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The Profile of Vitamin D among Type 2 Diabetes Mellitus Patients

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Objective: To evaluate vitamin D deficiency in type 2 diabetic patients and its association with poor control of diabetes.

Design: A Cross-Sectional Study.

Setting: Diabetes Outpatient Clinic, A'Ali Health Center, Bahrain.

Method: Two hundred sixty-eight patients were included in this study. Serum 25-hydroxy vitamin D concentrations were measured from May 2012 to September 2012. Other parameters of diabetes control were measured.

Result: One hundred seventy-six (65%) patients had vitamin D deficiency (<50 ng/mL). Vitamin D deficiency appears to be prevalent among the diabetic Bahraini population. Association of vitamin D status and glycemic control could not be confirmed in this study.

Conclusion: Due to the high prevalence of hypovitaminosis D in diabetics, vitamin D status should be routinely evaluated for diabetics as part of regular preventive care.

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Vitamin D is associated with calcium metabolism and bone structure. Recently, vitamin D has been implicated in other conditions namely cancer, multiple sclerosis, cardiovascular disease and diabetes. Evidence has indicated the potential association of low vitamin D nutritional status with an increased risk of type 2 diabetes (T2DM) and poor glycemic control. Nevertheless, evidence for the role of vitamin D in type 2 diabetes genesis and control is contradictory and inconclusive[1].

Vitamin D is a fat-soluble vitamin with steroid nucleus; therefore, it is usually described as a hormone and acts through intracellular receptors which belong to the thyroid-steroid receptor super family. The principal role of vitamin D is the enhancement of intestinal absorption of calcium and phosphorus[2]. The best indicator of vitamin D deficiency is plasma 25-hydroxycholecalciferol (25OH-D3)[1,2].

In addition to a potential role for vitamin D in insulin resistance and β-cell function, there is an emerging evidence that low 25(OH) D levels may be associated with increased risk of the metabolic syndrome (MetS), which represents a cluster of risk factors for type 2 diabetes[1-10].

The role of vitamin D in glucose homeostasis include: the presence of vitamin D receptors (VDRs) on β-cells, the expression of 1-α- hydroxylase enzyme in β-cells, the presence of a vitamin D response element in the human insulin gene promoter, the presence of VDR in skeletal muscle[9].

The prevalence of vitamin D deficiency was quoted to be as high as 91% in type 2 diabetics compared to 58% in a case-control study done in North India. In that study, levels of vitamin D correlated with age[11,12].

The Bahrain nutritional survey published in 1995 addressed the need to estimate the prevalence of micronutrients' deficiencies including vitamin D[13]. In 2013 and 2014, four studies were published in Bahrain, which highlighted the prevalence of hypovitaminosis D and the impact of the deficiency if any[14-17]. These studies revealed a high prevalence of hypovitaminosis D ranging from 60%-90%, a predilection for females and associated with lack of sun exposure, smoking and high BMI. Further studies on vitamin D in the region suggest that a large proportion of adolescent females, up to 70% in Iran and 80% in Saudi Arabia had 25(OH)D3 levels below 25 nmol/L[16,18,19]. Diarrhea, maternal vitamin D and infants, gender, clothing style and socioeconomic factors in older children are reported to be independent risk factors for 25(OH)D3 levels[19-24]. Predictors of low vitamin D levels in adults are older age, female gender, multi-parity, winter season, conservative clothing, low socioeconomic status and urban living. The negative impact of low vitamin D on mineral metabolism was illustrated in the inverse relationship between vitamin D and PTH levels noted in Lebanese, Emirati and Iranian females[25-27].

The aim of this study is to evaluate vitamin D deficiency in type 2 diabetic patients and its association with poor control of diabetes.

METHOD

A cross-sectional study of T2DM was performed from May 2012 to September 2012 in A'Ali health center because of the high prevalence (15%) of diabetes in the Central Governorate.

