

## Is Vitamin D Level Associated with Glycemic Control in Patients with Type-2 Diabetes Mellitus: An Experience from Taif City, Kingdom of Saudi Arabia

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### ABSTRACT

**Background:** Few Saudi studies have been carried out showed that vitamin D deficiency is significantly associated with diabetes mellitus. However, up to our knowledge, no previous community based studies have been conducted in Taif, (KSA) addressing the association between two health problems.

**Objectives:** To investigate the association between vitamin D level and diabetes control among type 2 diabetic patients in Taif Region, Saudi Arabia.

**Subjects and Methods:** A cross-sectional study was conducted at Family Medicine outpatient clinics at Al-Hada Armed Forces hospitals, Taif, Kingdom of Saudi Arabia. It included all adult type 2 diabetic patients attending outpatient clinics throughout the study period (January, 2018). Data were collected using a checklist including items of age, gender, vitamin D level (ng/mL) and glycated haemoglobin percentage.

**Results:** The study included 155 patients. Their age ranged between 18 and 91 years with a mean±SD of 52.6±14.1 years. Females represent 78.7% of them. Vitamin D level ranged between 6 and 101 ng/mL with a mean±SD of 25.2±12.2 ng/mL whereas hbA1c (%) ranged between 3.7 and 15.5% with a mean±SD of 6.2±1.6%. There was negative not significant

correlation between vitamin D level and glycated hemoglobin Percent; overall and according to age and gender distribution.

**Conclusion:** No association was observed between vitamin D level and glycated hemoglobin among our type 2 diabetic patients. However, further study is recommended including more representatives, enough sample from different institutions in Taif Region, Saudi Arabia.

**Keywords:** Vitamin D, Glycated Hemoglobin, Correlation, Saudi Arabia.


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### INTRODUCTION

Vitamin D deficiency is associated with a decreased insulin release, insulin resistance and type 2 diabetes in experimental and epidemiological studies.<sup>1</sup> Numerous studies documented that vitamin D deficiency is related to the development of diabetes mellitus type 2.<sup>2-6</sup> In addition, Pittas et al. 2007 observed that mild to moderate vitamin D insufficiency has been found to be a risk factor for type 2 diabetes.<sup>7</sup> Furthermore, in high risk patients, higher plasma vitamin D has been proved to be associated with a lower risk for the development of diabetes mellitus.<sup>8</sup>

Vitamin D deficiency has been reported in the metabolic syndrome<sup>9</sup>, specific vitamin D receptor gene polymorphisms having been found to be a component of the metabolic syndrome.<sup>10</sup> Also, vitamin D appears to affect glucose homeostasis, vitamin D levels having been reported to be inversely related to glycosylated hemoglobin levels in gestational diabetes mellitus.<sup>11</sup>

Few Saudi studies have been carried out in Southern Region<sup>12</sup>, and Arar<sup>13</sup> showed that vitamin D deficiency is significantly associated with diabetes mellitus. However, up to our knowledge, no previous community based studies have been conducted in Taif, (KSA) addressing the association between two health problems. Therefore, this study was carried out to investigate the association between vitamin D level and diabetes control among type 2 diabetic patients in Taif Region, Saudi Arabia.

### SUBJECTS AND METHODS

A cross-sectional study was conducted at Family Medicine outpatient clinics (n=6) at Al-Hada Armed Forces hospitals, Taif, Kingdom of Saudi Arabia. It included all adult type 2 diabetic patients attending outpatient clinics throughout the study period (January, 2018).

The minimum sample size for this study has been decided according to Swinscow, as follows:

$$n = \frac{Z^2 \times P \times Q}{D^2}$$

Where: n: Calculated sample size

Z: The z-value for the selected level of confidence (1- α) = 1.96.

P: An estimated prevalence of of vitamin D deficiency in type 2 diabetic patients assumed as 76.7% according to a recent Saudi study<sup>12</sup>.

Q: (1 – 0.77) =23%, i.e., 0.23

D: The maximum acceptable error = 0.05.

So, the calculated minimum sample size was:

$$n = \frac{(1.96)^2 \times 0.77 \times 0.23}{(0.05)^2} = 272$$

All eligible type 2 diabetic patients attending Family Medicine outpatient at Al-Hada Armed Forces hospitals in Taif Starting from 1<sup>st</sup> January, 2018 were invited to participate in the study till the minimum requires sample size reached.

