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Assessment of Vitamin D Levels in Diabetic Patients

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ABSTRACT

Objectives: Diabetes is considered as a major public health problem that has direct impact on both the economic and functional aspects of individuals and country. The vitamin D is widely known for its role in various body functions. In the past few years, it has been associated with many important systemic diseases including diabetes. Thus, the present study aims to compare vitamin D levels in both the diabetic and non-diabetic individuals in order to depict the relation of vitamin D with the glycemic control of diabetic patients. **Methods:** For this purpose two groups were formed named as experimental and control groups, each consisting of 120 patients were formed. The demographic characteristics, disease duration, anthropometry, and haemoglobin A1C were recorded during data collection. This was followed by data analyzation through SPSS 17 with utilization of chi square test, students t-test and regression analysis. **Results:** In diabetic individuals, mean value of vitamin D was 17.6 ± 9.1 ng/dl, whereas, for non-diabetic individuals, it was 29.5 ± 10.9 ng/dl (p = 0.001). On the other hand, in diabetic group, 79 (65.83 %) patients were vitamin D deficient, whereas, in the control group, 43 (35.83 %) patients were vitamin D deficient. Thus, the vitamin D deficiency was more prevalent in the diabetic patients. Moreover, it was found to be dependent on factors such as gender, BMI, disease duration, RBS and HbA1C. **Conclusion:** It is concluded that vitamin D supplements can be used as an essential component of diabetic patient's treatment.

Key words: vitamin D, diabetes, vitamin D deficiency, diabetes mellitus

Introduction

Vitamin D and its metabolite, calcitriol, have long been associated with calcium regulation. The bone health and skeletal integrity are two important attributes of this hormone (Mathieu, 2015). Conversion of vitamin D into cholesterol and its presence in bone cells and parathyroid depicts its significance (Bayani, et al., 2014). Although vitamin D is produced in body through sunlight stimulation, large number of people depends on milk and supplements to fulfil their vitamin D requirements (Christakos, et al., 2013). On the other hand, many others ignore the importance of this substantial vitamin due to which a large number of people have either vitamin insufficiency or deficiency. The deficiency of vitamin D has found to be common in hospitalized people with chronic diseases and disorders (Zoppini, et al., 2013).

In recent years, extra-skeletal functions of vitamin D have gained vital interest (Li-min, et al., 2013). Previous studies have indicated its linkage with metabolic syndromes (Kayaniyil, et al., 2013), cancer, cardiovascular disorders, autoimmune diseases and glucose homeostasis (Herrmann, et al., 2015). Consequently, it has been related to the development and complications of various chronic diseases, including diabetes mellitus type 2 (Lim, et al., 2013). Vitamin insufficiency has been associated with higher risk for diabetes (Song, et al., 2013), whereas, higher levels of vitamin D in plasma have been linked with lower risk for diabetes mellitus (Mitri & Pittas, 2014). On the other hand, diabetic patients have more probability of being vitamin D deficient as compared to the non-diabetics (Van Belle, et al., 2013). Previous research work has also indicated that by maintaining vitamin D above 800 IU/day, diabetes type 2 can be reduced by 33% (Gao, et al., 2015). A survey showed that diabetic patients, among 15 thousand individuals, had the lowest vitamin D (Harinarayan, 2014). It is proposed that combined supplementation of vitamin D and calcium can work together to reduce diabetes in highly risked people (Dutta, et al., 2014). Heaney et al (Heaney, et al., 2013) claimed that insulin resistance and vitamin D concentration are inversely related with vitamin D levels ranging from 16 to 36 ng/ml. This is due to the fact that vitamin D is responsible for stimulating the expression of insulin receptor (Griz, et al., 2014).

