The Level of Vitamin D among Diabetic Patients

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Objective: To evaluate vitamin D deficiency in diabetic patients.

Design: A Retrospective Study.

Setting: Primary Health Care Department, Bahrain Defence Force Hospital, Bahrain.

Method: One-hundred twenty-seven patients with type 2 Diabetes Mellitus (DM) were evaluated for vitamin D level. The patients were divided into two groups according to vitamin D supplementation. The first group had 55 (43.3%) patients who received vitamin D supplementation and the second group had 72 (56.7%) patients who did not receive vitamin D supplementation.

Result: Vitamin D deficiency was found in 24 (18.9%) patients. Vitamin D insufficiency was found in 99 (78%) patients and only 4 (3.1%) patients were sufficient. None of the patients was having vitamin D toxicity. One hundred one (79.5%) patients were Bahrainis; 21 (16.5%) were deficient, 76 (59.8%) were insufficient and 4 (3.1%) were sufficient. Twenty-six (20.5%) were non-Bahrainis; 3 (2.4%) were deficient and 23 (18.1%) were insufficient and none was sufficient.

No significant differences were found in vitamin D level in diabetic patients among the following variables: age, nationality and gender.

Conclusion: In this study, 18.9% of patients were deficient and 78% of patients were insufficient. Only 3.1% patients were sufficient. The majority were Bahrainis.

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Vitamin D insufficiency is often detected in diabetic patients, and it is believed to be linked to the disease development and severity[1,2,3].

The World Health Organization (WHO) predicts that Diabetes Mellitus (DM) would be the seventh leading cause of mortality by the year 2030. The incidence of diabetes is rising, from 4.7% in 1980 to 8.5% in 2014. Type 2 DM accounts for 90% of diabetic patients. It is due to the body's inefficient use of insulin which is caused by insulin resistance[1]. Glucose and lipids (triglycerides including cholesterol) metabolism are affected in diabetic patients.

Vitamin D is available in two forms, D2 and D3. The D3 form is synthesized from 7-dehydrocholestirol under UV light in the skin or taken from fortified dairy products and fish oil, while the D2 form is derived from the plant sterol ergosterol[4,5]. Vitamin D3 has higher affinity compared to D2[5]. Vitamin D is hydrolyzed to its hormonal form which is an active form that serves as the ligand for the vitamin D receptor[4]. Vitamin D is involved in skeletal development, thyroidal metabolism, immune response regulation, cardiovascular health and in the glucose-mediated insulin secretion via regulation of insulin receptor expression[1].

The level of vitamin D in blood varies depending on the season, geographical location, body mass index and diet[6]. The genetic component plays a significant role in the vitamin D status[6].

Vitamin D supplementation may increase insulin production and secretion by acting via the regulation of the vitamin D receptors dependent calcium and phosphorus metabolism cascade in pancreatic beta cells[7,8]. However, vitamin D could act as an expression modifier of inflammatory cytokines, such as tumor necrosis factor alpha and interleukin 6, which in turn affect insulin resistance in muscle and adipose tissues[7]. Animal studies confirm that vitamin D is required for normal insulin secretion[8].

A study revealed that vitamin D levels in type 2 diabetics are significantly lower than in the healthy controls and in general population[8]. However, the serum vitamin D values vary between populations.

Bahraini database lacks the statistical data regarding vitamin D level in diabetic patients, whether in the supplemented or non-supplemented patients; this study is intended to fill such gaps in knowledge.

The aim of the study is to evaluate vitamin D deficiency in diabetic patients.

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METHOD

One hundred twenty-seven type 2 diabetic patients were included in the study and reviewed from 1 March 2016 to 31 March 2016; the age ranged between 29 and 80 years. The patients were divided into two groups according to vitamin D supplementation. The first group was 55 patients who received vitamin D supplementation and the second group was 72 patients who did not receive vitamin D supplementation. One hundred twenty-four patients had other chronic diseases. All patients received medication for their comorbidities alongside with taking the antidiabetic medicine.

