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Vitamin D Status in Children with Iron Deficiency and/or Anemia

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Abstract

Background

Iron and vitamin D inadequacy are both essential wellbeing issues, an extra advancement has been the vitamin D extra skeletal role. Late collecting proof demonstrates that vitamin D inadequacy is pervasive in people with pallor, we meant to recognize a potential relationship between vitamin D lack and iron insufficiency.

Materials and Methods

A case control study was done in Erbil, Iraq during April 2015 to April 2016, on 160 children aged 1-5 years who referred to Raparin hospital. Blood test was acquired from every kid for measuring hemoglobin, serum iron and vitamin D level.

Results

The mean estimation of vitamin D was lower 21.3ng/dl in iron deficiency group in contrast with control group and it was essentially lower in gathering that had hemoglobin of under 11gm/dl (19.7ng/dl) in contrast with those with more than 11gm/dl. There was a direct relationship between serum iron, hemoglobin and vitamin D levels (r=0.520, P<0.05 and r=0.418, P<0.05 for serum iron and hemoglobin respectively).

Conclusion

There was significant moderate positive correlation between vitamin D and serum iron level.

Key Words: Children, Iraq, Iron deficiency, Vitamin D.

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1- INTRODUCTION

As the standard of living has improved and fortified food ingredients are widely distributed, it is difficult to identify diseases caused by nutritional deficiencies; however, some micronutrients remain insufficient, which causes various problems (1). Iron and vitamin D are important micronutrients for normal growth and development of children, yet they are frequently overlooked (2). Numerous adverse effects have been observed in infants aged ≤ 24 months with iron and vitamin D deficiencies. Even in asymptomatic cases, these adverse effects may be problematic because infants are rapidly growing at this age.

Iron deficiency (ID) can lead to growth and developmental delay, cognition and memory problems, impaired immune function, frequent infections. Intestinal iron absorption is controlled and dependent on the body's need for iron. Since proteins such as flavor protein and cytochrome are involved in this process, the effects of iron deficiency are diverse (3). Iron passes through the blood-brain barrier, enters nerve cells, and is involved in neurotransmission and myelin formation (4). Vitamin D is primarily involved in bone metabolism. Vitamin D deficiency may cause rickets in childhood, which primarily occurs at 3-18 months of age (5). It was recently discovered that vitamin D receptor is widely expressed in osteoblasts, lymphocytes, mononuclear cells, and most organs such as the small intestine, colon, brain, heart, skin, gonads, prostate, and breast (6).

A significant association between vitamin D deficiency and anemia has been reported throughout the world (7). Several studies in various populations all over the world suggest a high degree of association between Iron deficiency anemia and vitamin D deficiency. Vitamin D receptor has already been reported in bone marrow (8) and levels of 1, 25-dihydroxyvitamin D (1, 25-(OH) 2D) (active form of vitamin D) is several hundred folds higher in bone marrow compared to plasma. It imparts an important role in erythropoiesis the mechanism of Red Blood Cell (RBC) formation. Several mechanisms have been proposed to explain the association of vitamin D deficiency and anemia. Vitamin D influences Hemoglobin levels through a direct effect on erythropoiesis. Erythroid precursors are directly stimulated by vitamin D suggesting the latter's immense role in erythropoiesis. The storage and retention of Iron and reduction of pro-inflammatory cytokines is also aided by vitamin D (9).

Thus vitamin D deficiency reduces the ability of RBCs to become active. Vitamin D possibly modulates the level of systemic cytokine production, thus reducing the inflammatory milieu leading to anemia of chronic diseases. Absorption of vitamin D may be impaired due to Iron deficiency in the same way it impairs fat and vitamin A intestinal absorption. It is still controversial which deficiency causes the other but this association should be addressed in view of better treatment proposal (10).

Aims: Anemia and vitamin D deficiency are both very important health issues, recent accumulating evidence shows that vitamin D deficiency is prevalent in individuals with anemia; we aimed to detect a potential relationship between vitamin D deficiency and iron deficiency anemia.

