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Prevalence, Risk Factors, and relation of Vitamin D Deficiency with Bone Health Markers in Baghdad among Women of Reproductive Age

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ABSTRACT
The countries in the Middle East are very prone to the deficiency of vitamin D despite the excessive amount of sunlight, which is strange when considering the fact that the culture of the country restricts the exposure to the sun. The hypothesis of the cross-sectional research was to establish the occurrence of vitamin D deficiency among the reproductive-aged women (18-45 years) and how this condition was correlated with the bone health indicators. Between March and September 2024, 280 women who visit outpatient clinics at Baghdad Teaching Hospital were enrolled with the help of the convenience sampling method. Measurements were done on serum 25-hydroxyvitamin D [25(OH)D], calcium, phosphorus, and alkaline phosphatase (ALP), as well as parathyroid hormone (PTH). Structured questionnaires were used to gather information on sun exposure, dietary intake and physical activity. Findings indicated overall prevalence of vitamin D deficiency (25(OH)D <20 ng/mL) of 72.5% (n=203), severe deficiency (25(OH)D <10 ng/mL) of 28.2% and deficiency (10-19.9 ng/mL) of 44.3% with insufficiency (20-29.9 ng/mL) of 19.3% and sufficient levels (30 ng/mL Wearing full covering clothing, limited outdoor activity, low dietary vitamin D intake and multiparity were significant risk factors (aOR= 3.42, p=0.001, aOR= 2.64, p=0.001, aOR= 2.18, p=0.003, aOR= 1.86, p=0.012, respectively). Weak women possessed much more PTH and ALP and less calcium. Such findings show that there is an urgent need of public health interventions such as supplementation programs and awareness programs.

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1. INTRODUCTION

Deficiency of vitamin D has proven to be an international health disease with about one billion individuals in the world being at risk of it. Ironically, even though the Middle East nations have plenty of sun all year round, the area records some of the highest rates of reduced vitamin D levels in different populations, with 50-90% of the population reported to be affected (1). This has been blamed on the cultural and religious activities that do not expose people to direct sunlight especially the women.

Vitamin D is important in calcium and phosphorus homeostasis and is vital to the health of bones. Deficiency causes secondary hyperparathyroidism, bone turnover acceleration and osteomalacia and osteoporosis. In addition to skeletal effects, vitamin D deficiency is linked to many other factors that predispose people to autoimmune diseases, cardiovascular diseases, diabetes, cancer, and negative pregnancy outcomes (2).

Reproductive age women are more prone to vitamin D deficiency because of several reasons such as exposure to sun is limited, physiological needs are high during pregnancy and while lactating, and cultural beliefs. Fetal and neonatal morbidities have been linked to vitamin D deficiency in pregnant women: gestation diabetes, preeclampsia, premature birth, and skeletal

malformation of the child. Moreover, maternal levels of vitamin D influence infant stores of vitamin D and could have long-term health effects on children (3).

There is a dearth of information on the vitamin D status of women of reproductive age in Iraq and, especially, its biochemical effects on bone metabolism. The purpose of this study was to identify how common the practice of vitamin D deficiency is in this vulnerable population and to evaluate its relationship with bone health parameters such as PTH, calcium, and ALP and present some evidence to inform the interventions of the general population and clinical treatment plans (4).

2-MATERIALS AND METHODS

Study Design and Setting

The analytical study is a cross-sectional study that was carried out in the outpatient clinics of the Baghdad Teaching Hospital between March and September 2024. It is a large tertiary care hospital that accepts referrals in Baghdad and neighboring regions. The duration of the study was six months because it would accommodate the possible variation of vitamin D within a season.

Sample Size Calculation

The lowest sample size was estimated by assuming that the prevalence of vitamin D deficiency in the region is 60 percent as reported in the literature, a level of confidence (Za=1.96) of 95 percent and a margin of error of 6 percent. The result of this was a minimum sample of 256 participants. A final population of 280 women was recruited to consider potential exclusions and lack of data.

Sampling Method and Population of the Study.

The sampling method was based on convenience that was utilized to identify the participants by the researcher as women who were eligible and attended the outpatient clinics within the study period were approached in order to reach the intended sample size. There were 280 apparently healthy women that were enrolled (18-45 years old). The exclusion criteria were as follows: pregnancy, lactation, chronic kidney disease (eGFR <60 mL/min/1.73m2), chronic liver disease, malabsorption syndromes (celiac disease, inflammatory bowel disease), the use of vitamin D supplements or drugs that influence its metabolism (anticonvulsants, glucocorticoids, cholestyramine), and parathyroid disorders.

Table 1: The instruments in this study.

No.	Instrument	Company	Origin
1	Chemiluminescent Immunoassay Analyzer (ADVIA Centaur XP)	Siemens	Germany
2	Chemistry Analyzer (Cobas c501)	Roche	Germany
3	Centrifuge	Eppendorf	Germany
4	Digital Weight Scale	Seca	Germany
5	Stadiometer	Seca	Germany

Data Collection

A questionnaire in the form of a structured one was used to obtain information about demographics, obstetric history (parity, history of pregnancy complications), sun exposure patterns, dietary habits, and physical activity. Anthropometric data in terms of height, weight, and BMI were measured.

