Original Article

Correlation of 25-Hydroxyvitamin D Deficiency with Ferritin, Thyroid-Stimulating Hormone, and Other Biochemical Parameters of Women in Baghdad Province

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Abstract

Background: The importance of vitamin D in facilitating the absorption of calcium and phosphorus from the intestines and maintaining appropriate levels of these minerals in the blood for normal bone mineralization is well-established. **Objectives:** Beyond its role in bone health, vitamin D has been shown to exert a significant influence on various biochemical processes and may impact the development of certain diseases, including infections, obesity, heart disease, and certain cancers. This study aimed to investigate the differences in vitamin D levels among women from Baghdad province and its potential associations with ferritin and thyroid-stimulating hormone (TSH).**Materials and Methods:** This cross-sectional study involved 171 apparently healthy women, categorized into two age groups: the menstrual age group (group A, mean age 36.4 ± 9.2) and the menopausal age group (group B, mean age 57.7 ± 8.4). Vitamin D levels, serum ferritin levels, and hemoglobin levels were assessed to understand the interplay between these parameters. **Results:** The results revealed that both groups exhibited low levels of vitamin D (group A: 916.56 ± 8.33; group B: 16.86 ± 10.45), low serum ferritin (group A: 11.9 ± 10.66; group B: 28.2 ± 13.67), and low hemoglobin levels (group A: 10.97 ± 1.74; group B: 11.42 ± 1.68). Notably, the results observed no significant differences in all studied parameters between these groups, except for serum ferritin ($P < 0.05$). Additionally, the finding demonstrated a significant positive association between vitamin D and serum ferritin levels in both groups (group A, $r = +0.569$, $P < 0.000$; group B, $r = +0.405$, $P < 0.01$). Also, there was a significant moderate positive correlation between vitamin D and hemoglobin levels (group A, $r = +0.43$, $P < 0.001$; group B, $r = +0.312$, $P < 0.04$). However, no significant correlation was found between vitamin D and TSH, urea, and creatinine levels. **Conclusion:** The implications of this study suggest that vitamin D deficiency may serve as a useful predictor and have an adverse effect on anemia in women.

Keywords: Vitamin D, serum ferritin, thyroid-stimulating hormone, anemia, 25-OH D

Introduction

Vitamin D (also known as Calciferol) is a fat-soluble vitamin that is mainly involved in bone metabolism and acts by absorbing calcium and phosphate in the intestine.[1] Its deficiency can cause rickets in childhood and musculoskeletal disorders like osteomalacia and osteoporosis in teenagers and adults. In addition to bone metabolism, vitamin D (25-hydroxyvitamin D, 25-OH D) shows a significant function in a variety of other diseases, such as controlling infections, immune response for autoimmune diseases, respiratory infections, cancer suppression, etc.[1] Its common variants D3 and D2, come to the human body considered very important and essential chemical compounds to produce active vitamin D after undergoing hydroxylation in the liver and kidney.[2] Body requirements for vitamin D are fulfilled by exposure to sunlight (ultraviolet) for a sufficient period or by food ingestion rich with it,[1] whereas ferritin is a

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protein that represents intercellular iron storage in the body and acts as an acute phase reactant. Since ferritin is a vitally important storage of iron, it is considered the greatest parameter for diagnosis of Iron deficiency.[3] Moreover, it is well known that low concentrations of serum ferritin may be linked with diseases such as iron-deficient anemia and low bone density, while high levels of serum ferritin may be linked with heart diseases, liver diseases, insulin resistance, and hyperthyroidism.[4] Regarding the above information, the current study is focused on investigating the relationship between vitamin D with serum levels of ferritin as well as other important biochemical parameters like thyroid-stimulating hormone (TSH), kidney (creatinine, and urea), hemoglobin, and packed cell volume (Hb, and PCV) in apparently healthy women with different ages.

Materials and Methods

This cross-section study was conducted on 171 apparently healthy females attending Abdul Majeed Hussain Hospital in Baghdad province from January 2022 until March 2023. Most of the participants have signs of low vitamin D levels, such as hair falling, tiredness, paleness, bone pain, etc. Participants were divided into two groups regarding their menstrual and menopause age: group A, females with ages ranging from 16 to 46 years old, and group B, a female with age 47 years and above [Table 1]. Detailed information about each participant was recorded, such as age, gender, marital status, referring doctor, etc. Patients who were taking vitamin D supplements or iron therapy, diabetic patients, renal impairment patients on erythropoietin, pregnant, thyroid, and liver diseases were excluded. Samples (5 ml) were collected by venipuncture into a dry gel tube (without anticoagulant) to perform vitamin D, ferritin, and TSH analysis. For Hb and PCV analysis, EDTA tubes have been used. Samples with gel tubes were allowed to stand for 10 min to make a clot and then centrifugated for 10 min at a speed of 3000 (rpm). Next, supernatant serum was taken and stored at -22°C until the time of analysis. Cobas type E411 (Roche, Germany, ElectroChemiLuminescence [ECL] technology for immunoassay analysis) and Cobas C111 device have been used to perform the studied biochemical parameters. Furthermore, participants were classified regarding vitamin-D status according to the range provided by Roche-kit, as shown in Table 2.