Various mechanisms have been proposed by previous researchers to explain the relationship between vitamin D and diabetes. The levels of vitamin D have been associated with the secretion of insulin as the vitamin D receptors are present on β-cells of the pancreas (Talaei, Mohamadi, & Adgi, 2013). Thus, by treating vitamin D deficiency, glucose tolerance and insulin resistance can be improved (Papandreou & Hamid, 2015). It has been noted that decrease in vitamin D reduces insulin secretion. In animals, it has observed that vitamin D supplementation restores insulin

secretion. Another important mechanism proposed by researchers involves the effect of calcium on insulin secretion (Nakashima, et al., 2016). As vitamin D is responsible for normalizing extracellular calcium, lower levels of vitamin D can result in a decrease of calcium's function of effecting insulin secretion (Sheth, et al., 2015). It has also been found that fluctuating vitamin D is influencial on the glycemic control of diabetic patients (Kostoglou-Athanassiou, et al., 2013). A previous study has reported that vitamin D stimulates expression of insulin receptor to increase insulin action, increase glucose transport through boosting of insulin responsiveness, imposing calcium effect on insulin secretion and by influencing cytokines through systemic inflammation (Harinarayan, 2014).

Diabetes is an important health problem throughout the world, at present. Although tremendous development has been witnessed in the previous few years, there is no treatment for diabetic patients (Din, 2014). It consists of life-long complications, which deteriorate health condition of the patients. Diabetes is reported to increase morbidity and mortality rates due to abrupt increase in its prevalence. At present, the global prevalence of diabetes is estimated to be 8% with 415 million diabetic patients all over the world (Basit, et al., 2015). Unfortunately, 5 million deaths have been reported on average to occur in a year due to diabetes. It is expected that in year 2040, diabetic patients will be 642 million. Awfully, majority of the diabetic patients remain undiagnosed in their life (International Diabetes Federation, 2012).

About 80% of the individuals suffering from diabetes are reported to belong to developing regions including South Asian countries. Pakistan is a renowned country of South Asia with a population of 85.044 million (Hussain & Ali, 2016). Increased urbanization and poor dietary intake has resulted in enhancing prevalence of diabetes in Pakistan. Resultantly, 7 million people are patients of diabetes in Pakistan (Shera, et al., 2007). This makes Pakistan to rank 8th in world ranking for prevalence of diabetes. Moreover, in year 2025, it is expected to rank 4th and consist of 15 million diabetic patients. Thus, double fold increase is expected in prevalence of diabetes for Pakistan (Tarin, 2010).

It is hypothesized that vitamin D deficiency is more prevalent in the type 2 diabetic patients due to its influence on the glucose control of the patients. In Pakistan, no recent research work has been dedicated to explore relation of vitamin D with diabetes. Thus, this study aims to depict the levels of vitamin D in the diabetic patients for understanding the influence of vitamin D on the glycemic control of the patients. The attributes including demographic characteristics, disease duration, anthropometry, and haemoglobin A1c will also be measured. This will help in taking measures towards prevention of diabetes. A general awareness among population of Pakistan can also be achieved

Materials and Methods

The study was conducted from October 2014 to October 2015 on the patients visiting hospitals of Lahore, Pakistan. The individuals were divided into two groups: experimental and control group. The experimental group consisted of 100 patients, aged 25-60 years, having diabetes mellitus type 2 from the area of Lahore, Pakistan. The control group comprised of 120 individuals, who did not have any systemic disorder and had no history of drug intake that might interfere with vitamin D metabolism. All the samples were collected in one season to avoid seasonal changes that may take place in the level of vitamin D. Vitamin sufficiency was considered for samples having a serum concentration of 25(OH) D more than 30 ng/ml, insufficiency was considered for samples having a serum concentration of 25(OH) D in between 20-30 ng/ml, and the deficiency was considered for samples having a serum concentration of 25(OH) D less than 20ng/ml.

For determination of weight, Seca Alpha digital electronic balance was used, whereas, for determination of height, a Harpenden digital stadiometer was used. BMI was estimated with formula weight/height^2. A Holtain flexible metallic tape was used to determine waist and hip circumferences. Three observations were taken for each characteristic and mean value was used for analysis. The tape was held tightly against the body of patients, while the individuals were standing in a relaxed position. The slenderest part of torso was considered as waist, whereas, horizontal part surrounding buttock and pubic symphysis region was considered as hip circumference. The waist/hip ratio (WHR) was estimated through formula waist circumference/hip circumference. The data was collected by trained staff.