Participants were identified as type 2 diabetics based on their age of onset of diabetes and previous use of oral hypoglycemic agents according to the criteria of American Diabetes Association (ADA). Insulin resistance was identified by the waist circumference and C-peptide levels according to ADA criteria[28].

Exclusion criteria were severely ill patients, pregnant women, patients with diseases other than diabetes known to be associated with vitamin D deficiency, such as autoimmune diseases or tuberculosis, patients on medications that interfere with vitamin D or calcium (steroids, antituberculous medications, Thiazides, Antacids, Phenobarbital, Phenytoin, Primidone, Valproic acid and Orlistat). Immune compromised state and acute complications of DM at the time of recruitment were also part of the exclusion criteria.

The level of education was grouped into low if the patient only reads and writes and primary school graduates; middle if patients finished intermediate and secondary school; and high if patients achieved higher education. Data was analyzed using SPSS version 19.

Vitamin D deficiency is defined as 25(OH) D below 20 ng/mL (50 nmol/L) and insufficiency 21–29 ng/mL (52.5–72.5) nmol/L. Vitamin D sufficient is above or equal to 70 nmol/L[29,30].

Informed consent was obtained from all the participants.

RESULT

Two hundred sixty-eight patients were included in this study. All patients completed their interview and blood tests.

One hundred seventy-six (65.7%) patients were vitamin D deficient; 77 (28.7%) were vitamin D insufficient; 15 (5.6%) were vitamin D sufficient. The prevalence of both vitamin D deficiency and insufficiency was 94.4%.

The average age of the population is 57.6 years (SD±10.6). One hundred fifteen (43%) were male; 153 (57%) were female, see table 1. One hundred twenty-two (45.5%) had a low education; 92 (34.3%) had middle education and 42 (15.7%) achieved a high education. The level of education of 12 (4.5%) could not be identified. One hundred sixteen (43.3%) were housewives and 74 (27.6%) were retired. Sixty-seven (25%) were government employees, 11 (4%) could not be identified. The average parity of the female patients was 4.5 (SD±2.9) children. All patients were non-vegetarians. Table 1 depicts some personal characteristics and vitamin D level. The average diabetes duration for the sample was 8.5 years (SD±12.08). All patients in this sample had a family history of diabetes.

Table 1: Patient Characteristics and Vitamin D level

		Vitamin D		
Variables		**Deficiency**	**Insufficiency**	**Sufficiency**
Age (mean ± SD) years		53± 5.6	52± 5.6	66± 2.8
Sex	**Males 43%**	20.1%	67.5%	12.4%
	Females 57%	100%	0%	0%
Level of Education	**Low 45.5%**	64.7%	28.6%	6.7%
	Middle 34.4%	58.3%	37.4%	4.3%
	High 15.6%	81%	10.5%	8.5%
Diabetes Duration (mean±SD) years		12.5± 6.36	3.5± 4.24	12.5± 17.7

Table 2 depicts some of the physical and biochemical characteristics of the participants and vitamin D level.

Table 2: Means of Physical and Biochemical Parameters and Vitamin D Level

Parameter	Vitamin D		
	Deficiency	Insufficiency	Sufficiency
BP mean±SD mmHg	115/70(±16/11)	130/80 (±15/7)	120/70 (±11.5/6.6)
BMI mean±SD (kg/m2)	38.75(±8.6)	23.05 (±6)	30.8 (±4.5)
Waist circumference mean±SD cm	112(±12.3)	89.75 (±16.34)	104.5 (±16.34)
Fasting blood sugar mean±SD mmol/L	7.8 (±3.3)	11.9 (±4.3)	6.2 (±3.16)
HbA1c mean±SD %	4.7 (±2.25)	7.35 (±5.10)	8 (±1.92)
Fasting Insulin mean±SD µIU/ml	66.7 (±22.27)	7.35 (±37.1)	7.2 (±8.6)
Vitamin D mean±SD nmol/L	27.1 (±8.9)	59.5 (±5.4)	71.5 (±9.4)
Calcium mean±SD mmol/L	2.24 (±0.10)	2.32 (±0.08)	2.15 (±0.10)
Phosphorous mean±SD mmol/L	1.2 (±0.17)	1.0 (±0.16)	1.1 (±0.15)
PTH mean±SD mg/dL	11.45 (±0.88)	4.25 (±0.61)	2.90 (±0.21)

The average vitamin D level was 45.5 nmol/L (SD±15.1). The average vitamin D level for the vitamin D deficient group was 27.1 nmol/L (SD±8.9), for the vitamin D insufficient group was 59.5 nmol/L (SD±5.4) and for the vitamin D sufficient group was 71.5 nmol/L (SD±9.4).

