

Association between hypovitaminosis D and diabetic retinopathy in type II diabetes mellitus

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Abstract

Background: Diabetes mellitus is associated with considerable morbidity and mortality with its prevalence increasing every year. Vitamin D plays an important role in calcium metabolism and vitamin D deficiency is associated with many diseases, including cancer, cardiovascular disease, and type 2 diabetes mellitus. The studies showing the effect of vitamin D on diabetic retinopathy are controversial and have shown inconclusive results. So there is the need to study the effect of vitamin D on diabetic retinopathy in patients with type 2 diabetes mellitus. **Aims and Objectives:** To quantitatively estimate the levels of vitamin D in serum and assess diabetic retinopathy in cases and controls. To find the association between status of Vitamin D and diabetic retinopathy in type 2 Diabetes mellitus. **Materials and Methods:** This study was conducted in department of Ophthalmology Gadag Institute of medical sciences Gadag, Karnataka. 50 patients with diabetic retinopathy were compared with 50 patients with diabetes and without diabetic retinopathy after taking an informed consent. Vitamin D was estimated by Chemiluminescence Immuno Assay (CLIA) method. Retinopathy was assessed using indirect ophthalmoscopy fasting and post prandial blood sugar was estimated by GOD-POD method. **Results:** vitamin D ($p=0.015$) was highly significant in patients with diabetic retinopathy as compared with diabetics without retinopathy. The study showed a negative correlation between vitamin D and diabetic retinopathy. **Conclusion:** Decreased vitamin D levels are statistically highly significant in diabetic retinopathy. Hypovitaminosis D is negatively correlated with diabetic retinopathy.

Key Word: Diabetes mellitus, Diabetic Retinopathy (DR), hypovitaminosis D

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INTRODUCTION

Diabetes mellitus is associated with considerable morbidity and mortality with its prevalence increasing every year (1,2). Incidence of type 2 Diabetes mellitus is 7.1% in India. Many modifiable and non modifiable risk factors contributing to diabetes mellitus have been found out but identification of easily modified risk factor is needed to reduce the incidence of type 2 diabetes³. T2DM

is a disorder associated with insulin resistance to the cells and decreased insulin secretion due to beta cell dysfunction⁴. Vitamin D plays an important role in calcium metabolism and vitamin D deficiency is associated with many diseases, including cancer, cardiovascular disease, and type 2 diabetes⁵. There is growing body of evidence that vitamin D deficiency is an important contributing factor in the development of both type 1 and type 2 diabetes. The β -cell in the pancreas which secretes insulin contains vitamin D receptors⁶. Several studies have shown that treatment with vitamin D is found to improve glucose tolerance and insulin resistance^{7,8}. Vitamin D deficiency leads to reduced insulin secretion⁹. Studies have also shown that vitamin D has an indirect effect on insulin secretion, by the effect of calcium on insulin secretion. Vitamin D brings up the calcium levels, leading to normal calcium flux through cell membranes, so decreased vitamin D may bring down calcium's ability to affect insulin secretion¹⁰. Diabetes mellitus contributes to the major threats to global health. Long standing diabetes

mellitus are more prone for going into vascular complications. It is been proposed that among the patients going in for vascular complications, 35% of patients have diabetic retinopathy (DR), about 7% have proliferative DR (PDR), 7% of patients have diabetic macular oedema, and 10% are grouped in vision-threatening conditions¹¹ Although many mechanisms have been proposed studies showing the relation between vitamin D and Diabetic retinopathy are controversial. So the present study is been designed to find the status of vitamin D in Diabetic retinopathy so as to reduce the risk of diabetes mellitus and its progression to ocular complications related with it.

OBJECTIVES

Measurement of fasting blood sugar (FBS) levels and post prandial blood sugar (PPBS) levels and vitamin D levels in cases and controls. To find the association between status of Vitamin D with diabetic retinopathy in type 2 Diabetes mellitus.

