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Prevalence and determinants of vitamin D deficiency amongst patients in Erbil, Kurdistan region of Iraq

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Abstract

Aim: This study aims at calculating the prevalence of Serum Vitamin D deficiency and determining risk factors associated with deficiency amongst patients in Erbil, Kurdistan Region of Iraq.

Material and methods: This was a prospective cross-sectional study conducted on 424 patients from September to November 2021 in the Outpatient Department of Kurdistan Cardiac Center – Surgical Specialty hospital.

Results: Results showed that study population consisted of adults aged 30 years and above, 171 (40.3%) females and 253 (59.7%) males. The majority of the study population (51.9%) were Serum Vitamin D deficient, 27.6% were Serum Vitamin D insufficient and 20.5% had normal Vitamin D levels. Serum Vitamin D deficiency was seen more frequently among female gender, increased BMI, previous infection of COVID 19, Diabetes Mellitus and those with abnormal lipid profiles.

Conclusion: There is a high prevalence of Serum Vitamin D deficiency in Erbil, Kurdistan Region of Iraq. In addition, there were associations between Serum Vitamin D deficiency and many other diseases. Therefore, medical practitioners should consider more education of patients regarding importance of vitamin D status in the body.

Key words: vitamin D, prevalence, deficiency, risk factors, prospective cross-sectional study

Introduction

Vitamin D is a fat-soluble vitamin that has a remarkable role in homeostasis of phosphorus and calcium [1]. Like so many other vitamins, it has an essential role in human health and wellbeing. The two main existing forms of Vitamin D are D2 (Ergocalciferol) and D3 (Cholecalciferol). Ergocalciferol is acquired from sources of plant, while cholecalciferol is acquired from exposure to sunlight and animal derivates [2].

When ultraviolet B (UVB) radiation of wavelength 290-315 nm hits the skin, 7-dehydrocholesterol gets converted to pre-vitamin D3, and vitamin D3 is produced upon its isomerization. However, the amount of vitamin D produced can vary depending on the individual's age, skin complexion, day time, sunscreen product usage, latitude, and seasonal changes [3].

Due to its long half-life, serum concentration of 25-hydroxyvitamin D [25(OH)D] is considered the main indicator of vitamin D status, which reflects total vitamin D in the human body [4]. In today's world, there is a widespread prevalence of vitamin D deficiency that is primarily caused by under-appreciation of the important role of moderate sun exposure in supplying vitamin D for humans [5]. Furthermore, the amount of vitamin D found naturally in food is very limited, and foods that contain vitamin D are insufficient to meet an individual's needs [6]. The prevalence of Vitamin D deficiency appears to be highest in countries such as Asia, the Middle East, Africa, and amongst immigrants residing in regions of higher latitudes [7].

Vitamin D has long been known for its impact on bone and muscle health. However, it is becoming increasingly evident that vitamin D is essential for overall wellbeing and has a role in conditions other than its main role in the musculoskeletal system [8]. It has been noticed that it may also have extensive regulatory effects on both innate and adaptive immune cells and contributes to inflammation in the body [9]. Vitamin D status has also been linked to diabetes mellitus [10] as it appears to have a direct influence on insulin sensitivity and resistance [11]. It also possesses regulatory roles in cardiovascular diseases [12], chronic kidney disease [13], and different types of cancer [14]. Furthermore, deficiency in vitamin D has been linked to obesity as a cause and consequence through direct and indirect mechanisms [15].

Since vitamin D has an important role in maintaining the homeostasis of the body, it is essential to have sufficient data of vitamin D status among the population and its correlations with different diseases. Having said that, in the Kurdistan region of Iraq, there is limited studies and investigations implemented regarding the status of vitamin D amongst the population. Thereby, this study was conducted to inspect prevalence of vitamin D and its association with various conditions in the body.

Material and methods

Study population and design of the study

Prospective cross sectional study conducted amongst 424 male and female patients of different regions in Iraq, seeking medical consultation in outpatient department in Kurdistan Cardiac Center- Surgical department.

