



Original Article

The Association between Vitamin D Deficiency and Diabetic Retinopathy in Type 2 Diabetes

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Abstract

Background: *Diabetes mellitus is major and most common non-communicable disease in worldwide, specially developing country like India. Diabetic retinopathy is main complication of DM. It is major cause of blindness worldwide. Vitamin D deficiency is increase in world because of more indoor work and less exposure to sunlight. Vit. D has Anti- oxidant and Anti- angiogenesis property, its deficiency increase the chances of early retinal changes in diabetes patients in the form of Non- proliferative DR, proliferative DR, glaucoma other complications. Given these associations, we sought to determine the relationship between vitamin D insufficiency and diabetic retinopathy.*

Aims and Objectives

- 1) To estimate the serum Vitamin D levels in Diabetes.
- 2) Establish the association between the serum Vitamin D levels and Diabetic Retinopathy.

Materials and Methods: *Total of 98 diabetic patients either attending OPD or admitted in Department of Medicine, R.L. Jalappa Hospital and Research center, were assessed during September 2018 to November 2018. Patients were tested for HbA_{1c} levels and serum Vitamin D and labeled insufficient for Vitamin D when serum levels were <30ng/ml. Patients also underwent detail Fundoscopic examination and were classified into No Background Diabetic Retinopathy(BDR), Non Proliferative Diabetic Retinopathy(NPDR) of mild, moderate, severe grade and Proliferative Diabetic Retinopathy(PDR).*

Results: *Total 98 diabetic patients were included in study all patients were Vit D insufficient. 39 patients of diabetes with Vit D insufficiency had No background diabetic retinopathy, 38 patients were in mild-moderate NPDR group. 15 patients were in severe NPDR and 6 patients had Proliferative DR. In patients with No BDR the mean Vit D levels were 27.91±3.01 ng/ml. In mild- moderate and PDR the Vit D levels were 20.80±6.75 and 15.52±0.92 ng/ml respectively. In severe NPDR the Vit D levels were in range of 12.05±2.41ng/ml for Proliferative DR the Vit D levels were in range of 11.17±.1.91 ng/ml.*

Conclusion: *This study suggests that diabetic subjects, especially those with NPDR and PDR, have lower Vitamin D levels than those without diabetes.*

Keywords: *Diabetes Mellitus, Diabetic Retinopathy, Vitamin D.*

Introduction

Diabetes mellitus is a major cause of mortality and morbidity among non-communicable diseases. Diabetes mellitus is become like epidemic worldwide with an estimated prevalence increases from 2.8% 171 million of patients in 2000 to 4.4%366 million of patients by 2030 and constitutes one of the major threats to global health by 2030¹. Diabetes is well recognized in Indian population with 62 million diabetic individuals. India has maximum number of diabetic patients in the world. The diabetes is further compounded by various catastrophic microvascular and macrovascular complications targeting the vital organs in the body.

Diabetic retinopathy is major global complication related to diabetes and one of the major causes of blindness between the ages of 20 and 74 and it is 25 times more common than blindness due to other factor. Blindness in Diabetes is result from progressive diabetic retinopathy and neo vascularisation while it has been well established that intensive blood glucose control can lower the risk of microvascular complications from diabetes, the pathophysiology of retinopathy progression is not completely understood.²⁻⁴

Vit D deficiency is becoming major health problem around the world because of more indoor work and less exposure to sunlight. Vitamin D insufficiency has been implicated in the development of diabetes and also correlated with an elevated risk of cardiovascular disease, cancer, and mortality.⁵⁻⁷ Vit D has Anti proliferative, Anti-oxidant, Anti-angiogenesis property.

Vitamin D may play as important factor in the pathogenesis of diabetic retinopathy through its effects as a Anti proliferative, Anti-oxidant, Anti-angiogenesis property. Vitamin D exerts an anti-inflammatory effect by decreasing the proliferation of effect on inflammatory markers like lymphocytes, natural killer cells and several pro-inflammatory cytokines.⁸ It has been shown Calcitriol, which is active metabolite of Vit D is a potent inhibitor of retinal neovascularization in oxygen-induced ischemic retinopathy in both

animal and human model.⁹ Given these associations, we sought to determine the relationship between vitamin D insufficiency and diabetic retinopathy.

