ORIGINAL ARTICLE

Vitamin D Status in Diabetic and Non-Diabetic Patients of Coronary Artery Disease

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ABSTRACT

Objective: To assess and compare the level of hypovitaminosis D in diabetic and non-diabetic patients of coronary artery disease (CAD).

Study Design: Cross-sectional observational.

Place and Duration of Study: The study was conducted from May 2014 to November 2014 at Pakistan Railways Hospital, Islamic International Medical College, Rawalpindi.

Materials and Methods: A total of 149 patients of coronary artery disease were selected in this studyby convenient sampling technique including 77 male and 72 female patients. Out of 149 patients, 75 were diabetic and 74 non-diabetic. These participants were assessed for their individual serum vitamin D levels(ng/ml). Family history of coronary artery disease and treatment modalities was also obtained from all the patients. The data was analyzed through SPSS 21. Descriptive statistics and t test were used to analyze the data.

Results: The serum levels of Vit D among diabetic and non- diabetic patients suffering from CAD were 16.4(±9.7) ng/ml and 17.4(±7.9)ng/ml respectively. These values suggest a deficiency of Vit D in both diabetic and non-diabetic patients suffering from CAD. However the difference in Vit D levels of the two subgroups of CAD was statistically not significant (p = 0.4).However vitamin D levels were found to be significantly lower in patients with positive family history of CAD (p=0.04).

Conclusion: There is no significant difference in the level of Hypovitaminosis D in diabetic and non-diabetic CAD patients.

Key Words: *Vitamin D, Vitamin D Receptor, Type 1 Diabetes Mellitus, Type 2 Diabetes Mellitus, Hypovitaminosis D, Islet β Cells, Insulin Secretion, Insulin Sensitivity.*

Introduction

Vitamin D is a secosteroid prohormone which is synthesized in the skin from 7-dehydrocholesterol by ultraviolet B-irradiation. Almost 80 percent of vitamin D is provided through cutaneous synthesis while 20 percent is obtained from various dietary resources.[1] Vitamin D has been known for its key role in bone metabolism and calcium homeostasis. However its extra-skeletal effects have attracted much attention because of recent discovery of Vit D receptor (VDR) expression in almost all tissues of the body including immune, endocrinal, vascular and myocardial cells.[2] Vit D deficiency is considered as a risk factor for diabetes type-2 diabetes and higher plasma levels of vitamin D are shown to decrease the risk for development of diabetes mellitus.[3,4]

Diabetes mellitus is a very common condition which affects over 300 million people worldwide and accounts for significant morbidity and mortality.[5] Ziegler et al found that vitamin D administration in type 1 diabetes can protect the function of pancreatic islet β cells. Deficiency of vitamin D has been investigated to affect the synthesis and secretion of insulin both in human and animal models.[6] Vitamin D supplementation not only restores the synthesis but also secretion of insulin and therefore decreases blood glucose concentration.[7] Palomer et al also reported that vitamin D deficiency can predispose to glucose intolerance and vitamin D supplementation improves insulin secretion in type 2 diabetes mellitus.[8]

Both genetic and environmental factors are known to be etiological in causing type 1 diabetes mellitus (T1DM), a chronic disorder that results from autoimmune response against the beta cells of the pancreatic islets of Langerhans at early stages of life. It is hypothesized that vitamin D has a role in the therapy of T1DM due to its immune-modulating effects. Chronic insulinitis is found in islet cells

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Funding Source: NIL ; Conflict of Interest: NIL
Received: March 26, 2015; Accepted: January 14, 2016

involving CD8+, CD4+ T cells, B lymphocytes and macrophages. It has been reported that vitamin D inhibits the production of IFN-γ and IL-2 cytokines which are responsible for the destruction of pancreatic islet cells.[9] Vitamin D also reduces the activity of APCs and regulates the production of CD4+ lymphocytes.[10] Cytokines cause apoptosis. 1,25(OH)2D3 protects beta cells by reducing exposure of MHC-1 molecules. As a result A20 protein which inhibits apoptosis is activated and a decrease in expression of a transmembrane cell surface receptor occurs.[9]

