# VITAMIN D DEFICIENCY IN PATIENTS WITH DIABETIC RETINOPATHY

Farzana Khan<sup>1</sup>, Robina Usman<sup>2</sup>, Shafaq Zafar<sup>3</sup>, Shamaila Wadud<sup>4</sup>

1-4 Peshawar Medical College, Peshawar - Pakistan. Address for Correspondence: Dr. Farzana Khan House No. 355, Sector P/II, Street 11, Phase 4 Hayatabad, Peshawar - Pakistan. Email: drfsalman@yahoo.com Date Received: August 25, 2016 Date Revised: April 18, 2017 Date Accepted: April 28, 2017

# ABSTRACT

**Objective:** To determine the relationship of vitamin D deficiency with diabetic retinopathy (DR) in patients with type 2 diabetes mellitus.

**Methodology:** This comparative study recruited one hundred cases from January to April 2012 from the Department of Endocrinology, Hayatabad Medical Complex, Peshawar; 50 with DR and 50 without DR. Frequency of Vitamin D levels was assessed and compared between the groups. The data was analyzed using SPSS v.17 and to compare the groups, Chi square test was used.

**Results:** Mean age of the cases with DR was  $53.0 \pm 10.6$  years and those without DR  $54.0 \pm 8.5$  years. Significant vitamin D deficiency was demonstrated in diabetics with any stage of retinopathy as compared to those without retinopathy. Among cases with non-proliferative retinopathy (NPDR) 41 (82%) had normal to low levels of vitamin D. In cases with PDR 9(18%) had normal to low levels of vitamin D levels. P-value was highly significant (p=0.001).

**Conclusion:** Diabetics with retinopathy were found to have significal vitamin D deficiency as compared to those without retinopathy. As the DR increased, levels of vitamin D decreased.

Key Words: Vitamin D, Diabetic retinopathy, Diabetes mellitus

This article may be cited as: Khan F, Usman R, Zafar S, Wadud S. Vitamin D deficiency in patients with diabetic retinopathy. J Postgrad Med Inst 2017; 31(2): 196-8.

## **INTRODUCTION**

Vitamin D is a fat-soluble vitamin, well known for its enhancing effects on the immune system. It has anti-oxidant, anti-inflammatory and anti-proliferative functions in all areas of the body including the eyes¹. There is considerable data to suggest that vitamin D can inhibit angiogenesis either by a direct action on endothelial cells or indirect effect through angiogenic signaling or combination of both². According to a study, vitamin D plays an important role in prevention of diabetic retinopathy (DR) because on one hand it is essential for normal insulin release and glucose metabolism while on the other hand it decreases the level of inflammatory cytokines that are up-regulated in diabetes².

People without any eye disease were found to have highest serum vitamin D levels while those with proliferative retinopathy had the lowest levels<sup>3</sup>. A study has shown that levels of vitamin D were inversely correlated with a higher grade of retinopathy in type-2 diabetic patients with more advanced retinopathy, especially lower levels were associated with proliferative retinopathy<sup>4</sup>. According to a study, 33.3% of their diabetic population was suffering from diabetic retinopathy, a condition amenable to timely and cost effective treatment<sup>5</sup>.

Type-2 diabetic patients have significant association between the existence of proliferative retinopathy and a decrease in vitamin D levels<sup>6</sup>. The plasma concentration of vitamin D has been inversely correlated with development and severity of diabetic retinopathy<sup>7</sup>. Low levels of vitamin D might act as a risk marker for development or progression of diabetic retinopathy<sup>8</sup>.

Diabetic retinopathy is a leading cause of visual disability and blindness. Although the treatment of diabetic retinopathy has greatly improved but the management of progressive changes remains a challenge. Determining an association between vitamin D deficiency and severity of diabetic retinopathy can help establish a preventive measure that can have a beneficial effect on the prognosis of diabetic retinopathy and thus improve the quality of life of those suffering from this devastating disease. Therefore, this study was planned to determine the relationship of vitamin D deficiency with diabetic retinopathy (DR) in patients with type 2 diabetes mellitus.

### **METHODOLOGY**

This comparative study was conducted from January to April 2012 in Endocrinology Unit of Hayatabad Medical Complex, Peshawar. During this period, 100 subjects,

	•	•	. ,	
	Normal	Diabetic Reti- nopathy	Total	P-Value
Vitamin D Low Levels (<8.2ng/ml)	(1) 2%	(18) 36%	(19) 19.0%	
Vitamin D Normal to High Levels (8.2-37.4 ng/ml)	(49) 98%	(32) 64%	(81) 81%	0.001
Total	(50) 100%	(50) 100%	(100) 100%	

Table 1: Relationship of vitamin D deficiency and diabetic retinopathy

admitted in the unit, were included in the study after obtaining informed consent; 50 being cases with DR and 50 without DR, using convenient sampling. Exclusion criteria included patients having known risk factors related to diabetic retinopathy especially people who were hypertensive or pregnant and lactating women. Rest all type 2 diabetics admitted in Endocrinology Unit of Hayatabad Medical Complex, Peshawar were included.

Written consent was obtained from all the subjects and ethical approval was taken from the ethical board of the institution. Data was collected from subjects on a pre-designed proforma filled by the principal investigator. Detailed information on their diabetic status was obtained which included family history and current clinical status.

25-hydroxy vitamin D concentrations were assessed in all 100 patients. The qualified nurse of the unit took the blood. The serum of the patients' was assessed by ELISA technique using commercially available kit Euroimmun 25-hydroxy Vitamin D ELISA (Germany) <sup>9</sup>. The principal investigator did the payment of the tests. Retinopathy was assessed using Canon CR-1 Mark II Digital Retinal Camera<sup>10</sup>. For this, a trained technician deputed in the unit for this purpose took the pictures. Diabetic retinopathy was graded by the consultant endocrinologist as none, non-proliferative (NPDR) and proliferative retinopathy (PDR).

