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Study of Vitamin D Status and its Correlation with Glycated Haemoglobin in Type 2 Diabetes Mellitus

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Abstract

Introduction: Few published researches have surveyed the correlation between Vitamin D status and glycaemic control in type 2 diabetes mellitus (T2DM). The present study was conducted to investigate the status of vitamin D and its correlation with glycated haemoglobin in type 2 diabetes mellitus.

Method: A cross-sectional single centre study was conducted in 2440 patients with T2DM attending the Diabetes Centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018. Eligible patients were 20 years or older.

Results: There were 2440 patients with T2DM. Vitamin D deficiency (25-OHD<50 nmol/l) was found 47.5%. Patients with HbA1c<7% were younger than patients with HbA1c 7%-9% and >9% (55.3 ± 16.0 vs. 58.4 ± 15.2 vs. 57.1 ± 15.4 respectively, p<0.0001). The mean 25-OHD concentration was statistically significant lower in patients with Hba1c>9% compared to patients with Hba1c<7% and 7%-9% (49.7 ± 27.0 vs. 61.8 ± 31.4 vs. 56.9 ± 28.8 respectively, p<0.0001). The frequency of vitamin D deficiency was statistically significant higher in patients with Hba1c>9% compared to patients with Hba1c<7% and 7%-9% (40% vs. 48% vs. 61% respectively, p<0.0001). The frequency of vitamin D deficiency was upward across HbA1c groups as age advanced with highest frequency of vitamin D deficiency was found to be statistically significant in HbA1c>9% compared to HbA1c< and 7%-9% groups in the age group 50-59 years and ≥60 years with males most frequently predominant than females in all age group associated with HbA1c 7%-9% and 9%. HbA1c was significantly positively correlated with age whereas 25-OHD concentration was significantly negatively correlated with age.

Conclusions: We report vitamin D deficiency and its inverse association with Glycated Haemoglobin in type 2 Diabetes Mellitus.

Keywords: Type 2 Diabetes mellitus, Glycated haemoglobin and Vitamin D status

Introduction

Type 2 Diabetes Mellitus (T2DM) is a major health concern globally. The total number of Diabetics is expected to reach 366 million by 2030 [1]. The prevalence of T2DM in Saudi Arabia is one of the highest reported in the world, reaching up to 30% [2]. Vitamin D deficiency remains a major health problem in many parts of the world [3]. The main marker of vitamin D status is the metabolite 25-hydroxyvitamin D (25(OH)D) [4,5] It is now increasingly recognized that vitamin D deficiency is defined as serum 25(OH)D concentration <50 nmol/L [5].

The prevalence of vitamin D deficiency in the general world population including Saudi Arabia is as high as 50-80% [6-9]. Evidence suggests a link between vitamin D deficiency and T2DM [10-15]. 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 [16,17]. It has been postulated that vitamin D has an influence on glycemic control [18]. Pancreatic beta cell function may be affected by the existence of specific vitamin D receptors in the beta cells [19]. Additionally, vitamin D is essential for pancreatic β cells insulin secretion regulation and calcium absorption [20]. It is thought that vitamin D stimulates glucose transport and preventing systemic inflammation [21,22].

Few published researches have surveyed the prevalence of vitamin D deficiency in Saudi patients with T2DM and the correlation between Vitamin D status and glycemic control [23]. Hence the present study was conducted to investigate the status of vitamin D and its correlation with glycated haemoglobin in type 2 diabetes mellitus.

Methods

A cross-sectional single centre study was conducted in 2440 patients with T2DM attending the Diabetes Centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018. Eligible patients were 20 years or older. Exclusion criteria were known hepatic or renal disease, metabolic bone disease, malabsorption, 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. Glycosylated hemoglobin (HbA1c) was measured by the high performance liquid chromatography method

(Bio-Rad Laboratories, Waters, MA, USA). The total numbers of cohort were separated on basis of age values into five groups: 20-29 years, 30-40 years, 40-49 years, 50-59 years and ≥60 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 analysed using the chi-square test. The relationship between continuous variables was assessed using coefficients of correlation. P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

There were 2440 patients with T2DM, 875 male and 1565 female (35.9% vs. 64.1% respectively) **(Table 1)**. The mean age was 56.8± 15.6 years. The mean and median 25-OHD concentrations were 57.2± 29.9 and 51.7 respectively. Vitamin D deficiency (25-OHD<50 nmol/l) was found in 1160 (47.5%). The mean and median HbA1c were 7.7± 1.9 and 7.5 respectively.

Patients with HbA1c<7% were younger than patients with HbA1c 7%-9% and >9% (55.3± 16.0 vs. 58.4 ± 15.2 vs. 57.1 ± 15.4 respectively, p<0.0001) **(Table 2)**. Females were statistically significant more frequent across all HbA1c groups.

