Relation between 25-hydroxy vitamin D and diabetic retinopathy in Egyptian patients with type 2 diabetes mellitus

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Background/aim
Diabetic retinopathy (DR) is one of the leading causes of blindness in people whose ages range from 20 to 64 worldwide. This study aims to evaluate the association of serum 25-hydroxy (OH) vitamin D deficiency and DR in type 2 diabetes mellitus (T2DM) patients.
Patients and methods
A cross-sectional study was conducted on 90 Egyptian patients with T2DM. Patients were divided into two groups: group I included 44 patients without retinopathy and group II included 46 with retinopathy. Group II was subdivided into two subgroups, group IIa, which included 26 nonproliferative DR patients and group IIb, which included 20 proliferative DR patients. Anthropometric data and laboratory investigations, including fasting and the postprandial blood sugar, glycated hemoglobin, lipid profiles, and serum vitamin D level. A fundus examination was also performed.
Results
The present results exhibited a significant decrease ($P<0.05$) of serum vitamin D (25-OH-vitamin D) in patients with T2DM and this deficiency is more in group II in comparison to group I and in a patient with proliferative DR (group IIb) compared to nonproliferative DR (group IIa). Also, there was a downward trend in serum vitamin D with the severity of DR. Also 25-OH-vitamin D level was inversely correlated with fasting, postprandial blood sugar, and glycated hemoglobin. A cut-off value for serum vitamin D levels of less than or equal to 12.03 ng/ml served as a sensitive indicator for DR.
Conclusion
25-OH-vitamin D deficiency is highly prevalent in Egyptian patients with T2DM and this deficiency is highly associated with the presence and severity of DR.

Keywords:
25-hydroxy-vitamin D, diabetic retinopathy, nonproliferative, proliferative

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Introduction

The type 2 diabetes mellitus (T2DM); one of main threats to aging population health in the 21st century, is described as a global epidemic since it affects health and economy of almost all the countries irrespective of their socioeconomic status or their geographic location [1].

Diabetic retinopathy (DR) is one of the leading causes of blindness in people 20–64 years of age [2]. It is believed that nearly all the patients with type 1 and 60% of the type 2 diabetes will have evidence of DR on examination 20 years after the onset of diabetes [3]. DR, is characterized as a neurovascular disease entity that results from hyperglycemia-induced changes in blood–retinal barrier and the retinal vasculature [4].

Many vasoactive factors are evoked by hyperglycemia and retinal hypoxia. These factors induce pathology in a variety of cell types, including glia, neurons, and microvasculature. A primary factor in the regulation of vessel patency throughout the body and retina is vascular endothelial growth factor (VEGF). Early in diabetes, the VEGF system is disturbed, and there is an interaction between it and other vasoactive factors, which stimulate the breakdown of blood–retinal barrier and causes angiogenesis leading to proliferative diabetic retinopathy (PDR) [5].

Insufficiency of vitamin D is very prevalent worldwide. 25-hydroxy-vitamin D3 (abbreviated as 25OH-D3) is a form of vitamin D, produced in the liver by hydroxylation of vitamin D3 (cholecalciferol) by the enzyme vitamin-D 25-hydroxylase. Different epidemiological studies have shown that more than

40% of adult populations are at risk of inadequate 25-OH vitamin D. Moreover, strong correlations exist between 25-OH vitamin D status, obesity, and T2DM. However, it was found that 25-OH vitamin D deficiency is predisposing factor for diabetes development and increasing hearing loss [6]. Animal studies have suggested that 25-OH vitamin D active metabolite supplementation protects against retinal neo-vascularization and other studies have documented the anti-angiogenic effects of 25-OH vitamin D primarily in the tumor models [7].

Many previous studies addressed the potential role of 25-OH vitamin D in the pathogenesis of DR [8–10]. To our knowledge, in Egypt, there is data about the association of diabetic peripheral neuropathy and the 25-OH vitamin D deficiency in T2DM [11] and T1DM in children [12]. Our study aimed to assess the association between DR and 25-OH vitamin D status in T2DM in a sample of Egyptian patients and the relation between 25-OH vitamin D deficiencies and the severity of retinopathy.

