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Vitamin D Deficiency in Saudi Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Vitamin D deficiency and type 2 diabetes mellitus (T2DM) remain major health problems in many parts of the world. We conducted a cross sectional study to investigate the prevalence vitamin D deficiency in patients with T2DM.

Method: A cross-sectional single center study was conducted in 4053 patients with T2DM. Patients with T2DM attended the Diabetes Center at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018 were recruited. The serum concentration of 25(OH)D and HbA1c were measured.

Results: There were 4053 patients with T2DM, 1145 male and 2908 female (28.3% vs. 71.7% respectively. The mean age was 53.9±16.5 years. Vitamin D deficiency (25-OHD < 50 nmol/l) was found in 1916 (47.3%). Moreover, vitamin D deficiency was significantly more prevalent among females than males with male to female ratio 1:2.0 (66.8% vs. 33.2% respectively, p<0.0001). In addition, Vitamin D deficient patients were statistically significant younger than non-vitamin D deficient (50.3±16.2 vs. 57.2±16.0 respectively, p<0.0001). Vitamin D deficient patients have statistically significant higher HbA1c than non-vitamin D deficient (8.0±2 vs. 7.4±1.8 respectively, p<0.0001).

The mean 25-OHD was upward as age advanced with highest frequency of vitamin D deficiency was found in the fourth and sixth decades with males statistically significant most frequent than females in the third, fifth to eighth decades. 25-OHD concentration was significantly positively correlated with age (r=0.187, p<0.0001) and significantly negatively correlated with HbA1c (r= - 0.161, p<0.0001). Regression analysis of odd ratio of risk factors for patients with vitamin D deficiency showed that female gender, age and HbA1c were statistically significant associated with vitamin D deficiency.

Conclusion: The prevalence of vitamin D deficiency in patients with T2DM is high and that more females with T2DM are affected with vitamin D deficiency than males.

Keywords: Type 2 diabetes mellitus; Vitamin D deficiency

Abbreviations: T2DM: Type 2 Diabetes Mellitus; OR: Odds Ratio.

Introduction

Vitamin D deficiency remains a major health problem in many parts of the world [1]. Vitamin D affects various

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tissues besides bones, sun exposure and vitamin D intake determines its concentration [2]. The main marker of vitamin D status is the metabolite 25-hydroxyvitamin D (25(OH)D), which is synthesized in the liver [1,3]. Hypovitaminosis D is defined as serum 25(OH) D concentration <50 nmol/L [4,5]. Current studies confirm that the prevalence of vitamin D deficiency in the general world population is actually as high as 50-80%, even occurring in countries located in geographical areas which receive sunshine year-round [6]. The Middle East and the North African region in general including Saudi Arabia have very high prevalence of hypovitaminosis D even in the normal asymptomatic population [7-9].

The prevalence of type 2 diabetes mellitus (T2DM) in Saudi Arabia is one of the highest reported in the world, reaching up to 30% in a recent study [10]. It has been demonstrated that vitamin D deficiency is associated with T2DM [11-19]. It has been reported that insulin secretion is dependent upon vitamin D and there is a positive correlation of vitamin D concentration with insulin sensitivity [20-25]. The prevalence of vitamin D deficiency in patients with T2DM varies from 70 to 90%, depending on the threshold used to define vitamin D deficiency [26-28]. Few published researches have been found that surveyed the prevalence of vitamin D deficiency in patients with T2DM in Saudi Arabia [29]. We conducted a cross sectional study to investigate the prevalence vitamin D deficiency in patients with T2DM.