Table 1: Number of participants and classification according to menstrual and menopause age

Group (n = 171)	Age ± SD
Group A (n = 79)	36.4 ± 9.2
Group B (n = 92)	57.7 ± 8.4

Statistical analysis

Statistical analyses were generated using SPSS V26 (IBM, USA). Data and quantitative analysis were written as mean ± SD. An independent sample t-test was used for comparison among studied groups, and coefficient r (Pearson's correlation) was used to find out the relationship between the studied parameters.

Results

This study was performed on female participants (171) who attended Abdul-Majeed Hussain Hospital/Baghdad and were divided into two groups, as shown in Table 1. Group A's mean age was 36.4 ± 9.2 (menstrual), and Group B with 57.7 ± 8.4 (menopausal). Table 3 shows the prevalence of vitamin D levels among all participants, which indicates 121 (71%) have deficiency <20 ng/ml, 31 (18.4%) have insufficiency, and only 11 (9.6%) have sufficient level. Table 4 shows serum ferritin was significantly lower in group A (11.9 ± 14.66) than in group B (30.2 ± 28.67) with a P-value (0.001), while for other studied variables, Table 4 illustrates vitamin D levels not statically different between the two examined groups (16.56 ± 8.33 group A), (16.86 ± 10.45 group B), hemoglobin (10.97 ± 1.74 group A), (11.42 ± 1.68

Table 2: Vitamin D status according to kit provided by Roche Company

25-Hydroxyvitamin D level (ng/ml)	Description
≤3	Severe deficiency
4–20	Deficiency
21–29	Insufficiency
≥30 ng/ml	Sufficient

Table 3: Vitamin D distribution among all participants

Vitamin D distribution	Mean ± SD	Status
n = 121 (71%)	11.6 ± 4.6	Deficiency
n = 31 (18.4%)	23.69 ± 2.01	Insufficiency
n = 11 (9.6%)	40.38 ± 13.1	Sufficient

Table 4: Assessment of vitamin D with other biochemical variables between studied groups

Parameters	Group A	Group B	P-value
Vitamin D (ng/ml)	16.56 ± 8.33	16.86 ± 10.45	N.S
Serum ferritin (ng/ml)	11.9 ± 10.66	28.2 ± 13.67	0.001
Hemoglobin (Hb) (g/dl)	10.97 ± 1.74	11.42 ± 1.68	N.S
Packet cell volume (PCV)%	34.25 ± 4.61	34.15 ± 5.82	N.S
Creatinine (mg/dl)	0.642 ± 0.127	0.77 ± 0.32	N.S
Urea (mg/dl)	23.4 ± 5.1	30.9 ± 21.9	N.S
Thyroid-stimulating hormone (TSH) (uIU/ml)	1.69 ± 0.83	1.97 ± 1.1	N.S

N.S (statically not-significant)

Table 5: Correlation of vitamin D with biochemicals variables for group A

Group A	Pearson correlation coefficient (*r*)	*P*-value
Ferritin	+ 0.569	0.000
Hemoglobin	+ 0.43	0.001
PCV	+ 0.42	0.001
Creatinine	-0.056	N.S
Urea	+0.16	N.S
TSH	+0.044	N.S
Age	+0.087	N.S

N.S (statically not-significant)

Table 6: Correlation of vitamin D with biochemical variables of group B

Group B	Pearson correlation coefficient (*r*)	*P*-value
Ferritin	+0.405	0.01
Hemoglobin	+0.312	0.04
PCV	+0.21	0.039
Creatinine	+0.047	N.S
Urea	+0.05	N.S
TSH	-0.063	N.S
Age	+0.03	N.S

N.S (statically not-significant)

group B), PCV (34.25 ± 4.61 group A) (34.15 ± 5.82 group B), creatinine (0.642 ± 0.127 group A), (0.77 ± 0.32 group B), urea (23.4 ± 5.1 group A), (30.9 ± 21.9 group B), and TSH (1.69 ± 0.83 group A), (1.97 ± 1.1 group B).

Table 5 indicates vitamin D of group A has a highly significant positive correlation with ferritin (r = +0.559, P-value 0.000), hemoglobin (r = +0.43, P-value 0.001), and packed cell volume (r= +0.42, P-value 0.001). However, nonsignificant correlations were found with creatinine, urea, and TSH. Table 6 exhibits that vitamin D of group B has a highly significant positive correlation with ferritin (r = +0.405, P-value 0.01), hemoglobin (r = +0.312, P-value 0.04), and PCV (r= +0.21, P-value 0.03), while no significant correlation for creatinine, and TSH.

