



## A STUDY ON THE CORRELATION OF DIABETIC RETINOPATHY IN TYPE II DIABETES MELLITUS WITH SERUM VITAMIN D LEVELS

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### ABSTRACT

**INTRODUCTION:** Diabetes mellitus is a major public health problem with significant morbidity and mortality. Diabetic retinopathy is one of the most common microvascular complications of Diabetes mellitus causing blindness. Vitamin D is a fat soluble vitamin involved in maintenance of mineral homeostasis and bone remodelling. Vitamin D deficiency is highly prevalent in type I and type II Diabetes. **METHOD:** 38 diabetic without ocular disease and 30 diabetic with retinopathy were taken as cases and 38 age sex matched healthy persons were taken as controls. Serum Vit D and glucose were estimated and retinopathy was diagnosed by fundus examination. The results were statistically analysed. **RESULTS:** Statistical analysis of the results shows a negative correlation between FBS and HbA1C with Vitamin D level in diabetic retinopathy patients. **CONCLUSION:** Patients with Diabetic retinopathy has lower serum Vitamin D level than diabetic patients without retinopathy.

**KEYWORDS :** Diabetes Mellitus, Diabetic retinopathy, Vit D deficiency

### INTRODUCTION:

Diabetes Mellitus (DM) is a large public health problem which affects more than 300 million individuals in the world, with significant morbidity and mortality worldwide.<sup>1</sup> Diabetic retinopathy is among the most common diabetic complications and is the leading cause of blindness among working aged individuals worldwide.<sup>2</sup> In 2018, more than 500 million cases of type 2 Diabetes Mellitus have been reported worldwide.<sup>3</sup> Diabetic retinopathy is one of the most common microvascular complications of Diabetes Mellitus and is one of the leading cause of preventable blindness and visual impairment.<sup>4</sup> Diabetes is the cause of 2.6% of global blindness.<sup>5</sup>

Vitamin D deficiency is highly prevalent worldwide.<sup>6</sup> Serum 25-hydroxy vitamin D<sub>3</sub> [25(OH)D] is a better indicator of vitamin D sufficiency than the active hormone, that is 1,25 dihydroxy vitamin D<sub>3</sub>.<sup>7</sup> The main biological actions of Vitamin D include the maintenance of mineral homeostasis and the regulation of bone remodelling.<sup>8</sup> Multiple studies have previously shown that Vitamin D deficiency is highly prevalent in type I and type II Diabetes.<sup>9</sup> Additionally there is a growing interest on the potential role of vitamin D deficiency in the development of diabetic micro and macroangiopathic complication.<sup>9,10</sup> However, different studies show that there is an association between Vitamin D deficiency and Diabetic retinopathy while some other studies contradict the role of Vitamin D level with Diabetic retinopathy.

### AIMS AND OBJECTIVES:

- To estimate the serum Vitamin D levels in individuals with type II Diabetes Mellitus.
- To establish the association between Vitamin D deficiency and Diabetic retinopathy in Type II Diabetes Mellitus.

### Study Design:

This study was an institution based observational study conducted at Regional Institute of Ophthalmology in collaboration with Central Clinical Laboratory (Biochemistry) of Gauhati Medical College & Hospital

### Study Population:

- The subjects were divided into 3 groups
- Controls: healthy persons without diabetes
  - Cases 1: diabetics without ocular disease
  - Cases 2: diabetics with retinopathy

### Sample Size:

106 samples were taken of which 38 were controls, 38 diabetics without ocular disease and 30 diabetics with retinopathy were taken as

cases. An informed and written consent was obtained from the study participants. Institutional Ethical Committee clearance was taken prior to conducting the study.

### Inclusion Criteria:

- Diagnosed cases of type II Diabetes Mellitus patients.
- Age group between 20 years to 80 years and both sexes were included.

### Exclusion Criteria:

- Any media opacity occluding the fundus examination.
- Conditions mimicking Diabetic retinopathy, hypertensive retinopathy, retinal vascular occlusion, age related macular degeneration, macular oedema due to other causes.
- Patients with renal and hepatic diseases were excluded.
- CVS complications like Coronary artery disease, peripheral artery disease etc.
- Patients taking oral Vitamin D or calcium supplements.