Collection of blood samples

A total of 424 blood samples were collected from participants. The serums were used for the measurement of: serum gamma glutamyl transferase (S. GGT), total cholesterol, serum high density lipoprotein (S.HDL), serum low density lipoprotein (S.LDL), serum very low-density lipoprotein (S. VLDL), serum triglyceride (S.TG), S. 25 OH vitamin D, creatinine, and C reactive protein (CRP).

Inclusion and exclusion criteria

Both genders, adults aged 30 years and above attending the medical outpatient department due to any medical reason were included.

Exclusion criteria involved those on vitamin D or multivitamin supplements and/or calcium supplementation taken within 12 months before interview was conducted. Cancer patients (undergoing regular treatment and/or diagnosed with malignancies), those with chronic kidney disease (stage 3 Renal failure or higher), liver dysfunction (including viral hepatitis, cholestasis jaundice) and ischemic or hemorrhagic stroke during 12 months before interview was conducted.

Study timeline

The present study was carried out from 15th of September 2021 to the 15th of November 2021 at the outpatient department of SSH/Cardiac Center- Erbil/ Iraq.

Statistical analysis

All statistical data were analyzed using SPSS Statistics 26 (SPSS Inc., Chicago, IL, USA)

Questionnaire form design

Data was collected through direct administration of a face-to-face questionnaire that was pretested with modifications made before its use in the study. Along with access to medical records or records which contain intimate personal information, and are individually identifiable and not publicly available. The questionnaire included demographic variables (name, age, gender, home address, time of administration, date and socioeconomic status), clinical risk factors of the patient, family history, and smoking habitual of the patient.

Ethical considerations

Ethical approval was obtained from the ethics committee of Hawler Medical University. Verbally informed consent was taken from each patient. A complete explanation of the nature and aim of the study was given to each participant and reassured about the confidentiality of the data and their anonymity.

Laboratory Parameters:

Cholesterol	mg/dL Good: <200 Borderline: 201-239 High: >240
TG	mg/dL Good: <159 Borderline: 160-199 High: >200
HDL cholesterol	mg/dL 30-55
LDL cholesterol	mg/dL Good: <100 Borderline: 101-130 High: >130
S. VLDL	mg/dL Good: 2-30 Borderline: 30-40 High:>40
Serum creatinine	Normal: 0.6-1.2 mg/dL High: >1.3 mg/dL
Vitamin D	ng/mL Risky: >100 Normal: 30-100 Insufficient: 21-29 Deficient: <20
CRP	Mg/Dl Normal: <5 High: >6
GGT	IU/L Normal: 0-30 Abnormal: >30

Results

This was a cross sectional prospective study with a sample size of 424 cases. The study population consisted of 171 (40.3%) females and 253 (59.7%) males. According to age, the majority of the population were between the age group 60-69 (32.2%) and 50-59 (30.2%), followed by the 40-49 age group (21.9%), >70 age group (11.3%) and lastly the <39 age group which consisted of only 4.2% of the population (Table 1).

Concerning the BMI of the cases, the majority of them were overweight (37.7%) and obese class I (36.8%) followed by normal weight (15.3%), obese class II (7.5%) and obese class III (2.6%) (Table 1).

Among the study population, 207 (48.8%) of them had a previous history of COVID-19 infection (Table 1).

According to the serum vitamin D levels, the study population was divided into three categories: those with serum vitamin D deficiency (<20 ng/ml), serum vitamin D insufficiency (21-29 ng/ml), and those with normal serum vitamin D levels (30-100 ng/ml).

Table 1 Distribution of age, gender, BMI class and previous COVID 19 infections in the sample

Characteristic	Frequency	Percentage (%)
Age Group		
<39	18	4.25
40-49	93	21.93
50-59	128	30.2
60-69	137	32.3
>70	48	11.32
Gender		
Males	253	59.7
Females	171	40.3
*BMI		
Normal weight	65	15.33
Overweight	160	37.73
Obese Class I	156	36.8
Obese Class II	32	7.54
Obese Class III	11	2.6
Previous COVID-19 Infection		
Yes	207	48.8
No	217	51.2

*BMI: Body Mass Index

The majority (51.9%) were vitamin D deficient, (27.6%) were insufficient and (20.5%) had normal vitamin D levels (Figure 1).

