IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 10 Ser.3 (October. 2020), PP 42-47
www.iosrjournals.org

A Study on Relationship between Diabetic Retinopathy and Hypovitaminosis D in Eastern India

Rajarshi As[1],SrilaGhoshChowdhury[2],Manika Sadhu Ghorai[3]
MoumitaMandal[4]
MD –PGT[1]; Department of Physiology,
Assist Professor [2];Departmentof Physiology,
Professor &Head [3]; Department, of Physiology
Demonstrator [4]; Department of Physiology.
Calcutta National Medical College, Kolkata.India
Corresponding author: Srila Ghosh Chowdhury.

Abstract
DM is rapidly escalating globally as well as in India affecting all age groups. Diabetic retinopathy (DR) is one of the most prominent pathological microvascular complications in diabetes. Several studies reported an association between hypovitaminosisDand an increased risk of diabetic retinopathy in type 2 diabeticpatientsin various populations all over world. Studies considering an association between hypovitaminosis D withdiabetic retinopathy are not adequate particularly in eastern India.The present study was conducted in a tertiary care teaching hospital approved by the institutional Research and Ethics Committee, aimed to evaluate the relationship of Diabetic retinopathy and hypovitaminosis ThisStudyconducted on 107 type 2 diabetic patients of 40 yearsof age& above.Results were analyzed by using SPSS version16.Statistical analysis used Chi square test for qualitativevariables.Results showed that there was significant association of hypovitaminosis D with Diabetic retinopathy.

Keywords*: diabetic retinopathy,hypovitaminosisD, type 2 diabetes(T2DM),vitamin D*

Date of Submission: 26-09-2020 Date of Acceptance: 09-10-2020

I. Introduction

Diabetesmellitus is asevereandgrowingpublichealthproblemwithasubstantial economicburden worldwide. More than 300 million individualsare suffering, with significant morbidity and mortality [1]. In addition to the deleteriouseffects of the disease itself, its long-term complications can conspicuously decrease the quality of life of diabetes patients. Diabetes patients withuncontrolled or poorly-controlled blood glucose are at high risk of microvascular complications. Diabetic retinopathy is among the most common diabetic complications, and is the leading cause of blindness among working-aged individuals worldwide [2].

In India, in spite of adequate sunlight exposure throughout theyear, several reports documented hypovitaminosisD.Vitamin D plays important roles in the metabolism of glucose. It directly stimulates insulin secretion from betacells of pancreas and increases the number of insulin receptor and sensitivity. T2DM is a state of chronic low-grade chronic inflammation and beinganti-inflammatory in nature, vitamin D exerts beneficial effects on glycemic control and prevention of development of complications like diabetic retinopathy (DR)[3].

The prevalence of DR varies from 20% to 80% in different studies. Recent estimates suggest that the number of people with diabetic retinopathy will increase to 191 million by 2030 [4]. More than 60% of type 2 Diabetic are found to have retinopathy after 20 years of their illness.While vitamin D deficiency is a global issue, several studies reported an association of vitamin D deficiency with increased prevalence of retinopathy in diabetic patients though few studies showed conflicting results.

Aims: To evaluate the prevalence of vitamin D deficiency in patients with type2 diabetes mellitus and the relationship between vitamin D status and presence of diabetic retinopathy.

II. Materials & Methods

A cross sectional study was conducted with 107type 2 diabetic patients,aged 40 years and above; attending Diabetic clinic;CNMC, Kolkata. The inclusion criterion was patientswith type 2 DM and the exclusion criterion was patients who were on vitamin D supplementation for last 6 months. Allpatients underwent direct ophthalmoscopy (β Heine-200) after taking detailed history, & relevant blood investigation for evaluation of glycaemic status &Vitamin D.

Serum 25-hydroxyvitamin D [25 (OH) D] concentration is measured to assess vitamin D status. In our study level of vitamin D was classified according to serum 25-hydroxyvitamin D (25(OH)D) into three groups,sufficient, insufficient and deficient.