SPSS version 17 was used to analyze the data. Vitamin D levels were categorized as low levels and normal to high levels. The range taken was from 8.2ng/ml to 37.4ng/ml for normal to high levels. P value was determined using chi square tests for the comparison of both the groups.

## RESULTS

The sample included 50 patients with DR and 50 without DR. Mean age of the DR cases was  $53.0 \pm 10.6$  years and those without DR was  $54.0 \pm 8.5$  years. There were 25 (50%) males in patients with DR while 32 (64%) in patients without DR. The P-value was highly significant between both the groups (p=0.001). (Table 1)

An increased frequency of vitamin D deficiency was demonstrated in diabetics with progressively increasing

retinopathy. Among 50 cases with DR, non-proliferative DR was in 41 (82%) cases, out of which 12 were with low vitamin D levels and 29 with normal to high vitamin D levels. Out of 9 (18%) cases of proliferative DR, 6 were with low Vitamin D levels and 3 with Normal to high vitamin D levels

## DISCUSSION

This study showed that as progression of DR increases the levels of vitamin D decreases. To our knowledge, this is the first study done in Peshawar-Pakistan, which showed the frequencyof low levels of vitamin D and progression of diabetic retinopathy in type 2 diabetics.

There was 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 study<sup>11</sup>. A clinical based cross sectional study suggested that patients with diabetes especially those with PDR have low levels of vitamin D as compared to those without diabetes<sup>12</sup>. Study done by Suzuki et al<sup>8</sup> suggested that subjects with PDR have low serum 25-OH vitamin D concentration than those without retinopathy and those with early diabetic retinopathy. Another study done by Patricia et al<sup>13</sup> suggested an association between severity of diabetic retinopathy and prevalence of vitamin D deficiency.

#### CONCLUSION

Diabetics with retinopathy were found to have significal vitamin D deficiency as compared to those without retinopathy. As the DR increased, levels of vitamin D decreased. Low levels of vitamin D areimportant not only for the development of retinopathy but also for its progression.

#### REFERENCES

- Millen AE, Sahli MW, Nie J, LaMonte MJ, Lutsey PL, Klein BE et al. Adequate vitamin D status is associated with the reduced odds of prevalent diabetic retinopathy in African Americans and Caucasians. Cardiovasc Diabetol 2016; 15:128.
- Maj E, Papiernik D, Wietrzyk J. Antiangiogenic cancer treatment: The great discovery and greater complexity

- (Review). Int J Oncol 2016; 49:1773-84.
- Klein BEK, Klein R. Lifestyle exposures and eye diseases in adults. Am J Ophthalmol 2007; 144:961-9.
- 4. Kaur H, Donaghue KC, Chan AK, Benitez-Aguirre P, Hing S, Lloyd M et al. Vitamin D deficiency is associated with retinopathy in children and adolescents with type 1 diabetes. Diabetes Care 2011; 34:1400-2.
- Kiyani H, Rehan N, Ullah N. Frequency of retinopathy among diabetics admitted in a teaching hospital in Lahore. J Ayub Med Coll Abottabad 2003; 15:53-6.
- Joergensen C, Hovind P, Schmedes A, Parving HH, Rossing P. Vitamin D levels microvascular complications and mortality in type 1 diabetes. Diabetes care 2011; 34:1081-5.
- Aksoy H, Akcay F, Kurtul N, Baykal O, Avci B. Serum 1,25 dihydroxy vitamin D (1,25(OH)2D3), 25 hydroxy vitamin D (25(OH) D) and parathormone levels in diabetic retinopathy. Clin Biochem 2000; 33:47-51.
- 8. Suzuki A, Kotake M, Ono Y, Kato T, Oda N, Hayakawa N et al. Hypovitaminosis D in type 2 diabetes mellitus: association with microvascular complications and type of treatment. Endocr J 2006; 53:503-10.
- Takashi H, Shibuya M. The vascular endothelial growth factor (VEGF) receptor system and its role under physiological and pathological conditions. Clin Sci (London) 2005; 109:227-41.

- Bates DO, Curry FE. Vascular endothelial growth factor increases permeability via a Ca<sup>+2</sup> dependent pathways. Am J Physiol 1997; 273:H687-94.
- 11. Wirostko B, Wong TY, Simo R. Vascular endothelial growth factor and diabetic complications. Prog Retin Eye Res 2008; 27:608-621.
- Gao BB, Clermont A, Rook S, Fonda SJ, Srinivasan VJ, Wolkowski M, et al. Extracellular carbonic anhydrase mediates hemorrhagic retinal and cerebral vascular permeability through prekallikrein activation. Nat Med 2007; 13:181-8.
- Patrick PA, Visintainer PF, Shi Q, Weiss IA, Brand DA. Vitamin D and retinopathy in adults with diabetes mellitus. Arch Ophthalmol 2012; 130:756-60.
- 14. Khan F, Usman R, Wadud S, Zafar S, Abideen ZU. Association of vitamin D with retinopathy in patients with type 2 diabetes mellitus. J Med Sci 2015; 23:58-61.

#### **CONTRIBUTORS**

FK Conceived the idea, collected data and drafted the manuscript and final revision of the manuscript. RU helped compilation and interpretation of data and statistical analysis. SZ did literature survey and statistical analysis. SW did Proof reading and references management. All authors contributed significantly to the submitted manuscript.