The mean 25-OHD concentration was statistically significant lower in patients with Hba1c>9% compared to patients with Hba1c<7% and 7%-9% (49.7± 27.0 vs. 61.8± 31.4 vs. 56.9± 28.8 respectively, p<0.0001). The frequency of vitamin D deficiency was statistically significant higher in patients with Hba1c>9% compared to patients with Hba1c<7% and 7%-9% (40% vs. 48% vs. 61% respectively, p<0.0001).

Variable		Values
Total		2440
Age (years)		56.8 ± 15.6
Gender	Male	875 (35.9)
	Female	1565 (64.1)
HbA1c (%)		7.7 ± 1.9
25-hydroxyvitamin D (nmol/L)		57.2 ± 29.9
Vitamin D deficiency		1160 (47.5)

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

Variable		HbA1c			P values
		<7	7-9	>9	
Numbers		983 (40.3)	897 (36.8)	560 (23.0)	
Age (years)		55.3± 16.0	58.4± 15.2	57.1± 15.4	<0.0001
Gender	Male	279 (28.4)	357 (39.8)	239 (42.7)	<0.0001
	Female	704 (71.6)	540 (60.2)	321 (57.3)	
HbA1c (%)		5.9± 0.6	7.9± 0.6	10.5± 1.3	<0.0001
25-hydroxyvitamin D (nmol/L)		61.8± 31.4	56.9± 28.8	49.7± 27.0	<0.0001
Vitamin D deficiency		(39.5) 388	(47.7) 428	344 (61.4)	<0.0001

Table 2: HbA1c levels among type 2 diabetes mellitus patients (mean± standard deviation or number (%)).

The frequency of vitamin D deficiency was upward as age advanced **(Figure 1)**. The frequency of vitamin D deficiency was upward across HbA1c groups as age advanced with highest frequency of vitamin D deficiency was found to be statistically significant in HbA1c>9% compared to HbA1c< and 7%-9% groups in the age group 50-59 years and ≥ 60 years **(Figure 2)** with males most frequently predominant than females in all age group associated with HbA1c 7%-9% and 9% **(Figure 3)**. HbA1c was significantly positively correlated with age (r= 0.055, p=0.007) **(Figure 4)** whereas 25-OHD concentration was significantly negatively correlated with age (r=-0.161, p<0.0001) **(Figure 5)**.

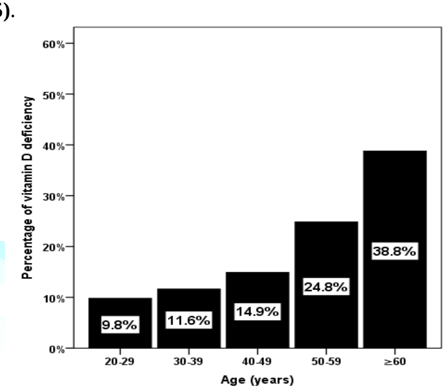

Figure 1: The percentage of vitamin D deficiency in relation to age groups.

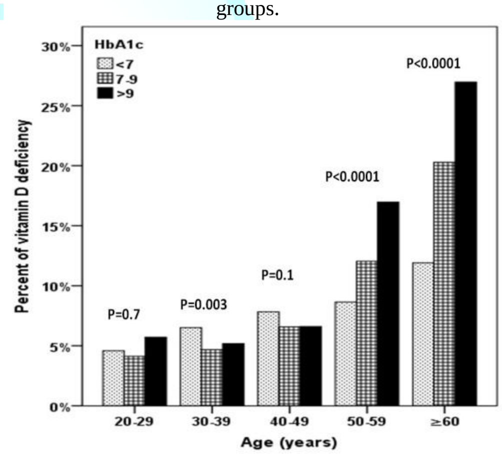

Figure 2: The percentage of vitamin D deficiency in relation to HbA1c in correlation to age groups.

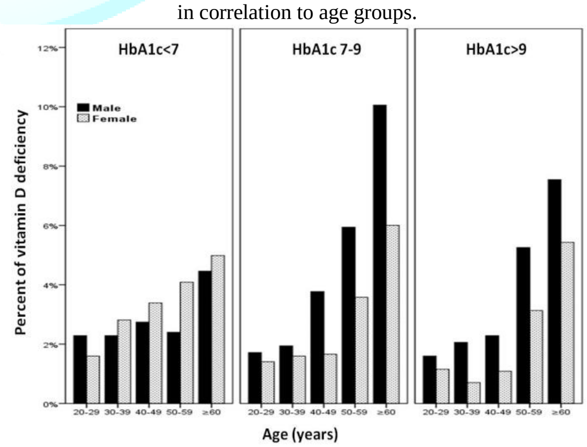

Figure 3: The percentage of vitamin D deficiency in relation to HbA1c in correlation to gender and age groups.

