüktü ($p<0.05$). Kontrol grubunda gelişme geriliği olan çocuk bulunmazken, hasta grubunun %16.7'sinde gelişme geriliği vardı ($p<0.001$). Vitamin D eksikliği çok yüksek prevalansa sahiptir ve ağır demir eksikliği anemisi olan hastalarda Vitamin D düzeyi anlamlı olarak düşük bulunmuştur. Sonuç olarak, ciddi demir eksikliği anemisi olan hastalar Vitamin D eksikliği açısından değerlendirilmeli ve tedavi edilmelidir.

Anahtar Kelimeler: Ağır demir eksikliği anemisi; D vitamini eksikliği; Çocukluk; Gelişimsel gerilik; Transfüzyon

Received 11.09.2020 Accepted 27.11.2020 Online published 30.11.2020

Cite this article as:
Cobanusagi M, Acipayam C, Gunes H, Temiz F, Seringec Akkececi BN, Inanc Tolun F, Vitamin D Level in Pediatric Patients with Severe İron Deficiency Anemia, Osmangazi Journal of Medicine, 2021;43(3):202-210 Doi: 10.20515/otd.793743

1. Introduction

It has been difficult to identify diseases caused by nutritional deficiencies together with the improvement of living standards and the widespread use of enriched food (1,2). However, some micronutrients may be insufficient and this causes various problems (1,2). Although iron and vitamin D levels are important in the normal growth and development of children, they are often ignored (2).

Iron deficiency is the most common nutritional deficiency in children, and the prevalence of anemia worldwide is found to be 32.9% in 2010, and it has been reported that children under 5 are most commonly affected (3). There are studies reporting that the prevalence in our country is around 7-9% (4). Vitamin D is a fat-soluble vitamin. foods naturally contain vitamin D, vitamin D dermal synthesis is the main source. (5). Vitamin D sourced from diet or the Although very few dermal synthesis is not biologically active and enzymatic reactions are required to turn it into active metabolites (5). Serum 25-OH-D levels which indicate deposits of Vitamin D in the body are generally low in cases such as rickets and osteomalacia. (5). Although the incidence of nutritional rickets varies according to age and regions, the most common age is between 3-18 months (6). It is known that vitamin D deficiency and iron deficiency anemia are related (7). A number of studies shows that vitamin D has an effective role in erythropoiesis (8). Besides vitamin D has erythropoietic functions, it also has effects on iron metabolism and immune system (9). It is thought that vitamin D regulates systemic cytokine production and therefore reduces the inflammatory process in chronic disease /inflammation anemia (9).

Vitamin D deficiency, which can be seen with severe iron deficiency anemia, can cause growth retardation and important problems in children. This study has been planned to determine the frequency of vitamin D deficiency in children with severe iron deficiency anemia.

2. Materials and Methods

Our study included 60 patients with severe iron deficiency anemia between 6-72 months and 60 healthy children of the same age group. Ethics committee approval (2018/02-09; 17.01.2018) was obtained from Clinical Research Ethics Committee and then the study was started prospectively. The parents of the children included in the study were given detailed information about the study and a written informed consent was obtained.

Severe iron deficiency, as in the definition of World Health Organisation (WHO); blood hemoglobin level was considered to be below 7 g/dl (10). Patients diagnosed as severe iron deficiency anemia with blood hemoglobin level below 7 g/dl were included in the patient group. While establishing the control group, the criteria of being compatible with the patient group in terms of age and gender, and not having any chronic disease or anemia were taken as a basis.

Of all cases age, sex, body weight in kilograms, height in centimeters, head circumference in centimeters, breast milk intake status, and whether they received erythrocyte suspension was recorded. Taking into account the body measurement rates, children are classified according to whether they have growth and developmental delays. Evaluation of cases in terms of developmental retardation was made according to the definition that growth rate was not suitable for the age and according to the age, body weight, and head circumference percentiles were evaluated (11). Those with developmental retardation were selected from those whose height and body weights were below 3 percentile according to the age.

