Vitamin D status among patients of a tertiary health-care center in Makkah, Saudi Arabia: a retrospective study

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Abstract

Background: The prevalence of vitamin D deficiency has been reported to be quite high (30%–50%) in many areas of the world. Saudi Arabia is one of the sunniest areas of the globe and exposure to sunlight may maintain adequate vitamin D status. Yet studies performed as early as 1982 among the Saudi population pointed to the presence of a high prevalence of vitamin D deficiency. In the last 3 to 4 decades, the lifestyle and dietary habits of children and adults in Saudi Arabia have changed tremendously.

Objective: To report the occurrence of vitamin D deficiency and assess the factors associated with it and to report the pattern of supplementation in a tertiary center in Makkah, Saudi Arabia.

Materials and Methods: Retrospective data collection was done for patients, for whom vitamin D serum level was assayed between May 2011 and December 2013. Patients were divided into two groups based on their vitamin D serum concentration using 30 ng/mL as the cutoff point. Demographic and clinical characteristics were analyzed to detect the association with vitamin D inadequacy.

Result: Of the 594 patients included, more than 80% had inadequate vitamin D level at some point of time. The mean age was 44.59 ± 15.6 and 49.20 ± 16.48 years for groups with inadequate and adequate Vitamin D, respectively ($p = 0.006$). In the multivariate model and after adjusting for vitamin D supplementation status, only age and kidney disease were significantly associated with vitamin D status. The records did not show a clear pattern of vitamin D assay and follow-up in relation to the supplementation.

Conclusion: This study makes it very clear that many patients without known risk factors may have inadequate vitamin D concentrations. This may call for wider screening for vitamin D status in the Saudi population. To optimize vitamin D assay and to make supplementation effective, guidelines for supplementation and follow-up need to be put in place.

KEY WORDS: Vitamin D, deficiency, risk factor, retrospective

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Introduction

Vitamin D is an important fat-soluble vitamin, which has substantial roles in calcium and phosphorus metabolism and in the maintenance of a healthy skeleton.[1] It also plays various nonskeletal functions in different body systems by regulating more than 200 different genes that in turn regulate a wide variety of biologic processes.[2–4] Deficiency of vitamin D is responsible for the development of osteomalacia in adults and rickets in children. Vitamin D is also postulated to play an important role in reducing the risk of many chronic diseases including hypertension, diabetes, rheumatoid arthritis, infectious diseases, heart disease, and some types of cancers.[4] Many factors were found to be associated with vitamin D deficiency including age, obesity, skin color, low vitamin D intake, gender, sunscreen use, and the use of some medications.[5,6]

Definitive diagnosis of hypovitaminosis D is done by serum vitamin D testing and despite improvement in health services, vitamin D deficiency is among the most commonly missed medical conditions in children and adults.[7] This is because signs and symptoms of vitamin D deficiency do not show unless there is severe deficiency. There is no absolute consensus on the cutoff value of a low level of vitamin D. It is generally recommended for the normal level of 25-hydroxyvitamin D (25OHD) to be ≥30 ng/mL and it is agreed to define vitamin D insufficiency as a level of 20–29 ng/mL and deficiency as a level ≤20 ng/mL.[8] However, in many institutions, vitamin D deficiency is defined at a serum cutoff value of 10 ng/mL or lower.[9]

The prevalence of vitamin D deficiency has been reported to be quite high (30%–50%) in many areas of the world including the United States, the Middle East, Europe, India, Australia, New Zealand, and Asia.[10–13] Saudi Arabia is one of the sunniest places of the globe and exposure to sunlight may maintain adequate vitamin D status. Yet studies performed as early as 1982 among the Saudi population pointed to the presence of a high prevalence of vitamin D deficiency. In the last 3 to 4 decades, the lifestyle and dietary habits of children and adults in Saudi Arabia have changed tremendously.[14]

King Abdullah Medical City (KAMC) is a tertiary care center that serves a wide sector of the population in Makkah and is a big referral center. The main objective of this retrospective cross-sectional study is to report the occurrence of vitamin D deficiency among patients referred of vitamin D level determination. A close look is also paid to the factors associated with vitamin D deficiency and to the pattern of supplementation and follow-up among patients from KAMC.

Material and Methods

This study included all patients for whom vitamin D serum level was assayed between May 2011 and December 2013. After obtaining the Institutional Review Board approval, the hospital information system (HIS) was accessed to locate the records of those patients. Patients were divided into two groups, a group with inadequate vitamin D level in whom vitamin D level was less than 30 ng/mL on at least one occasion and a group in whom vitamin D level was adequate (≥30 ng/mL).