Not all patients had C-peptide performed due to budget issues. One hundred forty-five (54.1%) had serum C-peptide. The normal range for a C-peptide test is 0.17-0.90 nmol/L. The average C-peptide reading for this sample was 0.58 nmol/L (SD±0.80). The average C-peptide reading for the vitamin D deficient group is 0.54 nmol/L (SD±0.87), see figure 1.

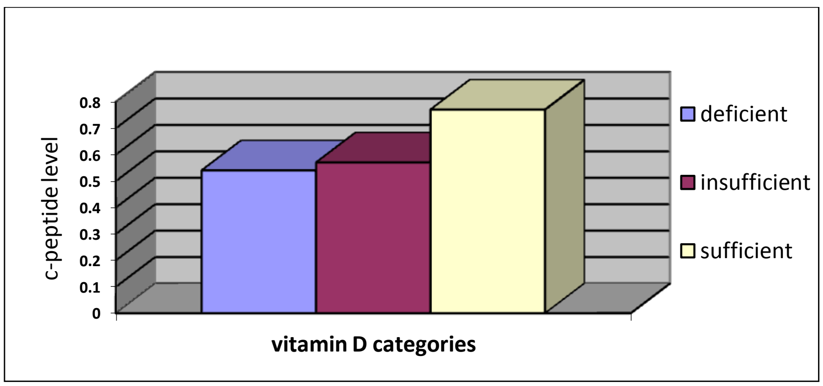

Figure 1: Average C-Peptide Level and Vitamin D Categories

The average fasting insulin reading was 66.7 µIU/ml (SD±26.74). The normal range is considered 5 to 25 µIU/ml. The average fasting insulin reading for the vitamin D deficient group is 66.7 µIU/ml (SD±22.27), see table 2.

Data were classified into vitamin D insufficient (≤50 nm/L) and vitamin D sufficient (>50 nm/L).

Table 3 depicts the association of vitamin D level and selected parameters: gender, fasting Insulin, BMI, waist circumference and PTH had statistically significant association with vitamin D level.

Table 3: Association of Vitamin D Level and Selected Parameters

Significance Relations	P-value
HbA1c	0.12
FBS	0.23
Fasting Insulin	0.037*
PTH	0.0449*
Age	0.9
Gender	0.0001*
Level of education	0.34
Diabetes duration	0.55
BMI	0.0078*
Waist Circumference	0.0065*
C-Peptide	0.4

DISCUSSION

Two studies from Bahrain revealed the extent of hypovitaminosis D among adults and mothers and their newborns in the labor room. Both studies addressed the controversies that entails the diagnosis and management of hypovitaminosis D and highlighted a striking fact of high prevalence of hypovitaminosis D in a very sunny community like Bahrain[14-17].

The relevance of the existing methods of evaluating vitamin D levels biochemically was debated; the debate was on optimal blood levels in humans, age, geographical and seasonal variations in 25(OH) D levels and the levels where supplementations of vitamin D are mandatory. However, there was a consensus that levels around 20 ng/mL (50 nmol/L) would be sufficient to cover the requirements of 97.5% of the population. Serum vitamin D levels of below 20 ng/mL (50 nmol/L) are alarming. Not enough data is available to support the benefits or harms of higher serum levels[31].