For the etiology of anemia from the patient group, hemogram, reticulocyte (N:0.76-2.25%), serum iron (N:50-175 mg/dl), iron binding capacity (N:250-450 µg/dl), transferrin saturation (N:>15%), ferritin (N:10-250 µg/L), vitamin B12 (N:211-911 pg/ml), folic acid (N:5.38-24 ng/ml), and for vitamin D (N:20-70 ng/ml) serum level tests a blood sample was taken. From the control

group a blood sample was taken for the serum Vitamin D levels, hemogram, ferritin, folic acid and vitamin B12 tests. The results obtained were compared statistically. In this study, serum vitamin D level lower than 20 ng/ml was defined as vitamin D deficiency.

Ferritin, vitamin B12 and folic acid tests were studied using commercially available kits in Cobas 8000 c 702 system autoanayzer (Roche Diagnostics, Rotkreuz, Switzerland), Hemogram and reticulocyte count in Symex XN-3000 autoanalyzer (Sysmex Corporation, Kobe, JAPAN). Vitamin D level was studied with Dionexultimate 3000 uHPLC analyzer (Thermofisher scientific, US).

Statistical Analysis

The results obtained from the experiments were evaluated by using the statistical package program "SPSS 18.0 for Windows". The conformity of the data to normal distribution was tested with the Kolmogorov-Smirnov and Shapiro Wilk Tests. "Independent Sample T Test" was used in the analysis of independent samples that fit the normal distribution and whose variances are homogeneous, and "Mann-Whitney U Test" was used in the analysis of data that did not fit the normal distribution and whose variances were not homogeneous. “Chi-square Test” was used in the analysis of qualitative data. Pearson correlation coefficients were used to analyze the relationship between parameters that provide parametric test conditions, and Spearman correlation coefficients to analyze the relationship between parameters that do not meet parametric test conditions. All values are shown as mean (standard deviation) and/or median (minimum-maximum). The probability of error (p value) was set to 0.05 for statistical significance.

3. Results

Our study included 60 patients with severe iron deficiency anemia between 6-72 months and 60 healthy children of the same age group. The mean age of the patient group was 20.52±16.36 months, while the control group was 20.60±16.33 months (p=0.939). In the patient and control groups, boys were 60% and girls 40% (p=1.000) (Table 1). The average number of siblings of children in the patient group was 2.17±1.82 (median=2, min-max=0-10).The frequency of vitamin D deficiency (<20 ng/ml) was significantly higher in the patient group 75% (n=45) when compared to the control group 1.7% (n=1) (p<0.001). Breastfeeding rate was 95% (n=57) in the patient group. Erythrocyte suspension transfusion was given to 53.3% of the patient group. When the histories of breastfeeding were questioned, only 5.0% of them never took breast milk. Finally, 63.3% of patients with severe anemia use vitamin D preparations. When the body weight, height, head circumference measurements and growth retardation were compared between the patient and control groups, the mean body weight was 10.7±2.7 kg in the patient group and 11.4±3.6 kg in the control group; mean height was 78.9±10.5 in the patient group, 82.4±12.9 cm in the control group, and the mean head circumference was 45.4±2.3 in the patient group, and 46.2±1.8 cm in the control group. There was no significant difference between the patient and control groups in terms of these three variables (p>0.05). While none of the subjects in the control group had developmental retardation, 16.7% (n= 10) of the patient group had developmental retardation. In the patients, developmental retardation was found more frequently than the controls (p<0.001) (Table 2). In the patient group; WBC (White Blood Cell) was 9960±3172 mm3, RBC (Red Blood Cell) was 4.4±0.6 x106/mm3, HGB (Hemoglobin) was 6.1±0.8 g/dl, HCT (Hematocrit) was 23.8±2.8, MCV (Mean Corpuscular Volume) was 54.3±4.2 fL, MCH (Mean Corpuscular Hemoglobin) was 13.9±1.8 pg, MCHC (Mean Corpuscular Hemoglobin Concentration) was 25.6±1.7 g/dl, RDW (Red Cell Distribution Width) was 22.7%, MPV (Mean Corpuscular Volume) was 8.9±0.5 fL, PLT (Platelet Count) was 528±233 x103/mm3, folic acid was 12.8±6.1 ng/ml, ferritin was 7.7±9.2 µg/L, vitamin B12 was 431.8±311.6 pg/ml and vitamin D was 16.2±13.3 ng/ml (Table 3). When the patient and control groups were compared; RBC, HGB, HCT, MCV, MCH, MCHC, MPV, ferritin, folic acid and vitamin D (Figure 1) levels were significantly higher in the control group when compared to the patient group (p<0.05) (Table 3). In contrast,