>30 ng/mL: sufficient.
20 -30 ng/ml: insufficient
<20 ng/ml: deficient

Diabetic Retinopathy was classified clinically into three groups according to **International Clinical Diabetic Retinopathy Disease Severity Scale[5]:**

Proposed Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
No Apparent Retinopathy	€ No abnormalities
Mild Non-Proliferative Diabetic Retinopathy	Microaneurysms only
Moderate Non-Proliferative Diabetic Retinopathy	More than just microaneurysms but less than Severe NPDR
Severe Non-Proliferative Diabetic Retinopathy	Any of the following: € More than 20 intraretinal haemorrhages in each of 4quadrants € Definite venous beading in 2+ quadrants € Prominent IRMA in 1+ quadrant And no signs of proliferative retinopathy
Proliferative Diabetic Retinopathy	One or more of the following: € Neovascularization € Vitreous/preretinal haemorrhage

The data was analysed through SPSS version 16. Descriptive statistics of the mean, standard deviation and standard error was used to examine the data. Pvalue ≤0.05 deemed statistically significant.

III. Results

Table 1: Distribution of study participants according to their socio-demographic characteristics (N=107)

Characteristics	**Frequency (%)**	**Descriptive statistics**
Age		Mean-56.19 years Median-56 SD- 8.51 Maximum-82 Minimum- 40 Range- 40 -82
40-49	22(20.6)	
50-59	48(44.9)	
60-69	28(26.2)	
70-79	8(7.4)	
80-89	1(0.9)	
Gender		
Female	64(59.8)	
Male	43(40.2)	

Table 2: Comparison of age, Duration of DM, blood sugar level (FBS, PPBS), HbA1C, Vit D level in presence or absence of diabetic retinopathy in our study group (Mann Whitney Test)

variables	No DR N=46 Mean ± SD	DR N=61 Mean ± SD	*P* value
Age	56.41± 8.42	56.02 8.65	0.897
Duration of DM	7.54± 6.24	11.73± 7,60	0.002***
FBS	148.72±63.32	149.38±47.07	0.483
PPBS	205.64±108.25	221.10±85.14	0.060
HbA1C	7.72±2.08	8.73±1.36	<0.001***
Vit D	25.21±15.29	18.18±5.71	0.001**

Table 3: Frequency & percentage of different grades of diabetic retinopathy in our study according to International Clinical Diabetic Retinopathy Disease Severity Scale

Grading ofDiabetic Retinopathy	Frequency	%
No Apparent Retinopathy	46	42.9
Mild NPDR	12	11.3

Moderate NPDR	33	30.8
Severe NPDR	13	12.2
PDR	3	2.8
Total	107	100

Table4: Frequency & percentage of patients with deficient, insufficient & sufficient VitD level.

Vit D status	Frequency	%
Deficient	55	51.4
Insufficient	44	41.1
Sufficient	8	7.5
	107	100

92.5% of study population are hypovitaminosis **D**

Table 5: Relationship between grading of retinopathy & HbA1C

HbA1C	No Retinopathy	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	*P* value
<6.5%	9	0	0	0	0	<0.001***
6.5 -7%	17	0	1	0	0	
7.1 -8%	8	7	10	1	0	
8.1 -10 %	7	2	20	9	2	
>10%	5	3	2	3	1	

Table 6: Association between gender and severity of diabetic retinopathy (Pearson's Chi Square test for independence of attributes) (N=107)

Gender		DR					Total	
		No Retinopathy	Mild NPDR	Moderate NPDR	Severe NPDR	PDR		*P* Value
	Female	35(76.09)	6(50)	19(57.58)	2(15.38)	2(66.67)	64(59.81)	0.001***
	Male	11(23.91)	6(50)	14(42.42)	11(84.62)	**1(33.33)**	43(40.19)	
Total		46(100)	12(100)	33(100)	13(100)	3(100)	107(100)	

Table 7: Association ofVitamin Dstatus with severity of diabetic retinopathy (Fisher 's Exact test).