The level of glycosylated haemoglobin HbA1c and vitamin D were measured for both the groups. In order to measure vitamin D levels, radioimmunoassay (RIA) was utilized. There are two main steps in this procedure. In the first step, hydroxylated metabolites and 25(OH)D were extracted from plasma by acetonitrile. Through competitive RIA, the assay was conducted on the

samples with the help of antibodies. After incubation at 20–25 °C for 90 min, the samples were re-incubated for 20 min with second antibody. At the last step, phase separation was conducted.

High-performance liquid chromatography (HPLC) was used to measureHbA1c levels through separation on cation cartridge. Samples and a buffer gradient were injected in the cartilage. The haemoglobins got separated on the cartridge, which were passed under the photometer for analysis.

For statistical analysis of data, SPSS 17 was used. In order to compare experimental and control group, the student *t*-test and chi square test were performed with p value less than 0.05 considered as significant. For analysing the association between HbA1c and vitamin D levels, regression was conducted.

Results

Both the experimental and control groups consisted of 60 males and 60 females. The mean value for age of control group individuals was 45.45 ± 7.70, whereas, it was 43.14 ± 9.11 years for the experimental group. In diabetic individuals, mean value of vitamin D was 17.6±9.1 ng/dl, whereas, for non-diabetic individuals, it was 29.5 ± 10.9 ng/dl (p = 0.001). In male diabetic patients, mean value of vitamin D was 13.23 ± 8.87 ng/dl, whereas, for male non-diabetic patients it was 25.54 ± 13.57 ng/dl (p = 0.132). In female diabetic patients, mean value of vitamin D was 16.17 ± 13.63ng/dl, whereas, for female non-diabetic patients it was 29.17 ± 15.13 ng/dl (p = 0.001), as shown in the Table 1. In diabetic group, 79 (65.83 %) patients were vitamin D deficient, 23 (19.16 %) were vitamin D insufficient and 18 (15 %) were vitamin D sufficient. In the control group, 43 (35.83 %) patients were vitamin D deficient, 41 (34.16 %) were vitamin D insufficient and 36 (30 %) were vitamin D sufficient.

Chi square test and t-test were applied to compare various characteristics of patients in both the groups. Vitamin D deficient patients have been shown along with their characteristics in Table 1. The p value of attributes such as gender, BMI, disease duration, RBS and HbA1C is less than 0.05. Thus, the null hypothesis is rejected, which depicts the dependency of vitamin deficiency on these characteristics.

Table 1. Comparison of Vitamin D deficiency with patient characteristics in experimental and control groups

Characteristics	Control group		Experimental group		t-test	p value
	Mean	SD	Mean	SD		
Age (Years)	45.45	7.70	43.14	9.11	0.451	0.429
Gender						
Male	25.54	13.57	13.23	8.87	0.029	0.132
Female	29.17	15.13	16.17	13.63	- 143	0.001
Disease Duration (Years)	5.32	4.13	7.25	2.42	- 2.814	< 0.001
Height (cm)	173.12	8.61	134.17	6.32	0.374	0.417
Weight (kg)	72.12	5.173	42.41	5.28	- 0.291	0.021
BMI (Kg/m^2)	22.21	2.21	23.12	1.51	- 1.382	0.002
Waist (cm)	89.61	11.37	69.42	14.34	- 0.194	0.517
Hip (cm)	99.14	13.36	104.12	15.73	- 0.527	0.521
WHR	0.80	0.12	1.39	0.75	- 0.284	0.438
HbA1C (mg/dl)	5.31	0.72	8.13	3.24	- 3.194	< 0.001
RBS (mg/dl)	149.51	33.37	213.23	51.38	- 4.563	< 0.001
Chi square test p value used						

The multiple linear regression analysis was performed to evaluate the relation of vitamin D with various factors as shown in the Table 2. The p values for RBS, BMI and HbA1C were found to be less than 0.05. Thus, vitamin D is associated with these factors.