RDW, monocyte and PLT levels were significantly higher in the patient group when compared to the control group ($p<0.05$) (Table 3). There was no significant difference between the patient and control groups in terms of WBC, neutrophils, lymphocytes, eosinophils and vitamin B12 ($p>0.05$) (Table 3). In addition, iron binding capacity in the patient group was 442.64±81.89 µg/dl (median=454.00 µg/dl, min-max=281.00-603.00 µg/dl), transferrin saturation was 3.94% (median=2.93%, min-max=0.70-15.00%) and reticulocyte was 1.92% (median=1.73%, min-max=0.05-5.20%).

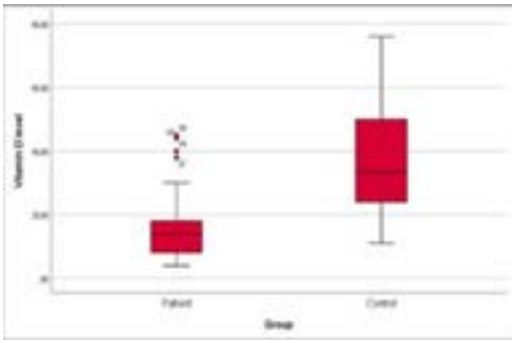

Figure 1. Vitamin D levels in patient and control groups.

Table 1. Comparison of age and gender in the patient and control groups

	Group				Total		p
	Patient		**Control**				
	N	%	N	%	n	%	
Gender							
Female	24	40.0	24	40.0	48	40.0	1.000**
Male	36	60.0	36	60.0	72	60.0	
Age (Month)							
Mean (SD)	20.52±16.36		20.60±16.33		20.56±16.27		0.939*
Median (min-max)	14.50 (6-72)		15.00 (6-72)		15.00 (6-72)		

*SD = standard deviation, * Mann Whitney U test, ** Chi-square Test*

Table 2. Comparison between patient and control groups in terms of body weight, height and head circumference measurements.

Group	Patient	Control	p
Body weight (kg)			
Mean±SD	10.7±2.7	11.4±3.6	0.205*
Median (min-max)	10.5 (5.8-18.0)	10.5 (7.2-27.0)	
Height (cm)			
Mean±SD	78.9±10.5	82.4±12.9	0.098*
Median (min-max)	77.5 (58.0-108.0)	80.5 (63.0-123.0)	
Head circumference (cm)			
Mean±SD	45.4±2.3	46.2±1.8	0.100*
Median (min-max)	45.5 (39.0-49.0)	46.0 (42.0-50.0)	