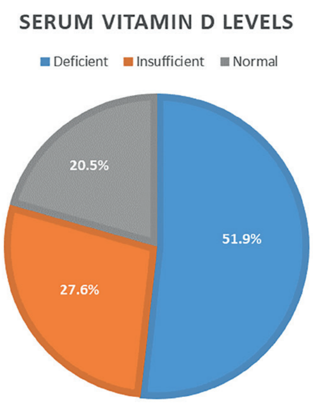

Figure 1 - The distribution of serum Vitamin D levels amongst patients

Upon comparing the serum vitamin D levels between the different sexes, the following findings were observed: amongst the female participants (55.5%) were vitamin D deficient, (20.5%) were vitamin D insufficient and (24%) had normal levels.

Amongst the males; (49.4%) were vitamin D deficient, (32.4%) were vitamin D insufficient and (18.2%) had normal levels of vitamin D.

This slightly higher level of deficiency seen among the females was statistically significant with a (P = 0.02) (Table 2).

Concerning the incidence deficiency amongst the different BMI classes: (41.5%) of the normal-weight, (48.8%) of the overweight, (55.1%) of the obese class I, (65.6%) of the obese class II and (72.7%) of the obese class III were vitamin D deficient, respectively.

Table 2 Association between gender and serum vitamin D status

Serum Vitamin D levels	Gender	
	Females n (%)	**Males n (%)**
Deficient	95 (55.5%)	125 (49.4%)
Insufficient	35 (20.5%)	82 (32.4%)
Normal	41 (24%)	46 (18.2%)
P Value	0.021	

This rising percentage of deficiency associated with increasing BMI was statistically significant (P = 0.004) (Table 3).

Upon analyzing the existence of a relationship between a previous COVID-19 and Vitamin D deficiency, it was discovered that (45.9%) of those with a previous COVID-19 had vitamin D deficiency, while (25.6%) had insufficiency and (28.5%) had normal Vitamin D levels. In contrast, amongst those without a previous COVID-19 infection, (57.6%) of patients had deficiency, (29.5%) of them had insufficiency and only (12.9%) had normal levels. This was a highly significant association with a P value <0.001 (Figure 2).

Among the study population, (35.4%) were considered diabetic while (64.6%) were not. The proportion of adults with diabetes were more common among participants with deficient and insufficient Vitamin-D, (61.3%) and (20.7%) respectively. This difference was significant with a P value of 0.013 (Table 4).

Regarding a previous percutaneous coronary intervention (PCI) performed on the population, (29.5%) of patient had undergone the procedure. Results showed that 88% of patients who had a previous PCI had either insufficient or deficient Vitamin-D levels. This was also statistically significant (P = 0.016) (Table 5).

When investigating the relation between serum Vitamin D deficiency and serum lipid levels, the following categories were defined. High cholesterol (> 200 mg/dl) was found in (37.7%) of the patients. Similarly, (39.2%) of the cases had high values of TG, 20% had high VLDL levels, 38.7% had high LDL levels and 33% had low HDL levels (Figure 3).

Aside from the lipid levels; CRP, creatinine and GGT blood levels were also measured. Only 20 out of the 424 patients (4.7%) presented with high creatinine levels. Cases of high CRP were more abundant amongst the patients (21.9%). GGT elevation was found in (38.2%) of the patients (Figure 3).

Table 3 Association of serum vitamin D levels with BMI class

Serum Vitamin D levels	*BMI				
	Normal weight n (%)	**Overweight n (%)**	**Obese Class I n (%)**	**Obese Class II n (%)**	**Obese Class III n (%)**
Deficient	27 (41.54%)	78 (48.8%)	86 (55.1%)	21 (65.6%)	8 (72.7%)
Insufficient	14 (21.54%)	53 (33.1%)	41 (26.3%)	9 (28.1%)	0 (0%)
Normal	24 (36.92%)	29 (18.1%)	29 (18.6%)	2 (6.3%)	3 (27.3%)
P Value	0.004				

*BMI: Body Mass Index

Table 4 Association between Serum Vitamin D levels and Diabetes.