Materials and Methods

This study included patients of Type 2 Diabetes mellitus attending OPD and IPD of R. L. Jalappa Hospital, Tamaka, Kolar, from September 2018 to November 2018. Those patients with type 1 Diabetes, younger than 18 years, taking vitamin D supplements, on medications such as Rifampicin, phenobarbital were excluded from study.

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients

Patients were screened to determine their diabetes status, age, sex. Patients underwent routine ophthalmic examination, including dilated Fundoscopy, complete medical history questionnaire and their blood tested for hemoglobin A1c, 25-hydroxy vitamin D (25(OH)D). Hemoglobin A_{1c} levels will be measured using high performance liquid chromatography (HPLC). The Vitamin D levels will be measured from serum samples via an automated competitive immunoassay detected by chemiluminescence. Vitamin D insufficiency is considered when serum levels were less than 30ng/ml and Diabetes mellitus when HbA_{1c} level more than 6.4.

Patient were divided into no background diabetic retinopathy (No BDR) group consisted of patients with type 2 diabetes but no evidence of diabetic retinopathy, nonproliferative diabetic retinopathy (NPDR) group had evidence of retinopathy, such as microaneurysms, cotton-wool spots, intraretinal hemorrhages, or macular edema, but no evidence of retinal or iris neovascularization, proliferative diabetic retinopathy (PDR) group consisted of

neovascularization on the optic disc, retina, or iris, with or without vitreous hemorrhage or prior panretinal photocoagulation.

Results

Total 98 diabetic patients were included in study all patients were Vit D insufficient. Majority of the patients with diabetes were in age of 41-70 years of age. No gender predominance observed in patients of diabetes in our study. 46 patients of diabetes had VitD level in range of 12-24 ng/ml. (Table 1)

Table 1: Vit D Level distribution of patients studied

Vit D Level	No. of patients	%
<12	10	10.2
12-24	46	46.9
>24.1	42	42.9
Total	98	100.0

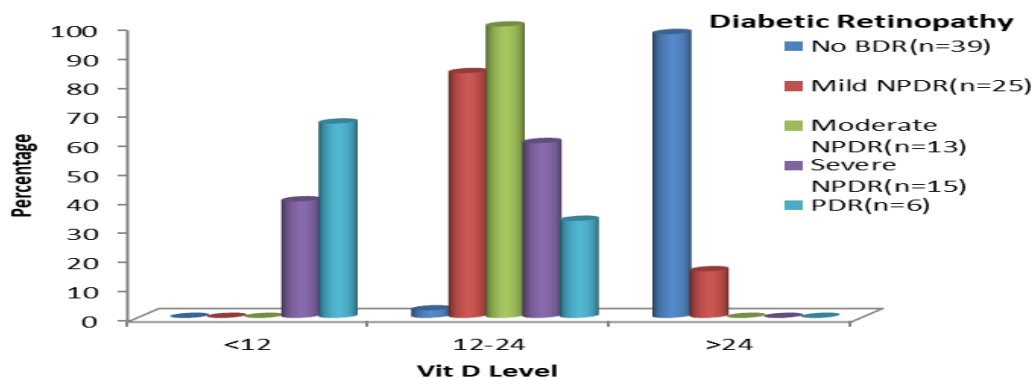
Mean ± SD: 21.00±7.59

39 patients of diabetes with Vit D insufficiency had No background diabetic retinopathy, 38 patients were in mild- moderate NPDR group. 15 patient were in severe NPDR and 6 patients had Proliferative DR.(Table 2)

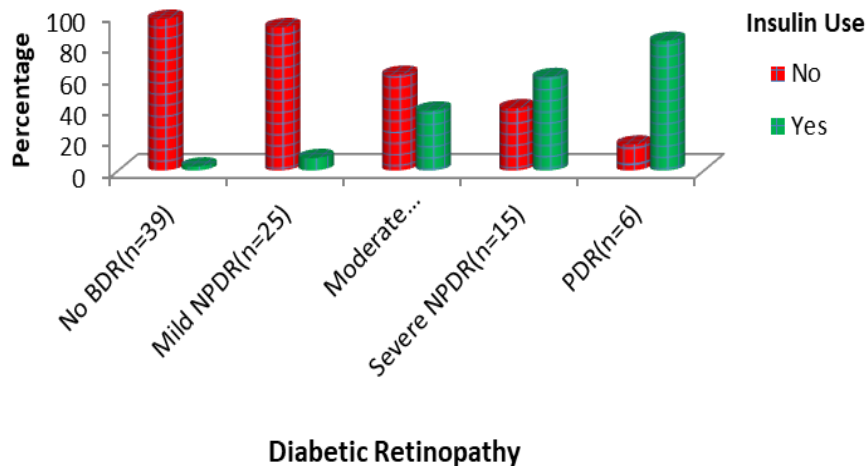
Table 2: Diabetic Retinopathy distribution of patients studied