The biochemical criteria used for evaluating hypovitaminosis D prevalence in this study was based on the American Endocrine Society Clinical Practice Guideline. The prevalence of vitamin D deficiency was 65.7% which is less than that of the non-diabetic population in neighboring countries[19]. Compared to the studies performed in Bahrain, the prevalence of hypovitaminosis D in the first study, performed on young males, was 64%. The biochemical criteria used in that study is comparable to our criteria, but the target population is slightly different being mainly males and of younger age group and non-diabetic. The prevalence of hypovitaminosis D in that population was 64% while in our male was 88%.

The prevalence of hypovitaminosis D in the second and third study was 90% in mothers and infants and 64% in males; the criteria used in both studies was comparable to our criteria, but the age groups were slightly different and non- diabetic[16,17]. The Mean total serum 25(OH)D concentration in the fourth study was 19.3 nmol/L and it was significantly lower in females than males; the criteria used in the fourth study is different and thus cannot be compared to our study though their population is compared to ours[17]. The prevalence in our study is less than a study performed in North India on diabetics, where they found that vitamin D deficiency was 91% compared to non-diabetic control[12].

Vitamin D level seasonal variation has been documented with increased levels during summer season[32-34]. Our study was done in the summer which might explain the relatively decreased prevalence of vitamin D deficiency compared to neighboring countries.

The average vitamin D level in our population was 45.5 nmol/L (SD ±15.1). In North India, the mean 25(OH) D was 7.88 ng/mL (19.5nmol/L) in the diabetic group[12]. The difference in average vitamin D level could be explained by the larger number of diabetics in our study with a predominance of females. All the female diabetics in our cohort have vitamin D deficiency which constitutes 89% of the vitamin D deficient group.

Female gender was significantly associated with vitamin D deficiency in our study. This is well-documented in other studies. Cultural, hormonal and nutritional factors have been proposed to contribute to such difference[22,33,35].

Age was not an important factor in the prevalence of vitamin D deficiency in our cohort because the means of both groups were comparable (53 years in the vitamin D insufficient group compared to 56 years in the vitamin D sufficient group).

The level of education was considered an element of financial ability. The middle education group had significantly less vitamin D deficiency than the lower education group. Nevertheless, the high education group vitamin D level was not significantly lower than either the low or the middle education group. This may be explained by the small number of patients with high education in this cohort.

In our sample, the level of education was mildly associated with vitamin D level which is consistent with the study of Naugler et al in which low vitamin D levels were found in low educated subjects[36]. In the same study and others, age was a predictor of vitamin D deficiency[36-38]. This is not the case in our sample, where age was not associated with vitamin D levels. This may be due to the small age variability of our sample.

Average diabetes duration was 8.5 years for the whole sample. No statistically significant relation of diabetes duration and vitamin D levels rendering this variable non-influential. In a study, no association was found between hypovitaminosis D and diabetes duration[36].

The association between hypovitaminosis D and diabetes complications is well-documented in many studies[34-38]. The number of complications in our sample is insufficient to draw conclusions. Nevertheless, all the patients with nephropathy, and 54% of retinopathy patients were vitamin D deficient. Sixty percent with IHD were vitamin D deficient. These complications are usually associated with poorer glucose level.

The waist circumference and BMI showed significant association with vitamin D level in our group. These anthropometric association with hypovitaminosis D are well-documented[37,38].

Eighty-seven percent of our patients who were vitamin D deficient had osteoporosis; this is similar to another study[38].

Low vitamin D was not associated with glycemic control in our sample; similar studies showed that the level of glycemic control was not strongly associated with vitamin D deficiency[34-38].

CONCLUSION

Low serum 25(OH)D was of association to greater insulin resistance, poorer β-cell function and a higher prevalence of the metabolic syndrome, and possibly related to poorer glycemic control.

Randomized controlled study is recommended to evaluate the association of serum 25(OH)D with the diabetes control, insulin resistance, β-cell function, and the metabolic syndrome.

Potential Conflicts of Interest: None.

Competing Interest: None. **Sponsorship:** None.

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Ethical Approval: Approved by the Research Committee, Ministry of Health, Kingdom of Bahrain.

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