

Deficiency of calcitriol in diabetic retinopathy patients of south Indian population

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Abstract

Background: Diabetes mellitus (DM) is a large public health disorder which affects more than 300 million individuals worldwide, with significant morbidity and mortality. The prevalence of Diabetic Retinopathy varies from 20% to 80% in different studies according to previous literature. The increased physical activity is highly associated with less severe levels of Diabetic Retinopathy. serum 25-hydroxyvitamin D (25(OH)D) levels were almost decreased in type 2 diabetic patients with retinopathy when compared with type 2 patients who had no microangiopathy. **Objectives** The purpose of this study was to evaluate the evidence for an association between diabetic retinopathy (DR) and vitamin D deficiency. **Materials and Methods:** This study was conducted from July 2016 to Dec 2016 in Ophthalmology department of ESIC Medical College and Hospital, Santhnagar, Hyderabad. During the study period, 100 subjects of both the sexes were included in the study after obtaining informed consent; 50 being cases with Diabetic Retinopathy and 50 without Diabetic Retinopathy, using convenient sampling. Exclusion criteria included patients having known risk factors of diabetic retinopathy mainly people who were hypertensive or pregnant and lactating women. The serum of the patients' samples were assessed by Chemiluminescence immunoassay [CLIA] of serum 25 hydroxy Vitamin D determination at ESIC Medical College and Hospital, Santhnagar, Hyderabad. Retinopathy was assessed using ZEISS VISUCAM 500 fundus camera at ESI Hospital, Nacharam, Hyderabad. **Results:** The sample included 50 patients with Diabetic Retinopathy and 50 without Diabetic Retinopathy. Mean age of the DR cases was 51.0 ± 10.4 years and those without DR were 52.0 ± 8.2 years. There were 25 (50%) males in patients with DR while 33 (66%) in patients without DR. The P-value was highly significant between both the groups ($p=0.001$). **Conclusion:** There is a statistically significant association between vitamin D deficiency and DR.

Key Word: Diabetic Retinopathy (DR), calcitriol, vitamin D Deficiency (VDD), serum 25-hydroxyvitamin.

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Received Date: 18/06/2018 Revised Date: 22/07/2018 Accepted Date: 10/08/2018

DOI: <https://doi.org/10.26611/1009722>

Access this article online

Quick Response Code:



Website:

www.medpulse.in

Accessed Date:
14 August 2018

INTRODUCTION

Diabetes mellitus (DM) is a large public health disorder which affects more than 300 million individuals worldwide, with significant morbidity and mortality¹. The

prevalence of Diabetic Retinopathy varies from 20% to 80% in different studies according to previous literature. Recent studies suggests that the number of people and its prevalence with diabetic retinopathy will increase to 191 million by 2030². Praidou *et al.* found that increased physical activity is highly associated with less severe levels of Diabetic Retinopathy³. The detailed pathophysiological mechanisms and other Diabetic Retinopathy risk factors are not fully clarified yet. Inukai *et al.* reported that serum 25-hydroxyvitamin D (25 (OH) D) levels were almost decreased in type² diabetic patients with retinopathy when compared with type 2 patients who had no microangiopathy⁴. However, others researchers suggested that no significant differences in calciferol status were found between type 2 diabetes with or without diabetic retinopathy. Alam *et al.* found there was no

How to cite this article: Gannaram Laxmi Prasad, Porika Ram Mohan Lal. Deficiency of calcitriol in diabetic retinopathy patients of south Indian population. *MedPulse International Journal of Ophthalmology*. August 2018; 7(2): 15-17.

<https://www.medpulse.in/Ophthalmology/>

association at all between serum 25(OH) D levels and the presence and the severity of diabetic retinopathy in his study population.⁵ Presently, there is insufficient evidence depicted whether serum vitamin D deficiency is related to diabetic retinopathy, and the determination of this relationship has rarely been conducted and observed. To address this issue, we carried out this analysis by pooling the results from observation studies to examine the highest potential association between vitamin D and diabetic retinopathy.

MATERIALS AND METHODS

This study was conducted from July 2016 to December 2016 in Ophthalmology Department of ESIC Medical College and Hospital, Sanathnagar, Hyderabad. During the study period, 100 subjects of both the sexes were included in the study after obtaining informed consent; 50 being cases with Diabetic Retinopathy and 50 without Diabetic Retinopathy, using convenient sampling.