*SD = standard deviation, * Mann Whitney U test, ** chi-square test*

Table 3. Comparison of laboratory test results in patient and control groups

Group	Patient			Control			p
	Mean±SD	Median	Min- Max	Mean±SD	Median	Min- Max	
WBC (mm^3)	9960±3172	9325	3940-19940	9506±2546	9375	5160-16380	0.430**
RBC ($x10^6/mm^3$)	4.4±0.6	4.5	3.1-5.6	4.8±0.4	4.8	4.0-5.9	**<0.001****
HGB (g/dL)	6.1±0.8	6.4	3.7-7	12.1±0.8	12.0	11.0-14.1	**<0.001***
HCT (%)	23.8±2.8	24.6	16.4-27.9	36.2±2.3	36.0	32.3-42.6	**<0.001***
MCV (fL)	54.3±4.2	54.5	45.1-71.4	75.8±4.0	76.0	70.0-83.8	**<0.001***
MCH (pg)	13.9±1.8	13.8	11.1-22.8	25.1±2.1	25.3	18.7-28.5	**<0.001***
MCHC (g/dL)	25.6±1.7	25.4	21.4-31.9	33.2±1.3	33.2	29.5-35.9	**<0.001****
RDW (%)	22.7±2.8	22.2	18.4-31.1	14.5±2	14.1	12.3-23	**<0.001***
MPV (fL)	8.9±0.5	8.9	8-10	9.4±0.6	9.3	8.2-11.2	**<0.001****
Monocyte (mm^3)	934±473	840	340-2630	742±204	700	470-1370	**0.025***
PLT ($x10^3/mm^3$)	528±233	498.5	150-1341	368±88	354.5	214-598	**<0.001***
Folic acid (ng/ml)	12.8±6.1	12	2-31.6	18.8±7	17.8	9-40	**<0.001***
Ferritin (µg/L)	7.7±9.2	4.1	0.5-48.6	29.3±22.1	23	4-106.5	**<0.001***
Vit B12 (pg/ml)	431.8±311.6	357	145-1582	436.4±213.2	381.5	145-1073	0.157*
Vit D (ng/ml)	16.2±13.3	14	3.4-71	36.3±15.1	31.5	11-76	**<0.001***

*WBC: White Blood Cell, RBC: Red Blood Cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, RDW: Red Cell Distribution Width, PLT: Platelet count, MPV: Mean Platelet Volume, SD = standard deviation, * Mann Whitney U test, ** Independent t test*

Correlation coefficients and statistical evaluations showing the relationship between parameters in the patient group are given in Table 4. There was a statistically significant negative correlation between age, body weight and height and WBC, lymphocyte and folic acid, and a statistically significant positive correlation between vitamin B12 levels. There was a statistically significant positive correlation between head circumference and RBC and HCT values. There was a statistically significant positive correlation between folic acid and MCH and lymphocyte values. There was a statistically significant negative correlation between vitamin B12 and lymphocyte, PLT and folic acid levels. There

was a statistically significant positive correlation between vitamin D and eosinophil and folic acid levels ($p<0.05$) (Table 4).

Table4. Correlation coefficients and statistical evaluations showing the relationship between parameters in the patient group

