

# A pilot Study of 25-Hydroxy Vitamin D in Egyptian Diabetic Patients with Diabetic Retinopathy

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**D**iabetic retinopathy is a highly specific vascular complication and a sight-threatening problem related to diabetes. It is characterized by gradually progressive alterations in the retinal microvasculature, leading to retinal non-perfusion, increased vascular permeability and pathologically intraocular proliferation of retinal vessels <sup>(1)</sup>.

The cause of complications in the diabetic state has been a subject of intense research for over half of a century. However, two major clinical trials established the relationship of poor glycemic control to diabetic retinopathy <sup>(2, 3)</sup>. The precise relationship of other factors to diabetic complications is still not clear.

Vitamin D is now recognized as an important prohormone in health and disease <sup>(4)</sup>. Recently, vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes <sup>(5)</sup>.

## **Objective:**

To study the presence of any relationship between 25 (OH) vitamin D level and different stages of diabetic retinopathy.

## **Research Design and Methods:**

This study was conducted on 50 type 2 Egyptian diabetic patients (divided into two groups):

- Group (I): 25 patients with diabetic retinopathy.
- Group (II): 25 patients without diabetic retinopathy.

And 50 healthy volunteers matched by age and sex selected as a control group (Group III).

The patients were subjected to:

- Full history taking and thorough clinical examination.
- Fasting blood sugar and HbA1c.
- Renal functions, liver functions, lipid profile.
- Serum calcium, serum phosphorous.
- Intact parathyroid hormone (i-PTH) and serum 25 hydroxy vitamin D<sub>3</sub> (25-OH D<sub>3</sub>) levels.
- A complete ophthalmic and fundus examination was done for all patients.

The diabetic patients with retinopathy divided according to fundus examination as follows:

Non proliferative diabetic retinopathy (NPDR)		Proliferative diabetic retinopathy (PDR)
Moderate	Severe	
When more than microaneurysms are present but none of the “severe characteristics” are observed.	When any one of these three parameters is detected in ophthalmic fundus examination: (1) More than twenty intraretinal hemorrhages in each of four quadrants; (2) Venous beading in two quadrants; (3) Prominent intraretinal microvascular abnormality in one quadrant and no signs of proliferative retinopathy.	Progressive disorder characterized by the presence of retinal vessel microaneurysms, hemorrhages, exudates and edema <sup>(6)</sup> .
<b>± clinically significant macular edema (CSME)</b>		

**Exclusion Criteria:** Type 1 diabetic patients. Type 2 diabetic patients who are receiving vitamin D or VDR agonist or calcium supplements or any medications that may affect vitamin D level. Pregnant women, smokers, patients with acute hyperglycemic states. Patients with chronic liver disease, patients with serum creatinine > 1.5 mg/dl in male or > 1.4 mg/dl in female, patients with GFR < 90 ml / min/1.73 m<sup>2</sup> and cancer patients.

## Results:

Table (1): Comparison between the different studied groups

	<b>Group I (type 2 diabetics with DR) (N=25) Mean <math>\pm</math>SD</b>	<b>Group II (type 2 diabetics without DR) (N=25) Mean <math>\pm</math>SD</b>	<b>Group III (control) (N=50) Mean <math>\pm</math>SD</b>	<b>P</b>
Age (years)	53.80 $\pm$ 8.67	53.08 $\pm$ 7.77	51.60 $\pm$ 6.85	>0.05
Duration of type 2 DM (years)	<b>17.96 <math>\pm</math> 4.08</b>	15.44 $\pm$ 3.54	-	<b>&lt;0.05*</b>
BMI (Kg/m <sup>2</sup> )	28.85 $\pm$ 3.90	27.93 $\pm$ 3.89	27.02 $\pm$ 3.06	>0.05
SBP (mmHg)	<b>140.60 <math>\pm</math> 13.10</b>	131.40 $\pm$ 15.11	121.30 $\pm$ 5.23	<b>&lt;0.01**</b>
DBP (mmHg)	<b>89.60 <math>\pm</math> 7.90</b>	81.98 $\pm$ 4.68	79.70 $\pm$ 4.09	<b>&lt;0.01**</b>
FBS (mg/dl)	<b>252.60 <math>\pm</math> 50.50</b>	210.08 $\pm$ 51.40	83.18 $\pm$ 10.59	<b>&lt;0.01**</b>
HbA1c %	<b>10.01 <math>\pm</math> 1.82</b>	8.24 $\pm$ 1.76	4.82 $\pm$ 0.47	<b>&lt;0.01**</b>
S. Cr. (mg/dl)	0.80 $\pm$ 0.08	0.85 $\pm$ 0.14	0.80 $\pm$ 0.06	>0.05
GFR (ml/min /1.73 m <sup>2</sup> )	109.32 $\pm$ 18.77	110.44 $\pm$ 6.67	115.38 $\pm$ 18.47	>0.05
Urinary albumin/creatinine ratio ( $\mu$ g/mg)	<b>124.44 <math>\pm</math> 30.32</b>	86.07 $\pm$ 20.80	12.84 $\pm$ 2.44	<b>&lt;0.01**</b>