Diabetes	Serum Vitamin-D level				P-value
	Deficient n (%)	**Insufficient n (%)**	**Normal n (%)**	**Total n (%)**	0.013
Yes	92 (61.3%)	31 (20.7%)	27 (18.0%)	150 (100%)	
No	128 (46.7%)	86 (31.4%)	60 (21.9%)	274 (100%)	
Total	220	117	87	424	

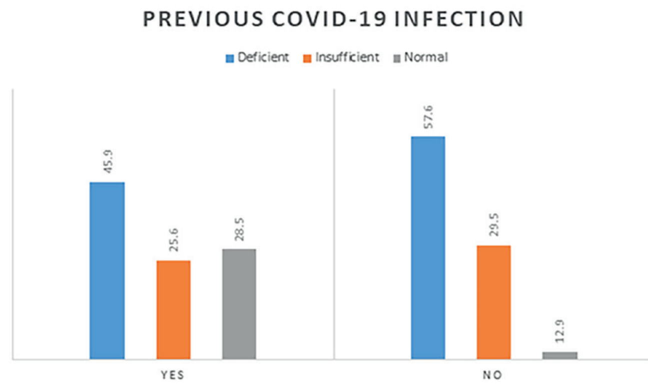

Figure 2 - Relationship between previous COVID-19 infection and Vitamin D amongst patients

Table 5 Vitamin D levels amongst patients who had undergone previous PCI or not

Previous PCI	Serum Vitamin-D level				p-value
	Deficient	**Insufficient**	**Normal**	**Total**	
Yes	72(57.6%)	38(30.4%)	15(12.0%)	125	0.016
No	148(49.5%)	79(26.4%)	72(24.1%)	299	
Total	220	117	87	424	

Table 6 Association of serum vitamin D levels with cholesterol and triglycerides

Serum Vitamin D levels	Serum Cholesterol		Serum Triglyceride	
	Normal n (%)	**High n (%)**	**Normal n (%)**	**High n (%)**
Deficient	124 (47%)	96 (60%)	130 (50.4%)	90 (54.2%)
Insufficient	76 (28.8%)	41 (25.6 %)	65 (25.2%)	52 (31.3%)
Normal	64 (24.2%)	23 (14.4%)	63 (24.4%)	24 (14.5%)
P value	0.015		0.038	

Table 7 Association of serum vitamin D levels with LDL, HDL and VLDL.

Serum Vitamin D levels	Serum *LDL		Serum *VLDL		Serum *HDL		
	Normal n (%)	**High n (%)**	**Normal n (%)**	**High n (%)**	**Low n (%)**	**Normal n (%)**	**High n (%)**
Deficient	132 (50.77%)	88 (53.7%)	171 (50.44%)	49 (57.6%)	80 (57.1%)	140 (50%)	0 (0%)
Insufficient	74 (28.46%)	43 (26.2%)	90 (26.55%)	27 (31.8%)	41 (29.3%)	73 (26.1%)	3 (75%)
Normal	54 (20.77%)	33 (20.1%)	78 (23.01%)	9 (10.6%)	19 (13.6%)	67 (23.9%)	1 (25%)
P value	0.84		0.04		0.018		

*LDL: Low Density Lipoprotein
*VLDL: Very Low Density Lipoprotein
*HDL: High Density Lipoprotein

Table 8 Association of serum vitamin D levels with creatinine, GGT and CRP.

Serum Vitamin D levels	Serum Creatinine		Serum *CRP		Serum *GGT	
	Normal n (%)	**High n (%)**	**Normal n (%)**	**High n (%)**	**Normal n (%)**	**High n (%)**
Deficient	204 (50.49%)	16 (80%)	160 (48.3%)	60 (64.5%)	133 (50.8%)	87 (53.7%)
Insufficient	115 (28.47%)	2 (10%)	105 (31.7%)	12 (12.9%)	76 (29%)	41 (25.3%)
Normal	85 (21.04%)	2 (10%)	66 (19.9%)	21 (22.6%)	53 (20.2%)	34 (21%)
P Value	0.032		0.001		0.704	