Data were collected using a checklist including items of age, gender, vitamin D level (ng/mL) and glycated haemoglobin percentage. Vitamin D level (recent) and glycated haemoglobin (within the last three months) were recorded for each type 2 DM patient of at least one year history of the disease, visiting Family Medicine clinics.

Permission from the regional Research and Ethics Committee at Al-Hada Armed Forces hospital was obtained. Also, permission from the medical director and head of Family Medicine department at Al-Hada Armed Forces hospital was obtained. A verbal consent was obtained from each patient.

Collected data were entered into an own computer and were analyzed using the SPSS version 23 with a significance of p-value < 0.05. Data were presented in the form of frequency and percentage. Continuous variables were presented by mean and standard deviation. Sperman`s correlation test was used to test for the correlation between vitamin D and glycated haemoglobin variables, since the data were abnormally distributed as evidenced by significant K-S test, p<0.001.

**Table 1: General characteristics of the study population (n=155)**

	Number	%
<b>Age (years)</b>		
<60	108	69.7
≥60	47	30.3
Range	18-91	
Mean±SD	52.6±14.1	
<b>Gender</b>		
Male	33	21.3
Female	122	78.7
<b>Vitamin D (ng/mL)</b>		
Range	6-101	
Mean±SD	25.2±12.2	
<b>HBA1c (%)</b>		
Range	3.70-15.50	
Mean±SD	6.2±1.6	

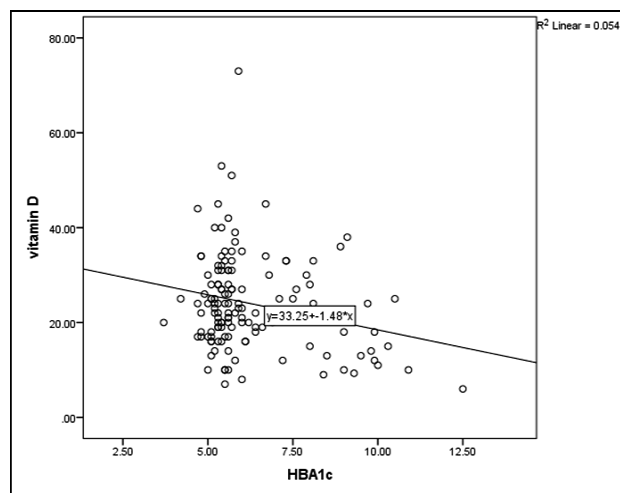
**Table 2: Spearman correlation coefficient between vitamin D level and glycated hemoglobin, overall and according to age and gender distribution**

	r*	p
<b>Overall</b>	-0.126	0.148
<b>Males</b>	-0.162	0.402
<b>Females</b>	-0.080	0.416
<b>&lt;60 years</b>	-0.083	0.441
<b>≥60 years</b>	-0.246	0.104