2- MATERIALS AND METHODS

After approval was obtained from the ethic committee of Hawler Medical University, a case-control study was conducted from April 1st 2015 to April 1st 2016 in Raparin Teaching hospital in Erbil city, Eraq. A convenience sample(n=80) of children aged 1-5 years with iron deficiency anemia attending the outpatient clinics and those who were admitted to Raparin teaching hospital during the period of study as well as same number of control were included in this study. Patients who have had history of any blood diseases, such as Thalassemia, leukemia, Glucose-6-phosphate dehydrogenase deficiency (G6PD), and those with severe illness were excluded. Data including information on socio-demographic data, past medical disease and history of admissions to hospital, medication history; including iron and/or multivitamin including vitamin D was gathered by research team through direct interview with the parents of children, clinical and laboratory examination (Vitamin D, hemoglobin, serum iron) were done.

Iron deficiency was defined as serum iron < 30 mg/dl while anemia was defined as hemoglobin <11 g/dl, vitamin D deficiency was defined as 25(OH)D ≤ 20 ng/dl, vitamin D insufficiency (VDI) as 25(OH)D of 20-30 ng/dl, and normal (vitamin D sufficiency [VDS]) as 25(OH)D > 30 ng/dl (11). The statistical significance level was set at $P < 0.05$. Descriptive statistics are reported as mean and standard deviation (SD). All continuous variables were compared using independent sample t-tests, and frequency was compared by using the Chi-squared test. Linear regression was used to examine the association of vitamin D, serum iron and hemoglobin level.

3- Results

A cohort was classified according to serum iron level to two groups; patients group (s. iron < 30 µg /dl) and control group (s. iron ≥ 30 µg /dl). The overall mean age of patient group was 2.8 ± 0.4 years old, control group was 3.2 ± 0.8 years old, males were 50% of patient group,49.4% of control group, females were 49.3% of patient group and 50.7% of control group, no significant difference was reported with regards to mean age or gender distribution between two groups. The results demonstrated that the mean value of vitamin D was significantly lower in patient group (21.3 ng/dl) in comparison to control group (37.0 ng/dl), P=0.001 and the mean value of vitamin D was significantly lower in subjects who had hemoglobin (Hb) level of <11gm/dl in comparison to those with Hb of ≥11gm/dl (P=0.001) as seen in **Table.1**.

The results of current study revealed that the subjects with serum iron level of less than 30 µg /dl reported lower percentages of vitamin D level (6.3%) in comparison to those with iron level of more than 30 µg /dl (59.3%) and this difference was statistically significant (P=0.001) as seen in **Table.2**.

The results showed there was a significant direct correlation between serum iron, and vitamin D level(r=0.5, P=0.001), same significant direct correlation was reported with Hemoglobin level (r=0.4, P=0.001) as seen in **Table.3** and **Figure.1**.

The results showed that the percentage of subjects who had sufficient vitamin D > 30 was not differed significantly between male and females although the female subjects reported higher percentage (35.6%), same finding was reported with regards to duration of feeding, where the subjects with duration of feeding of more than six months reported higher percentage of sufficient vitamin D level (36. 2%).The children of exclusive breast feeding showed a higher percentage of sufficient vitamin D in comparisons to others feeding types, no significant difference was reported with all parameters under study just those who had sufficient vitamin D reported significant lower frequency of admission as seen in **Table.4**.

Regression analysis by using the changes in hemoglobin and serum iron level as predictor to changes in vitamin D level showed that each change in one degree in hemoglobin or serum iron level predicted to produce decrease in vitamin D level (1.7, 0.19) respectively as seen in **Table.5**.

Table -1: Mean value of vitamin D of studied groups according to serum iron and hemoglobin status

Variables	Study groups	Number	Mean± SD	P-value
Vitamin D level	Serum iron			
	Patients (serum iron≤30 µg /dl)	80	21.3(8.647)	0.001
	Control (serum iron>30 µg /dl)	80	37.0(15.115)	
Vitamin D level	Hemoglobin			
	≤11gm/dl	60	19.7(8.2)	0.001
	>11gm/dl	100	34.8(14.6)	

Table-2: Association between serum iron and vitamin D of study group

Variables			Vitamin D range ng/dl			Total	P-value
			<15	15-29	>30		
Serum iron range	≤30 µg /dl	Count	11	63	5	79	0.001
		% within Serum iron range	13.9	79.7	6.3	100.0	
	>30 µg /dl	Count	5	28	48	81	
		% within Serum iron range	6.2	34.6	59.3	100.0	