The following groups were excluded: Diabetic patients who were not tested for vitamin D level; Diabetic patients who needed admission; Diabetic patients with severe comorbidities and Diabetic patients who were followed in diabetic specialist clinic.

The LIAISON 25 OH Vitamin D Total Assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of 25-hydroxyvitamin D and other hyroxylated vitamin D metabolites in human serum, EDTA-plasma or lithium heparin plasma to be used in the assessment of vitamin D sufficiency using the LIAISON analyzer family.

The ranges are as follows: <25 Deficiency, 25-75 Insufficiency, 75-250 Sufficiency and >250 Toxicity

Statistical Analysis

All data were expressed as mean ± standard deviations (SD). Normality of data distribution was analyzed by the Kolmogorov-Smirnov test. T-test for comparing mean values was used. Fisher exact two-tailed test was used to compare the two groups of patients. Regression analysis was performed to estimate predictive variables for vitamin D levels in diabetics using linear model. P-value < 0.05 was considered to be statistically significant. Data were analyzed using SPSS Version 24.

RESULT

One hundred twenty-seven type 2 diabetic patients were included in the study; 69 (54.3%) were females. Vitamin D deficiency was found in 24 (18.9%) patients. Vitamin D insufficiency was found in 99 (78%) patients and only 4 (3.1%) patients were sufficient. None of the patients was having vitamin D toxicity. In the study, 101 (79.5%) patients were Bahrainis; 21 (16.5%) were deficient; 76 (59.8%) were insufficient and 4 (3.1%) were sufficient. Twenty-six (20.5%) patients were non Bahrainis; 3 (2.4%) were deficient and 23 (18.1%) were insufficient and none was sufficient, see tables 1 to 3 and figure 1.

Table 1: Vitamin D Level among Bahrainis

Bahrainis	101 (79.5%)
Deficiency	21 (16.5%)
Insufficiency	76 (59.8%)
Sufficiency	4 (3.1%)

Table 2: Vitamin D Level among Non-Bahrainis

Non Bahrainis	26 (20.5%)
Deficiency	3 (2.4%)
Insufficiency	23 (18.1%)
Sufficiency	0

Table 3: Vitamin D Level by Nationality

	N	Mean	SE	SD	Lower Value	Upper Value	Skewness	Kurtosis
Bahraini	101	38.537	1.7078	17.16	12.1	94.7	0.95±0.2	0.6±0.5
Non-Bahraini	26	44.900	3.4033	17.35	18.1	74.3	0.45±0.45	-0.76±0.9

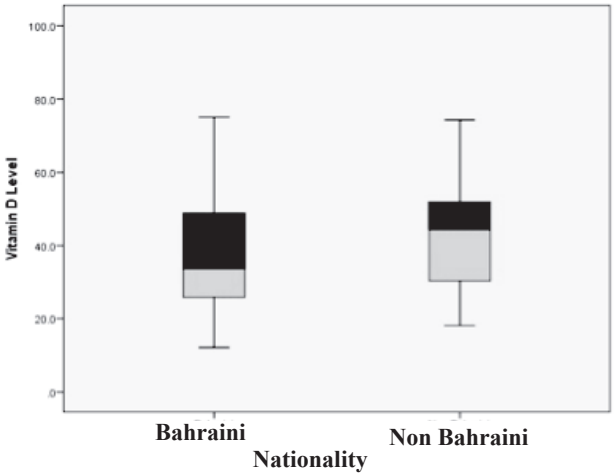

Figure 1: Vitamin D Distributions between Nationalities

Fifty-eight (45.7%) patients were males. Analysis of vitamin D level distribution between genders did not show significant differences, see figure 2. The mean level of vitamin D of males was 40.63±2.15 ng/mL and female was 39.17±2.18 ng/mL. The mean value of vitamin D was higher in male patients. However, the variability of vitamin D values was broader in female patients, see table 4.