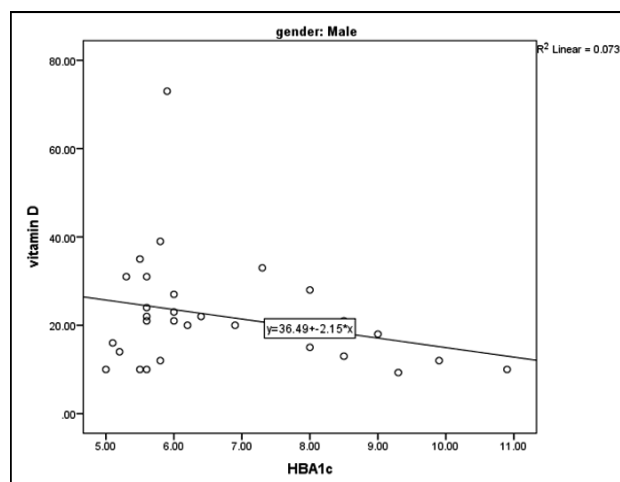
\* Correlation coefficient

**RESULTS**

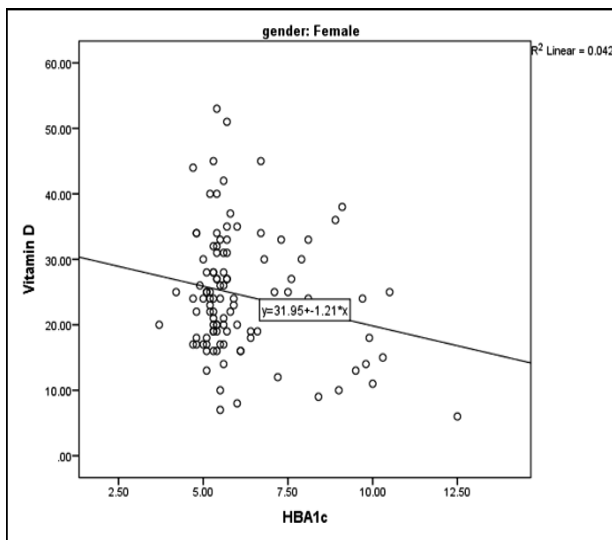
The study included 155 patients. Their age ranged between 18 and 91 years with a mean±SD of 52.6±14.1 years. Females represent 78.7% of them. Vitamin D level ranged between 6 and 101 ng/mL with a mean±SD of 25.2±12.2 ng/mL whereas hbA1c (%) ranged between 3.7 and 15.5% with a mean±SD of 6.2±1.6%. (Table 1) As demonstrated from table 2 and figures1-5, there was negative not significant correlation between vitamin D level and glycated hemoglobin Percent; overall and according to age and gender distribution.



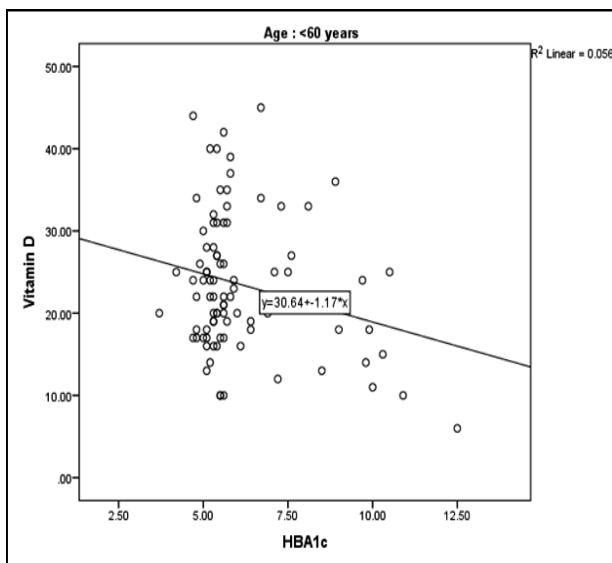
**Figure 1: Correlation between vitamin D level and glycated hemoglobin percent among type 2 diabetic patients.**



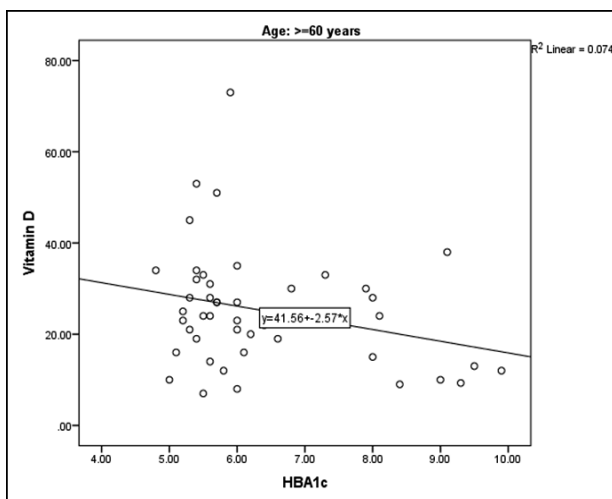
**Figure 2: Correlation between vitamin D level and glycated hemoglobin percent among male type 2 diabetic patients.**



**Figure 3: Correlation between vitamin D level and glycated hemoglobin percent among female type 2 diabetic patients.**



**Figure 4: Correlation between vitamin D level and glycated hemoglobin percent among type 2 diabetic patients aged below 60 years.**



**Figure 5: Correlation between vitamin D level and glycated hemoglobin percent among type 2 diabetic patients aged 60 years or more.**

**DISCUSSION**

Type-2 diabetes mellitus and Vitamin D deficiency are both common among Saudi Arabian population.<sup>12,13</sup> Despite of that, few studies investigated the association between the two health problems. In this study, we intended to correlate the level of vitamin D with glycated hemoglobin percentage among a sample of type 2 diabetic patients. The study revealed negative not significant correlation between vitamin D level and glycated hemoglobin percentage among those patients.