Patients and methods

Patients

This cros- sectional study included 90 Egyptian participants, aged between 31 and 65 years from April 2019 to March 2020. Patients were recruited from the Internal Medicine, Endocrinology, and Ophthalmology Departments of Al-Zahraa University Hospital. This study was done in accordance with the Declaration of the Helsinki guidelines. A written informed consent was taken from all the participants after a full explanation. Approval of the Ethics Board of Al Azhar University was obtained.

The included participants were divided into two groups as follows:

Group I consisted of 44 patients without DR.

Group II included 46 patients with DR. According to the Early Treatment Diabetic Retinopathy Study [13], this group was further divided into two subgroups, group IIa: 26 nonproliferative diabetic retinopathy patients (NPDR) and group IIb: 20 PDR patients.

Inclusion criteria

Adult patients aged 31–65 years diagnosed as having T2DM based on the American Diabetes Association criteria were included in this study.

Exclusion criteria

The exclusion criteria including T1DM, patients with history of hypertension, cardiovascular diseases, chronic kidney or liver disease, cancer, hypoparathyroidism, or hyperparathyroidism. Patients on 25-OH vitamin D replacement therapy, antioxidants,or medications affecting 25-OH vitamin-D metabolisms, such as phenobarbital, phenytoin, and rifampin were excluded.

Ocular exclusion criteria: dense media opacities, history of uveitis, any systemic diseases or medications affecting the retina, exposure to ocular trauma or surgery. Patients who had any posterior segment pathology except DR were also excluded.

Examination protocol and study measurements

The following examinations were conducted on all patients:

Full medical history, including duration and treatment of diabetes, complete physical examination, calculation of BMI according to the formula weight divided by the square of the height (kg/m^2) [14]. In addition to, complete ophthalmic examination including the uncorrected and the best-corrected visual acuity using Landolt's ring chart, refraction, and examination of slit lamp. Intraocular pressure was measured using Goldman applanation tonometer. A dilated fundus examination for DR grading was performed with the aid of +90 D noncontact lens.

Laboratory investigations

The laboratory investigations, which included fasting blood sugar (FBS) and postprandial blood glucose levels, total cholesterol, triglycerides, a high-density lipoprotein cholesterol and a low-density lipoprotein cholesterol were carried out using an automated chemistry analyzer (Cobas c311; Roche, Sandhofer Strasse 116 68305 Mannheim, Germany), according to manufacturer's instructions. Glycated hemoglobin (HbA1c) measurement was performed using the turbidimetric inhibition immunoassay method, according to the manufacture instruction of dimension x-pand plus supplied from Siemens (Siemens Healthcare Diagnostics Inc., Newark, Delaware, USA). Serum calcium and phosphorus were measured by a biochemical automatic analyser (Cobas c702; Roche, Shanghai, China).

Determination of serum 25-OH vitamin D was performed using the enzyme immunoassay method using the kit supplied from MicroVue (Quidel Corporation, San Diego, California, USA). Interpretation of the test: deficient: less than 20,

insufficient: 20–29, while sufficient: 30–100 ng/ml, according to the method of Holick [15].

Statistical analysis

Data were collected, revised, coded, and entered into Statistical Package for the Social Science (IBM SPSS, Chicago, Illinois, USA), version 15. Quantitative data were presented as the mean±SD. Comparision of the two groups was done using independent *t* test, while comparison between more than two independent groups with the parametric distribution was conducted by using the one-eay analysis of variance. Qualitative variables were presented as the number and the percentages. Comparing the groups regarding the qualitative data was conducted using the χ^2 test. The correlation between different studied parameters was done using Pearson's correlation coefficient. A *P* value less than 0.05 is considered significant. Receiver operating characteristic curve was used for prediction of DR.

Results

Demographic data of studied patients

The present study included 35 (39%) males and 55 (61%) females of Egyptian patients with T2DM. Their ages ranged from 31 to 65 years. All patients underwent fundus examination and according to the findings, our patients were divided into two groups: group I: included 44 diabetic patients without retinopathy and group II that included 46 diabetic patient with DR. The demographic and laboratory data of both groups are shown in Table 1. By comparing group I and group II there was an insignificant difference as regard age and sex while disease duration significantly increase ($P<0.05$) in group II in comparison to group I, but BMI was significantly low ($P<0.05$) in the group II compared to the group I (Table 1).

