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ASSOCIATION OF VITAMIN D WITH TYPE 2 DIABETES MELLITUS IN KARACHI, PAKISTAN

Yasir Mahmood[1], S. M. Shahid[1, 2], Asher Fawad[3], Abdul Basit[3] and Abid Azhar[1]

[1]*Dr. A. Q. Khan Institute of Biotechnology and Genetic Engineering, University of Karachi, Karachi, Pakistan*
[2]*School of Medicine, Faculty of Medical & Health Sciences (FMHS), University of Auckland, Auckland, 85 Park Road, Grafton Campus, New Zealand*
[3]*Baqai Institute of Diabetology and Endocrinology, Baqai Medical University, Karachi, Pakistan*
Corresponding Author: m.shahid@auckland.ac.nz

ABSTRACT

Hypovitaminosis D has become a pandemic in the world populations and is believed to be related with the diabetes mellitus (DM). The aim of study was to assess the status of vitamin D along with other parameters in type 2 diabetic patients. Vitamin D (VD), calcium (Ca), phosphorous (Ph), random blood glucose (RBS) and HbA1c levels were assessed in 192 diabetic subjects. Hypovitaminosis D was prevalent in diabetic patients while, Ca and Ph levels were found in normal physiological range. RBS and HbA1c showed negative association with VD levels in vitamin D deficient and diabetic patients with good glycemic control.

Key words: Vitamin D, HbA1c, Diabetes mellitus type 2.

INTRODUCTION

Low levels of VD (Hypovitaminosis D) have become a major health associated problem over the globe (Holick, 2017). In addition to its role in bone formation, several studies have claimed a correlation between hypovitaminosis D and onset of many health disorders like diabetes type 1 and 2, chronic kidney disease (Nakashima *et al*., 2016), hypertension (Afzal and Nordestgaard, 2017), cardiovascular diseases (Norman and Powell, 2014), autoimmune disorders (Paolino *et al*., 2016), obesity (Fernandez-Garcia *et al*., 2016), metabolic syndrome (Mitri and Pittas, 2014, Schmitt *et al*., 2017), and some types of cancers (Manousaki and Richards, 2017).

The association of hypovitaminosis D with DM (Both Type1 and 2) is still in the research process. Inverse association of VD levels and onset of DM has been observed (Nakashima *et al*. , 2016). Animal studies showed that diabetes mellitus impaired the circulating levels of vitamin D (Ishida *et al*., 1983). While, VD supplementation showed preventive effects from diabetes mellitus in the animal model (Altieri *et al*., 2016). VD affects the functions of beta cells by increasing the insulin secretion from the pancreas (Borissova *et al*., 2003) and associated with sensitivity of insulin (Kayaniyil *et al*., 2010). VD deficiency has been linked to DM and related problems like diabetic nephropathy, retinopathy, macro and microvascular complications, endothelial dysfunction and erectile dysfunction (Alcubierre *et al*., 2015; Basit *et al*., 2016; Caretta *et al*., 2016; Dalan *et al*., 2016; Herrmann *et al*., 2015). Hypovitaminosis D has shown an indirect association with coronary heart diseases in type 2 diabetic patients (Roberts *et al*., 2015).

Diabetes mellitus is one of the common health associated problems in our society. It was estimated that diabetes mellitus type 2 is 11.77% prevalent in Pakistani population; more common in male as compared to female and residents of cities as compared with rural population (Meo *et al*., 2016). Hypovitaminosis D has been linked with DM (type 2) and its complications have been studied in different parts of this country (Bashir *et al*., 2016; Iqbal *et al*., 2016; Shahzad *et al*., 2017; Tariq *et al*., 2016). The guidelines of 'Endocrine Society' revealed that less than 20ng/mL of serum VD is considered as deficiency; above 20 but below 30 ng/mL as insufficiency and more than 30 ng/mL as normal levels (Holick *et al*., 2011).

The purpose of this study was to explore the status of VD levels and its association with type 2 DM.