The major factors involved in the etiology of type 2 diabetes mellitus are insulin resistance, disorders of pancreatic beta cells and inflammation. Vitamin D facilitates pancreatic beta cell function through direct actions in which vitamin D is activated in pancreatic beta cells by intracellular 1-α-hydoxylaseenzyme. Vitamin D not only increases insulin secretion but also enhances beta cell survival through the effects of cytokines. Vitamin D also has indirect actions in which it regulates calbindin, a calcium-binding protein present in beta cells. Calcium then influences insulin secretion because this process is calcium dependent. In this way calcium indirectly affects insulin secretion via calcium binding protein calbindin. One more mechanism involved can be that low vitamin D levels cause secondary hyperparathy roidism. Parathyroid hormone then inhibits insulin secretion and also causes resistance in target cells because of its effects on regulation of calcium levels.[9]

An inverse relationship of insulin resistance was found at Vit D levels between 16 and 36ng/ml in arecent study.[10] Other cross-sectional, case control, prospective observational and longitudinal studies showed that higher Vit D concentrations were associated with a lower risk for diabetes mellitus type 2 and lower levels were negatively correlated with diabetes and glycosylated haemoglobin levels. However these studies did not reveal consistent results, neither vitamin D supplementation was found to improve glucose control in type 2 diabetes in all the subjects.[11]

The levels of blood glucose and vitamin D have been shown to be different in Third National Health and Nutritional Examination Survey and a negative correlation was found in healthy white post-menopausal women and in Mexican American men and women but not in Hispanic black population. This finding suggests that the effect of vitamin D may differ by ethnicity.[12]

The present study was undertaken to assess and compare the level of hypovitaminosis D in diabetic and non-diabetic patients of CAD because of paucity of research work on this therapeutically important subject.

Materials and Methods

This study was conducted at department of Biochemistry IIMC Rawalpindi. It was a cross-sectional observational study. The Study was conducted from May 2014 to November 2014.

Blood samples were drawn from 149 patients of coronary artery disease comprising of 77 males and 72 females from OPD, emergency department and ICU of Railways General Hospital Rawalpindi, a 480 bedded teaching hospital affiliated with IIMC. These patients were divided into two groups:

Group I consisted of diabetic patients of coronary artery disease while group II comprised of patients without diabetes. Patients of coronary artery disease between ages of 40 years to 55 years were included in the present study. Patients with renal, liver, parathyroid and thyroid disorders were excluded from the study. Patients taking vitamin D and calcium supplements and those on medication that affect vitamin D metabolism such as anticovulsants were also not recruited in this study.

Venous blood was drawn from the patients which was centrifuged at 300 rpm for separation of serum and then stored at -20 degree centigrade in laboratory freezer till further analysis. Serum levels of 25(OH)D was measured by enzyme linked immunosorbent assay. Statistical analysis was carried out for finding out significant p values ($p<0.05$) and t test was used to evaluate the data. SPSS version 21 was used for data processing.

A total of 149 patients with coronary artery disease were selected to participate in the study that fulfilled the inclusion criteria and gave informed consent. All the participants were assessed for their individual serum vitamin D levels (ng/ml). The diabetic patients were questioned about the mode of treatment, either oral hypoglycaemic agents or insulin therapy to control their diabetes.

Results

Out of a total of 149 patients selected to participate in the study, 77 were male and 72 were female patients. Of these, 75 male and female patients were diabetic whereas 74 were non-diabetic male and female participants. The mean age of the male participants was 49.1+4.1(in years) and of the female participants was 47.4+4.5(in years).

The mean serum vitamin D level in diabetics was 16.4 ng/ml and in non-diabetics was 17.4 ng/ml(Fig 1). However the difference was not statistically significant (p value= 0.4)(Table I). The serum Vitamin D level in the female diabetic participants was 16.8 ng/ml and in the male diabetic participants it was 16.0 ng/ml. The serum vitamin D level in non-diabetic female patients was 19.0 ng/ml and in male non-diabetic participants it was 15.9 ng/ml.

Vitamin D deficiency was considered when the serum vitamin D was < 20ng/ml, insufficiency if the serum vitamin D was between 21-29ng/ml and normal if serum vitamin D was > 30 ng/ml. Vitamin D deficiency was seen in 100(67.1%), insufficiency was seen in 39(26.2%) and normal Vitamin D was present in 10(6.7%) of the participants. The percentage of deficiency and insufficiency was 93% in the sample population.

Family history of coronary artery disease was present in 63(84.0%) of the diabetic patients and in 53(71.6%) of the non-diabetic patients. Vitamin D levels in patients with and without family history of CAD were 7.7(±9.2)ng/ml and 14.2(±7.1)ng/ml respectively. The difference was significant (p= 0.04)(Table II).