		Age (Month)	Body weight (kg)	Height (cm)	Head circumference (cm)	Folic acid (ng/ml)	Vit B12 (pg/ml)	Vit D (ng/ml)
Age (Month)	r	-	0.824	0.842	0.573	-0.433	0.389	-0.157
	p	-	**0.001**	**0.001**	**<0.001**	**0.001**	**0.002**	0.230
Body weight (kg)	r	0.824	-	0.835	0.601	-0.367	0.362	-0.186
	p	**<0.001**	-	**0.001**	**<0.001**	**0.004**	**0.005**	0.155
Height (cm)	r	0.842	0.835	-	0.546	-0.331	0.462	-0.119
	p	**<0.001**	**0.001**	-	**<0.001**	**0.010**	**0.001**	0.365
Head circumference (cm)	r	0.573	0.601	0.546	-	-0.206	0.091	-0.111
	p	**<0.001**	**0.001**	**0.001**	-	0.143	0.520	0.433
WBC (mm^3)	r	-0.281	-0.338	-0.370	-0.122	0.030	-0.147	0.078
	p	**0.030**	**0.008**	**0.004**	0.388	0.818	0.263	0.553
RBC ($x10^6/mm^3$)	r	-0.133	0.024	0.011	0.295	0.013	0.008	-0.167
	p	0.309	0.857	0.932	**0.034**	0.922	0.949	0.203
HGB (g/dL)	r	-0.157	-0.099	-0.159	0.189	0.214	-0.087	-0.035
	p	0.231	0.452	0.224	0.179	0.100	0.509	0.792
HCT (%)	r	-0.066	0.047	-0.038	0.299	0.105	-0.128	-0.178
	p	0.615	0.723	0.770	**0.032**	0.424	0.331	0.174
Lymphocyte (mm^3)	r	-0.525	-0.533	-0.474	-0.126	0.340	-0.327	0.203
	p	**<0.001**	**0.001**	**0.001**	0.375	**0.008**	**0.011**	0.120
PLT ($x10^3/(mm^3)$)	r	-0.141	-0.137	-0.280	0.044	0.009	-0.352	0.100
	p	0.282	0.297	**0.030**	0.758	0.943	**0.006**	0.447
Reticulocytes (%)	r	-0.148	-0.088	-0.227	-0.003	-0.010	-0.366	-0.118
	p	0.259	0.501	0.082	0.983	0.938	**0.004**	0.371
Folic acid (ng/ml)	r	-0.433	-0.367	-0.331	-0.206	-	-0.371	0.321
	p	**0.001**	**0.004**	**0.010**	0.143	-	**0.004**	**0.012**
Vit B12 (pg/ml)	r	0.389	0.362	0.462	0.091	-0.371	-	-0.060
	p	**0.002**	**0.005**	**0.001**	0.520	**0.004**	-	0.646

Vit D (ng/ml)							
	r	-0.157	-0.186	-0.119	-0.111	0.321	-0.060	-
	p	0.230	0.155	0.365	0.433	**0.012**	0.646	-

WBC: White Blood Cell, RBC: Red Blood Cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, RDW: Red Cell Distribution Width, PLT: Platelet count, MPV: Mean Platelet Volume, Spearman correlation coefficients (r = correlation coefficient, p = level of significance)

4. Discussion

Together with the improvement of living conditions, it is difficult to determine the diseases caused by nutritional deficiencies as a result of widespread use of enriched foodstuffs. However, some micronutrients are inadequate and cause various problems. Iron and vitamin D are two important micronutrients in children's normal growth and development. In this study, we found that patients with severe iron deficiency anemia had significant vitamin D deficiency.

The vitamin D content of breast milk is low, and the American Academy of Pediatrics recommends 400 IU vitamin D supplements per day to babies who are breastfed, regardless of whether they receive formulation support or not(12). In our study, the rate of breastfeeding was 95% (n = 57) in the patient group. The data we obtained are similar to these studies, and those with severe iron deficiency anemia often switch late to supplementary food during feeding and are fed only with breast milk, and vitamin D deficiency is common in these patients.

Iron deficiency anemia is one of the causes of growth and development retardation as well as many clinical problems (13). Soliman et al. (13) evaluated 40 children with iron deficiency anemia in terms of growth and development before and after treatment and reported that iron deficiency anemia impairs growth and development. In our study, there was no developmental retardation in any cases of the control group, while 16.7% (n=10) of the patient group was determined developmental retardation. The parameters reflecting the state of anemia; hemoglobin levels, hematocrit, MCV, RBC and MPV were found to be low in the patient group consistent with the literature. Mean ferritin levels were also lower in the patient group when compared to the control group, consistent with the literature. Also, reactive thrombocytosis was seen in iron deficiency anemia (14). As consistent with the literature in also our study, the mean platelet count of the patient group was higher than that of the control group.

In our study, the frequency of vitamin D deficiency (<20ng/ml) was significantly higher in the patient group 75% (n=45) compared to the control group 1.7% (n=1). We found that the mean vitamin D level was significantly lower in the patient group (16.2±13.3 ng/ml) when compared to the control group (36.3±15.1 ng/ml).