The Dietary Intake and Sun Exposure Assessment.

The sun exposure was evaluated by asking questions about: (1) hours of outdoor activity between 10:00 and 15:00 hours (peak UV-B radiation); (2) dressing style characterized as: partial coverage (face and hands not covered), hijab (face and hands covered), or full coverage including niqab/abaya; (3) the use of sunscreen. Less than 30 minutes/day of direct sunlight exposure during the peak hours was considered as little outdoor activity. Vitamin D in dietary intake was evaluated with the help of a short food frequency questionnaire that included the intake of foods rich in vitamin D (fatty fish including salmon, sardines, and tuna; eggs; and fortified dairy products). A low intake of vitamin D in the diet was the definition of the intakes of such foods less than twice in a week.

Laboratory Analysis

Venous blood samples (5 mL) were taken off the participants in between 8:00-10:00 AM. Centrifugation of serum was done at 3000 rpm during 10 minutes and serum was kept at -20degC till analysis. Chemiluminescent immunoassay on ADVIA Centaur XP analyzer was used to measure serum 25 (OH) D and intact PTH (intra-assay CV <8%). The measurement of serum calcium, phosphorus, and alkaline phosphatase (ALP) was done with colorimetric measures on Cobas c501 analyzer.

Definitions

The classification of vitamin D status was based on the Clinical Practice Guidelines of the Endocrine

Society severe deficiency (less than 10 ng/mL), deficiency (10-19.9 ng/mL), insufficiency (20-29.9 ng/mL) and sufficiency ([?]30 ng/mL). To aid analysis, the participants were grouped into two categories, including Deficient (25(OH)D <20 ng/mL) and Non-deficient (25(OH)D [?]20 ng/mL, both insufficient and sufficient). Secondary hyperparathyroidism was considered PTH over65 pg/mL with vitamin D deficiency and normal serum calcium levels.

Statistical Analysis

The SPSS version 26 was used in data analysis. Mean +- SD was used as the measure of continuous variables and independent t-test or one-way ANOVA was used to compare them. The categorical variables were provided in frequency and percentages and they were compared by chi-square test. Continuous variables had relationships calculated using Pearson correlation. Multivariate logistic regression was done to determine independent risk factors of vitamin D deficiency, where p<0.1 in univariate analysis was introduced as an entering variable. Hosmer-Lemeshow test was used to evaluate the model fit. P-value that was below 0.05 was deemed significant.

Ethical Considerations

The Institutional Review Board of College of Medicine, University of Baghdad approved the study protocol and assigned it Approval No.: COM-UB-2024-VD-019. All the participants were informed and signed the informed consent written informed consent beforehand. Those participants who were determined to have a deficiency in vitamin D were advised on the same and were referred to get the condition managed. All the processes were performed on the background of the ethical principles of the Declaration of Helsinki, and the data confidentiality and anonymity were observed closely.

3-RESULTS

A total of 280 women had been enrolled with an average age of 32.4+-7.8 years with mean BMI of 27.8+-5.2 kg/m2. Mean serum 25(OH)D was 14.8+-8.6 ng/mL. The prevalence of overall vitamin D deficiency (25(OH)D <20 ng / ml) was 72.5% (n=203). As far as the status of vitamin D distribution is concerned: 28.2% (n=79) were severely deficient (less than 10 ng/mL), 44.3% (n=124) were deficient (10-19.9 ng/mL), 19.3% (n=54) were insufficient (20-29.9 ng/mL), and only 8.2% (n=23) possessed sufficient vitamin D levels (30 ng/mL). The demographic and biochemical characteristics are indicated in Table 2.

Table 2: demographic and Biochemical Characteristics.

Variable	Deficient* (n=203)	Non-Deficient** (n=77)	P-value
Age (years)	33.2 ± 8.2	30.4 ± 6.8	0.012
BMI (kg/m²)	28.6 ± 5.4	26.2 ± 4.6	0.001
25(OH)D (ng/mL)	11.2 ± 4.8	28.4 ± 6.2	<0.001
PTH (pg/mL)	68.4 ± 24.6	42.8 ± 16.2	<0.001
Calcium (mg/dL)	8.8 ± 0.6	9.4 ± 0.4	<0.001
Phosphorus (mg/dL)	3.6 ± 0.8	3.8 ± 0.6	0.068
ALP (U/L)	98.6 ± 32.4	72.4 ± 22.8	<0.001

**Deficient: 25(OH)D <20 ng/mL; **Non-Deficient: 25(OH)D ≥20 ng/mL (insufficient + sufficient)*

Table 3 provides the multivariate logistical regression analysis. The independent risk factors that were found to be significant in causing vitamin D deficiency included full covering clothing, limited outdoor nature, low dietary vitamin D and multiparty as well as obesity. The Hosmer-Lemeshow test showed that it was a good model (kh2=5.86, p=0.663).