Table-3: Correlation among serum iron, hemoglobin and vitamin D level

Variables		Serum iron level	Hemoglobin level	Vitamin D level
Serum iron level	Pearson Correlation	1	.590**	.520**
	Sig. (2-tailed)		.000	.001
Hemoglobin level	Pearson Correlation	.590**	1	.418**
	Sig. (2-tailed)	.001		.001
Vitamin D level	Pearson Correlation	.520**	.418**	1
	Sig. (2-tailed)	.001	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

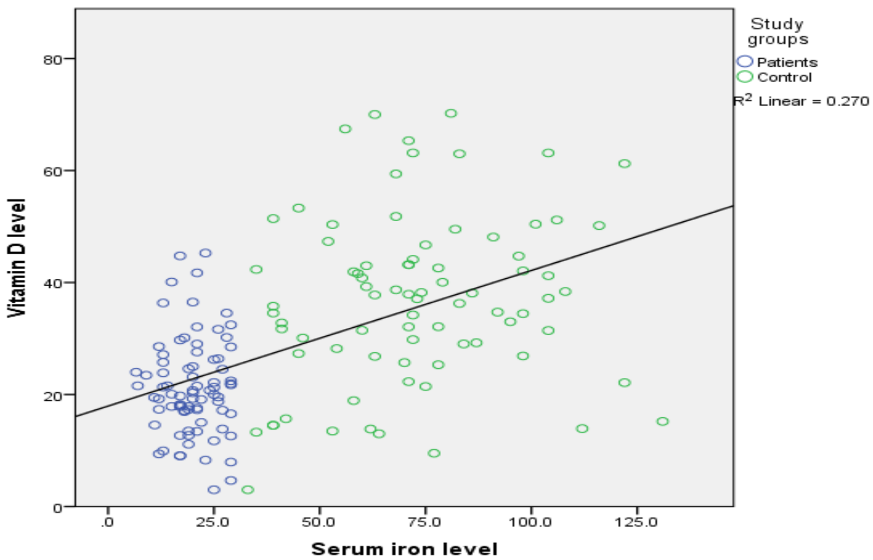

Fig.1: Correlation between serum iron and vitamin level

Table-4: Relationship between vitamin D statues and several parameters in patient group

Variables		Vitamin D range (ng/dl)						P-value
		<15		15-29		>30		
		Count	Row N %	Count	Row N %	Count	Row N %	
Gender	Male	6	6.9%	50	57.5%	31	35.6%	0.1
	Female	10	13.7%	41	56.2%	22	30.1%	
Duration of breast feeding	<6 months	9	9.9%	54	59.3%	28	30.8%	0.2
	>6 months	7	10.1%	37	53.6%	25	36.2%	
Feeding in the first year	Exclusive breast feeding	4	14.8%	10	37.0%	13	48.1%	0.4
	Bottle feeding	6	10.0%	41	68.3%	13	21.7%	
	Mixed feeding	6	8.2%	40	54.8%	27	37.0%	
Number of serving of eggs /week	1/day	5	9.6%	28	53.8%	19	36.5%	0.3
	< 2/wk.	5	8.9%	30	53.6%	21	37.5%	
	>2/wk.	1	3.1%	20	62.5%	11	34.4%	
	Other	5	25.0%	13	65.0%	2	10.0%	
Number of serving of milk per day	<1 glass	5	11.4%	29	65.9%	10	22.7%	0.06
	>1 glass	4	5.2%	43	55.8%	30	39.0%	
	Not drinking	7	17.9%	19	48.7%	13	33.3%	
period of sun exposure of child in the past weeks	>5 minute per day	6	20.7%	14	48.3%	9	31.0%	0.1
	5-15 minutes/day	4	5.1%	48	60.8%	27	34.2%	
	15-30 minutes/day	5	20.0%	14	56.0%	6	24.0%	
	> 30 minutes/day	1	3.7%	15	55.6%	11	40.7%	
Multivitamins supplement	Yes	2	6.1%	22	66.7%	9	27.3%	0.1
	No	14	11.0%	69	54.3%	44	34.6%	
Previous Hospital admission	Yes	8	19.5%	25	61.0%	8	19.5%	0.01
	No	8	6.7%	66	55.5%	45	37.8%	