Gamma-Glutamyl Transferase
*CRP: C-Reactive Protein

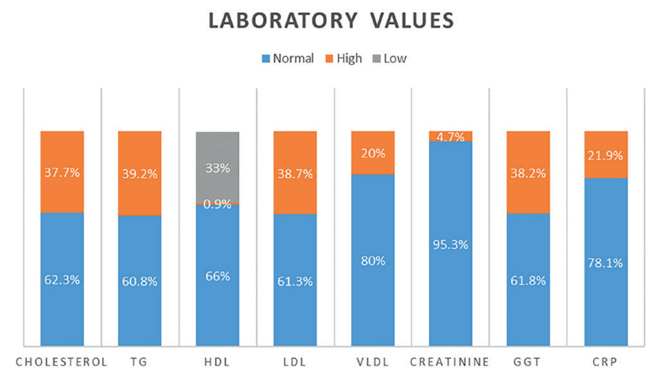

Figure 3 - The relationship between Serum Vitamin D levels amongst different laboratory parameter

Results had shown that 60% of patients with high serum cholesterol levels were vitamin D deficient and 25.6% were insufficient. Patients with normal serum cholesterol levels were vitamin D deficient only in 47% of the cases and insufficient in 28.8%. The calculated P value for serum cholesterol and serum vitamin D relationship was 0.015 (Table 6).

As for the serum TG levels, 54.2% of those with high serum TG levels were found to be deficient, and 50.4% of patients with normal serum TG levels lacked sufficient vitamin D (Table 6).

Of the 20% of patients with high serum VLDL levels, 57.6% were Vitamin D deficient and 31.6% were insufficient. For the patients with normal serum VLDL levels, 50.4% of them were deficient (Table 7).

Although connection was implied between high serum TG ($p = 0.038$), serum VLDL ($p = 0.040$) and serum vitamin D levels, the results for serum LDL levels didn't appear significant. Amongst those patients with high serum LDL levels, 53.7% were found serum vitamin D deficient, while 50.8% of patients with normal serum LDL presented with deficiency as well (Table 7).

While 57.1% of patients with low serum HDL levels were simultaneously serum vitamin D deficient, only 50% of patients with normal serum HDL had shown Serum Vitamin D deficiency (Table 7).

Regarding the serum CRP and creatinine levels, 80% of patients with high serum creatinine were found to be deficient in vitamin D, while 64.5% of those with high serum CRP levels were deficient. These findings were both significant with P values of 0.032 and 0.001, respectively (Table 8).

Concerning the serum GGT levels, 53.7% of those with high serum GGT levels were Serum Vitamin D deficient. For those without serum GGT elevation, deficiency was described in 50.8%. However, the P value was 0.704 and therefore the result was not statistically significant (Table 8).

Discussion

Out of the 424 participants that were included in the study, it was noted that (55.6%) females and (49.4%) males were serum vitamin D deficient, similar results were shown in Jinzhong city, China whereby (75%) of women and (69%) of men had inadequate level of vitamin D [16]. Also, (51.9%) were vitamin D deficient, (27.6%) were insufficient and (20.5%) had normal vitamin D levels. Likewise, prevalence of vitamin D deficiency was (50,8%) and vitamin D insufficiency was (19.6%) among 1111 visitors of single consultation outpatient clinic in Isfahan City, Iran [17]. According to our results, BMI was inversely proportional to vitamin D deficiency, which was in accordance with a meta-analysis of 23 articles, suggesting a positive association between vitamin D deficiency and BMI [18]. A suggested cause for that may be due to extra body fat retaining vitamin D metabolites, and that body fat sequesters cholecalciferol taken from diet or produced through the skin is partly before it is hydroxylated by the liver [19].

Vitamin D has a host of extra skeletal effects. Studies have showed that vitamin D plays a pivotal role in preserving the function of islet cells. Low vitamin D levels have repeatedly been shown to be associated with increased risk of diabetes mellitus (DM) [20]. From the 424 participants involved in the study it was evident that there was a significant correlation between vitamin D levels amongst those patients diagnosed with DM. The proportion of adults with diabetes were more common among participants with deficient levels (51.9%) and insufficient levels (27.6%). A study conducted in the Babylon governorate of Iraq claimed that DM as well as hypertension is the most common reported chronic non-communicable diseases that correlated significantly with serum vitamin D inadequacy [21].