VitD		DR					Total	
		No Retinopathy	Mild NPDR	Moderate NPDR	Severe NPDR	PDR		*P*Value
	Deficient	15(32.61)	5(41.67)	20(60.61)	12(92.31)	3(100)	55(51.4)	0.003***
	Insufficient	24(52.17)	6(50)	13(39.39)	1(7.69)	0(0)	44(41.12)	
	Sufficient	7(15.22)	1(8.33)	0(0)	0(0)	0(0)	8(7.48)	
Total		46(100)	12(100)	33(100)	13(100)	3(100)	107(100)	

shows more is the Vitamin D deficiency, there is chance of more severe retinopathy.

Table8: Comparison between grading of retinopathy &duration of DM, Vit D, HbA1C

	No Retinopathy N=46 Mean ± SD	MildNPDR N=12 Mean ± SD	Moderate NPDR N=33 Mean ± SD	Severe NPDR N=13 Mean ± SD	PDR N=3 Mean ± SD	*P* Value
Age	56.41± 8.42	51.83 ±7.92	57.18 ±7.78	58.46 ± 10.67	49.33 ±3.79	0.129
Duration	7.54 ±6.24	10.46 ±8.42	13.39 ±7.21	10.15±7.92	5.33 ± 2.08	0.004***
FBS	148.72 ±63.32	176.25 ±73.23	139.94 ±38.81	152.31 ±32.74	133 ±14.11	0.581
PPBs	205.64 ±108.25	265.08±118.11	202.69 ±67.77	240.46 ±83.68	163.73 ±25.95	0.082
HbA1C	7.72 ±2.08	8.84 ±2.12	8.37 ±0.93	9.38±1.26	9.30 ±1.31	<0.001***
VIT D	25.21 ±15.29	20.45 ±6.36	18.43 ±5.88	16.46 ±4.36	13.71 ±3.07	0.004***

shows as duration prolongs, more hypovitaminosis D; poor control of HbA1C is significantly associated with severe diabetic retinopathy.

Table 9: Correlation betweenVit D & grading of retinopathy, HbA1C, FBS& PPBS

Spearman's rho	DR grading	Correlation Coefficient	*P* Value
		- *0.374*	<0.001***
	HbA1C	- 0.385	<0.001***
	FBS	- 0.231	0.017*
	PPBs	- 0.272	<0.005***

