



COMPARATIVE STUDY OF VITAMIN D3 LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND NON-DIABETICS.

General Medicine

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ABSTRACT

Back Ground:

Diabetes is defined as disturbance in intermediary metabolism manifesting as chronic sustained hyperglycemia, primarily due to either an absolute or relative lack of insulin. During the last 2 decades research and data is showing that vitamin D3 deficiency could be a risk factor in many chronic diseases like Diabetes mellitus, Hypertension, Dyslipidemia Cardiovascular diseases, Auto immune disorders, Tuberculosis and some cancers. Many studies have demonstrated an inverse relationship between vit D3 levels and Diabetes mellitus. Studies in India have demonstrated that the level of vitD3 in the population is low and there is high prevalence of chronic diseases like Diabetes, Hypertension and cardiovascular disease among vit D3 deficient subjects. However there is a paucity of literature regarding the levels of Vit D3 in type2 DM, which is common in our community. In view of the above facts that the present study has been undertaken.

Methods:

Cross sectional study. Cases of type2 Diabetes Mellitus admitted in the wards of Government General Hospital , Kakinada diagnosed as per the ADA criteria, between ages of 35-75 y ears (inclusion criteria).

Results:

VitD3 was found to be significantly lower in the study group (19.91 +/- 7.0) as compared to the control group (32.22 +/- 4.0).

Conclusions:

Significant Vitamin D deficiency was present in Diabetic patients compared to healthy subjects.

KEYWORDS

vitamin D, Diabetis Mellitus

INTRODUCTION:

Diabetes is defined as a disturbance in intermediary metabolism manifesting as chronic sustained hyperglycemia, primarily due to either an absolute or a relative lack of insulin. Diabetes is a polygenic and multi-factorial disease involving many pathways and mechanisms. The worldwide prevalence of Diabetes has dramatically increased over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013. Based on current trends; the International Diabetes Federation expects that 592 million individuals will have diabetes by the year 2035.

Vitamin D deficiency was associated with poor bone growth and development and development of rickets in children and osteoporosis in adults. During the last two decades new research and data is showing that vitamin D deficiency could be a risk factor in many chronic diseases like diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, some cancers, autoimmune disease and tuberculosis.

Many epidemiological studies [1,2] have demonstrated an inverse relationship between vitamin D levels and diabetes mellitus. Studies in India have demonstrated that the level of vitamin D in the population is low and there is high prevalence of chronic diseases like, diabetes, hypertension and cardiovascular disease.

However, there is a paucity of literature regarding the levels of vitamin D in type 2 diabetes, which is common in our community. In view of the above facts, the present study has been undertaken to determine the occurrence of hypovitaminosis D in Type 2 Diabetes Mellitus and to compare these with that of non-diabetic controls.

AIMS AND OBJECTIVES

- To study plasma 25-Hydroxycholecalciferol (Vitamin D3) levels in patients of type-2 diabetes and to compare it with age and sex matched control subjects.
- To study the correlation if any, with severity and duration of disease with vitamin D3 levels.

PATIENTS AND METHODS

Type 2 diabetic patients admitted to the medical wards of Government General Hospital, Kakinada diagnosed as per the ADA criteria were included in this study. The study was conducted on 30 diabetic cases

and 30 age and sex matched controls. Informed written consent was obtained from cases and controls for participation in the study and for conduction of investigations.

STUDY PERIOD:

The study was conducted between the period of august 2017 and July 2018.

INCLUSION CRITERIA

- Type 2 diabetic patients
- Age 31 - 75 years

EXCLUSION CRITERIA

- Age \leq 30 years or $>$ 75 years
- Type 1 diabetic patients
- Associated co-morbid conditions likely to influence Vitamin D levels in blood
 - Patients with chronic kidney disease
 - Liver disease
 - Cardiovascular disease
 - Cerebrovascular disease
 - Patients taking drugs effecting vitamin D metabolism e.g. anti-epileptics, steroids, rifampicin, ART, antacids, orlistat, statins, cholestyramine etc.
 - Patients taking vitamin D and/or calcium supplements
 - Patients with hypertension
- Patients not giving consent for the study.

METHOD OF COLLECTION OF DATA

Complete clinical history was taken and physical examination of 60 patients was done. All patients underwent the following investigations:

- Fasting blood glucose level
- Post prandial blood glucose level
- Serum calcium
- Serum creatinine
- Urine for micro-albumin
- Plasma 25-hydroxy Chole-calciferol
- Serum Parathyroid hormone

DATA ANALYSIS:

Data was entered in MS EXCEL and analysed by using Epi- info 7 th version software.

RESULTS:

The baseline characteristics of the study and control population were similar. Out 30 of cases 22 (73.4%) were males and 8 (26.6%) were females and out of 30 controls 23 (76.7%) were males and 7 (23.3%) were females.

Among the diabetics 11 (36.66%) of them were diagnosed to be diabetic less than or equal to year from the time of study, 14 (46.66%) were diagnosed between 2 to 5 years , 4 (13.34%) of them were diagnosed between 5 to 10 years and only 1 (3.34%) had long standing diabetes of greater than 10 years.

All of them were on anti-diabetic medications with 19 (63.34%) of them on OHA's, 7 (23.33%) patients on insulin only, and 4 (13.33%) patients were on a combination of both insulin and metformin.