For both groups, the following data were extracted directly from the HIS and patient hospital files: date of birth, gender, weight, height, diagnosis, vitamin D level, comorbidities, medications, and the number of subsequent vitamin D levels requested. We also extracted data about vitamin D and calcium supplementation.

Statistical Analysis

Statistical package for social science software version 21.0 (SPSS, IBM. Inc. USA) was used for data entry and analysis. Nominal data were presented as percentages. Quantitative data were presented as mean ± standard deviation if normally distributed, or median and interquartile range if not. For categorical data, chi-square test was used to compare groups, whereas for continuous data, comparisons were done by Student-*t*-test or Mann–Whitney *U*-test according to data distribution pattern.

A logistic regression model was constructed with vitamin D status (inadequate versus adequate) as the dependent variable and all the suspected risk factors as independent ones. Initially, factors were individually examined in univariate models followed by inclusion of all statistically significant factors in a multivariate model. A two-sided α was set at 0.05 for all comparative analyses.

Results

Study Population Characteristics

Five hundred and ninety-four individuals were found to have at least one vitamin D level available, of whom, 81% had inadequate vitamin D concentration. The mean age was 44.59 ± 15.6 and 49.20 ± 16.48 years for groups with inadequate and adequate concentrations, respectively (p = 0.006). The majority of the individuals were Saudis (75.8%) and lived in Makkah (93.1%). The most frequently seen comorbidities were hypertension, diabetes, and cardiovascular diseases [Table 1]. We found that 58.5% of the vitamin D assays were ordered from the internal medicine clinics, 7.4% from the orthopedic clinics, and 6.2% from the surgical clinics, and 6.9% were referred by the Ear Nose and Throat department. This study sample did not show a significant association between the intake of anticonvulsant or antifungal medications and vitamin D inadequacy ($p > 0.47$). On the other hand, the glucocorticoid and Anti-Tuberculosis medications were significantly more encountered in the group with adequate vitamin D level ($p < 0.001$) [Table 2].

The assessment and comparison of laboratory values in both groups are shown in Table 3. Only the random blood sugar and Blood Urea Nitrogen (BUN) levels showed a statistical significant difference between the groups ($p < 0.005$.)

Vitamin D Supplementation Among the Two Groups

A total of 121 of the studied patients were already on vitamin D supplementation when vitamin D assay was made. They constituted 31.3% of those with adequate vitamin D concentration. Only 17.8% of those with inadequate vitamin D concentration were on vitamin D at the time of the assay (p = 0.002) [Table 4]. Those already on vitamin D had a statistically higher vitamin D concentration as compared with those who were not (21.8 ± 15.4 ng/ml versus 16.8 ± 12.5 ng/ml, respectively, p = 0.001).

Considering cases with inadequate vitamin D level, who were not already on vitamin D therapy at the first vitamin D assay (396 patients), we found a record of subsequent

Table 1: Demographic characteristics of the two groups that are classified based on vitamin D level (*N* = 594)

Variable		Total	Inadequate vitamin D level (<30)	Adequate vitamin D level (>30)	*p*-Value
		(*n* = 594)	(*n* = 482)	(*n* = 112)	
Age at level (mean ± SD)			44.59 ± 15.601	49.20 ± 16.476	0.006
BMI (mean ± SD)			30.49 ± 8.13	29.29 ± 7.52	0.156
Gender	Male	202 (34.1%)	173 (35.9%)	29 (26.1%)	0.050
	Female	391 (65.9%)	309 (64.1%)	82 (73.9%)	
Nationality	Saudi	449 (75.8%)	352 (73.2%)	97 (87.4%)	0.002*
	Non-Saudi	143 (24.2%)	129 (26.8%)	14 (12.6%)	
Residency	Within Makkah	540 (93.1%)	446 (94.7%)	94 (86.2%)	0.002*
	Outside Makkah	40 (6.9%)	25 (5.3%)	15 (13.8%)	
Osteoporosis/osteomalacia		22 (4.3%)	10 (2.2%)	12 (18.2%)	0.000*
Chronic kidney disease		17 (3.3%)	12 (2.7%)	5 (7.4%)	0.046*
Malabsorption syndromes		5 (0.9%)	3 (0.7%)	2 (2.4%)	0.127
Bariatric surgery		18 (4.0%)	17 (4.1%)	1 (3.3%)	0.841
Hyperparathyroidism		9 (1.6%)	7 (1.5%)	2 (2.2%)	0.626
Hypertension		175 (31.3%)	135 (29.3%)	40 (40.0%)	0.037*
Diabetes mellitus		161 (28.8%)	126 (27.5%)	35 (35.0%)	0.131
Cardiovascular disease		97 (17.4%)	68 (14.8%)	29 (29.0%)	0.001*

BMI, body mass index; SD, standard deviation.
**p*-Value = a statistically significant appearance.