Figure 9 A

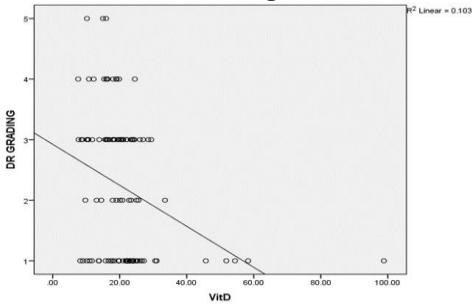

Figure 9B

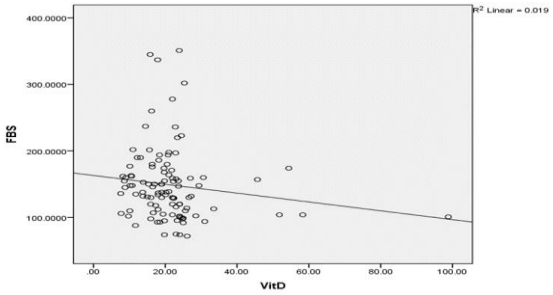

Figure 9C

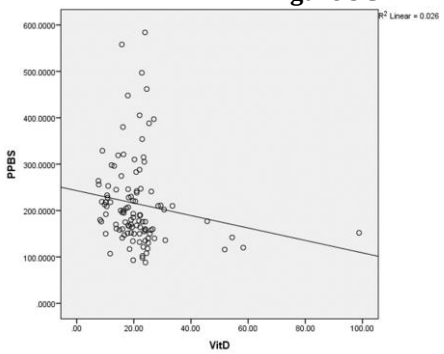

Figure 9D

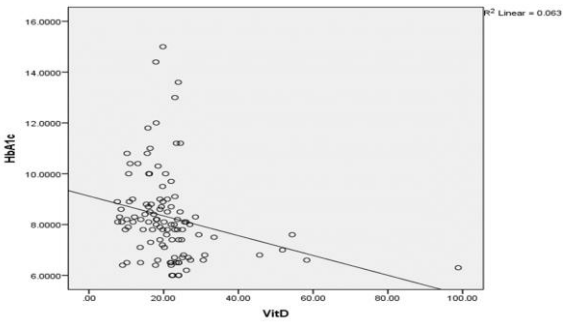

Fig 9A Scatter diagram shows that there is a linear & inverse or negative correlation between serum ***VitD*** level and severity of diabetic retinopathy (**DR**), strength of which is medium (within the range of -0.3 to -0.5) &*P*value is statistically significant.

Fig 9B diagram shows that there is a linear & inverse or negative correlation between serum Vit D level & FBS, but the strength is weak and P value is significant.

Fig 9C shows that there is a linear & inverse or negative correlation between serum Vit D level & PPBS strength is weak and P value is significant.

Fig 9D Scatter diagram shows that there is a linear & inverse or negative correlation between serum **VitD level & HbA1C**, the strength of which is medium.

IV. Discussion

Vitamin D deficiency is an independent risk factor for diabetic retinopathy. The effects of Vit D on theimmune system andangiogenesis in retina is well known. Vitamin D exerts anti-inflammatory effect by decreasing theproliferation of lymphocytes, natural killer cells, and several pro-inflammatory cytokines[6]A mouse oxygen-induced ischemic retinopathy model([7]) showed thatcalcitriol,the active metabolite of vitamin D, is a potent inhibitor of retinalneovascularization& vascular muscle proliferation . Recent study foundan association between vascular endothelial dysfunctionwithvitamin D deficiency in middle aged and elderly adults[8].,[16]

In our study, mean age of all patients was 56.19 ±8.51. Maximum were in 50-59 years,females were 59.8%while males were 40.2% (table1). According to the Centers for Disease Control and Prevention (CDC) in 2012, adults aged 45 to 64years were the most diagnosed age group for diabetes mellitus & it is similar to our study.Age is not significantly associated with presence & severity of DR in our study(table 2,8) which is similar to the findings of Lima et al [9].We found malesare more affected with DR than that of female & it is statistically

significant .84.62% of severe NPDR group was male patients. (table 6). This observation is similar to other studies.[17]

Mean duration of diabetes mellitus in 'No DR' group is 7.54yrs while that of PDR is 11.73yrs.i.emore is the duration of diabetes, more is the chance of severity of diabetic retinopathy (table 2); The relation between duration of diabetes& presence ofdiabetic retinopathy is statistically significant(P 0.002).The relation between duration of diabetes&severity of diabetic retinopathy is statistically significant(P 0.004) (table 8). this observationis similar tostudy done by Bajajet al.[10]

An optimal concentration of vitamin D is strongly proven to be necessary for efficient insulin secretion and function, and vitamin D receptors (VDR) expressed in every human tissue, including retina. Vitamin D may play a protective role through its effects on glycemic control. Poor glycemic status is a significant risk factors for the development and progression of diabetic retinopathy.[11]. Hypovitaminosis D is found in 92.5% patients in our study. Most of the patients are deficient(<20ng/ml) in vit D status (51%), 41% are insufficient (Table 2) in our study population. (table 4). Similar results have been reported by various studies[8,12].