Moreover, there was significant increase ($P<0.05$) in fasting, postprandial blood sugar, and HbA1c in group II (221±80, 291±85 mg/dl, and 9.96±2.07%, respectively) when compared to group I (182±76, 238±88 mg/dl, and 8.74±2.09%, respectively), while, there was significant decrease ($P<0.05$) of serum 25-OH vitamin D and very low-density lipoprotein in group II (11.66±1.60 ng/ml and 28.79±6.68 mg/dl), when compared to group I (15.52±9.94 ng/ml and 44.62±21.80 mg/dl). Also, there was an insignificant difference between the two groups as regards other parameters (Table 1).

As regard grading of retinopathy, our patients with DR in group II were divided into two groups, group IIa, which includes 26 NPDR patients, and group IIb, which involved 20 PDR patients.

Table 1 Comparison between the diabetic group without retinopathy (group I) and the diabetic group with retinopathy (group II) as regards demographic and biochemical data

Parameters	Group I (diabetic without retinopathy) *N*=44	Group II (diabetic with retinopathy) *N*=46	*P* value
Age (years)	48.68±6.74	52.26±7.75	0.101
Sex [*n* (%)]			
Male	22 (50)	15 (32.6)	0.094**
Female	22 (50)	31 (67.4)	
Disease duration (years)	8.38±6.28	15.35±6.912	0.000*
Weight (kg)	96.01±18 .94	86.11±16.44	0.000*
Height (cm)	165.18±8.07	163.59±8.34	0.359
BMI (kg/m^2)	35.06±5.43	31.59±5.30	0.003*
FBS (mg/dl)	182±76	221±80	0.000*
PBS (mg/dl)	238±88	291±85	0.005*
HbA1c (%)	9.85±2.09	9.96±2.07	0.007*
Calcium (mg/dl)	9.06±0.52	9.01±0.59	0.642
Phosphorus (mg/dl)	4.53±0.47	4.56±0.79	0.833
Albumin (gm/dl)	4.11±0.30	4.20±0.45	0.574
Cholesterol (mg/dl)	188.39±42.97	199.20±42.38	0.233
Triglyceride (mg/dl)	189.34±90.45	179.22±72.06	0.558
HDL (mg/dl)	39.23±8. 24	41.36±8.77	0.239
LDL (mg/dl)	111.31±43.89	119.62±37.85	0.282
VLDL (mg/dl)	44.62±20.80	28.79±6.68	0.006*
25-OH vitamin D (ng/ml)	15.52±9.94	11.66±1.60	0.011*
Oral treated [*n* (%)]	11 (25)	20 (43.5)	0.053**
Insulin treated [*n* (%)]	33 (75)	26 (56.5)	

FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PBS, postprandial blood sugar; VLDL, very low-density lipoprotein. *Significant difference at *P* value less than 0.05, using independent *t* test. **Insignificant difference at *P* more than 0.05, using χ^2 test.

On comparing between the two subgroups, as regard demographic and biochemical data, where there was significant increase ($P<0.05$) in disease duration in group IIb in comparison to group IIa, also there was significant increase ($P<0.05$) in fasting, postprandial blood sugar and HbA1c in group IIb (225.75±89.73, 307.95±97.87 mg/dl, and 10.11±2.01%, respectively) in comparison to group IIa (217.08±72.26, 277.58 ±72.56 mg/dl and 9.85±2.16% respectively). Also, 25-OH vitamin D level was significantly lower ($P<0.05$) in group IIb (11.06±1.59) when compared with group IIa (12.13±1.47), as shown in Table 2.

Also, there is an insignificant difference ($P>0.05$) between males and females regarding weight, BMI, and 25-OH vitamin D level, as shown in Table 3.