Discussion

Widely recognized that 25-OH D has a significant role in bone and mineral metabolism.[5,6] Most of the recent studies have focused on the effect of vitamin D on inflammation.[7-9] However, none of the investigations have considered the relationship between 25-OH D deficiency and ferritin along with kidney and thyroid functions. Ferritin is a protein that acts as a nutritional marker of iron status storage in the body as well as an acute phase reactant that would rise in the body responding to inflammation.[10,11] Creatinine and urea are specific tests that can tell about the renal status,[12] while TSH is liberated by the pituitary gland to motivate the thyroid gland to release thyroxin T4 and triiodothyronine T3, these hormones work together to regulate many metabolic functions and energy in the body.[13,14] This study is focused on finding if there is any relationship between vitamin D deficiency and the above parameters for two age groups apparently healthy based on the fertility period [Table 1]. Exhibited deficiency of vitamin D levels 121 (71%), insufficient 31 (18.4%), and only 11 (9.6%) were sufficient for both studied groups, which were very common in our society, and the reason might be either lack of nutrition or sunlight exposure. The results also showed low levels of Hb and PCV (anemia, according to WHO) for both groups, while creatinine, urea, and TSH were in normal range (supporting our investigation to exclude the effect of thyroid and kidney diseases). The outcomes additionally showed there were no significant differences between all studied parameters for both groups except for ferritin, group A (11.9 ± 10.66) lower than group B (28.2 ± 13.67), menstruation can lead to iron depletion in females, as they lose blood containing iron during their menstrual cycles. This can contribute to lower serum ferritin levels and potentially lower hemoglobin levels as well, 10.97 ± 1.74 and 11.42 ± 1.68 for groups A and B, respectively. Additionally, The results clearly indicated there was a directly proportional connection between deficiency of 25-OH D with low ferritin levels in both groups, as shown in Tables 4 and 5; Figures 1 and 2 (group A: r = +0.569, P-value 0.000, group B: r = +0.405, P-value 0.01).

Similar findings acquired in another study (Al-Zuhairy *et al.*) were in agreement with our study in which deficiency of 25-OH D is positively correlated with low levels of ferritin in infants and toddlers (r = 0.542, P-value = 0.000).[15] Moreover, in other studies, findings showed children with rickets (active) have hemoglobin levels lower than cured children with rickets.[16] Another study in Korean children and adolescents may boost our finding on the association of vitamin D and iron,[17] indicating a low level of 25-OH D (deficiency) is linked with an increased chance of anemia, particularly anemia with iron deficiency in healthy females of children and teenagers. Dissimilar findings were observed by Saadat *et al.*,[18] as they found a nonsignificant correlation between vitamin D and serum ferritin in anemic patients. The impact of vitamin D in ferritin (iron storage) can come with a possible mechanism of affecting vitamin D in the hepcidin hormone that regulates iron absorption and distribution in the body[19] and influences red blood cells proliferation of bone marrow by stimulation of progenitor cells in erythroid in synergic approach with erythropoietin.[19] Additionally, vitamin D has been shown to modulate inflammatory processes, and inflammation can affect iron metabolism and ferritin levels.[20] Also, iron works as an essential coenzyme for various enzymes such as 1α-hydroxylase, which is necessary for the hydroxylation of 25(OH) D to 1,25(OH)2D (an active form of vitamin D) and might cause deficiency.[21] Moreover, our study was investigated whether vitamin D levels associated with TSH