### Study Duration:

1 (one) year

### METHODS:

All study participants were subjected to detailed history and clinical examinations and findings were documented. Systemic examination was done. A detailed eye examination was done. Retinopathy was classified according to the International Clinical Disease Severity Scale. Diabetic macular oedema if present was again graded. Fundus photograph and Optical Coherence Tomography (OCT) imaging of all diabetic retinopathy cases were recorded. Fundus Fluorescence Angiography and OCT was done only when required. With all aseptic and antiseptic measures 5 ml whole blood is to be drawn from the median cubital vein and centrifuged in a centrifuge machine for 5 minutes at the rate of 3000 rpm for Laboratory investigations.

### Laboratory investigations:

- Routine blood investigations: Hb%, TLC, DLC, ESR
- Routine urine examination for sugar, albumin, pus cells, RBCs
- Serum creatinine
- Blood glucose estimation: Fasting plasma glucose, 2 hour postprandial glucose and HbA<sub>1c</sub>
- Fasting lipid profile
- Liver function test
- Serum 25(OH)D<sub>3</sub>

Test for estimation of serum 25(OH) OD<sub>3</sub> was done using the VITROS ECi/ECiQ/5600 Immunodiagnostic Systems and serum plasma

glucose by micro slide using photometry, both in VITROS 5600.

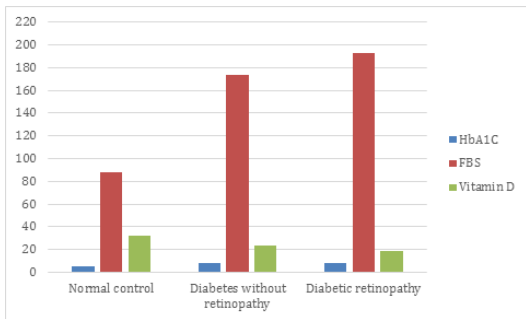
**RESULTS AND OBSERVATIONS:**

**Table 1: Age And Sex Distribution Of Subjects**

Variables	Groups	Groups					
		No diabetes and no ocular disease (n=38)		Diabetic without ocular disease (n=38)		Diabetic retinopathy (n=30)	
		Number of subjects	Percentage	Number of subjects	Percentage	Number of subjects	Percentage
Age in years	20 - 40	18	47.37	14	36.84	13	43.33
	41 - 60	15	39.47	17	44.74	11	36.67
	61 - 80	5	13.16	7	18.42	6	20
Sex	Male	18	47.37	17	44.74	15	50
	Female	20	52.63	21	55.26	15	50

**Table 2: Demographic profile of different groups viz. Normal control, Diabetes without retinopathy and Diabetic retinopathy**

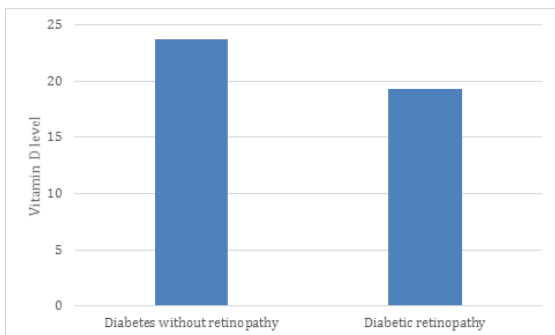
Variables	No diabetes and no ocular disease (n=38)	Diabetic without ocular disease (n=38)	Diabetic retinopathy (n=30)
Age (Years)	44.68 ± 12.62	48.79 ± 11.01	46.37 ± 11.99
Sex (Male/Female)	18/20	17/21	15/15
FBS (mg/dl)	88 ± 14.24	173.21 ± 27.63	192.83 ± 33.64
HbA1C (%)	4.97 ± 0.55	8.41 ± 1.07	8.52 ± 1
Vitamin D	31.82 ± 14.87	23.71 ± 2.46	19.3 ± 6.73



**Figure 1 Shows The Statistical Difference In Parameters HbA1C, FBS And Vitamin D Between Different Groups**

**Table 3: Statistical comparison of different parameters between Diabetics without retinopathy and Diabetics with retinopathy. Difference between Vitamin D level is significant (p<0.05)**