As regard serum 25-OH vitamin D was within the normal level of four (4.4%) patients, 76 (84.4%) patients had insufficient level, while 10 (11.2%) patients had deficient level. There was a significant decrease in vitamin D level in group IIb (11.06±1.59) when compared to group IIa and group I (12.13±1.47, 15.52±9.94, respectively) and post-hoc test revealed a highly significant difference between group I and group

Table 2 Comparison between nonproliferative diabetic retinopathy (group IIa) and proliferative diabetic retinopathy (group IIb) groups as regards demographic and biochemical data

Parameters	Group IIa (NPDR) (*N*=26)	Group IIb (PDR) (*N*=20)	*P* value
Age (years)	56.96±8.60	55.35±7.79	0.000*
Sex [*n* (%)]			
Male	5 (19.2)	10 (50.0)	0.020**
Female	21 (80.8)	10 (50.0)	
Disease duration (years)	13.42±6.40	19.35±11.44	0.000*
Weight (kg)	86.88±14.94	85.10±18.56	0.033*
Height (cm)	163.15±7.97	164.15±8.98	0.607
BMI (kg/m^2)	32.29±5.97	30.69±4.26	0.007*
FBS (mg/dl)	217.08±72.26	225.75±89.73	0.032*
PBS (mg/dl)	277.58±72.56	307.95±97.87	0.010*
HbA1c (%)	9.85±2.16	10.11±2.01	0.024*
Calcium (mg/dl)	9.10±0.60	8.89±0.58	0.377
Phosphorus (mg/dl)	4.35±0.87	4.84±0.59	0.038*
Serum albumin (g/dl)	4.08±0.48	4.32±0.43	0.520
Cholesterol (mg/dl)	211.81±44.72	182.80±33.49	0.034*
Triglyceride (mg/dl)	186.81±74.01	169.35±70.07	0.652
HDL (mg/dl)	41.95±8.82	40.59±8.88	0.435
LDL (mg/dl)	128.31±43.21	108.33±26.44	0.101
VLDL (mg/dl)	29.10±6.71	28.44±7.05	0.026*
Vitamin D (ng/ml)	12.13±1.47	11.0 6±1.59	0.035*

FBS, fasting blood sugar; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NPDR, nonproliferative diabetic retinopathy; PBS, postprandial blood sugar; PDR, proliferative diabetic retinopathy; VLDL, very low-density lipoprotein. *Significant difference at *P* value less than 0.05, using independent *t* test. **Insignificant difference at *P* more than 0.05, using χ^2 test.

Table 3 Comparison between males and females in all patients with diabetic retinopathy (group II), nonproliferative diabetic retinopathy (group IIa) and proliferative diabetic retinopathy (group IIb) groups regarding weight, BMI, and 25-hydroxy vitamin D level

	Group II: total diabetic with retinopathy			Group IIa: NPDR			Group IIb: PDR		
	Female	Male	*P* value	Female	Male	*P* value	Female	Male	*P* value
Weight	83.23±14.35	92.07±19.26	0.087*	85.62±14.39	92.20±17.80	0.387*	78.20±13.62	92.00±20.89	0.097*
BMI	31.75±5.70	31.28±4.52	0.784*	32.40 ±6.15	31.84±5.75	0.856*	30.38±4.61	31.00±4.10	0.754*
Vit D	11.65±1.71	11.69±1.40	0.945*	12.02 ±1.59	12.60±0.72	0.440*	10.89±1.78	11.23±1.46	0.638*
Normal [*n* (%)]	0	0	0.459**	0	0	0.369**	0	0	0.329**
Insufficient [*n* (%)]	24 (77.4)	13 (86.7)		18 (85.7)	5 (100.0)		6 (60.0)	8 (80.0)	
Deficient [*n* (%)]	7 (22.6)	2 (13.3)		3 (14.3)	0		4 (40.0)	2 (20.0)	

NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy. Insignificant difference at *P* value more than 0.05 using independent *t* test* or χ^2 test**.

