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Deficiency of Vitamin D and Iron in Anemic Female Iraqi Patients

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ABSTRACT

Vitamin D deficiency is highly prevalent in the population through the world and it's underestimated due to lack of screening tests. It's also associated with numerous diseases. Vitamin D deficiency and anemia are common in the Middle East, and vitamin D deficiency has been reported to be associated with an increased prevalence of iron deficiency anemia. **Aim**: To investigate the link between vitamin D status and anemia in healthy individuals and to examine the prevalence of vitamin D deficiency in young healthy female individuals.**Materials and Methods:** This study was conducted at Al-Hussein Medical City/ Al-Husain Teaching Hospital / Kerbala,-Iraq. All samples 176 apparently are healthy female subjects as controls 80 and 96 female patients non-obese having iron deficiency anemia during the period from Nov. 2015 to Sep. 2016 with age ranged between (15- 50) years. The data of body mass index (BMI), Vitamin D3, serum iron levels, total iron binding capacity, creatinine and complete blood count in blood were measured.**Results:** The results showed that serum vitamin D3 level was significantly decreased in iron deficiency anemia patients than that found in controls subjects (11.20 ±6.70±51.64vs. 18.86 ±9.91 ng/mmol, respectively), at ($p<0.0001$). Similarly the serum iron level (27.95 ±52.64µg/dl vs. 62.84 ±23.52 µg/dl, $P<0.0001$), Hb (9.39 ±1.53vs13.04 ±0.66g/dl, $p<0.0001$) and serum T.I.B.C level were significantly higher in iron deficiency anemia patients than in controls subjects (491.04 ±445.69 vs. 282.06 ±56.81µg/dl, $p<0.0001$). The patients female iron deficiency anemia, there was a significant positive correlation between serum vitamin D and serum iron ($r =0.168$, $P<0.05$) and Hb ($r=0.360$, $p<0.001$). **Conclusion**: It was concluding that iron deficiency anemia patients have significantly low levels of serum vitamin D3 than that in healthy. High prevalence rate of vitamin D deficiency was stronger in female population of Kerbala city in Iraq.

INTRODUCTION

Vitamin D is a fat-soluble steroid hormone ingested in the diet and produced in the skin following exposure to ultraviolet rays in sunlight, and conversion to active forms of vitamin D occurs in the liver and kidneys[1]. Most of the required cholecalciferol or vitamin D3 is derived from the biosynthetic pathway under the skin from 7-dehydrocholesterol through exposure to sunlight[2]. Most experts recommend an optimal concentration greater than 30 ng/mmol in serum and vitamin D3 deficiency is less than 30 ng/mmol[3]. In addition to its role in regulation of bone and mineral metabolism, cellular proliferation and differentiation. Vitamin D deficiency (VDD) is also an important issue in public heath because it is associated with a wide range of illnesses and chronic conditions, such as osteoporosis, cancer and metabolic syndrome[4,5]. The role of vitamin D in erythropoiesis has also been suggested by several clinical observations [6, 7]. Vitamin D has been demonstrated in bone marrow to affect marrow function[8]. Anemia is a major global health concern due to its high prevalence and association with substantial morbidity and mortality[9, 10]. The World Health Organization (WHO) estimates that about 2 billion people in the world are suffering from this disease and that approximately 50% of all anemia cases are diagnosed as iron deficiency anemia (IDA), patients with iron deficiency anemia (IDA) their hemoglobin less than (<12 mg/dl)[11]. Recent years, an increasing body of evidence indicates that VDD was associated with increased risk for anemia. However, this study had yet to demonstrate the relationship between vitamin D and hemoglobin levels in the general female population. New insights into the biologic functions of vitamin D3 have led to interest in the clinical consequences of vitamin D deficiency. Using the database of a large integrated health plan, we sought to assess the prevalence and risk of anemia in a population of subjects with documented D3 deficiency compared with those with normal D3 levels. Researchers have discovered a relationship between vitamin D deficiency and anemia female in a sample of patients without chronic kidney disease.