Vitamin D has been shown to play a role in erythropoiesis and vitamin D deficiency poses a great risk for anemia (8). In addition, vitamin D deficiency can decrease erythropoietin receptor expression from stem cells and cause anemia (16). Iron is an essential element for cytochrome P450 functions and some of these cytochromes (CYP27A1, CYP24A1) play a role in vitamin D hydroxylation (17). Iron deficiency can affect the functions of these enzymes and lead to vitamin D deficiency (17). Our study confirms the literature information. Since patients with anemia have chronic fatigue and weakness, their exposure to the sun decreases, and as a result, sufficient sunlight exposure cannot be provided for vitamin D synthesis (15). Kartal et al. (18) reported that they have reservations about the association of iron deficiency anemia and vitamin D deficiency, that measurement methods, nutrition, medications and infections may affect this association, and that more comprehensive studies should be conducted considering these factors. Smith et al. (19) stated that vitamin D supports erythropoiesis and creates a protection against anemia.In our study, vitamin D levels were found to be significantly low in patients with severe iron deficiency.

Jin et al. (20) in their study, which included 102 children in 2010-2011; found 67% vitamin D deficiency in children with iron deficiency anemia. In the same study, it was found that vitamin D levels were below normal in those with iron deficiency anemia and there was a significant relationship between hemoglobin and 25 (OH) D levels (20). In addition, although iron supplementation did not improve the vitamin D level in patients, a positive correlation was found between the serum iron level of the patients and vitamin D levels (21). Kaymak Cihan et al. (7) found that iron deficiency anemia and vitamin D deficiency were related to each other in their study, which included 117 children Sharma et al. (22) reported that anemia was observed statistically significantly in children with vitamin D deficiency in their study involving 263 children.

In our study, when the serum vitamin D levels of the patient and control groups were compared; the mean vitamin D level of the patient group was found to be statistically significantly lower than that of the control group. However, in the correlation analysis, no correlation was found between the vitamin D levels of the patient group and the laboratory parameters for anemia. In the light of these data, we concluded that iron deficiency anemia and vitamin D deficiency are related entities, similar to the literature reviews mentioned above.

There are some limitations of our study. One of them is; patients with moderate and mild iron deficiency anemia or only iron deficiency who did not develop anemia yet were not included in the study. More studies are needed on iron deficiency and vitamin D relation in these patient populations. Other limitations of our article include the fact that the time of breastfeeding and the time of starting supplementary food were not specified. In addition, the lack of data on post-treatment blood values and development of the patients can be considered as another limitation. Studies including this point are needed with more cases. The strength of our study is it is the first study to investigate Vitamin D levels in patients with severe iron deficiency anemia.

5. Conclusion

In conclusion, the frequency of vitamin D deficiency was found to be high and vitamin D level was significantly low in patient with severe iron deficiency anemia. Therefore, it was concluded that vitamin D levels should be routinely evaluated in patient with severe iron deficiency anemia and support should be provided accordingly.

***Contributors'Statement**:*

MC,CA,HG,FT,NSA,FIT,: conceptualized the research design and protocol, provided inputs on the research tool, analysis and interpretation of the data, and contribute to manuscript writing and revised it;

MC,CA,HG,FT,NSA,FIT: administrative and technical guidance on the research, design of research, and provided critical inputs on writing of the manuscript;

MC,CA,HG,FT,NSA,FIT: contributed to research design, conceptualized the research tool, and inputs to manuscript writing;

MC,CA,HG,FT,NSA,FIT: data collection, analysis, manuscript writing;

MC,CA,HG,FT,NSA,FIT analyzed the study results, supported interpretation and contributed to the manuscript writing and revision. All authors approved the final version of manuscript, and are willing to be accountable for all aspects of study.

***Abbreviations:**Vitamin D; WBC, white blood cell RBC; red blood cell, HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; PLT, platelet count; MPV, mean platelet volume.*

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