Table 4 Comparison of serum 25-hydroxy vitamin D level in the diabetic group without retinopathy (group I), nonproliferative diabetic retinopathy (group IIa), and proliferative diabetic retinopathy (group IIb) groups

Vitamin D	Group I (diabetic without retinopathy) *N*=44	Group IIa (NPDR) *N*=26	Group IIb (PDR) *N*=20	*P* value
Mean±SD	15.52±9.94	12.13±1.47	11.06±1.59	
Range	9.93–63.2	8.59–15.4	8.59–13.8	0.035*
Normal [*n* (%)]	4 (9.1)	0	0	0.006*
Insufficient [*n* (%)]	39 (88.6)	23 (88.5)	14 (70.0)	
Deficient [*n* (%)]	1 (2.3)	3 (11.5)	6 (30.0)	
Post-hoc analysis				
Parameters	P_1	P_2	P_3	
Quantitative vitamin D	0.056	0.022*	0.612	
Qualitative vitamin D	0.089	0.002*	0.294	

NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy. *Significant difference at *P* value less than 0.05, using one-way analysis of variance test with post-hoc analysis using LSD. *P*1: comparison between diabetic without retinopathy (group I) and NPDR group (group IIa). *P*2: comparison between diabetic without retinopathy (group I) and PDR group (group IIb). *P*3: comparison between NPDR (group IIa) and PDR (group IIb) groups.

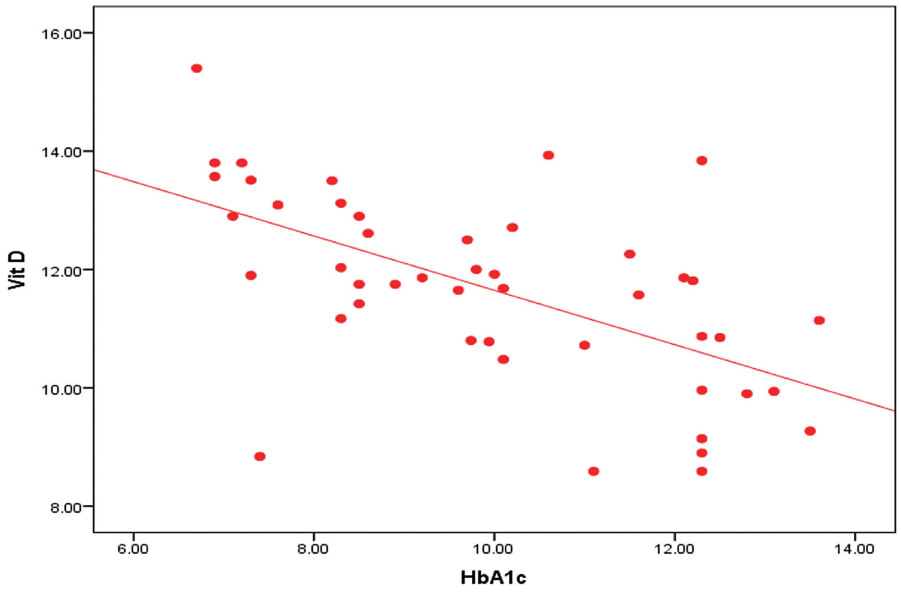
IIa, the distribution of number of patients in each group with respect to level of 25-OH vitamin D are shown in Table 4.

Pearson's correlation of 25-OH vitamin D with the studied parameters in group II (diabetic patients with retinopathy) showed a significant inverse correlation between it and each of fasting, postprandial blood sugar, and HbA1c (Fig. 1). Also a significant negative correlation between 25-OH vitamin D and serum calcium was noted in group II.

Receiver operating characteristic curve of 25-OH vitamin D level was conducted for the prediction of DR in diabetic patients. At serum concentration of 25-OH vitamin D level best cut off value is less than or equal to 12.03, sensitivity was 65.22%, specificity was 68.18%, the positive predictive value was 68.2%, and the negative predictive value was 65.2%.

Multivariate regression analysis using the backward: Wald method shows that age more than 49 and disease duration more than 9 years was found to be significantly associated to retinopathy with *P* value of 0.004 and 0.006, respectively, and with odds ration (OR) [95% confidence interval (CI)] of 7.945 (1.964–32.140) and 5.566 (1.619–19.135), respectively, followed by FBS more than 205 and BMI less than or equal to 34.3 with *P* value of 0.017 and 0.048, respectively, and with OR (95% CI) of 4.588 (1.307–16.103) and 3.335 (1.011–10.997), respectively; while 25-OH vitamin