MATERIALS AND METHODS

Location and Duration of the Study

This case-control study was conducted at Al-Hussein Medical City, Al-Hussein Teaching Hospital, Kerbala, Iraq, from November 2015 to September 2016.

Data collection

All subjects completed a questionnaire on age, gender, pregnancy, and history of any chronic diseases such as diabetes mellitus, hypertension, obesity, osteoporosis, osteomalacia, liver disease, renal disease, anemia, hypo- or hyperparathyroidism, vitamin and mineral deficiency, and steroid therapy. They were also asked about medications that could interfere with vitamin D metabolism, vitamin therapy, and whether they were taking vitamin D and calcium supplements during a face-to-face interview. One-hundred and twenty-one were subsequently excluded because of obesity (>25 kg/m^2), history of liver, renal, gestational, or endocrine disorder, medications that influence bone metabolism and current vitamin D and calcium intake, and vitamin B12 deficiencies, aplastic anemia, hemolytic anemia, sickle cell anemia, and thalassemia. Therefore, 176 females (age between 15–50 years) were included in the final study.

Biomarkers Determined

Body mass index (BMI), complete blood count (CBC), serum 25(OH) D3, iron level, total iron binding capacity (T.I.B.C) and creatinine.

Serum 25(OH)D3 levels were measured using the new [25(OH)D3] by ELISA assay kit which was designed for the determination of 25(OH)D3 in human serum or plasma samples (Eagle Biosciences Inc., MA, USA). BMI was determined by measuring weight (in kilograms) divided by the square of height (in meters); weight and height were measured by the same scale for all the sample subjects [BMI = weight (kg)/square height (m2)]. Serum iron level, total iron binding capacity and creatinine measured via spectrophotometry and complete blood count (Sysmex XP-300 Atomic Hematology Analyzer).

The mean ± SD of all parameters measured from patients iron deficiency anemia patients were determined and compared with the controls group.

The correlation coefficient *r* is used to describe the association between the different studied parameters; $P < 0.05$ was considered statistically significant.

Statistical analysis

Student's *t*-test was used to compare the biometric and biochemical parameters between patients and controls. Analysis of variance and Scheffe's post hoc test were used to compare the hemoglobin and other biometric and biochemical parameters between participants with

optimal, insufficiency, and deficiency of vitamin D. Pearson's correlation coefficients were used to examine the correlation between hemoglobin levels with serum total 25(OH) D3 and other variables. All statistical inferences were made based on a two-sided significance level of *P, 0.05* and were performed using IBM® SPSS® Statistics version 22.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

The distributions of biochemical and biometric parameters in patients and controls are shown in Table 1. Serum total 25(OH) D3 was significantly decreased in patients iron deficiency anemia than controls. Table 1 shows the results obtained for serum 25(OH) D3 in control group and the female patients iron deficiency anemia at $P < 0.0001$ and $P < 0.05$. The study group consists of one hundred seventy six (176) Vitamin D3 deficiency or insufficiency was present in 84.7% of the tested samples with low serum vitamin D levels < 30 ng/mmoL, in which 96 patients were had insufficient level with deficient level lower than that. The obtained data indicated that 25(OH) D3 was associated with hemoglobin, iron level and inversely associated with T.I.B.C, and it has positive correlation with Hb at $P < 0.0001$, whereas 25(OH) D3 was positively associated with Hb in a high significant correlation in patients and controls group at $P < 0.0001$ and significant at $P < 0.05$ in positive correlation with iron level, and inverse correlation with T.I.B.C. at $p<0.001$ in patient samples as shown in Table 2. Several factors were tested in order to find any relation with that vitamin D3 deficiency from this study such as three different seasons; summer, spring and winter the median of low vitamin D level was higher in winter months in comparison to spring and summer months ($p < 0.05$) as clear from figure 1. Several factors were tested in order to find any relation with that vitamin D3 deficiency from this study such as skin pigmentation, the median of increase vitamin D level was higher in white comparison to black and other skin pigmentation participant's figure 2**.**