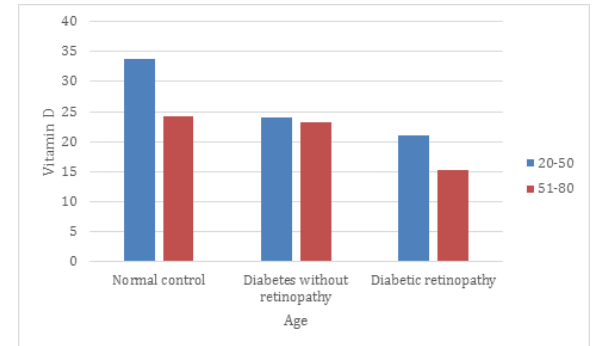
Variables	Diabetic without ocular disease (n=38)	Diabetic retinopathy (n=30)	t	p
Age (Years)	48.79 ± 11.01	46.37 ± 11.99	0.319	0.752
Sex (Male/Female)	17/21	15/15		
FBS (mg/dl)	173.21 ± 27.63	192.83 ± 33.64	2.41	0.023
HbA1C (%)	8.41 ± 1.07	8.52 ± 1	0.407	0.687
Vitamin D	23.71 ± 2.46	19.3 ± 6.73	3.201	0.003 (<0.05)



**Figure 2 Shows The Statistical Difference In Vitamin D Level Between Diabetics Without Retinopathy And Diabetics With Retinopathy**

**Table 4: Age wise difference in Vitamin D level in different groups**

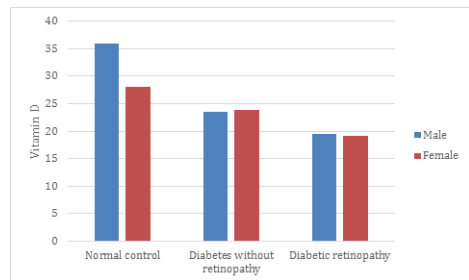
Age	Vitamin D level in different Groups		
	Normal control	Diabetes without retinopathy	Diabetic retinopathy
20-50	33.84	24.03	21
51-80	24.25	23.32	15.32



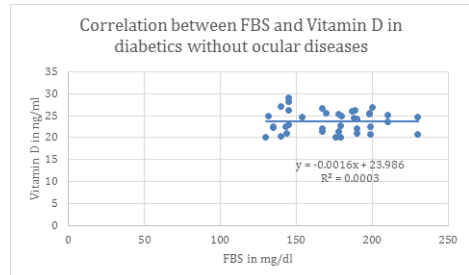
**Figure 3 Shows The Statistical Difference In Age Wise Vitamin D Level In Different Groups**

**Table 5: Gender Wise Difference In Vitamin D Level In Different Groups**

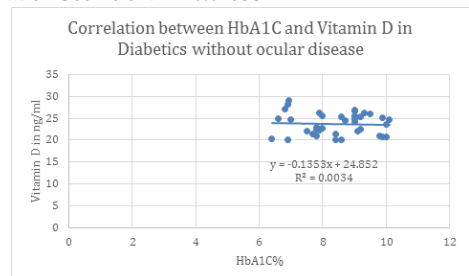
Sex	Vitamin D level in different Groups		
	Normal control	Diabetes without retinopathy	Diabetic retinopathy
Male	35.95	23.44	19.46
Female	28.11	23.94	19.14



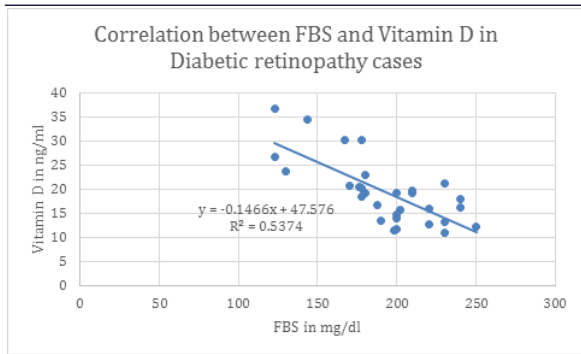
**Figure 4 Shows The Statistical Difference In Gender Wise Vitamin D Level In Different Groups**