Diabetic Retinopathy	No. of patients	%
NO BDR	39	39.8
MILD NPDR	25	25.5
MODERATE NPDR	13	13.3
SEVERE NPDR	15	15.3
PDR	6	6.1
Total	98	100.0

39 patients of diabetes with No BDR had serum Vit D level were > 24 ng/dl, mild –moderate, severe DR patients had serum Vit D level in range of 12-24 ng/ml. PDR patients had serum Vit D level < 12 ng/ml. (Graph 1)



Graph 1 percentage of patients with Vit D level



Graph 2 showing patients with DR and insulin use

Table 3 Comparison of age, HbA1c and Vit D levels according to Diabetic retinopathy

Variables	Diabetic Retinopathy					Total	P value
	No BDR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR		
Age in years	48.26±7.79	57.72±8.90	63.54±8.55	74.47±5.85	75.50±8.19	58.38±12.80	<0.001**
HbA1c%	7.02±0.22	8.02±0.39	8.32±0.33	9.33±0.57	9.47±0.80	7.95±0.98	<0.001**
Vit D Level	27.91±3.01	20.80±6.75	15.52±0.92	12.05±2.41	11.17±1.91	21.00±7.59	<0.001**

The mean ages for group of No BDR were 48.26±7.79 years, 75.50±8.19 years in group of PDR patients. The HbA1c levels for No BDR patients were in range of 7.02±0.22. In mild-moderate NPDR the HbA1c levels were 8.02±0.39 and 8.32±0.33 respectively. In Proliferative DR the HbA1c levels were in range of 9.47±0.80.

In patients with No BDR the mean Vit D levels were 27.91±3.01 ng/ml. In mild- moderate NPDR the Vit D levels were 20.80±6.75 and 15.52±0.92 ng/ml respectively. In severe NPDR the Vit D levels were in range of 12.05±2.41ng/ml for Proliferative DR the Vit D levels were in range of 11.17±.1.91 ng/ml.

Discussion

Our study was conducted to observe the relationship between Vit D and diabetes. It was observed that patients with diabetes had low levels of Vit D. It was also observed that, as the age of the patient and the duration of diabetes increased the levels of Vit D showed a steady decline. As the age advanced it was observed that the risk of acquiring complications of diabetes such as diabetic retinopathy also increased.

There was no significant difference in the distribution of male and females subjects in our study, however the mean vitamin D levels were seen to be of higher values in females as compared to Vit D levels in the male population as was observed in a similar study done by Payne et al¹⁰ and Joergensen et al.¹¹

HbA1c levels were also compared with the levels of Vit D in our study. Another significant finding was that the mean vitamin D levels were significantly more in subjects with lesser HbA1c levels than those with higher levels of HbA1c. The proportion of subjects with vitamin D insufficiency was seen to be more in those

subjects with higher HbA1c. Our findings were similar to Zoppinni et al¹² who also compared levels of HbA1c and levels of Vit D, and found that Glycated Haemoglobin was inversely related to Serum Vitamin D Levels in Type 2 Diabetics.

Another observation was done to assess the levels of Vit D with the various grades of retinopathy. There was also a significant and steady decline in mean serum vitamin D levels with increasing grades of Diabetic Retinopathy. The proportion of diabetics with vitamin D insufficiency is significantly more with increasing grades of Retinopathy. Payne et al¹⁰ found results comparable to our study.

Conclusion

Vitamin D plays a protective role through its effects on glycemic control and progression of diabetic retinopathy. It is possible that treating vitamin D insufficiency may lead to an improvement in blood sugar control, which could ultimately slow the progression of retinopathy. We, therefore propose that all patients with type 2 diabetes mellitus, besides undergoing afundoscopic examination to screen for retinopathy, must also be assessed for their vitamin D status at the point of diagnosis and supplemented appropriately if found insufficient so as to possibly prevent or even retard the progression of what has become the leading cause of blindness in the early adulthood till late ages.

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