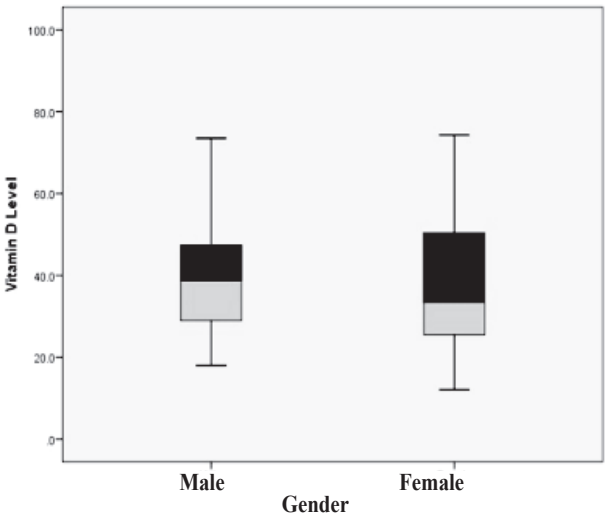

Figure 2: Vitamin D Distributions between Genders

Table 4: Vitamin D Level Distributions among Genders

	Mean	SE	SD	Lower Value	Upper Value	Skewness	Kurtosis
Male	40.633	2.1520	16.39	18	94.7	1.06±0.3	1.4±0.6
Female	39.172	2.1871	18.17	12.1	87.6	0.7±0.3	-0.4±0.6

Vitamin D values and age did not show a significant correlation, see figure 3.

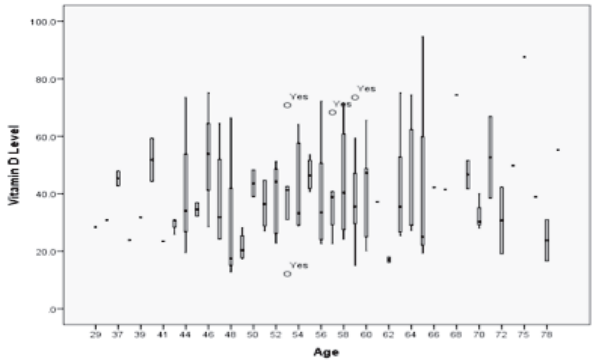

Figure 3: Distribution of Vitamin D Level According to Age

No significant differences shown by Fisher exact two-tailed test between the supplemented group and the non-supplemented in mean, see table 5. However, lower and upper values are a slightly lower in the group with supplementation, see table 5.

Table 5: Vitamin D Level in Supplemented and Non-Supplemented Groups

	N	Mean	SE	SD	Lower Value	Upper Value	Skewness	Kurtosis
Vitamin D Supplemented	55	36.273	2.3614	17.51	12.1	87.6	0.8±0.3	0.09±0.6
Vitamin D Non-Supplemented	72	42.564	1.9793	16.79	19.1	94.7	0.97±0.3	0.3±0.6

Regression analysis was performed for the variables in the study. There is no variable which could have predictive value, see table 6.

Table 6: Linear Regression Model for Vitamin D Levels

Model Summary				
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**
1	.307[a]	.094	.057	16.8262

a. Predictors: (Constant), age, gender, nationality, patient taking other medicines for other comorbidities, patient taking vitamin d supplementation or not

The measurement of vitamin D and the method used was dependable. The result of this study is dependable, reproducible and could be used for the modifications of treatment and management**.**

The mean of vitamin D level in the supplemented group is lower than non-supplemented, which indicates that the supplemented group may not be followed up properly or the treatment given is not effective. No adverse events during the study were encountered.

DISCUSSION

The mean value of vitamin D level is lower in the Bahraini patients with type 2 diabetes compared to other studies[6,9]. The upper limit of vitamin D values was significantly higher in Bahrainis, probably due to dietary vitamin D supplementation. In addition, a study found that vitamin D levels in type 2 diabetes mellitus patients are abnormally distributed which is similar to our study[8].