METHODOLOGY

Source of data: The subjects were selected from the patients coming to department of ophthalmology, Gadag Institute of Medical Sciences, Gadag. The study was carried out in the department of ophthalmology on the patients with type 2 Diabetes Mellitus. The patients with type 2 Diabetes Mellitus with retinopathy were considered as cases and patients with type 2 Diabetes Mellitus without retinopathy were included as controls. Both cases and controls were interviewed to obtain relevant data and the informed consent was taken to proceed with the study.

RESULTS

Table 1: Comparison of biochemical parameters between cases and controls

Variable	Cases (Mean±SD)	Controls (Mean±SD)	P value	Statistical significance
FBG(mg/dL)	170.7±38.3	122.2±8.5	0.005	HS
PPBG(mg/dL)	220±40.6	190.2±10.6	0.0014	HS
VIT D(ng/ml)	12.3±2.4	18.6±12.5	0.015	S

P value ≤ 0.05 is considered as statistically significant

FBG=Fasting blood glucose; PPBG = Post prandial blood glucose; VIT D= 25-OH Vitamin D ; HS = Highly Significant.

Table 2: shows the spearman correlation between the different parameters among type 2 diabetes mellitus cases

VARIABLE	r VALUE
Vit D and FBG in cases	-0.615
VIT D and PPBG in cases	-0.468

r value of -0.5 to -1.0 shows negative correlation

FBG = Fasting blood glucose; PPBG = Post prandial blood glucose; VIT D= 25-OH Vitamin D; r = spearman correlation coefficient

About 50 cases with type 2 diabetes mellitus with retinopathy and 50 cases with type 2 diabetes mellitus without retinopathy as controls were enrolled in the study. **Inclusion criteria:** Type 2 Diabetes mellitus cases having FBS of more than 120 mg/dl and PPBS of more than 180 mg/dl with and without retinopathy changes will be included in the study.

Exclusion criteria: type 1 diabetes mellitus cases, Obese subjects, smokers, gestational diabetes, hepatic failure, cases with pancreatic diseases or other systemic diseases, cases on vitamin D supplementation, patients on medications altering vitamin D metabolism like rifampin, phenytoin, or Phenobarbital, cases with hyperparathyroidism or hypoparathyroidism altering vitamin D levels were excluded from the study. Based on the inclusion and exclusion criteria, 50 cases and equal number controls were included in the study. Venous blood samples were collected from the subjects following a 12 hours fast, with all the aseptic precautions. The serum was separated by centrifugation and was used for the estimation of FBS and Vitamin D levels. blood sample was collected after one and a half hour of food to estimate PPBS. FBS and PPBS were estimated by Glucose oxidase (GOD-POD) method (12). Vitamin D was estimated by Chemiluminescence Immuno Assay (CLIA) method¹³ Diabetic retinopathy was evaluated in all patients after dilatation of both pupils with tropicamide plus phenylephrine combination eye drops with indirect ophthalmoscope examination in dark room. It was graded as No diabetic retinopathy, Non proliferative diabetic retinopathy and Proliferative diabetic retinopathy.