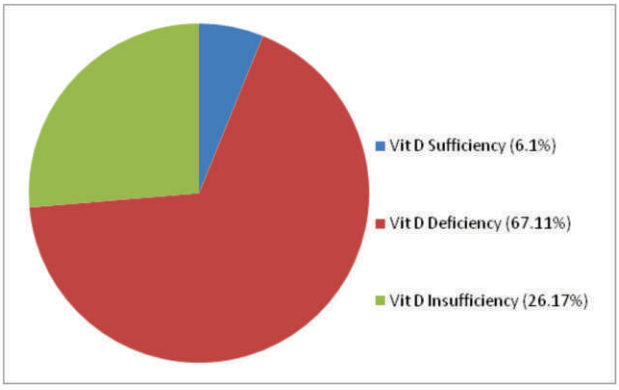

Fig 1: Percentage of hypovitaminosis in the study population

Table I: Comparison of Vitamin D levels between diabetic and non- diabetic patients

Disease	N=149	Vitamin D level (±SD)ng/ml	p- value
Diabetic population	75	16.4(±9.7)	0.4
Non-diabetic population	74	17.4 (±7.9)	

Table II: Comparison of vitamin D levels between patients with family history of coronary artery disease and patients with no family history of coronary artery disease

Family history of coronary artery disease	N=149	Vitamin D levels (±SD)ng/ml	P-value
Positive family history	116	7.7(±9.2)	0.04
No family history of CAD	33	14.2(±7.1)	

Discussion

This study was undertaken to assess the role of vitamin D in diabetes mellitus and to measure its levels in diabetic and non-diabetic patients of CAD. Our results did not reveal statistically significant difference in Vitamin D levels between diabetic and non-diabetic sample population (p= 0.4). This finding which is in contrast to many other observational studies may possibly be due to multiple confounding factors like obesity, sun exposure and/or methodological and measurement limitations. However cumulative percentage of vitamin D deficiency and insufficiency in the study population has been found to be about 93% which matches with one of the studies carried out by Bellen et al. in which hypovitaminosis D was reported in 95% of cases.[13]

A study performed by Daga et al. in North India showed that 91% of diabetic patients had hypovitaminosis D and the mean concentration was 7.88(±1.2)ng/ml. In non-diabetic patients the mean concentration was 16.46(± 7.83) ng/ml. This finding is in line with our results for non-diabetic patients.[14]

Hypovitaminosis D is reported worldwide mainly due to dietary insufficiency and use of sun protection clothing and sun screen. Studies on this subject in Saudi Arabia, Turkey, Australia, Arab Emirates and India have shown that 30-50% of children and adults had vitamin D levels of less than 20ng/ml. A Japanaese study has shown a prevalence of vitamin

D deficiency in 75% of the study population which is consistent with the findings of our study. The results of a study carried out in the United Kingdom also revealed the prevalence of vitamin D levels (below 20ng/ml) in more than 80% of the research participants.[15] Our study also revealed comparable results.

An interesting and therapeutically useful finding in this study is that patients taking oral hypoglycemic drugs had significantly lower vitamin D levels as compared to those on insulin therapy ($p = 0.05$). Another finding of the present research is a significant difference in Vit D levels while comparing results of patients with and without family history of coronary artery disease ($p = 0.04$).

The conclusive statement of a study carried out by Bellan et al. on this subject is "At variance with previous reports, we were unable to disclose negative effects of low 25(OH)D concentration on plasma glucose levels both in fasting conditions and after the oral glucose challenge after correction for multiple variables known to affect glucose metabolism".[16]

Another study postulates that vitamin D is needed to improve production and action of insulin in both diabetic and non-diabetic patients but the relationship between vitamin D, insulin resistance and β cell function is inconsistent. Additionally interventional studies with vitamin D in any form have also shown conflicting results. Therefore, interpretation of the results is difficult in view of lack of placebo-controlled studies.[17]

Conclusion

The results of the present study revealed that serum levels of Vit D in diabetic patients of coronary artery disease were not significantly lower than non-diabetic patients of coronary artery disease in our study. It is inferred from the current findings that diabetes mellitus is a multifactorial disease resulting from complex interaction of genetic and environmental factors. Vitamin D could only be one of the environmental variables and not an independent potential predictor of diabetes mellitus but rather could be a mediator of metabolic disturbances responsible for the long- term health outcomes.

Further large well-designed, randomized controlled studies are suggested to assess and clarify the correlation between vitamin D and glucose homeostasis in diabetes mellitus.

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