Table 1: Mean ± SD values of all parameters in iron deficiency anemia patients compared with controls group			
Parameter	**IDA patients**	**Controls Group**	**P value**
25-(OH)D3 (ng/mmol)	11.20 ± 6.70	18.86 ± 9.91	<0.001
Hb(g/dl)	9.39 ± 1.53	13.04 ± 0.66	<0.001
MCV (fl)	67.05 ± 6.50	83.66 ± 3.96	<0.001
MCH (pg)	20.92 ± 5.07	28.22 ±1.69	<0.001
HCT (pg)	31.24 ± 4.30	39.22 ± 2.42	<0.001
RDW-CV	17.91 ± 2.90	13.17 ± 1.32	<0.001
Iron level (µg/dl)	27.95 ± 51.64	62.84 ± 23.52	<0.001
T.I.B.C (µg/dl)	491.04 ± 445.69	282.06 ± 56.81	<0.01
GFR	132.10 ± 3.19	130.01 ± 25.18	NS
BMI (kg/m2)	24.16 ± 2.58	23.35 ± 2.67	<0.04
Age (years)	31.54 ±10.99	29.6 ±10.51	NS
Creatinine (mg/dl)	0.64 ± 0.23	0.65 ± 0.13	NS
Hb: Hemoglobin; MCV: mean corpuscular volume; 25-(OH)D3: 25-hydroxyvitamin D3; T.I.B.C.: total iron binding capacity; MCH: mean corpuscular hemoglobin; BMI: body mass index; GFR: glomerular filtration rate; RDW-CV: red blood cell distribution width*High significant correlation at P < 0.05. **High significant correlation at P < 0.001			

Table 2. Correlation between 25(OH)D3and other parameters in (IDA) patients compared with controls group							
Parameter		**Hb**	**MCV**	**Iron level**	**T.I.B.C**	**Creatinine**	
25-(OH)D3	**Patients**	0.360**	0.372**	0.169*	-0.178*	0.151	
		0.0001	0.0001	0.001	0.001	0.09	**P.value**
25-(OH)D3	**Controls**	0.067	0.122	-0.150	-0.097	0.148	
		0.265	0.361	0.45	0.31	0.12	**P.value**
*High significant correlation at P < 0.001. **High significant correlation at P < 0.0001							

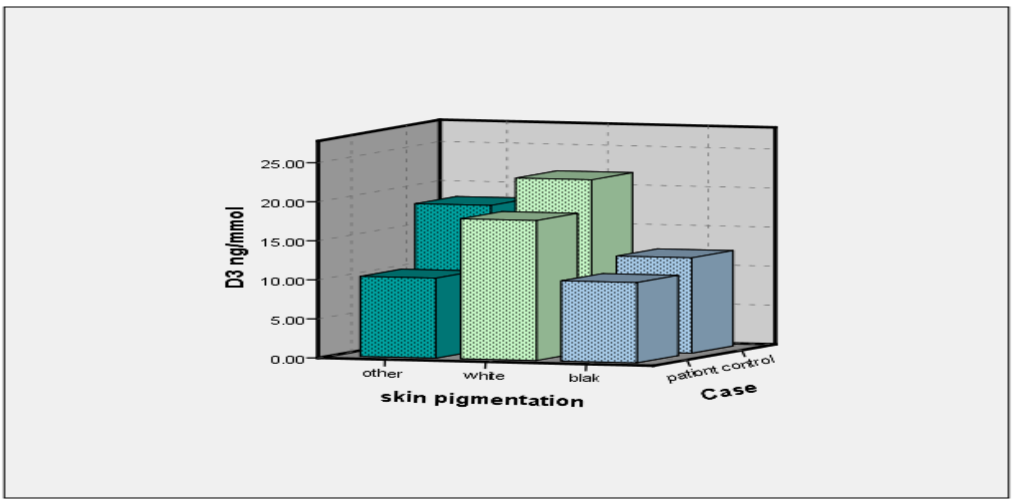

Figure (1): Distribution in IDA patients and controls group according to 25 (OH) D3 levels with skin pigmentation