<b>Total cholesterol (mg/dl)</b>	<b>250.64 ± 61.51</b>	234.76 ± 51.40	155.30 ± 19.18	<b>&lt;0.01**</b>
<b>Triglycerides (mg/dl)</b>	<b>178.48 ± 44.26</b>	173.24 ± 42.69	88.36 ± 21.19	<b>&lt;0.01**</b>
<b>LDL- cholesterol (mg/dl)</b>	<b>175.52 ± 43.65</b>	163.17 ± 40.09	86.89 ± 19.33	<b>&lt;0.01**</b>
<b>HDL- cholesterol (mg/dl)</b>	39.44 ± 7.74	36.68 ± 6.61	<b>50.86 ± 4.55</b>	<b>&lt;0.01**</b>
<b>Total calcium (mg/dl)</b>	9.28 ± 0.56	9.16 ± 0.56	9.26 ± 0.47	>0.05
<b>Serum phosphorus (mg/dl)</b>	3.59 ± 0.48	3.68 ± 0.46	3.69 ± 0.57	>0.05
<b>Intact Parathyroid Hormone (pg/ml)</b>	<b>46.68 ± 11.26</b>	41.21 ± 7.62	34.01 ± 8.03	<b>&lt;0.01**</b>
<b>25 (OH) vitamin D<sub>3</sub> (ng/ml)</b>	<b>18.78 ± 4.62</b>	24.17 ± 5.80	45.79 ± 11.08	<b>&lt;0.01**</b>