Table 2. Regression analysis for associations of vitamin D with patient characteristics

Model	B	Standard Error	T	p value	95 % Confidence Interval for B	
					Lower Bound	Upper Bound
(Constant)	23.411	7.281	1.374	0.002	7.373	39.283
Age (Years)	0.002	0.032	.033	0.816	- 0.291	0.321
Gender	1.413	0.721	2.431	0.213	- 0.462	1.734
Duration of Diabetes (years)	-0.342	0.231	- 1.384	0.113	- 0.723	- 0.013
BMI (Kg/m^2)	-0.324	0.216	- 1.183	0.032	- 0.734	- 0.031
HbA1C (mg/dl)	-0.321	0.222	- 1.738	0.014	- 0.523	- 0.052
RBS (mg/dl)	-0.012	0.006	- 4.013	< 0.001	- 0.034	- 0.031
Regression coefficient of determination (R^2) = 27.7						

Discussion

Chi square test, students' t-test and multiple linear regression were performed to analyse the relation of vitamin D deficiency with age, gender, disease duration, height, weight, BMI, waist, hip, WHR, BMI and HbA1C. The results affirm that there exists an association between vitamin D deficiency and gender, BMI, disease duration, RBS and HbA1C. An inverse relation was found between HbA1C and vitamin D. This depicts the association between vitamin D and glycemic control, supported by the works of Kostoglou-Athanassiou et al. (2013) and Zoppini et al. (2013). Another verdict confirms the relation between gender and vitamin D deficiency. This affirmation is justified by the work of Gao et al (2015). Schottker et al (2013) claimed that females have more association between vitamin D and diabetes. Consequently, females are more likely to suffer from diabetes. These findings are in accordance with the results of present study. However, the relation between vitamin D deficiency and disease duration is not supported by previous works (Papandreou & Hamid, 2015). Thus, more research should be conducted on the relation of these factors in order to get appropriate inferration.

The present study affirmed that the mean concentration of vitamin D in diabetic patients is less than that of healthy individuals. This finding is supported by the research work of Gao et al (2015). Thus, it was found that statistically significantly more patients of diabetes mellitus were suffering from vitamin D deficiency as compared to control group. The same was found by Kostoglou-Athanassiou et al (2013).

On the basis of results, the use of vitamin D supplements for the improvement of glucose control in type 2 diabetic patients is highly recommended. Consequently, type 2 diabetic patient have been administered with vitamin D (Breslavsky, et al., 2013. Previously, use of 2000 international units of cholecalciferol for 16 weeks has been found to be vital in improving beta cell function in individuals having high risk for diabetes. Vitamin D is observed to reduce albuminuria and oxidative stress in diabetic patients (Salum, et al., 2013.

Some important limitations were imposed on the present study. As this is an observational study, it is difficult to draw any concise if a cause and effect relation exists between vitamin D deficiency and onset of type 2 diabetes. On the other hand, 25(OH) D was selected for detecting vitamin D deficiency in accordance to the current recommendation. Anyhow, there are many blood circulating forms of vitamin D with active form being **$25(OH)_2D_3$. Thus, it is required that better tools should be opted in future for determining vitamin D deficiency, especially in diabetic patients. Moreover, research is required to understand the impact of vitamin D supplementation on glycemic control of type 2 diabetic patients. Consequently, it is also important that relation of vitamin D with other important chronic diseases is disclosed through future research work. Moreover**, the sample collection for the study was performed in one season only. The vitamin D level may get fluctuated as a result of sunshine duration changes, throughout the year. Thus, the future research works should undermine this fact.

Conclusion

It is concluded that vitamin D deficiency is more prevalent in the diabetic patients as compared to the healthy individuals. Thus, vitamin D supplements should be considered as an essential component of treatment rendered to diabetic patients. The present study is important in terms of therapeutic implications. The vitamin D levels present in blood are helpful in maintain glucose levels. In case of diabetic patients, this effect is essential in diabetic control. Another important implication is that the individuals having higher chances of developing diabetes should try to increase daily intake of vitamin D. This may slow down clinical development of diabetes in such people.

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