Correlation analysis was done and found that there was a significant negative correlation between serum 25(OH)D and PTH (r = -0.62, p<0.001) which showed compensatory secondary hyperparathyroidism to vitamin D deficiency. A secondary hyperparathyroidism (PTH >65 pg/mL and normal calcium) was observed in 48.3% (n=98) of the vitamin D deficient women highlighting the functional role of deficiency on bone metabolism.

Table 3: Multivariate Logistic Regression Analysis of the risk factors.

Risk Factor	aOR	95% CI	P-value
Full covering clothing (Niqab/Abaya)	3.42	2.08 - 5.62	<0.001
Limited outdoor activity (<30 min/day)	2.64	1.56 - 4.48	<0.001
Low dietary vitamin D (<2×/week)	2.18	1.28 - 3.72	0.003
Multiparity (≥3 children)	1.86	1.14 - 3.04	0.012
Obesity (BMI ≥30)	1.72	1.02 - 2.90	0.042

aOR = adjusted Odds Ratio; Model adjusted for age and education level

4-DISCUSSION

This research shows a very high rate of vitamin D deficiency in women of reproductive age in Baghdad (72.5) with one-third (28.2) of the respondents having severe deficiency. Notably, 8.2% of the participants had adequate levels of vitamin D. These results align with other reports of the Middle Eastern countries and highlight the seriousness of this public health issue in the area despite the numerous sunlight throughout the year (5).

The close relation between full covering clothing and vitamin D deficiency (aOR=3.42) identifies the cultural and religious practices in the constraint of the cutaneous vitamin D production. Vitamin D demands are met by skin production close to 90 percent of the total demands when exposed to UV-B. Although cultural and religious practices should be respected, the strategies of ensuring that the status of vitamin D is adequate should focus on alternative methods to guarantee that this trend is achieved, and this is through supplementing and food fortification policies (6).

The bone health indicators that were measured in the given study are a strong indication of the functional effect of the lack of vitamin D. Besides high PTH (68.4 vs 42.8 pg/mL, $p<0.001$) and ALP (98.6 vs 72.4 U/L, $p<0.001$), vitamin D deficient women also had significantly low levels of serum calcium (8.8 vs 9.4 mg/dl). The combination of the three findings, low calcium, high levels of PTH and high levels of ALP, all indicate that there is an elevated bone turnover and a biochemical evidence of secondary hyperparathyroidism with the possible long-term risk of osteomalacia and osteoporosis. Secondary hyperparathyroidism was found in almost a half of all vitamin D deficient women (48.3), which underlines the importance of screening and early treatment (7).

Our study findings of independent association between obesity and deficiency of vitamin D (aOR=1.72) are in line with other studies which have postulated sequestration of vitamin D into adipose tissue and volumetric dilution in obese patients. Vitamin D is a fat soluble one and excess adipose tissue has a possibility of being a sink that decreases its bioavailability. The observation highlights the importance of taking into account body weight when developing vitamin D supplementation plans because obese people might need more vitamin supplements to obtain the proper levels in the serum (8).

The correlation between multiparity with vitamin D deficiency (aOR=1.86) is indicative of the high physiological needs of pregnancy and lactation on the levels of vitamin D. Repeated pregnancies may result in depletion of maternal vitamin D in the absence of supplementation, and may have negative consequences on maternal bone mass and infant vitamin D status. This observation shows the significance of regular use of vitamin D supplements during pregnancy and the need to continue with the same supplements during lactation (9).

Study Limitations

This research has a number of limitations. First, its cross-sectional design excludes the possibility of causally relating vitamin D deficiency and the determined risk factors or bone markers. Second, the sample size was sampled via convenience sampling in one tertiary care hospital, and thus, the study findings might not be entirely applicable to reproductive women in the community; population-based research is required to validate these findings. Third, the sun exposure and dietary intake of vitamin D were self-reported and are also prone to recall and social desirability bias. Fourth, bone mineral density (BMD) by DEXA scan and radiological evidence of osteomalacia was not evaluated which would offer more explicit tests of bone health. Fifth, the levels of 25(OH)D were found to vary seasonally, which could not be completely measured within the six months of study period (winter and summer months). Lastly, the possible confounders, including skin pigmentation and application of traditional cosmetic products, were not determined.

CONCLUSION

The study reveals that the prevalence of vitamin D deficiency is very high in women of reproductive age in Baghdad with much regard to functional effects on bone metabolism as indicated by high levels of PTH and ALP and low levels of serum calcium. Risk factors were limited sun exposure as a result of clothing practices, insufficient dietary intake, multiparity and obesity. These results indicate that urgent intervention measures in the field of public health, such as: (1) regular screening of vitamin D deficiency in high-risk women, particularly those with full body covering, limited sun exposure, or multiple pregnancies; (2) vitamin D supplementation initiatives within primary and reproductive care; (3) food fortification policies of common foods eaten by the population, such as bread, dairy products, and cooking oil; (4) mass education regarding the significance of vitamin D and cultural practices; and (5) increased doses of supplements by obese women are required. Such all-encompassing measures should be implemented to eliminate this ubiquitous gap and the long-term health ramifications of the same.

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