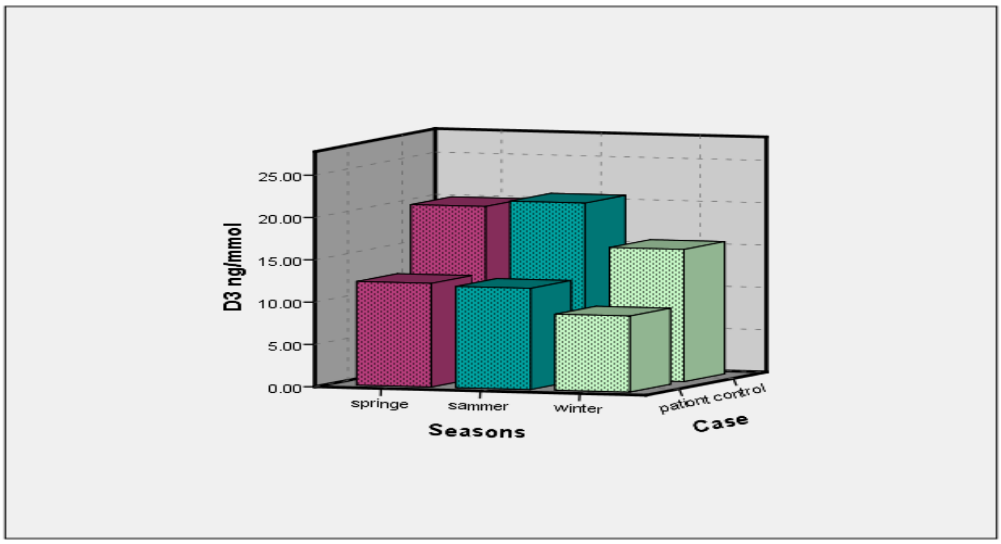

Figure (2): Correlation between the seasons and serum vitaminD3 levels.

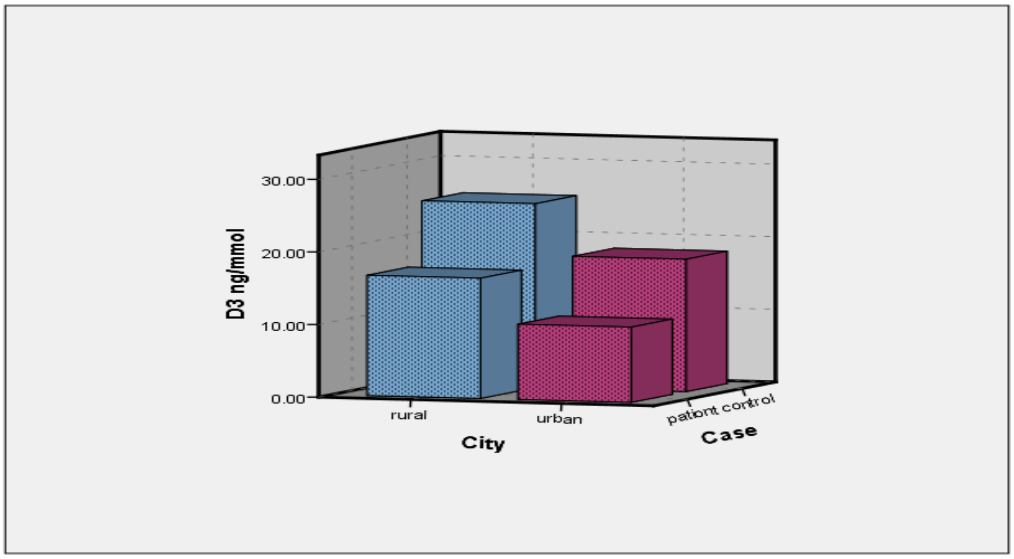

Figure3: Relationship between reduced 25-Hydroxyitamin D3 with city live rural, urban in patients deficiency vitamin D and controls.