In Southern Region, Saudi Arabia a study was carried out to estimate 25-OH vitamin D deficiency in patients with type-2 diabetes mellitus in comparison to normal age-matched non-diabetic control population. It was found that, the mean serum 25-OH vitamin D levels in the diabetic group were  $15.7 \pm 7.5$  ng/mL as compared healthy non-diabetic group having  $11.1 \pm 5.9$  ng/mL and a total of 340 patients (98.5%) from both groups were found to be deficient in 25-OH vitamin D.<sup>12</sup> Recently (2017), Abo el-Fetoh et al carried out a cross-sectional study to address the prevalence of vitamin D deficiency and its possible association with DM in Arar, KSA. Vitamin D deficiency (lower than 12 ng/ml) has been reported among 24.8% of the participants whereas insufficient level (12-20 ng/ml) was observed among 4.6% of them. Diabetes mellitus was more significantly prevalent among cases of vitamin D deficiency than those of normal level (16.3% versus 10.3%).<sup>13</sup>

Regarding overseas studies, Kostoglou-Athanassiou et al (2013) carried out a case-control study aimed to study levels of 25-hydroxy vitamin D3 [25(OH)D3] and the relationship between 25(OH)D3 levels and glycemic control in patients with diabetes mellitus type 2. The results showed that 25(OH)D3 levels were lower in the diabetes mellitus type 2 patients than in the control group, being  $19.26 \pm 0.95$  ng/ml and  $25.49 \pm 1.02$  ng/ml, in the patient and control groups, respectively,  $p < 0.001$ . 25(OH)D3 levels were found to be inversely associated with HbA1c levels in the diabetic patients,  $p = 0.008$ . 25(OH)D3 levels were found to be inversely associated with HbA1c when the patient and control groups were analysed together,  $p < 0.001$ .<sup>6</sup> Perez-Diaz et al (2015) reviewed the charts of a sample of postmenopausal women diagnosed with T2DM to determine the relationship between 25 (OH) D3 levels, glycemic control, bone mineral density (BMD), and the development of osteoporotic fractures among them. They found that in the group of patients with poorly controlled T2DM, 25 (OH) D3 levels were not significantly lower in comparison with the optimal control group ( $19.29 \pm 7.70$  versus  $17.26 \pm 6.93$ ). Also, no statistically significant linear relationship between HbA1c and 25 (OH) D3 levels was detected. The group with optimal glycemic control had an increased number of osteoporotic fractures events,  $p = 0.04$ .<sup>14</sup> In Spain, Calvo-Romero and Ramiro-Lozano studied serum levels of 25-hydroxyvitamin D (25(OH)D) and associated characteristics in 130 type 2 diabetic patients. Almost two thirds of patients (69.9%) had serum levels of 25(OH)D lower than 20 ng/mL. There was inverse correlation between serum levels of 25(OH)D and glycosylated hemoglobin ( $r = -0.74$ ,  $P = 0.01$ ).<sup>15</sup> In India, Kumar et al evaluated in a case-control study the correlation between Vitamin D status and Glycated Haemoglobin in Type 2 Diabetes Mellitus. The mean Vitamin D values in cases were 16.1 ng/ml and mean Vitamin D values in controls were 17.3 ng/ml. There was no significant difference between the mean values of Vitamin D in cases and

controls. Vitamin D insufficiency was observed in both cases and controls. No statistically significant correlation was observed between vitamin D levels and Glycated haemoglobin (in patients of Type 2 Diabetes Mellitus).<sup>17</sup>

In Italy, Zoppini et al carried out a cross-sectional study to test for correlation between A1C and 25(OH)D in a well characterized cohort of type 2 diabetic patients. Serum 25(OH)D levels were inversely associated with A1C levels ( $r=-0.116$ ,  $p=.003$ ). This relation maintains its independence after adjusting for other co-factors<sup>17</sup>. In another Indian study, Sur and Priya carried out a case-control study to find out the degree of association between glycemic status and vitamin D levels in type 2 Diabetes Mellitus patients in a tertiary care center. Controls were healthy subjects. Vitamin D showed a significant negative correlation in cases and vitamin D levels were decreased in cases as compared to controls.<sup>18</sup>

Among important limitations of the present study is the inclusion of patients from only one health institution and relatively small sample size which could affect the generalizability of results. In addition to the cross-sectional design of the study which doesn't permit temporal relationship between the two diseases.

In conclusion, no association was observed between vitamin D level and glycated hemoglobin among our type 2 diabetic patients. However, further study is recommended including more representatives, enough sample from different institutions in Taif Region, Saudi Arabia.

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