**Table (2): Comparison between the different studied groups of diabetic retinopathy:**

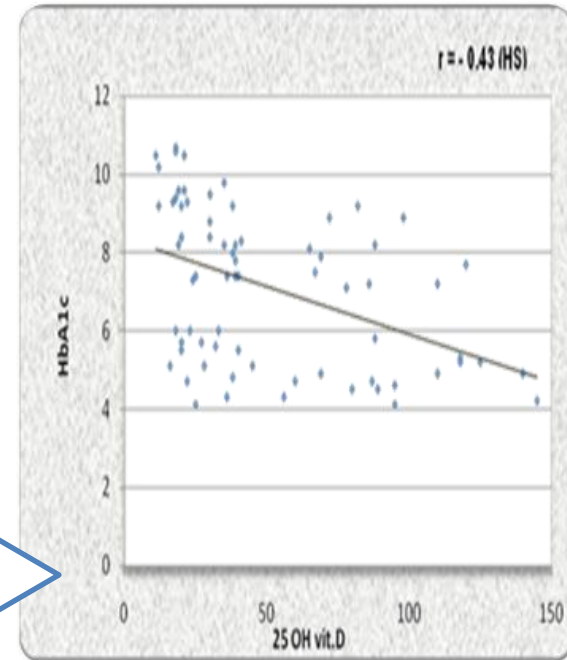
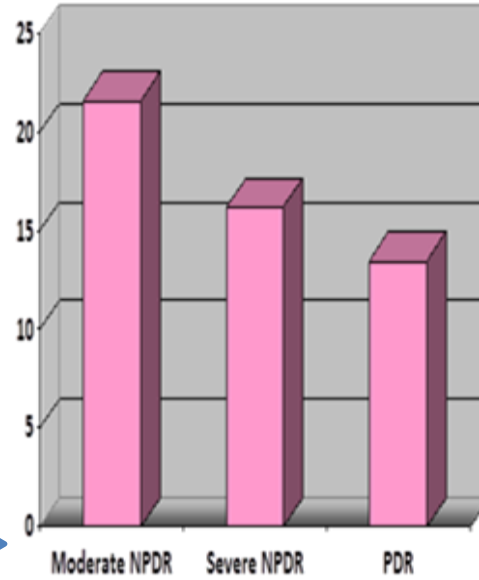
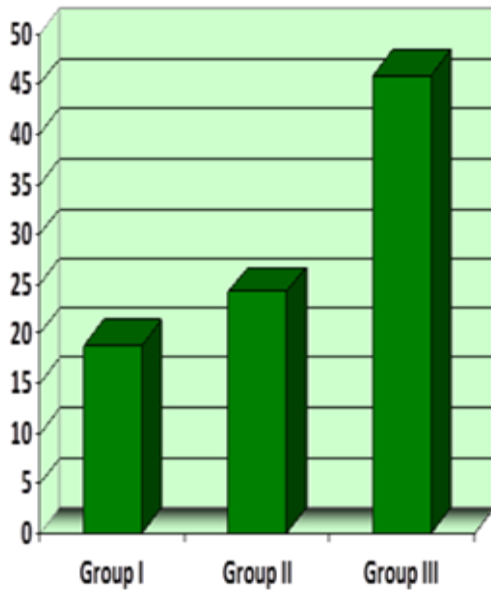
	<b>Moderate Non Proliferative Diabetic Retinopathy (N=15) Mean±SD</b>	<b>Severe Non Proliferative Diabetic Retinopathy (N=4) Mean±SD</b>	<b>Proliferative Diabetic Retinopathy (N=6) Mean ±SD</b>	<b>P</b>
<b>Age (years)</b>	46.87 ± 2.88	55.25 ± 2.50	<b>66.00 ± 3.74</b>	<b>&lt;0.01<sup>**</sup></b>
<b>Duration of type DM (years)</b>	14.80 ± 3.34	19.25 ± 1.50	<b>25.00 ± 3.16</b>	<b>&lt;0.01<sup>**</sup></b>
<b>BMI (Kg/m<sup>2</sup>)</b>	28.73 ± 3.76	27.08 ± 4.22	30.33 ± 4.19	>0.05
<b>SP (mmHg)</b>	136.30 ± 13.69	142.50 ± 9.57	<b>151.67 ± 7.53</b>	<b>&lt;0.05<sup>*</sup></b>
<b>DBP (mmHg)</b>	87.67 ± 7.99	86.25 ± 4.79	<b>96.67 ± 5.16</b>	<b>&lt;0.05<sup>*</sup></b>
<b>FBS (mg/dl)</b>	223.20 ± 33.57	273.00 ± 40.61	<b>301.50 ± 38.71</b>	<b>&lt;0.01<sup>**</sup></b>
<b>HbA1c %</b>	8.91 ± 0.94	10.63 ± 1.52	<b>12.35 ± 1.26</b>	<b>&lt;0.01<sup>**</sup></b>
<b>S. cr. (mg/dl)</b>	0.77 ± 0.05	0.78 ± 0.02	<b>0.86 ± 0.11</b>	<b>&lt;0.05<sup>*</sup></b>
<b>GFR (ml/min /1.73 m<sup>2</sup>)</b>	115.47 ±18.23	109.75 ± 22.23	<b>93.67 ± 7.55</b>	<b>&lt;0.05<sup>*</sup></b>
<b>UACR (µg/mg)</b>	101.52 ± 25.06	107.35 ± 25.86	<b>136.27 ± 25.73</b>	<b>&lt;0.05<sup>*</sup></b>