Table 1: comparison of vitamin D levels among cases and controls

VITAMIN D STATUS	CASES (%)	CONTROLS(%)	TOTAL (%)
DEFICIENT(<20NG/ML)	15(50.0)	0(0.0)	15(25.0)
INSUFFICIENT (21-30NG/ML)	13(43.3)	10(33.3)	23(38.3)
NORMAL(31-70NG/ML)	2(6.7)	20(66.7)	22(36.7)
TOTAL	30	30	60

The mean vitamin D in cases was 19.91+/- 7.0 and among controls was 32.22+/- 4.0 with p value <0.001

There was a significant inverse correlation between vitamin D and type 2 diabetes mellitus (p < 0.001).

DISCUSSION:

In Nurses' Health Study [3] – a large prospective, observational cohort, women with the highest calcium and vitamin D intake (> 1200 mg and > 800 IU daily, respectively) showed a 33% lower risk of type 2 diabetes mellitus than women with lowest calcium and vitamin D intake (< 600 mg and < 400 IU daily, respectively) [4]. Another large cohort study from Finland indicated an inverse association between serum 25(OH)D3 and risk of type 2 diabetes. These results were consistent with those from the Nurses' Health Study by Pittas et al [3], where an inverse association was observed for the intake of vitamin D supplements.

Several studies have ascribed an active role to vitamin D3 in the functional regulation of the endocrine pancreas, particularly the beta cells. The expression of calbindin-D28K has been shown to protect beta cells from cytokine-mediated cell death [5], thereby reducing the risk of type-2 diabetes.

Sheena et al [6] examined the cross-sectional association between vitamin D and beta-cell dysfunction in subjects at risk for type-2 diabetes and showed a positive association between vitamin D and beta-cell function. A high prevalence of hypovitaminosis D was noted among women with type 2 diabetes. Hyper-responsive insulin secretion after a glucose challenge has been found in older men with hypovitaminosis D [7].

A recent study by Enju Liu et al [8] examined the association between vitamin D status and insulin resistance in non-diabetic individuals and showed that higher vitamin D status was inversely associated with fasting markers of insulin resistance. A positive correlation of 25(OH)D concentration with insulin sensitivity and a negative effect of hypovitaminosis have been reported by Ken C Chiu et al [9]. Peeyush et al. [10] examined the effect of vitamin D supplementation on preventing the altered expression of GLUT-3 in STZ-induced diabetic rats leading to imbalanced glucose transport in the neurons of cerebellum. They concluded that supplementation with vitamin D has beneficial effects in reducing the alterations in GLUT-3. Hitman et al. [11] showed an association between the ApaI polymorphism (homozygous for the a allele) and lower insulin secretion in a healthy Bangladeshi Asian population who are at risk of type 2 diabetes living

in London with a high prevalence of vitamin D deficiency.

A study on 825 US hemo-dialysis patients to determine the relationship between vitamin D levels and mortality reported that 78% of the patients were vitamin D deficient and that this was associated with an increased early mortality [12]. Zhang et al. [13] reported that receptor-mediated vitamin D actions may be protective of kidneys in rats with diabetic nephropathy. In a study to determine the relationship between 25(OH)D and kidney functions on NHANES III participants, the level of 25(OH)D was significantly lower in persons with severely decreased glomerular filtration rate when compared with those with normal kidney function [14]. Diabetes has been associated with several neurological disorders including reduced loco-motor activity that in turn is associated with low levels of vitamin D [15].

Table 2 : Effects of vitamin D

Role of vitamin D	MECHANISM OF ACTION
Effect of vitamin D on insulin secretion	<ul style="list-style-type: none"> • Presence of vitamin D receptor in pancreatic beta cells and expression of 1,25 hydroxylase enzyme in pancreatic beta cells suggest a role of Vit .D in insulin secretion. • Vit.D alters calcium flux which can have adverse effects on insulin secretion, a calcium-dependent process. • Vit.D improves insulin secretion and glucose tolerance through regulation of the calcium levels. Vit. D may induce insulin secretion indirectly by increasing the intracellular calcium concentration. • Vit. D mediates the activation of calcium dependent endopeptidases, which facilitate the conversion of pro-insulin to insulin.
Effect of vitamin D on insulin action	<ul style="list-style-type: none"> • Vit. D mediates the transcriptional activation of human insulin gene (Vitamin D Responsive Element [VDRE] is present in human insulin gene promoter region) and also stimulates the expression of insulin receptor thereby enhancing insulin responsiveness for glucose transport.
	<ul style="list-style-type: none"> • Vit. D may have a beneficial effect on insulin action indirectly via its role in regulating extracellular calcium levels, as calcium is essential for insulin mediated processes in insulin responsive tissues.
Effect of vitamin D on Cytokines	<ul style="list-style-type: none"> • Vit.D may improve insulin sensitivity and promote beta-cell survival by modulating the effects of cytokines.
	<ul style="list-style-type: none"> • Vitamin D can down regulate the activation of NF-k B, which is an important regulator of genes encoding pro-inflammatory cytokines implicated in insulin resistance.

Conclusion:

The present study proves that significant hypovitaminosis D is prevalent in type 2 diabetic patients and there is significant inverse correlation between vitamin D and type 2 diabetes mellitus (p < 0.001). The present study and review of literature suggest that Vitamin D supplementation may have a role in reducing the risk of development of type 2 diabetes and it's supplementation may help in achieving better glycemic control and preventing complications.

CONFLICT OF INTEREST: NO CONFLICT OF INTEREST**REFERENCES**

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