Figure 1



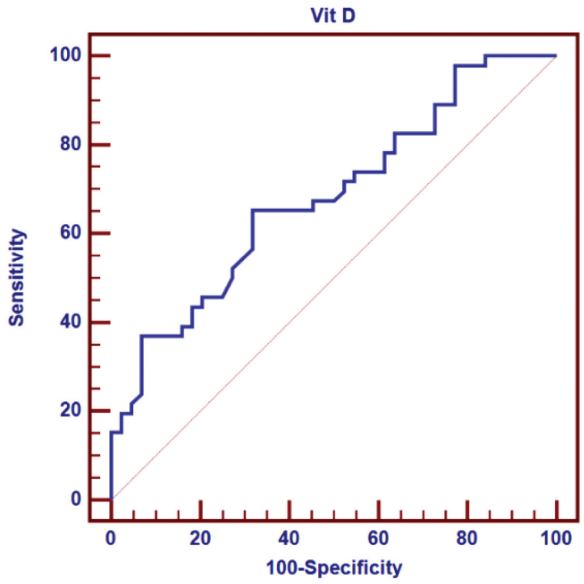
Pearson's correlation between HbA1c and 25-hydroxy vitamin D in diabetic patients with retinopathy (group II). HbA1c, glycated hemoglobin.

Table 5 Final model of multivariate logistic regression analysis using backward Wald method for the association between retinopathy and the other parameters

						95% CI for OR	
Parameters	*B*	SE	Wald	*P* value	OR	Lower	Upper
Vitamin D<12.03	0.996	0.600	2.754	0.097	2.708	0.835	8.781
BMI≤34.3	1.204	0.609	3.913	0.048*	3.335	1.011	10.997
DD>9	1.717	0.630	7.426	0.006*	5.566	1.619	19.135
Age >49	2.073	0.713	8.449	0.004*	7.945	1.964	32.140
FBS>205	1.523	0.641	5.654	0.017*	4.588	1.307	16.103
Constant	−4.218	0.946	19.886	0.000*	0.015		

Variable(s) entered on step 1: vitamin D, weight, BMI, disease duration, age, fasting blood sugar, and postprandial blood glucose. CI, confidence interval; OR, odds ratio. *Significant difference at *P* value less than 0.05.

Figure 2



Receiver operating characteristic (ROC) curve of 25-hydroxy vitamin D in diabetic patients with retinopathy (group II). The cut-off value is less than or equal to 12.03, sensitivity was 65.22%, specificity was 68.18%, positive predictive value was 68.2%, and negative predictive value was 65.2%.

D not found as an independent factor for retinopathy with *P* value of 0.097 and OR (95% CI) of 2.708 (0.835–8.781), as shown in Table 5, Fig. 2.

Discussion

In our study, there was a statistically significant decrease of serum 25-OH vitamin D in most patients with type 2 diabetes. This decrease was more in diabetic patients with retinopathy (group II) in comparison to patients without retinopathy (group I) and in patients with PDR (IIb) compared with NPDR (IIa). Also, there was a downward trend in serum 25-OH vitamin D with the severity of DR.

The relation between vitamin D deficiency and T2DM was reported more than 30 years ago. In 1988, Pietschmann *et al.* [16] found that serum vitamin D was lower in diabetic patients than nondiabetic control. Other studies concluded that serum vitamin D was low in T2DM and this is one of the contributing factors for the development of T2DM [17,18].

This agrees with the performed study by *Dave* et al. [19] *on* 98 patients with T2DM; all patients had vitamin D insufficient. Thirty-nine patients had no DR, 38 had mild to moderate NPDR, 15 had severe NPDR, and six patients had PDR. They found that 25-OH vitamin D decreased significantly in patients with PDR than those without retinopathy. In agreement with our study, Nadri *et al.* [20] found that serum 25-OH vitamin D was significantly low in T2DM patients and lowest in PDR patients. Their study was conducted on 72 patients with T2DM, 24 patients without retinopathy, 24 patients with NPDR, and 24 with PDR and vitamin D levels. Also consistent with our results Dinesh and Anil Kumar [21] in their study on 412 patients with T2DM, found that 7% had 25-OH vitamin D level more than 30 ng/ml, 13% had a level between 20 and 30 and 80% had less than 20 ng/ml. They concluded that T2DM patients with retinopathy were found to have significant 25-OH vitamin D deficiency compared to those without retinopathy.