Exclusion criteria included patients having known risk factors of diabetic retinopathy mainly people who were hypertensive or pregnant and lactating women. Rest all type 2 diabetics from general OP are admitted in Ophthalmology department, ESIC Medical College and Hospital, Sanathnagar, Hyderabad were included. Written and informed consent was obtained from all the subjects

and ethical approval was taken from the ethical committee of the institution. Data was collected from subjects on a pre-designed proforma filled by the principal investigator with the help of other investigators. Detailed information on their diabetic status was obtained which included family history and current clinical status, medication etc. Vitamin D concentrations were estimated in all 100 patients who were included in the study. The qualified nurse of the department collected the blood samples. The serum of the patients' samples were assessed by Chemiluminescence immunoassay [CLIA] of serum 25 hydroxy Vit-D determination at ESIC Medical College and Hospital, Sanathnagar, Hyderabad. Retinopathy was assessed using ZEISS VISUCAM 500 fundus camera at ESI Hospital, Nacharam, Hyderabad. For this, a trained technician deputed in the unit for this purpose took the pictures from the department of Ophthalmology. DR was graded by the consultant Ophthalmologist as none, non-proliferative and proliferative retinopathy from the department. SPSS version 17 was used to analyze the data. Calcitriol levels were categorized as low levels and normal to high levels. The range taken was from 8.6ng/ml to 37.2ng/ml for normal to high levels. P value was determined using chi square tests for the comparison of both the groups.

RESULTS

Table 1: Effect of Calciferol deficiency in Diabetic retinopathy patients

S. No	Levels of Calcitriol	Normal	Diabetic Retinopathy	Total	P-Value
1	Low (<8.6ng/ml)	3(6%)	17 (34%)	20 (20%)	<0.001
2	Normal to high (8.2-37.2 ng/ml)	47(54%)	33 (66%)	80(80%)	<0.001
3	Total	50 (100%)	50 (50%)	100(100%)	<0.001

The sample included 50 patients with Diabetic Retinopathy and 50 without Diabetic Retinopathy. Mean age of the DR cases was 51.0 ± 10.4 years and those without DR were 52.0 ± 8.2 years. There were 25 (50%) males in patients with DR while 33 (66%) in patients without DR. The P-value was highly significant between both the groups ($p=0.001$). Table 1. An increased vitamin D deficiency was demonstrated in Diabetics with progressively increasing retinopathy. Among 50 cases with Diabetic Retinopathy, non-proliferative Diabetic Retinopathy was in 40 (80%) cases, out of which 10 were with low vitamin D levels and 30 with normal to high vitamin D levels. Out of 10 (20%) cases of proliferative DR, 6 were with low Vitamin D levels and 4 with Normal to high vitamin D levels.

DISCUSSION

To the best of our knowledge, the role of vitamin D in cellular inflammation pathways, endothelial cell proliferation, and angiogenesis is well established, however, its role in DR has to date been obscured in clinical studies by disease pathogenesis (diabetes Type I vs Type II), varied DR classifications, and differing patient ethnic populations⁶. It was observed, no effect of age, gender or duration of diabetes in this study. The study also demonstrated the severity of vitamin D deficiency with progression of DR amongst type 2 diabetic patients. Similar finding have been reported in another study⁷. He *et al*, suggested that serum vitamin D levels may be used as a low cost Diabetic Retinopathy screening tool in Chinese patients, suggesting that such patients with diabetes and VDD should undergo more routine diabetic eye exams⁸. Aksoy *et al*. also suggested

that there exists an inverse relationship between serum vitamin D levels and the severity of DR⁹. In a previous studies, conducted in Lebanon, Japan, Italy, and China found significantly increased odds of vitamin D deficiency and lower serum 25(OH)D in patients with DR¹⁰. Suzuki *et al* suggested that subjects with PDR have low serum 25-OH vitamin D concentration than those without retinopathy and those with early diabetic retinopathy¹¹. Another study done by Patricia *et al* suggested an association between severity of diabetic retinopathy and prevalence of vitamin D deficiency¹². There are several important limitations to the present study as per or knowledge goes. The small number of studies eligible for this review and the different study designs prevented the extraction of more data regarding the highly association between vitamin D deficiency and DR. There are only 2 large population based studies from the United Kingdom and South Korea. Source of population in other studies are from clinics and subgroup of prospective study in diabetes, which may result in having different in population characteristics. However, the mechanism underlying ARMD (age related macular degeneration) also is thought to be ischemic in nature, with activation of angiogenic pathways responsible for the choroidal neovascularization and retinal edema seen in advanced ARMD. It seems to be there may be an important role for the supplementation of vitamin D and other antiangiogenic vitamins in the medical management of DR. The main strength of this study is giving strong evidence of the association of serum vitamin D and diabetic retinopathy. However, there were several limitations in this study. Future such eye screening studies will be more factual in terms of the information gleaned by the implementation of scientific sampling techniques, strict adherence to complete completion of standardized data entry forms along with better verification of the patients diabetic status and biochemistry.

CONCLUSION

The present study demonstrated a highly significant association between VDD and DR and a statistically significant difference in mean serum vitamin D levels between DR and non-DR patients. The definite causative

role of VDD and development of DR should be explored further. Vitamin D supplementation as a protective mechanism against the development and progression of DR warrants further investigation

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Source of Support: None Declared
Conflict of Interest: None Declared