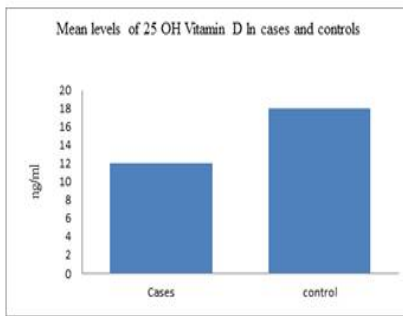


Figure 1

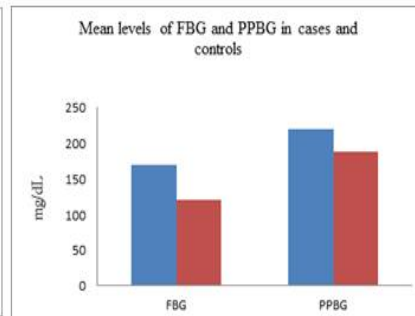


Figure 2

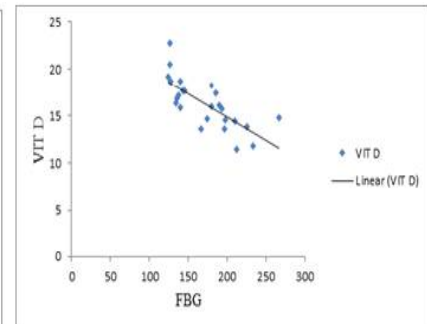


Figure 3

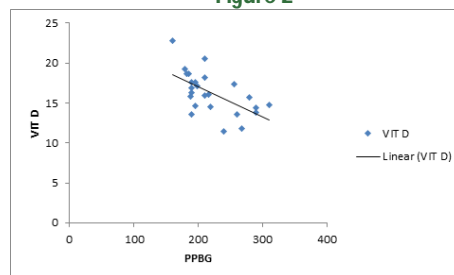


Figure 4

Figure 1: shows the mean 25 OH Vitamin D in the study group; **Figure 2:** shows the mean fasting blood glucose and post prandial blood glucose in the study group; **Figure 3:** Relationship between vitamin D and fasting blood glucose levels in the cases; **Figure 4:** Relationship between vitamin D and post prandial blood glucose levels in cases

DISCUSSION

Our study showed statistically highly significant mean values for fasting blood glucose levels and post prandial blood glucose levels and statistically significant mean values for 25 OH Vitamin D in cases as controls (table 1). Our study showed increased mean values for fasting blood glucose levels and post prandial blood glucose levels and 25 OH Vitamin D in cases as compared to controls (fig 1, fig 2). Our study revealed a negative correlation of 25 OH Vitamin D with fasting blood glucose levels and post prandial blood glucose levels in type 2 diabetes with retinopathy cases (table 2, fig 1, fig 2). Present study is similar to the study done by Bonakdaran *et al* who suggested that there is an inverse correlation between vitamin D insufficiency and diabetic retinopathy¹⁴. Our study is similar to study done by Patrick, P.A *et al* who reported that vitamin D levels are decreased in adults with diabetic retinopathy¹⁵. Results of study done by Aksoy *et al*. Are similar to our study which indicated that severity of DR is inversely related with vitamin D levels¹⁶. Present study shows similar results as various studies which indicated decreased vitamin D in diabetic retinopathy cases (17,18). Our study showed different results as compared to study done by Alam *et al* who found no association between vitamin D and diabetic retinopathy¹⁹. Various studies have shown the mechanisms related to vitamin D and diabetic retinopathy. Vitamin D receptors are present extensively in retina²⁰, the animal study have shown that

calcitriol is an inhibitor of neovascularisation in retina in a mouse model with an oxygen-induced ischemic retinopathy²¹. This evidence shows that vitamin D plays an important role in pathogenesis of diabetic retinopathy.

CONCLUSION

Our study indicates that there is a definite correlation between Vitamin D levels and diabetic retinopathy and poorly controlled diabetics have further lower values of Vitamin D which increases the severity of diabetic retinopathy. So the supplementation of Vitamin D in diabetics may improve the glycemic control of the patients and can decrease the rate of morbidity and mortality and can also improve the quality of life. Limitations of our study involved small sample size. Our study is cross-sectional in nature, there is also a need for prospective study with large population group to correlate the changes of vitamin D with different levels of progress of type 2 diabetes mellitus retinopathy changes. Seasonal changes were not included in our study as it is going to affect the synthesis of vitamin D by sunlight.

Implications: The present study will be useful to reduce the risk of diabetic retinopathy. If the association between Vitamin D and Diabetic retinopathy is proved then vitamin D supplementation can be given to the patients as it is one of the modifiable risk factor and can prevent the patients from going in to the complications related to DM.

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