Poor glycemicstatus of patients with DR was reflected in our study (table 5). Mean HbA1c was also found 8.3% in patients.similarly, Lima et al [9]observed that individuals with poor glycemic control (HbA1C>7%) were more likely to develop DR. Chronic hyperglycemia is responsible for a chain of events responsible for DR.

Astudy on Turkish type 2 diabetic subjects (with retinopathy) found no differences in serum 25(OH)D between type 2 diabetic patients according to the presence or absence of retinopathy and also to the severity of retinopathy [12]. In contrast, Suzuki et al. showed that Japanese type 2 diabetic patients with proliferative retinopathy had lower serum 25(OH)D [13]. A study inUSAshowed a greater prevalence of vitamin D deficiency with increased severity of retinopathy [8]. In our study mean serum 25(OH)D level without DR was 25.21±15.29ng/ml,whereas in patient with DR, vit D level was 18.18±5.7ng/ml. (table 2). Several researchers found a close relationship between Vit D deficiency and diabetic retinopathy. Our study confirms the association ofHypovitaminosis D withseverity of diabetic retinopathy in type 2 diabetes in eastern India.

A recent large, population-based, cross-sectional study in Korea confirmed that there is an inverse relationship of 25(OH)D concentrations with the presence of any retinopathy and also with proliferative retinopathy [15]. This study did not provide details on the type of diabetes of the included subjects. A close relationship between Vit D deficiency and DR showed an inverse association between vitamin 25(OH)D concentration and the severity of DR. [15] which is similar to our study. (table 9)

Most of the reports were able to identify an association between hypovitaminosis D and diabetic retinopathy. Additionally, those studies that performed a detailed characterization of the severity of retinopathy revealed that proliferative or advanced retinopathy grades were clearly associated withhypovitaminosis D[8,15,18]. Additionally, it is remarkable that, as in our study, most others have found an inverse association of vitamin D status and the severity of retinopathy [12,14.15,18)

Thus,ur study confirms the association of a higher frequency of hypovitaminosis D with diabetic retinopathy in patients with type 2 diabetesin eastern India. Further, these parameters of poor vitamin D status are also associated with the severity of diabetic retinopathy. These findings reveal the potential role of vitamin D in the pathogenesis of diabetic retinopathy.[8,15,17]So, our study is in accordance with the majority of previous reports.

V. Conclusion

India is facing epidemics of T2DM and hypovitaminosisD across all age groups in urban as well as rural region. Association of poor vitamin D statuswith the severity of diabetic retinopathy is further confirmed from this study. However, Patients with Vit D deficiency should be screened and treated as needed to prevent progression of the disease to proliferative stage.

Future research with a larger sample is needed to find whether vitamin D supplementation may treat or prevent DR in patient with type 2DM. However, we are in great need of well-designed prospective observational studies sufficiently powered to test the role of vitamin D status in the development of diabetic retinopathy.

References

[1]. Sherwin R., Jastreboff A.M. Year in diabetes 2012: the diabetes tsunami. J. Clin. Endocrinol. Metab. 2012;97:4293–4301. doi: 10.1210/jc.2012-3487. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[2]. Klein B.E. Overview of epidemiologic studies of diabetic retinopathy. Ophthalmic Epidemiol. 2007;14:179–183. doi: 10.1080/09286580701396720. [PubMed] [CrossRef] [Google Scholar]

[3]. Shilpa Balaji Asegaonkar ,Vitamin D and Type 2 Diabetes Mellitus: Indian Perspectives . *. Journal of Diabetic Complications & Medicine 2016

[4]. Zheng, Y.; He, M.; Congdon, N. The worldwide epidemic of diabetic retinopathy. Indian J. Ophthalmol.2012,60, 428–431. [PubMed]

[5]. Wilkinson C.P.,Ferris F.L., et al.Proposed International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales.Ophthalmol. 2012;130:756-760.(American Academy of Ophthalmology[The Eye M.D. Association]