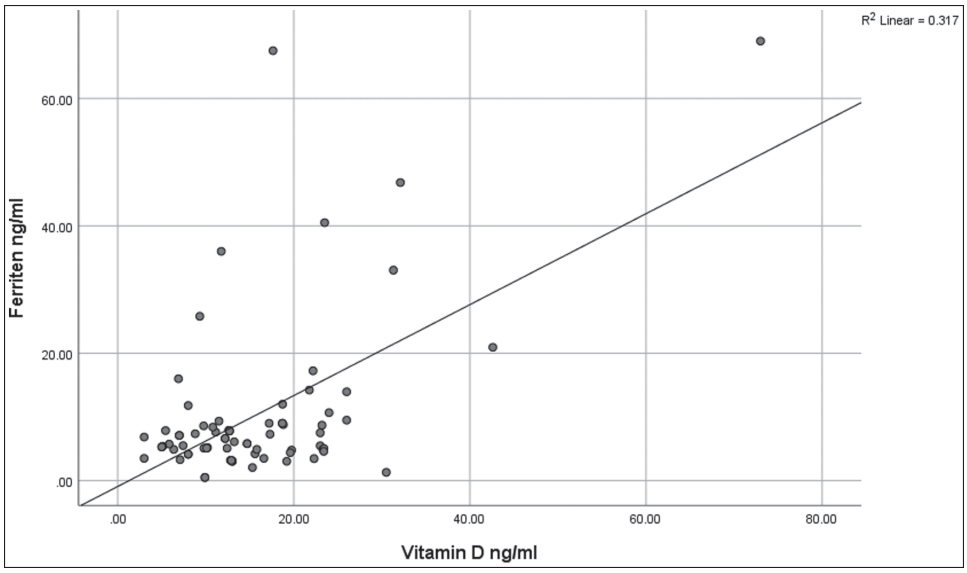

Figure 1: Correlation of vitamin D with serum ferritin for group A (menstrual age)

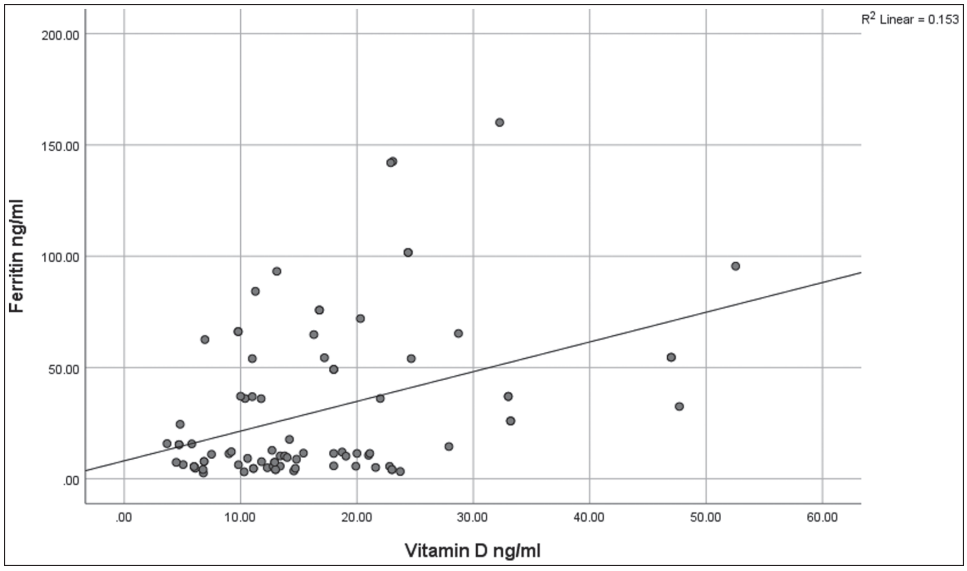

Figure 2: Correlation of vitamin D with serum ferritin for group B (menopausal age)

or vice versa; our finding revealed there was no significant correlation between vitamin D deficiency levels and TSH in both studied groups, as shown in Tables 4 and 5. This results in agreement with Muscogiuri *et al.*,[22] who found no association between 25(OH) vitamin D levels with TSH, TG-Ab, and FT4. While our results disagreed with Mackawy *et al.*,[23] they indicated an inverse correlation between vitamin D deficiency levels with TSH (r = -0.598, $P < 0.05$) in hypothyroidism patients.

Conclusion

Low serum 25-OH D concentration is positively correlated with ferritin and hemoglobin levels in both menstrual and menopausal age groups. While no association and correlation with TSH, creatinine, and urea in apparently healthy women. Thus, deficiency in vitamin D may be considered as a predictor parameter for anemia that should be treated and checked along with anemia treatment to enhance iron reabsorption and accelerate the cure. Further long-term investigation along with planned interventions need to be made by using vitamin D supplements, monitoring the level of ferritin for the same studied age groups, and knowing the results more clearly.

Ethical approval and consent to participate

All procedures involving human participants were conducted in accordance with the ethical standards outlined by the Ministry of Health in Iraq. Prior to participation, all participants provided informed consent after receiving

a detailed explanation of the study's objectives, procedures, potential risks, and benefits. Participants were assured of their voluntary participation and the confidentiality of their personal information.

Human ethics

Human ethics played a pivotal role in our research study, as we diligently ensured that all participants provided informed consent, their privacy was safeguarded, and any potential risks were minimized, demonstrating our commitment to upholding the fundamental principles of ethical conduct in research.

Consent for publication

Participation in the publication is entirely voluntary, and participants have the right to refuse consent without facing any negative consequences.

Availability of supporting data

Not applicable.

Financial support and sponsorship

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Conflicts of interest

There are no conflicts of interest.

Authors' contributions

The authors' contributions to this manuscript are as follows: Alaa Abbas Fadhel conceptualized the study, performed experiments, and conducted data analysis; Kahleed J. Khaleel conducted data analysis and drafted the manuscript.

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