The Bahraini group did not show any significant difference in the vitamin D levels between gender and age, which is dissimilar with other studies which revealed that vitamin D levels are significantly lower in females, especially in the elderly, which could be explained by the small sample size[6,7].

The only independent variable that has shown a weak correlation with vitamin D level according to the correlation analysis was the supplementation of vitamin D to treat its deficiency, which was logical and expected. What was not expected was the strength of correlation: theoretically, this correlation should be much stronger. However, the efficacy of treatment may depend on many factors including absorption, metabolizing and excretion rate as well as the type of supplement used for the treatment.

Even though we did not find significant differences or correlations between the analyzed variables and the vitamin D level in the blood, it is clear that the search for valuable predictors of hypovitaminosis D is needed due to recent insight on the functional role of this vitamin in the pathophysiology of the disease.

Lower vitamin D values adjusted for body mass index and biochemical parameters predict poorer glycemic control with the odds ratio of 4.86 at 95% confidence interval[10]. These findings are not completely consistent with the other studies[11,12].

Studies revealed an inverse association between vitamin D level and colorectal cancer in type 2 diabetics with the relative risk of 0.62. However, the benefit of vitamin D supplementation is lost when the levels of vitamin D are over the upper limit of the normal range[3].

Serum concentrations of vitamin D in type 2 diabetic patients demonstrated that hypovitaminosis D is associated with lower concentrations of calcium, phosphorus as well as with higher levels of low-density lipids and total cholesterol[13].

Prolonged vitamin D supplementation improved fasting glucose level and insulin resistance in type 2 diabetic patients; the fasting glucose level and insulin resistance index were significantly reduced after exercise regimen and vitamin D supplements[14].

A study of vitamin D supplementation in type 2 diabetics with coronary artery disease showed significant reduction in fasting plasma glucose, serum insulin, insulin resistance, and β cell function[15]. Hypovitaminosis D in diabetic patients was significantly correlated with the female gender, dyslipidemia and obesity[16]. Using multiple linear regression analysis, the

total cholesterol and body mass index were defined as predictors for vitamin D insufficiency in Brazilian population[16].

A study revealed positive correlation and association of vitamin D level with high blood pressure in diabetics; a higher concentration of vitamin D was associated with the elevated systolic blood pressure[17]. Vitamin D level and micronutrients are associated with cardiovascular health of type 2 diabetes mellitus[18].

Vitamin D is an important nutrient influencing multiple cellular functions. There are conflicting scientific reports on the specific phenomena associated with the level of vitamin D.

Bahraini database lacks the statistical data of vitamin D level of diabetic patients whether supplemented or non-supplemented and how effective the treatment of vitamin D deficiency. This study is intended to fill such gap in knowledge. The findings of this study indicate that the treatment of vitamin D deficiency is not effective as we thought it would be.

This study highlights an important fact that a costly treatment given to patients is not achieving its target while it is costing the health service and draining the budget. The study has few limitations: It is a retrospective study, which means no randomization or blinding, data was collected from the medical records where accuracy depends on what has been documented. Another limitation is the small sample size.

This study is very relevant for GCC countries where they are rated among the top ten in the incidence of diabetes. In GCC countries, males and females usually cover themselves from the sun for the protection of their skin; this attitude affects the level of vitamin D since the sun is an important source of vitamin D.

I believe that there should be GCC guidelines for patients with diabetes and vitamin D deficiency.

CONCLUSION

In this study, the level of vitamin D is lower than normal range in diabetic patients. Most Bahrainis were either deficient or insufficient; only four were sufficient. The study sample is small; therefore, it is advisable to perform multicentric prospective randomized controlled trial to assess the level of vitamin D in Diabetic patients and its associated complications.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

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Approval of the Study: Approved by the Research and Ethics Committee, Bahrain Defence Force Hospital, Royal Medical Services, Bahrain.

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