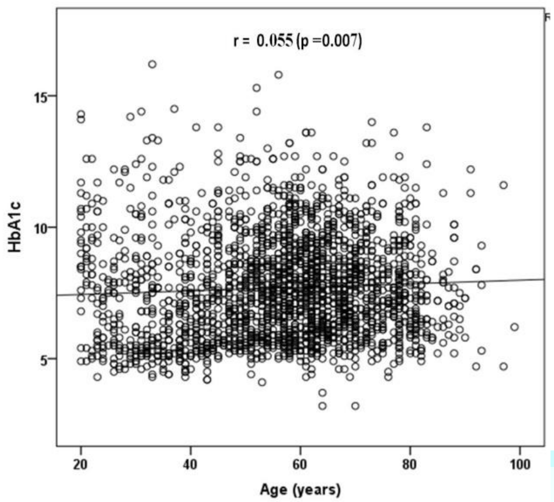

Figure 4: Scatter plot indicating negative correlation between HBA1C levels witt age.

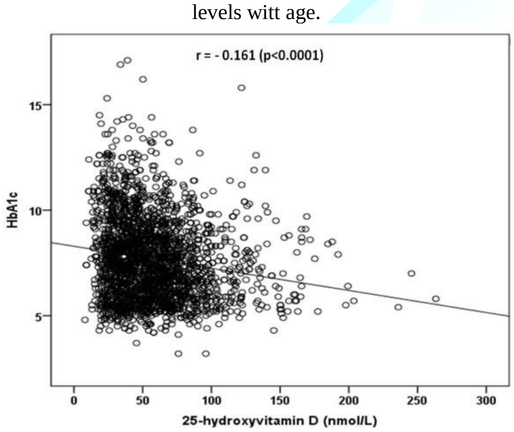

Figure 5: Scatter plot indicating negative correlation between HBA1C levels with Vitamin D levels.

Discussion

Diabetes mellitus is currently the most prevalent chronic illness in the world having a prevalence of around 9% in the adult population amd 30% in Saudi Arabia [2,24]. Vitamin D deficiency plays an important role in development of T2DM [25] We detected a significant negative correlation between plasma vitamin D and each of HbA1c levels in all studied groups in harmony with others [26-29]. 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.

In our study around 48% of the subjects were vitamin D deficient with a mean 25-OHD level of 57 nmol/l. Bashir et al reported that 81% of the studied subjects were vitamin D deficient with a mean 25-OHD level of 39nmol/l [30]. 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, changes in dietary habits, carbohydrate and saturated fat enhanced diet. These factors also contribute to both development of T2DM and poor control of diabetes.

Vitamin D deficiency has received special attention lately because of its high incidence and its implication in the genesis of multiple chronic illnesses. The high prevalence of vitamin D deficiency in our study population underlines the fact that vitamin D deficiency is more common in chronic diseases like diabetes mellitus. Our study showed that vitamin D was inadequate in a half of our population of patients with T2DM. Lower vitamin D levels were associated with a poor glycemic control. This was more strongly associated with HbA1c ($p<0.0001$). The study indicates a poor glycemic control (>9%) in a majority (61%) of patients compared to 40% patients with good glycemic control (7%). In patients having HbA1c greater than 7.0 vitamin D deficiency was significantly greater (67%) compared to 33% patients with good glycemic control (HbA1c<7) $p<0.0001$.There was a stronger co-relation between HbA1c levels and serum 25-OHD levels. These findings are supported by a number of international studies. Some studies showed no association of a low 25-OHD levels with HbA1c levels.30 But inverse correlation between the level of 25-OHD and HbA1c is well known [31,32]. In many studies 25-OHD levels were low in subjects having higher HbA1c values both in patients with diabetes mellitus indicating that they are inversely related [14,16,34-36].

In our study, the prevalence of vitamin D deficiency was much higher among the older age-group (39%), whereas serum 25(OH)D was statistically significant positively correlated with age r=0.193 ($p<0.0001$), in consistent with most studies whereas other studies reported the higher prevalence of vitamin D deficiency among the young people [37-42]. The positive correlation of 25(OH)D to age is in disagreement with a study carried out in the US, where severe vitamin D deficiency was found to be more common among the young, and less common among the elderly [43].

Growing scientific evidence has implicated vitamin D deficiency in a multitude of chronic conditions including T2DM [41]. With the growing prevalence of vitamin D deficiency across Saudi Arabia and its association with these leading causes of mortality, it has become more important than ever to delineate vitamin D's role in the pathogenesis of these diseases and use data to pinpoint established risk factors for vitamin D deficiency. The relationship between vitamin D deficiency and diabetes has long been explored, with growing evidence suggesting vitamin D deficiency is a contributing factor to the development of T2DM [40]. We had several limitations the study was done at one centre and was done at one point of time. The study sample confined to patients with T2DM but without comparable groups. We conclude that vitamin D deficiency and its inverse association with Glycated Haemoglobin in type 2 Diabetes Mellitus have been established in many studies. Such a finding was demonstrated in the present study. An interesting avenue in this aspect would be to see if supplementing with vitamin D can help improve glycemic control in diabetic population.

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