Table-5: Predictor of vitamin D by hemoglobin level and serum iron

Coefficients							
Model	Unstandardized Coefficients		Standardized Coefficients	t-test	P-value	95.0% Confidence Interval for B	
	Beta	Std. Error	Beta			Lower Bound	Upper Bound
Hemoglobin level	1.7gm/dl	0.8	0.17	2.049	0.04	0.06	3.51
Serum iron level	0.19 µg /dl	0.03	0.41	5.030	0.001	0.11	0.27
a. Dependent Variable: Vitamin D level							

4- DISCUSSION

Iron deficiency makes a large contribution to anemia. Iron and Vitamin D are two of the most important micronutrients for growth and development of children but they are ignored frequently (5). Children aged 1–5 years are in a time of rapid and dramatic postnatal brain development. This period is also a key transition time for the child who is transferred from a direct maternal nursing and caring/selection of diet-based nutrition to food selection more based on self-selection and self-gratification (12).

In this study we found that the level of vitamin D was significantly lower in group of patients who had low serum iron level as well as those who had low hemoglobin level in comparison to control group (13). This was consistent with a study done in south Korea, a study of Asian children aged ≤ 2 years showed a significant association between coexisting iron deficiency and vitamin D deficiency (14) , similar findings were also observed in recent Korean studies revealing that a coexisting vitamin D deficiency frequently accompanies iron deficiency (15,16), and this association might be due to suppressive effect of vitamin D on iron deficiency anemia (IDA) via Iron-Regulating Hormone Hepcidin which is a peptide hormone act as Master regulator of iron homeostasis, macrophages play a central role in iron recycling by engulfing senescent RBC. Iron receptor ferroportin binds iron and retain it in macrophages with the help of hepcidin, recent studies suggest that vitamin concentration are inversely proportional with hepcidin concentration and positively with hemoglobin and iron concentration (17), there were numerous adverse effects have been observed in under two children with iron and vitamin D deficiencies. Even in asymptomatic cases, these adverse effects may be problematic because children are rapidly growing at this age (18).

Known risk factors associated with vitamin D deficiency include gender (female), age (child or elderly), lack of sunlight exposure, residence (high latitude), low socio-economic status and malnutrition. Malnutrition and protein deficiency can lead to vitamin D deficiency by decreasing the concentration of vitamin D-binding proteins in the blood (19). The precise amount of sunlight exposure needed to maintain normal levels of vitamin D is unknown. This can be explained by the fact that the amount of sunlight exposure can be affected by many factors such as clothing, race, skin color, sunscreen use, weather, latitude of residence, time of day, and air pollution (11). The observed difference in our finding did not reached the significance level with regards to risk factors for vitamin D deficiency, in contrast to other study where those who had regular sun exposure achieved higher blood level of vitamin D compared to those who avoided direct sun exposure (20), but with regard to gender difference our result was consistent with a study in Korea (11) which stated that gender had no role in vitamin D deficiency in children. In humans, there is no known study regarding the long-term adverse effects of concurrent iron deficiency and vitamin D deficiency. Katsumata et al. (21) reported in a rat model that iron deficiency decreased the levels of 1, 25-dihydroxycholecalciferol, insulin-like growth factor-1, and osteocalcin concentrations, which resulted in decreased bone formation and bone resorption.

As the final hydroxylation of vitamin D is dependent on iron, iron-deficient rats had lower concentrations of the active form of vitamin D. Diaz-Castro et al. also reported that bone metabolism was impaired despite normal 25(OH) D levels in iron-deficient rats. The main cause of decreased bone matrix formation was shown to be related to a decreased type I collagen amount. However, it is unclear whether severe IDA in humans would lead to the same phenomenon observed in animal studies (22).

4-1. Limitations of the study

There are limitations in this study, as it does not represent the general population.

5. CONCLUSION

Iron-deficient children are more prone to vitamin D deficiency. The potential adverse effect of concurrent deficiencies is not yet known. Therefore, every child with IDA should also be evaluated for vitamin D deficiency. Educational efforts are needed to increase compliance with iron and vitamin D supplementation guidelines. Further studies with larger sample size and cohort design are needed to determine the causality.

6- CONFLICT OF INTEREST

No conflict of interest to be declared.

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