Methods

A cross-sectional single center study was conducted in 4053 patients with T2DM. Patients with T2DM attending the Diabetes Center at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018 were recruited. Eligible patients were 20 years or older. Exclusion criteria were known hepatic or renal disease, metabolic bone disease, mal-absorption, hypercortisolism, malignancy, immobility for more than one-week, pregnancy, lactation, and medications influencing bone metabolism. The serum concentration of 25(OH) D was measured by competitive protein binding assay using kits (Immunodiagnostic, Bensheim, Germany). Vitamin D deficiency was defined as serum 25-OHD concentration < 50 nmol/L [1]. Glycosylated hemoglobin (HbA1c) was measured by the high performance liquid chromatography method (Bio-Rad Laboratories, Waters, MA, USA). The total number of cohort was separated on basis of age values into six groups: 20-29 years, 30-40 years, 40-49 years, 50-59 years, 60-70 years and ≥70 years. The study was approved by the ethical committee board of King Fahad Armed Forces Hospital.

Statistical Analysis

Data are presented as means ± standard deviation (SD) or numbers (%). Quantitative variables were compared between two groups by using the Student's test. Differences in categorical variables were analyzed using the chi-square test. The relationship between continuous variables was assessed using coefficients of correlation. Logistic regression analysis was carried out to identify the independent predictors of vitamin D deficiency considering age, gender and HbA1c as risk factors and to estimate odds ratio (OR) and 95% CI. P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

There were 4053 patients with T2DM, 1145 male and 2908 female (28.3% vs. 71.7% respectively) (Table 1). The mean age was 53.9±16.5 years. The mean and median 25-OHD concentrations were 57.8±30.5 and 51.9 respectively. Vitamin D deficiency (25-OHD < 50 nmol/l) was found in 1916 (47.3%) (Table 2). Moreover, vitamin D deficiency was significantly more prevalent among females than males with male to female ratio 1:2.0 (66.8% vs. 33.2% respectively, p<0.0001). In addition, Vitamin D deficient patients were statistically significant younger than non-vitamin D deficient (50.3±16.2 vs. 57.2±16.0 respectively, p<0.0001). Vitamin D deficient patients have statistically significant higher HbA1c than non-vitamin D deficient (8.0±2 vs. 7.4±1.8 respectively, p<0.0001). As expected, the mean 25-OHD concentration was statistically significant lower in the vitamin D deficient patients compared to non-vitamin D deficient (34.2±9.7 vs. 78.9±27.3 respectively, p<0.0001).

Variable		Values
Total		4053
Age (years)		53.9 ±16.5
Gender	Male	1145 (28.3)
	Female	2908 (71.7)
HbA1c (%)		7.7 ±1.9
25-hydroxyvitamin D (nmol/L)		57.8 ±30.5

Table 1: Patient characteristics [mean ± standard deviation or number (%)].

Variable		Vitamin D Deficiency		P values
		Present	Absent	
Numbers		1916 (47.3)	2137 (52.7)	<0.0001
Age (years)		50.3 ± 16.2	57.2 ±16.0	
Gender	Male	637 (33.2)	508 (23.8)	<0.0001
	Female	1279 (66.8)	1629 (76.2)	
HbA1c (%)		8.0 ±2.1	7.4 ±1.8	<0.0001
25-hydroxyvitamin D (nmol/L)		34.2 ±9.7	78.9 ±27.3	<0.0001

Table 2: Vitamin D deficiency among Type 2 diabetes mellitus patients [mean ± standard deviation or number (%)].

The mean 25-OHD was upward as age advanced with highest frequency of vitamin D deficiency was found in the fourth and sixth decades (Figure 1 A and B) with males statistically significant most frequent than females in the third, fifth to eighth decades (Figure 2).