MATERIALS AND METHODS

The formal approval was taken from the institutional review boards of Dr. A. Q. Khan Institute of Biotechnology and Genetic Engineering, University of Karachi, and Baqai Institute of Diabetology and Endocrinology, Baqai University of Health Sciences, Karachi, Pakistan. Data was collected after obtaining written consent from diabetic patients. 192 diabetic patients enrolled comprised of 107 male and 85 female subjects). VD, Ca, Ph, RBS and HbA1c were analysed by automatic chemistry analyzer (Roche Diagnostic). Diabetic patients were

sub-divided into normal VD, insufficient and deficient groups. On the basis of "American Diabetic Association" guidelines, diabetic patients who had HbA1c value equal or more than 7% and less than 7% were divided as poor glycemic control, and good glycemic control groups respectively (American Diabetic Association, 2015).

Statistical Analyses

The student t-test was used to determine significance of difference between mean values. Regression and correlation analyses were carried out by using SPSS (Version 20) software.

RESULTS

Majority of the participants showed lower while, only 9.8% of diabetic patients had normal VD levels (Table 1). Results (Table 2) showed that blood glucose and HbA1c levels were statistically different ($p<0.05$) between VD deficient and insufficient groups, and between the VD deficient and normal VD groups, but not between VD insufficient and normal VD groups. The comparison of biochemical parameters between the poor glycemic control group (n=146) and good glycemic control groups (n=46) showed that VD, Ca and Ph levels were not significantly different from each other (Table 3). VD was found significantly associated ($p<0.05$) with RBS and HbA1c levels in diabetic patients with good glycemic control and VD deficient group but not in VD insufficient and poor glycemic control diabetic patients (Table 4).

Table 1. Distribution of diabetic patients on the basis of VD levels

VD status	Number of diabetic Patients (%)
VD deficient group (<20ng/mL)	96 (50%)
VD insufficient group (20-29 ng/mL)	77 (40.2%)
Normal VD group (>30ng/mL)	19 (9.8%)
Total	192

Table 2. Comparison of biochemical parameters on the basis of VD levels

Biochemical Parameters	VD deficient group	VD insufficient group	Normal VD group
RBS (mg/dL)	$159.5\pm5.0^{ab*}$	$178.6\pm7.4^{a*}$	$187.5\pm11.2^{b*}$
HbA1c (%)	$7.56\pm0.2^{ab*}$	$8.2\pm0.2^{a*}$	$8.8\pm0.5^{b*}$
Serum VD (ng/mL)	$16.4\pm0.7^{abc**}$	$25.2\pm0.3^{abc**}$	$35.7\pm1.8^{abc**}$
Ca (mg/dL)	9.6±0.1	9.6±0.1	9.3±0.2
Ph (mg/dL)	3.5±0.1	3.5±0.1	3.8±0.2

Values are given with ±SEM. 'a' represents $p<0.05$ between VD deficient and VD insufficient group. 'b' represents $p<0.05$ between VD deficient and vitamin D normal group. 'c' represents $p<0.05$ between VD insufficient and VD normal group. *$p<0.05$, **$p<0.01$

Table 3. Biochemical parameters in poor glycemic control and normal glycemic control groups.

Biochemical Parameters	Poor glycemic control n=146 (76%)	Normal glycemic control n=46 (24%)	p-value
RBS (mg/dL)	201.5±4.3	129.8±1.5	<0.01
HbA1c (%)	9.4±0.2	6.1±0.1	<0.01
VD (ng/mL)	20.4±0.8	19.6±1.1	0.32
Ca (mg/dL)	9.4±0.1	9.4±0.2	0.48
Ph (mg/dL)	3.6±0.1	3.5±0.1	0.22

Table 4. Coefficients of correlation values of different parameters with VD in different study groups.