Table 2: Concomitant medications with known association with vitamin D deficiency

Medication	Total	Inadequate (<30)	Adequate (>30)	*p*-Value
	(*n* = 594)	(*n* = 482)	(*n* = 112)	
Antifungal medications	23 (3.9%)	20 (4.1%)	3 (2.7%)	0.477
Anticonvulsant medications	84 (14.3%)	67 (14.0%)	17 (15.3%)	0.724
Glucocorticoids	13 (2.2%)	5 (1.0%)	8 (7.2%)	<0.001
Anti-TB medications	4 (0.7%)	0 (0.0%)	4 (3.6%)	<0.001

BMI, body mass index; SD, standard deviation.
**p*-Value = a statistically significant appearance.

Table 3: Summary and comparison of laboratory values in both groups

Variable	Inadequate (<30) (*n* = 482)	Adequate (>30) (*n* = 112)	*p*-Value	(95% CI)
	Mean ± SD	Mean ± SD		
BMI (in kg/m^2)	30.49 ± 8.13	29.29 ± 7.52	0.156	(–2.8–0.45)
Creatinine level (in mg/dL)	0.95 ± 0.95	1.07 ± 1.10	0.38	(–0.14–0.37)
BUN level (in mg/dL)	12.76 ± 6.89	16.70 ± 13.93	0.02*	(0.59–7.2)
Phosphorus level (in mg/dL)	3.50 ± 0.67	3.62 ± 0.69	0.315	(–0.11–0.36)
Random blood glucose level (mg/dL)	120.73 ± 69.82	107.08 ± 26.29	0.003*	(–33.01– –7.08)
Fasting blood glucose level (mg/dL)	120.73 ± 70.02	121.38 ± 39.79	0.96	(–27.49–28.80)
Calcium level (in mg/dL)	9.33 ± 5.24	8.98 ± 0.48	0.53	(–1.46–0.76)
Alkaline phosphatase level (in U/L)	98.97 ± 35.48	99.10 ± 37.22	0.98	(–12.34–12.61)
Parathyroid hormone level (in pg/mL)	75.32 ± 47.64	82.35 ± 63.30	0.58	(–18.64–32.71)

BMI, body mass index; CI, confidence interval; SD, standard deviation.
**p*-Value = a statistically significant appearance.

Table 4: The relation between vitamin D level adequacy and the vitamin D supplementation

Vitamin D supplementation	Total (*n* = 594) (%)	Group with inadequate level of vitamin D (*n* = 482) (%)	Group with adequate vitamin D level (*n* = 112) (%)	*p*-Value
Not on vitamin D supplement before the level	473 (79.6%)	396 (82.2%)	77 (68.8%)	0.002
On vitamin D before the level	121 (20.4%)	86 (17.8%)	35 (31.3%)	

Table 5: Results of univariate logistic regression analysis for the relation of different factors to the vitamin D status

Factor entered in regression	Odds ratio	95% CI	*p*-Value
Age	0.981	0.968–0.993	0.003
Gender	0.653	0.413–1.032	0.068
BMI	1.062	0.919–1.228	0.416
Kidney disease	0.502	0.423–0.595	<0.001
Hypertension	0.695	0.548–0.883	0.003
Diabetes mellitus	0.731	0.576–0.927	0.01
Cardiovascular disease	0.685	0.544–0.864	0.001
Antiseizure medication	1.04	0.62–1.744	0.883
Glucocorticoids	0.493	0.231–1.052	0.068
Antifungal medication	1.573	0.459–5.388	0.471
Anti-TB medication	0.367	0.099–1.36	0.134
Being on vitamin D supplementation at the time of assay	0.472	0.29–0.769	0.003

BMI, body mass index; CI, confidence interval; anti-TB.