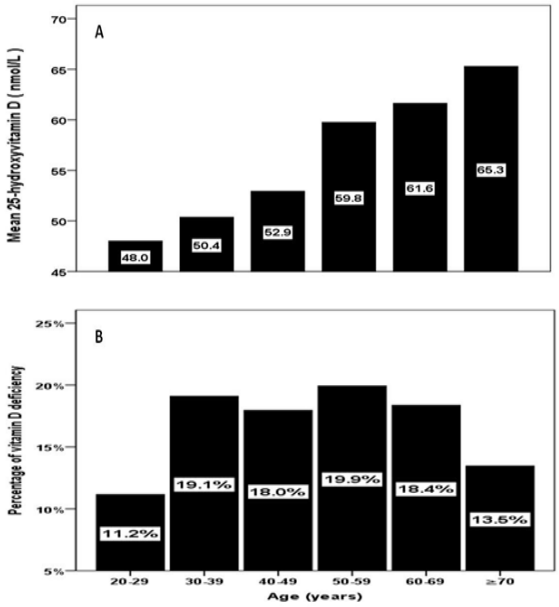

Figure 1: The mean of vitamin D concentration (nmol/l) (A) and the percentage of vitamin D deficiency (B) in correlation to age groups.

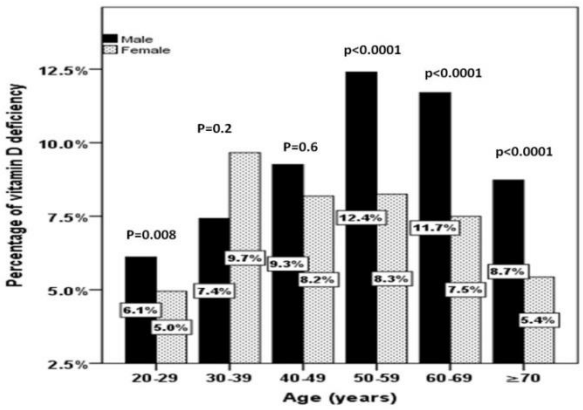

Figure 2: The percentage of vitamin D deficiency according to gender in correlation to age groups.

25-OHD concentration was significantly positively correlated with age (r=0.187, p<0.0001) and significantly negatively correlated with HbA1c (r= - 0.161, p<0.0001) (Figure 3 A and B). Regression analysis of odd ratio of risk factors for patients with vitamin D deficiency showed that female gender, age and HbA1c were statistically significant associated with vitamin D deficiency, (OR=1.579; 95% confidence interval [CI]=1.347, 1.878), p<0.0001), (OR=0.971; 95% CI=0.966, 0.977), p<0.0001) and (OR=1.206; 95% CI=1.153, 1.261, p<0.0001) respectively (Table 3).

Parameters	Odd Ratio (95% CI)	P value
Female gender	1.579 (1.347-1.878)	<0.0001
Age (years)	0.971 (0.966-0.977)	<0.0001
HbA1c	1.206 (1.153-1.261)	<0.0001

Table 3: Regression analysis for odd ratio of risk factors for patients with vitamin D deficiency.

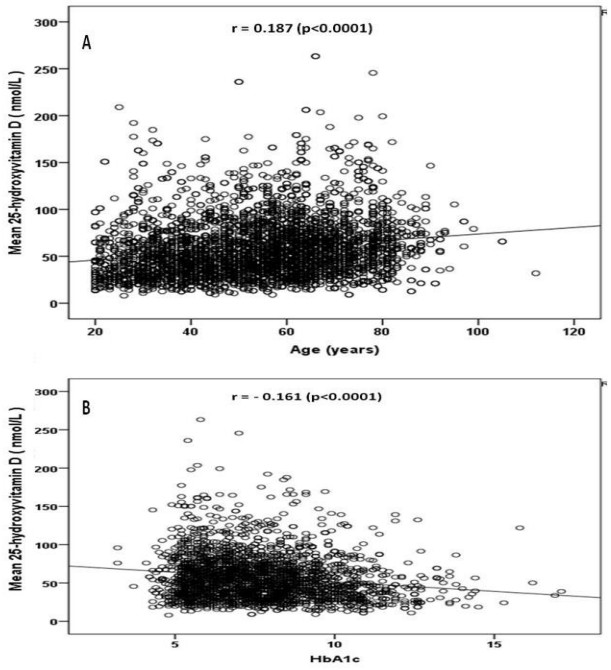

Figure 3: Correlation of 25-hydroxyvitamin D concentration and age (A) and HbA1c (B) in the study population.