<b>Total cholesterol (mg/dl)</b>	231.47 ± 50.84	258.50 ± 39.53	<b>293.00 ± 36.27</b>	<b>&lt;0.05*</b>
<b>Triglycerides (mg/dl)</b>	159.27 ± 33.56	188.75 ± 14.27	<b>207.83 ± 41.62</b>	<b>&lt;0.05*</b>
<b>LDL- cholesterol (mg/dl)</b>	158.49 ± 35.70	182.05 ± 38.59	<b>213.27 ± 34.54</b>	<b>&lt;0.05*</b>
<b>HDL- cholesterol (mg/dl)</b>	41.13 ± 7.84	38.75 ± 3.59	<b>31.90 ± 6.46</b>	<b>&lt;0.05*</b>
<b>Total calcium (mg/dl)</b>	9.39 ± 0.45	9.20 ± 0.87	9.03 ± 0.62	>0.05
<b>S.phosphorus (mg/dl)</b>	3.59 ± 0.50	3.70 ± 0.34	3.50 ± 0.54	>0.05
<b>Serum albumin (gm/dl)</b>	4.17 ± 0.28	4.35 ± 0.25	4.43 ± 0.30	>0.05
<b>Intact PTH (pg/ml)</b>	42.25 ± 10.56	47.65 ± 11.83	<b>60.43 ± 15.08</b>	<b>&lt;0.05*</b>
<b>25 (OH) vitamin D<sub>3</sub> (ng/ml)</b>	21.57 ± 5.38	16.20 ± 4.00	<b>13.53 ± 3.36</b>	<b>&lt;0.01**</b>



**Table (3): Correlation between Vitamin D and different parameters in group II**

	<b>Variables</b>	<b>r</b>	<b>P</b>
<b>25 (OH) vitamin D<sub>3</sub> (ng/ml)</b>	<b>Age (years)</b>	<b>- 0.52</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Duration of type 2 diabetes mellitus (years)</b>	<b>- 0.59</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Stages of diabetic nephropathy</b>	<b>-0.62</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Fundus findings</b>	<b>-0.40</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Body mass index (Kg/m<sup>2</sup>)</b>	<b>- 0.48</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Systolic blood pressure (mmHg)</b>	<b>- 0.73</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Diastolic blood pressure (mmHg)</b>	<b>- 0.69</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Fasting blood sugar (mg/dl)</b>	<b>- 0.84</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Glycated hemoglobin (HbA1c %)</b>	<b>- 0.75</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Serum creatinine (mg/dl)</b>	<b>- 0.16</b>	<b>&gt;0.05</b>
	<b>GFR /1.73 m<sup>2</sup>)</b>	<b>0.46</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Urinary albumin creatinine ratio (µg/mg)</b>	<b>- 0.82</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Total cholesterol (mg/dl)</b>	<b>- 0.71</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Triglycerides (mg/dl)</b>	<b>- 0.58</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Low density lipoprotein cholesterol (mg/dl)</b>	<b>- 0.71</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>High density lipoprotein cholesterol (mg/dl)</b>	<b>0.47</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Total calcium (mg/dl)</b>	<b>0.61</b>	<b>&lt;0.01<sup>**</sup></b>
	<b>Serum phosphorus (mg/dl)</b>	<b>0.20</b>	<b>&gt;0.05</b>
	<b>Serum albumin (gm/dl)</b>	<b>0.27</b>	<b>&gt;0.05</b>
	<b>Intact Parathyroid Hormone (pg/ml)</b>	<b>- 0.33</b>	<b>&lt;0.05<sup>*</sup></b>



- Mean 25(OH) vitamin D level was lower in type 2 diabetic cases than in control group ( $P < 0.01$ ).
- Mean 25(OH) vitamin D level was lower in type 2 diabetic cases with DR than type 2 ( $P < 0.01$ ).
- Patients with PDR have the lowest mean 25(OH) vitamin D level compared to patients with moderate NPDR and severe NPDR ( $P < 0.01$ ).
- 25(OH) vitamin D level was inversely correlated with age, duration of type 2 diabetes mellitus, degree of microalbuminuria, fundus findings, BMI, SBP, DBP, glycemic parameters, urinary ACR, total cholesterol, triglycerides, LDL-C ( $P < 0.01$ ) and iPTH level ( $P < 0.05$ ). 25(OH) vitamin D level was positively correlated with GFR, HDL-C and total calcium level ( $P < 0.01$ ) among all studied groups.

## Conclusion

This study found an association between vitamin D deficiency and development of diabetic retinopathy. It demonstrated a negative correlation between 25 (OH) vitamin D level and severity of diabetic retinopathy among patients with type 2 diabetes mellitus.

However, 25 (OH) vitamin D level is not the only predominant factor affecting the development and progression of diabetic retinopathy. It plays nearly an equal role to other traditional risk factors for diabetic retinopathy.

Given previous research indicating possible anti-inflammatory and antiangiogenic properties of vitamin D, the role of vitamin D in the progression of diabetic retinopathy warrants further study.

## References

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