Table 6: Results of multiple linear regression analysis for the relation of different factors to the vitamin D status

Factor entered in regression	Adjusted odds ratio	95% CI	*p*-Value
Being on vitamin D supplementation at the time of assay	0.328	0.19–0.565	<0.001
Gender	0.78	0.466–1.31	0.346
Age at vitamin D assay	0.971	0.957–0.986	<0.001
Kidney disease	0.411	0.329–0.512	<0.001
Hypertension	1.34	0.8–2.244	0.266
Diabetes mellitus	1.33	0.803–2.203	0.268
Cardiovascular disease	0.783	0.488–1.26	0.315
Being on vitamin D supplementation at the time of assay	0.472	0.29–0.769	0.003

CI, confidence interval.

supplementation in only 147 (37.1%) of them. Only 64 (44%) of those patients who were on supplementation had a record for a follow-up of second vitamin D assay.

Of the 147 cases for whom supplementation was started after obtaining the vitamin D concentration, 74 patients (50.3%) had their supplementation started within 1 month after performing vitamin D assay, 28 (19%) started within 1–3 months whereas 45 (30.6%) started their supplementation more than 3 months of obtaining vitamin D assay result.

Of those with inadequate vitamin D concentration, we found records of follow-up of vitamin D concentration assay in 153 cases, For 51 (33.3%) of those, no records of vitamin D supplementation were found. For the remaining 102 cases, 32 (32%) had the second assay before the recorded start of supplementation, 18 (18%) had it less than 3 months from the start of supplementation, and 52 (50%) had the second assay more than 3 months after starting the supplement. Those performing the assay less than or more than 3 months of supplementation showed a statistically significant increase in serum vitamin D.

Risk Factors

Table 5 shows the results of the univariate regression analyses. Vitamin D inadequacy is shown to be associated with younger age, Hypertension, Diabetes mellitus, kidney diseases, Cardiovascular disease, and vitamin D supplementation. All appear to be negatively associated with vitamin D inadequacy. In the multivariate model, all but the vitamin D supplementation, age, and kidney disease lost that significant association [Table 6].

Discussion

Many studies focused on vitamin D status and risk factors around the world, yet results were variable. This study shows that more than 80% of those referred for vitamin D assay had inadequate level. Earlier vitamin D deficiency prevalence studies have been performed in the Kingdom of Saudi Arabia. Examples include a study that has been conducted on 225 Saudi medical students and it stated that 75.2% had 25(OH)D levels <30 nmol/L.[15] The results of this study however cannot be used to comment on the prevalence of vitamin D inadequacy among the Saudi population because of its retrospective nature and the fact that the assay results analyzed belonged to patients referred for vitamin D measurement, probably for suspected deficiency. Furthermore, in a systematic review that included 27 studies, which used different types of vitamin D assay, it was concluded that different assay methods that have different specificity and sensitivity may lead to diagnostic inaccuracy and thus may lead to variations in the estimation of occurrence of vitamin D inadequacy in different studies.[16]

Despite the important role played by vitamin D in general health and the fact that literature is full of studies that probe into the risk factors of vitamin D insufficiency, still there is a debate around the relation between vitamin D deficiency and various potentially associated factors such as gender, certain comorbidities, body mass index, age, and certain medications.

In this study, deficiency was found to be more prevalent in female patients, being reported in 64.1% of the female patients compared with 35.9% of the male patients. In spite of this being statistically nonsignificant, similar observations have been reported in Saudi Arabia as well as in other countries. In a study by Hussain et al.,[17] a total of 10,709 people were enrolled during a 5-year period and the prevalence was 44.6% among Saudi women as compared with 28.3% among men. Another study was conducted on Saudi women from the western region and it reported around 80% of hypovitaminosis D.[18] A study conducted among University students in Shiraz, Iran, showed that the prevalence among female and male students was 51.2% and 44%, respectively.[19] Lack of statistical significance in the difference between men and women with regard to vitamin D status in this study may be due to the smaller number of records studied in comparison with other studies.

Vitamin D plays an important protective role on the cardiovascular system through regulation of growth and proliferation of smooth muscles and cardiomyocytes,[20] preservation of the endothelial function, and anti-inflammatory effects.[21] Some previous observational studies like that by Scragg et al.[22] reported a significant inverse association between serum 25(OH)D concentration and blood pressure, after adjustment for age, gender, ethnicity, and physical activity. Others suggested that vitamin D inadequacy resulted in a twofold increase in the risk of cardiovascular events.[20] Some randomized clinical trials even went further and tried vitamin D for lowering the blood pressure but failed to show a significant effect.[23] In this study, there was no significant association between hypertension or cardiovascular disease and vitamin D adequacy in the adjusted model.