Discussion

Diabetes mellitus is currently the most prevalent chronic illness in the world having a prevalence of around 9% in the adult population and 30% of Saudi adults [10,30]. Moreover, vitamin D deficiency is a worldwide epidemic. According to World Health Organization statistics, around one billion people are suffering from VD deficiency throughout the world even in the sunniest areas; vitamin D deficiency is common when most of the skin is shielded from the sun. Studies in Saudi Arabia, the United Arab Emirates, Australia, Turkey, India, and Lebanon, 30 to 50% of children and adults had 25-hydroxyvitamin D levels under 50 nmol/L [1,31-34]. Vitamin D deficiency has received special attention lately because of its high incidence and its implication in the genesis of multiple chronic illnesses. A most important finding in our study is that the frequency of vitamin D deficiency (47%) was higher among T2DM subjects in Saudis residing in Jeddah. It is of importance to state that the sample size is representative for a number of subjects suffering from T2DM in the area and study population of one institution does not represent the entire city of Jeddah, in addition the study sample confined to patients with T2DM but without comparable groups.

Vitamin D deficiency was observed in a half proportion (47%) of our study population with a mean vitamin D3 level of 34 nmol/l. This finding is lower than other study (83%) conducted in Saudi Arabia [29]. This finding is also corroborated by other studies in the region [35-39]. The causes of vitamin D deficiency could be due to changing life style with people adopting a more sedentary life, little exposure to sunlight, reduced outdoor activity and changes in dietary habits. These factors also contribute to both development of T2DM and poor control of diabetes.

The majority of our female patients (66.8%) were vitamin D deficient while (33.2%) of male patients. Earlier study in Saudi Arabia showed female patients (73.6%) were vitamin D deficient while (46.9%) of male patients. Other found no significant difference in vitamin D status of males and female [40]. Our result could be attributed to less sun exposure in female patients relative to male patients in our community. Vitamin D deficiency was reported as quite common in young, normal Saudi adults in 1981 [32]. Back then however, vitamin D deficiency was more common among the elderly in consistent to the findings in our study, in which serum 25(OH)D was strongly correlated with age, that is similar to the findings of Hashemipour et al. in a cohort of 1210 Iranians adult [41]. The strong correlation of 25(OH)D to age is also in agreement with a study carried out in the US, where severe hypovitaminosis D was found to be more common among the young, and less common among the elderly [42]. We found vitamin D deficient patients (8.0±2) have statistically significant higher HbA1c than non-vitamin D deficient (7.4±1.8), $p<0.0001$. Moreover, 25-OHD concentration was inversely correlated with HbA1c ($r= -0.161$, $p<0.0001$).

These findings are supported by a number of international studies. In contrast some studies show no association of a low vitamin D with HbA1c levels [43]. But inverse correlation between the level of vitamin D and glucose level is well known [44-46]. In many studies vitamin D levels were low in subjects having higher HbA1c values in patients with T2DM indicating that they are inversely related [18,27,47]. Vitamin D has various effects on glucose homeostasis. Besides its role in insulin secretion, it also has an influence on insulin resistance directly or via Ca indirectly [23,48]. Changes in Ca in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction, leading to decreased glucose transporter-4 activity [25]. The association between low vitamin D level and insulin sensitivity have been reported in cross-sectional and observational studies. The results from the trials on the effect of vitamin D and/or Ca supplementation on insulin resistance have showed improvement on insulin action [49]. We had several

limitations. Study was done at only one Center and was done at one point of time. The study sample confined to patients with T2DM but without comparable groups.

Conclusion

The prevalence of vitamin D deficiency in patients with T2DM is high and that more females with T2DM are affected with vitamin D deficiency than males. We recommend larger scale studies for detecting vitamin D deficiency in our population with T2DM and suggest planning strategies to supplement our population with vitamin D.

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