[6]. Palomer X, Gonzalez-Clemente JM, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes ObesMetab. 2008;10:185–197.
[7]. Albert DM, Scheef EA, Wang S, et al. Calcitriol is a potent inhibitor of retinal neovascularization. Invest Ophthalmol Vis Sci.m2007;48:2327–2334
[8]. J. F. Payne, R. Ray, D. G. Watson et al., "Vitamin D insufficiency in diabetic retinopathy," Endocrine Practice, vol. 18, no. 2, pp. 185–193, 2012.View at: Publisher Site | Google Scholar
[9]. Lima et al.risk factors for diabetic retinopathy: a case control study. Int J Retin vitr.2016:2:21
[10]. Bajaj S, Singh RP, Dwivedi NC, Singh K,Gupta A, Mathur M. Vitamin D levels andmicrovascular complications in type2diabetes. Indian J EndocrMetab2014;18:537-41
[11]. Klein R, Klein BE, Moss SE. Relationship of glycemic control to diabetic microvascular complications in diabetes mellitus. Ann Intern Med. 1996;124:90–96. [PubMed] [Google Scholar]
[12]. H. Aksoy, F. Akçay, N. Kurtul, O. Baykal, and B. Avci, "Serum 1,25 dihydroxy vitamin D (1,25(OH)2D3), 25 hydroxy vitamin D (25(OH)D) and parathormone levels in diabetic retinopathy," Clinical Biochemistry, vol. 33, no. 1, pp. 47–51, 2000.View at: Publisher Site | Google Scholar
[13]. A. Suzuki, M. Kotake, Y. Ono et al., "Hypovitaminosis D in type 2 diabetes mellitus: association with microvascular complications and type of treatment," Endocrine Journal, vol. 53, no. 4, pp. 503–510, 2006.View at: Publisher Site | Google Scholar
[14]. Sadat Ali M, Al Elq A. Osteoporosis in Saudi Arabia; A pilot study. Ann Saudi Med. 2006;26:450–454. [PMC free article] [PubMed] [Google Scholar) .Incidence of Vitamin D Deficiency in Patients with Type II Diabetes Mellitus and its Relation to the Severity of Retinopathy
[15]. D. Jee, K. d. Han, E. C. Kim, and D. Vavvas, "Inverse association between high blood 25-hydroxyvitamin D levels and diabetic retinopathy in a representative Korean population," PLoS ONE, vol. 9, no. 12, Article ID e115199, 2014. View at: Publisher Site | Google Scholar
[16]. .Jablonski KL, Chonchol M, Pierce GL, Walker AE, Seals DR. 25-Hydroxyvitamin D deficiency is associated with inflammation-linked vascular endothelial dysfunction in middle-aged and older adults. Hypertension. 2011;57:63–9. [PMC free article] [PubMed] [Google Scholar
[17]. P. A. Patrick, P. F. Visintainer, Q. Shi, I. A. Weiss, and D. A. Brand, "Vitamin D and retinopathy in adults with diabetes mellitus," Archives of Ophthalmology, vol. 130, no. 6, pp. 756–760, 2012. View at: Publisher Site | Google Scholar
[18]. R. He, J. Shen, F. Liu et al., "Vitamin D deficiency increases the risk of retinopathy in Chinese patients with Type 2 diabetes," Diabetic Medicine, vol. 31, no. 12, pp. 1657–1664, 2014. View at: Publisher Site | Google Scholar
[19]. The ACCORD Study Group and ACCORD Eye Study Group Effects of medical therapies on retinopathy progression in type 2 diabetes. N Engl J Med. 2010;363:233–44. [PMC free article] [PubMed] [Google Scholar]
[20]. Glen Y Ozawa 1, Marcus A Bearse Jr, Anthony J Adams,Male-female differences in diabetic retinopathy?2014 Dec 29. (Pub med)

Srila Ghosh Chowdhury, et. al. "A Study on Relationship between Diabetic Retinopathy and Hypovitaminosis D in Eastern India." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(10), 2020, pp. 42-47.