25-OH vitamin D has a suppressive function with anti-angiogenic and anti-inflammatory effects in the pathogenesis of DR. Mantell *et al.* [22] showed that retinal new vascularization was inhibited by vitamin D in induced ischemic retinopathy mouse model. 25-OH vitamin D inhibits VEGF induced endothelial cell proliferation, elongation, and sprouting. Also, Albert *et al.* [7] proposed that 25-OH vitamin D interrupts the angiogenesis signalling pathway and induces endothelial cell apoptosis. Chronic inflammation leads to the degeneration of retinal pigment cells. However the anti-inflammatory effect of vitamin D exerts by inhibition of proliferation of natural killer

cells, lymphocytes, and many pro-inflammatory cytokines. Also, metalloproteinase, MMP-9 production by inflammatory cells is inhibited by vitamin D [23].

Alcubierre *et al.* [24] reported the association of 25-OH vitamin D deficiency with the existence and extent of DR in T2DM in their study on two groups of patients. One humdred fourty-four without retinopathy and 139 patients with retinopathy, also patients with low concentration of vitamin D had advanced stage of DR.

In agreement with our findings, a Chinese study, which was conducted by He *et al.* [8] on 1520 patients with type 2 diabetes and was divided into three groups according to the results of their fundus oculi, where the percentage of patients with no DR were, 41.12%; non-PDR were 36.97%; and PDR were 21.91%, they concluded that patients with PDR 25-OH vitamin D was lower than other two groups, also there was a stepwise decrease in serum 25-OH vitamin D with the severity of DR.

Another research agrees with our findings [25] and found that patients with DR had significantly low serum vitamin D in comparison with those without retinopathy. They measured serum 25-OH vitamin D in 136 patients with T2DM and concluded that low serum 25-OH vitamin D level was an independent indicator of DR, diabetic neuropathy, and HbA1c in T2DM patients.

Also, our results are consistent with Suzuki *et al.* [26], who showed in their study on 581 Japanese diabetic patients and 51 normal participants that patients with microvascular complications had significantly low serum vitamin D when compared with patients without complications.

Another study agrees with our results, Gungor *et al.* [27], studied 50 early-stage DR patients with 25-OH vitamin D deficiency and 50 early-stage DR patients without 25-OH vitamin D deficiency. The same ophthalmologist examined all patients, and optical coherence tomography was used to determine the retinal nerve fiber thickness. Also 25-OH vitamin D levels were measured by using a radioimmunoassay. They reported that patients with 25-OH vitamin D deficiency had significantly low serum vitamin D and reduced mean of retinal nerve fiber thickness compared with patients without 25-OH vitamin D deficiency.

As regards the correlation of serum 25-OH vitamin D with studied parameters, it was found that there was a significant negative correlation between 25-OH vitamin D and each of fasting, postprandial blood sugar, and HbA1c. Our results agree with Ghavam *et al.* [28], who found an inverse linear relationship between 25-OH vitamin D with HbA1c, FBS, BMI, and disease duration. Also, in agreement with our results, a study was done by Alkhatatbeh and Abdul-Razzak [29], where there were significant inverse correlations between the duration of DM and HbA1c and fasting blood glucose levels. Extended previous studies are in agreement with our results [17,25,30].

Conclusion

This cross-sectional study demonstrated that vitamin D deficiency is highly prevalent in type 2 diabetic patients, and this deficiency is highly associated with the presence and severity of DR. These findings highlight the role of 25-OH vitamin D in the pathogenesis of the DR.

Recommendation

Further studies on large sample sizes are recommended to assess the role 25-OH vitamin D deficiency in the development of the DR and other diabetic microvascular complications. Also, further follow up of the patients after vitamin D supplementation to study the effect on retinopathy.

Authors' contributions: Fatma M. El-Senosy was responsible for conceptualization, methodology, formal analysis, validation, and writing – review and editing. Mervat E. Elwakeel was responsible for methodology and validation. Nesma S. Mohammed, and Heba M. Abdelrahman were taking a part in investigation, and visualization. Finally, Eman E. Ebrihem helped in investigation and methodology.

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Conflicts of interest

There are no conflicts of interest.

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