Some studies suggested that vitamin D deficiency is a risk factor for the development of diabetes mellitus.[24,25] Other studies suggested diabetes mellitus to be a risk factor or a worsening factor for vitamin D deficiency.[26,27] In this study, adjusted regression analysis failed to show a statistically significant association between diabetes and vitamin D adequacy. Likewise, Mitri et al.[28] in their systematic review had difficulties in making conclusion about the relation between vitamin D and type 2 diabetes. Another systematic review and meta-analysis by George et al.[29] could not confirm that vitamin D supplementation can improve glycemia or insulin resistance in patients with normal fasting glucose.

In this study and according to the results of multiple regression analysis, age, kidney disease, and vitamin D supplementation were the only significant factors associated with vitamin D deficiency. The sample examined in this study showed younger age to be associated with vitamin D inadequacy. This comes in contrary to the results of other studies such as that of MacLaughin and Holick.[30] Aging can reduce the production capacity of vitamin D3 in the skin more than twofold.[30] In Riyadh, one study was conducted in King Abdulaziz Medical City, a tertiary hospital where patients from different cities in Saudi Arabia seek medical advice. They included 3,475 patients with mean age 46.9 ± 16.3 years and had low vitamin D ($p < 0.0001$).[31] So is it that vitamin D deficiency may affect people of a younger age in Saudi Arabia? This needs further studies.

It is well-known that chronic kidney disease has a major effect on the rate of production of vitamin D in the active form.[32] In fact, the relation between secondary hyperparathyroidism and chronic kidney disease is due to 25OHD values that are <30 ng/mL.[33,34] In this study, kidney disease was actually negatively associated with vitamin D insufficiency (i.e., vitamin D level was higher in identified patients with kidney disease). This seems contradictory to the well-known fact that kidney disease leads to vitamin D deficiency. The explanation of this is the fact that patients with kidney disease in this study may have been very well managed in terms of vitamin D supplementation, which led to the correction of their vitamin D status.

Certain medications are known to be associated with low levels of vitamin D as some of them may interfere with its metabolism and decrease its bioavailability.[35,36] Such drugs include anticonvulsants, glucocorticoids, some antituberculous medications, and some systemic antifungal medications.[36] Such associations however could not be demonstrated in this study because of the relatively few patients on these drugs and the presence of several interplaying factors.

In this study, association of vitamin D deficiency and almost all known risk factors were lost in the multivariate analysis; these include gender, hypertension, diabetes mellitus, and cardiovascular disease. For some factors, there may not really be an association and for others bigger numbers may be needed to show it. Supplementation with vitamin D remained the only factor to retain a significant and explainable association with vitamin D inadequacy, such that patients who were on supplementation were less likely to be deficient. Even after adjusting for supplementation, patients older in age and those with kidney disease were less likely to be deficient. This only points to the fact that such patients, known to be vulnerable to vitamin D deficiency, receive much greater medical attention with this regard. This may take the form of a regular follow-up. Also in this study, supplementation was judged only by going back to the pharmacy records. Because of the retrospective nature of the study, no accurate data could be collected about the dose taken or the patients' compliance with therapy. Thus, patients with older age and kidney disease may have higher doses and stricter follow-up, which lead to the apparent association with a better vitamin D level.

This study shows that there is not a clear practice guideline for managing vitamin D level assay and supplementation. Some patients who were vitamin D deficient may repeat the level without being supplemented and some may have supplements without follow-up. Also the time of the follow-up does not seem to have consistent rules. Although it is generally believed that normalization of vitamin D status may take several weeks, many patients have the assay repeated before a month from the original assay.

Thus far, there is no consensus on screening asymptomatic adults to detect vitamin D deficiency.[37] In this study; however, those with less of the known risk factors were more likely to have inadequate levels. In other words, patients without known vitamin D risk factors may still have deficiency that passes unnoticed and uncorrected.

Conclusion

The records did not show a clear pattern of vitamin D assay and follow-up in relation to the supplementation. This study makes it very clear that many patients without known risk factors may have inadequate vitamin D concentrations. This may call for a wider screening for vitamin D status in the Saudi population. To optimize vitamin D assay and to make supplementation effective, guidelines for supplementation and follow-up need to be put in place.

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