Study groups	RBS (mg/dL)	HbA1c (%)	Ca (mg/dL)	Ph (mg/dL)
VD deficient group	-0.245*	-0.245*	-0.075	0.040
VD insufficient group	0.106	0.064	-0.035	-0.012
Normal VD group	0.169	0.168	-0.181	0.381
Poor glycemic control patients	-0.018	-0.066	-0.125	0.034
Good glycemic control patients	-0.411*	-0.411*	-0.022	0.054

*p<0.05

DISCUSSION

Elevated levels of blood glucose represent abnormality in glucose metabolism and higher values of HbA1c show its poor control. VD acts as a modulatory factor in glucose homeostasis and its deficiency could be a contributing factor in type 2 DM. The results showed that large proportion of this study group had either insufficiency or deficiency and only few diabetic patients had normal vitamin D levels. In spite of proper sunlight throughout the year, this condition of vitamin deficiency and insufficiency may be due to some other factors. The participants of this study belong to urban area in which chances of sunlight exposure are lesser as compared to the rural population. However, previous studies have shown prevalence of VD deficiency in diabetic patients and normal subjects, in both rural and urban areas of Pakistan (Bashir *et al*., 2016; Iqbal *et al*., 2016; Shahzad *et al*., 2017; Tariq *et al*., 2016). Not only life style modifications, but other factors may play a in vitamin D deficiency such as age, skin colour and genetics. It is observed that dark-skin individuals make lesser VD as compared with white skin individuals under same interval of sunlight exposure and capability of VD synthesis declines with aging. The blood glucose and HbA1c levels were negatively associated with VD levels in VD deficient group as compared to VD insufficient and normal VD groups. It may be hypothesized that vitamin D deficiency could be one of the contributing factors of type 2 DM in the study group.

HbA1c levels are used to assess the status of glycemic control in the diabetic patients. According to the guidelines of American Diabetic Association, diabetic patients were less than 7% HbA1c value represents good glycemic control and patients with equal or more than 7% poor glycemic control. Poor glycemic control in diabetic patients may lead to further complications such as diabetic retinopathy, neuropathy and other severe conditions (Herrmann *et al*., 2015). Most of the patients in this study had poorly controlled glycaemia and their mean value of VD was found at the border of VD deficiency. Only 24% diabetic patients showed good glycemic control but mean VD value was found to be in the VD deficiency range and was not found significantly different from poor glycemic control group. It appears that most of the patients could not maintain good glycemic control. The VD levels were also negatively correlated with blood glucose and HbA1c levels in good glycemic control group but not in poor glycemic control group. Therefore, it could be hypothesized that VD may modulate glycaemia up to a certain level.

VD deficiency was found equally present in all diabetic patients. Therefore, it might play a contributing role in the progression of type 2 DM and may lead to its complications especially, in poor glycemic control group.

Elevated levels of Ca are suggested as risk factor of type 2 diabetes mellitus (Rooney *et al*., 2016) and low levels of serum Ph have been shown link with type 2 diabetic patients. This may be impairment of phosphorus metabolism (Fang and Li, 2016). In this study, significant difference was not found in Ca and Ph levels among VD deficient, insufficient, and normal VD groups. Similarly, they were not found significantly different between poor glycemic control and good glycemic control groups. In all aforementioned groups, Ca and Ph values were found in normal physiological range. Ca and Ph values were not found significantly associated with VD, and did not represent any relation with blood glucose and HbA1c levels. It may be inferred that their levels were independent to type 2 DM in the study.

In the light of findings of previous studies, VD deficiency was prevalent in this population. It may be hypothesized that the definition of VD deficiency could be different in this population. Therefore, a population based study is needed addressing issues such as dietary habits, skin colour, sun exposure duration and life style to understand the actual status of VD in this population.

Conclusion

In this study diabetic patients showed low levels of VD and very small proportion had normal VD levels. Similarly, most of the diabetic patients showed poor glycemic control. Hypovitaminosis D was found significantly associated with blood glucose and HbA1c levels in VD deficient and poor glycemic control patients. Therefore, it may be associated with the progression of further complications. Therefore, it is recommended that normal VD levels should be maintained in diabetic patients either by proper sunlight exposure or VD supplementation in the diet to avoid any further complications of type 2 diabetes mellitus.

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