As one of the stages of Vitamin D synthesis takes place in the liver, GGT levels were taken into consideration when searching for the risk factors of vitamin D deficiency. Clinical studies have reported a relationship between chronic liver diseases and lowering of serum Vitamin D levels [22]. Vitamin D insufficiency was even described as a biomarker in chronic liver diseases [23]. However, among samples included in this study, no significant correlation was found in those with high serum GGT levels and those with serum Vitamin D deficiency.

When comparing the vitamin D levels in patients with high and normal serum creatinine, the results were seemingly significant. Up to (80%) of the patients with high creatinine levels presented with vitamin D deficiency. This would contradict the results of clinical study conducted in the Jawaharlal Institute of Postgraduate Medical Education and Research in India. According to the study, the total serum Vitamin D levels were not affected by chronic kidney disease [24]. Similar results were found in children with steroid sensitive nephrotic syndrome in the Institute of Child Health in Kolkata, India [25].

As there were only (4.7%) patients with high creatinine levels in this study, it is possible that the results were solely due to insufficient number of samples. To confirm the relationship additional research would be required.

Furthermore, the study showed significant associations between serum vitamin D deficiency and dyslipidemia. Low serum HDL, high serum cholesterol and high serum TG were significantly associated with a higher incidence of serum vitamin D deficiency and insufficiency [26]. This is similar to a study done by Jiang X conducted in Northern China which found a strong association between vitamin D levels and dyslipidemia. Specifically, serum Vitamin D was inversely correlated with LDL cholesterol and triglycerides levels, and positively correlated with HDL cholesterol level [27].

In contrast, a study done by Zittermann A conducted in North-easter Brazil showed no relation between serum vitamin D level and serum cholesterol [28].

It was also noted that there was no significant association between serum vitamin D levels and serum LDL, which was in contrast to the study conducted by Han YY in Taiwanese population which showed higher levels of serum LDL in vitamin D deficient cases [29]. The relationship between serum vitamin D levels and lipid profile can be explained by the lipid lowering actions of vitamin D through its effects on calcium metabolism and parathyroid hormone regulation [30].

A study done by Jin D showed that serum vitamin D levels and normal lipid profiles were directly related. Furthermore, this same study showed an inverse relationship between serum

Vitamin D levels and serum CRP, which was consistent to our own results [31].

Several studies, including our own, showed a clear link between serum vitamin D levels and serum CRP [32-34]. This obvious association can be explained by vitamin D's immunological and anti-inflammatory actions. Vitamin D plays a key role in reducing inflammation by acting on the innate and adaptive immune systems [35].

Limitations

All measures in the study were self-reported and subject to recall bias. Data collection only included individuals who were attending the outpatient department of Cardiac center and results collected from Cardiac center lab.

The samples were taken over a two-month period and were collected in the Autumn season in Erbil. Furthermore, 25(OH) D, has a relatively long circulating half-life (approximately 3 weeks) and is considered a good biomarker, but serum vitamin D levels may change throughout the day and season of the year. A single measurement of vitamin D may not reflect lifetime status.

The sample size included patients with chronic diseases such as diabetes mellitus, chronic kidney disease and liver dysfunction which might disrupt Vitamin D levels in the body.

Vitamin D levels were not determined in a control group of healthy individuals for the purpose of comparative analysis.

Recommendation

Based on our findings, practitioners should consider more education of patients regarding importance of vitamin D status in the body. Additionally, Vitamin D deficiency should be corrected using supplements, correct diet and safe sun exposure.

Further researches need to be conducted regarding prevalence of Vitamin D as well as causes of low Vitamin D and associated conditions among Kurdistan Region population. Future studies could include Calcium status and use of sunscreen products, with a bigger and more equivalent number of people involved in all parts of Kurdistan Region throughout all four seasons of the year.

Conclusion

Vitamin D deficiency is a prevalent condition in the Kurdistan Region of Iraq, with a large number of people suffering from its implications. Several factors proved to be associated with serum vitamin D deficiency, including a previous infection of COVID-19, female gender, increased BMI, diabetes mellitus, the presence of atherosclerotic heart disease, or other inflammatory processes.

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