DISCUSSION

This study indicates that vitamin D3 deficiency or insufficiency status was associated with an increased risk of anemia. The first population-based study to provide evidence that vitamin D deficiency is associated with anemia in healthy females Iraqi, working adult population. Vitamin D3 deficiency or insufficiency was present in 84.7% of the samples under the study, and serum 25 (OH) D3 levels lower in patients were associated with iron deficiency anemia when compared to individuals of non-obese healthy subjects (11.8 ± 8.8 vs. 18.0 ± 9.4 ng/mmol) respectively, whereas others showed association between vitamin D3 level and a risk of iron deficiency anemia patients without and chronic kidney disease[12,13]. The mechanism of association of vitamin D deficiency with iron deficiency anemia in human is not clearly known. This could potentially influence vitamin D deficiency could lead to increased risk of reticulocytosis and iron deficiency anemia[14]. The findings presented are consistent with the hypothesized mechanisms underlying the vitamin D–anemia relationship may be deficiency vitamin D has been recommended to have an effect on erythropoiesis, to the well-documented role of vitamin D in the regulation of bone and mineral metabolism, vitamin D may have an effect on erythropoiesis including cellular proliferation and differentiation [15,16]. In bone marrow, there are enormous vitamin D receptors and vitamin D is reported to stimulate erythroid precursors. High local concentrations of 25 (OH) D3 in hematopoietic tissues are suggested whereas vitamin D3 may direct to activate erythroid precursor cells in a paracrine fashion[17]. This study was associated between vitamin D status

and anemia in three seasons; summer, winter and spring. The results presented are supported by other epidemiologic studies done on Saudi Arabia's population that have**,** in which high prevalence of vitamin D deficiency in both summer and winter seasons recorded and even higher levels recorded in the winter season [18]. The data obtained revealed, the same result reported that skin exposure to solar ultraviolet radiation is a significant source of vitamin D, and in most cases, vitamin D deficiency occurs when individuals do not get enough exposure to and do not eat foods that are rich in vitamin[19]. This study are compatible with another studies the causes of vitamin D deficiency among the Middle Eastern population remain uncertain, as well as the factors that may increase their risk for low vitamin D. Studies indicate that lack of sun exposure in Middle Eastern population results from cultural practices such as conservative clothing in addition to their lifestyle habit of spending most time indoors[20]. This study same results recent studies have shown that the rate of vitamin D deficiency is also higher in the sunniest areas of the world, including the Middle East countries, such as Saudi Arabia, Qatar, and United Arab Emirates, Turkey, India, and Iran because of low exposure to sun due to cultural factors[19,21.22]. Skin pigmentation and dark skin may be one of the factors in this study are compatible with several studies as most of the population in this region is brown to dark colored skin which contains more melanin, possibly decrease skin vitamin D production and reduce the production of cholecalciferol[23]. This study clarified the entire samples significantly a lower level vitamin D3 in the females Iraqi living in holy Karbala city urban compare with lifestyle females the live in the rural. Perhaps in Middle Eastern countries that are poor in food fortification in general and lower vitamin D status in females live in urban compared to female live in rural could be explained by females spending more time indoors and/or the type of clothing that females wear and sun protection and sun avoidance attitudes seen in Iraqi[24,25]. The data obtained revealed, the same result reported that associated pattern of risk factors for VDD (younger age, female gender/covering clothing, residence in Australia for a longer time, decreased daylight exposure, and vitamin D level tested in winter or spring) indicates a reduction in exposure to UVR in affected individuals[**26**]**.**

CONCLUSION:

We can conclude that vitamin D deficiency is associated with anemia in healthy Iraqi females. These findings could have potentially broad public health implications given the high prevalence of vitamin D deficiency in Kerbala city of Iraq. Ultimately, if these results

can be replicated by others and extended, they could lead to patients clinical trials to evaluate vitamin D supplementation as therapy for patients with anemia.

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