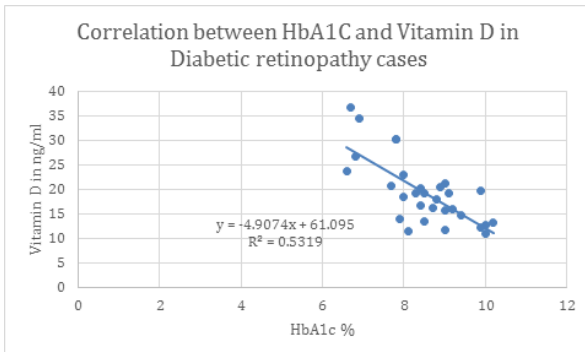
**Figure 5 Shows That There Is No Correlation Between FBS And Vitamin D Level In Diabetics Without Ocular Disease With Correlation Coefficient r = -0.01758**



**Figure 6 Shows That There Is No Correlation Between HbA1C And Vitamin D Level In Diabetics Without Ocular Disease With Correlation Coefficient r = -0.05872354**



**Figure 7 Shows That There Is Negative Correlation Between FBS And Vitamin D In Diabetic Retinopathy Cases With Correlation Coefficient  $r = -0.73308275$  Which Is Significant With  $P < 0.05$ .**



**Figure 8 Shows That There Is Negative Correlation Between HbA1c And Vitamin D In Diabetic Retinopathy Cases With Correlation Coefficient  $r = -0.72929118$  Which Is Significant With  $P < 0.05$ .**

#### DISCUSSION:

In the current study, we evaluated the serum levels of Vitamin D in normal persons, Diabetic patients without retinopathy and Diabetic patients with retinopathy. Findings show that Diabetics with retinopathy has lower mean Vitamin D concentration in serum than Diabetics without retinopathy (fig 2). These results are comparable to other studies. Payne et al found that diabetic patients, especially those with PDR, had lower 25 (OH) D levels than those without diabetes.<sup>11</sup> Similarly, Luo et al in their meta-analysis that included eight studies involving 13,435 participants showed vitamin D deficiency (serum 25 (OH) D levels  $< 20$  ng/mL) increased the risk of DR (OR = 2.03, 95% CI: 1.07–3.86)<sup>12</sup> On the contrary, some studies found no differences in serum vitamin D levels between diabetic patients with and without retinopathy.<sup>13,14</sup>

Evidence shows that vitamin D may affect the pathogenesis of DR via its effects on angiogenesis by changing the presence of hypoxia-inducible products, such as vascular endothelial growth factor (VEGF).<sup>15</sup> Ben-Shoshan et al found that 1, 25 (OH)<sub>2</sub>D<sub>3</sub> decreases the protein expression of both regulated hypoxia-inducible factor (HIF)-1 $\alpha$  subunit and the VEGF in human cancer cells.<sup>16</sup> Vitamin D reduces inflammatory products by decreasing the lymphocyte proliferation and cytokine production.<sup>17</sup> Moreover, vitamin D deficiency influences the activity of tissue matrix metalloproteinase (MMPs) and C-reactive protein (CRP) that are involved in microangiopathies.<sup>18</sup>

Older age is additional risk factor for diabetic retinopathy. In a study by Bonakdaran S et al, patients with proliferative diabetic retinopathy (PDR) were older age than patients with NPDR and NDR but differences were not significant<sup>19</sup>. This finding is similar to our study (table 4 and fig 3).

In correlation studies, it was found that there is no correlation between FBS and HbA1C with Vitamin D levels in diabetic patients without retinopathy (fig 5 and fig 6). But in diabetic retinopathy patients, negative correlation was found between FBS and HbA1C with Vitamin D level (fig 7 and fig 8). Hence higher the FBS and HbA1C, lower is the Vitamin D level. For the first time in 1999, Aksoy<sup>20</sup> found that severity of diabetic retinopathy was negatively related with serum level of 1, 25 dihydroxy vitamin D [1, 25 (OH)<sub>2</sub>D<sub>3</sub>]. This result is supported by other studies of adults with type 2 diabetes and children

and adolescents with type 1 diabetes.<sup>21,22</sup>

#### CONCLUSION:

From the findings of this study, it can be concluded that, patients with Diabetic retinopathy has lower serum Vitamin D level than diabetic patients without retinopathy. Vitamin D insufficiency also correlates with severity of Diabetes Mellitus.

#### Conflict Of Interest:

There is no conflict of interest between the authors. The study was self funded by the authors.

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