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# Association of Vitamin D Status with Diabetic Retinopathy in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study from Iran

## ABSTRACT

**Objective:** Diabetic retinopathy (DR) is a major microvascular complication of type 2 diabetes mellitus (T2DM). In addition to hyperglycemia, vitamin D may influence DR via anti-inflammatory and anti-angiogenic mechanisms. This study examined the relationship between serum vitamin D levels and the presence and severity of DR, while accounting for clinical, biochemical, and lifestyle factors.

**Methods:** A total of 120 patients with T2DM attending an ophthalmology clinic participated in this cross-sectional study. The presence of DR was determined through fundus photography and established DR criteria (ETDRS). Data included serum 25(OH)D, hemoglobin A1c (HbA1c), cholesterol, and clinical data. Patients were divided according to DR status as either DR or non-DR and further classified as non-proliferative diabetic retinopathy or proliferative diabetic retinopathy (PDR).

**Results:** Compared to non-DR patients, those with DR had lower mean serum vitamin D levels (19.43 ± 4.50 ng/mL vs. 26.48 ± 8.99 ng/mL, $P < .001$). Diabetic retinopathy was associated with longer duration of diabetes and higher HbA1c and cholesterol. Patients with DR and PDR were more susceptible to vitamin D deficiency and were less likely to receive supplemental vitamin D. In a stepwise-adjusted multivariate regression model, low vitamin D and longer duration were independent predictors of DR. The risk of DR was also associated with a history of smoking and insulin therapy.

**Conclusion:** Vitamin D deficiency is strongly associated with DR in Iranian patients with T2DM. Further research should clarify vitamin D's potential as a modifiable risk factor for prevention strategies.

**Keywords:** Diabetic retinopathy, glycemic control, risk factors, type 2 diabetes mellitus, vitamin D

## Introduction

Diabetic retinopathy (DR) is a common microvascular complication of diabetes and a major cause of vision loss. With rising rates of type 2 diabetes mellitus (T2DM), DR prevalence is increasing globally. Though chronic hyperglycemia is the main cause, factors like vitamin D status may also contribute to DR development.[1,2]

Beyond bone health, vitamin D plays roles in immunomodulation, inflammation, oxidative stress, and vascular regulation. Retinal tissues express vitamin D receptors, and active vitamin D (calcitriol) inhibits angiogenesis, reduces inflammation, and limits oxidative damage, all of which are relevant to DR pathogenesis.[3,4] Observational studies show lower serum 25-hydroxyvitamin D [25(OH)D] in patients with DR compared to those without.[5,6] Meta-analyses further support an inverse association, reporting a 27% reduction in DR risk per 10 ng/mL increase in 25(OH)D.[7,8] These findings suggest vitamin D deficiency may not only reflect poor health but may also contribute to DR pathophysiology.

This association is particularly relevant in the Middle East and North Africa, where both T2DM and vitamin D deficiency are highly prevalent. In Saudi Arabia, DR affects about 31% of patients with diabetes, with poor glycemic control and low vitamin D linked to a higher risk.[6] Studies in Qatar, Egypt, and Iran also suggest vitamin D deficiency contributes to DR despite abundant sunlight.[9,10]

Glycemic control, diabetes duration, and dyslipidemia are key predictors of DR. Other factors, including smoking, hypertension, and insulin therapy, may interact with vitamin D status.[4,11]Vitamin D supplementation shows promise in reducing inflammation and neovascularization, but its preventive role in DR is unclear. This study examines the relationship

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between vitamin D status and DR severity in Iranian patients with T2DM, controlling for clinical and biochemical variables.

## Methods

### Study Design and Participants

This cross-sectional study included 120 patients with T2DM attending a tertiary ophthalmology clinic. Participants were recruited via convenience sampling from individuals referred for routine DR screening from September 2024 to March 2024. Inclusion criteria were confirmed T2DM diagnosis, age >18 years, and availability of recent biochemical data. Exclusion criteria included type 1 diabetes, other retinal disorders, advanced renal/hepatic disease, recent vitamin D injections, or systemic autoimmune/inflammatory conditions. Patients were grouped based on DR status, determined by a trained ophthalmologist using fundus photography and fluorescein angiography, and further classified as non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) according to the early treatment diabetic retinopathy study criteria.

The study was approved by the Ethics Committee of Babol University of Medical Sciences (Approval code: IR.MUBABOL.REC.1403.103; Approval date: August 26, 2024). Written informed consent was obtained from all participants, who were free to withdraw from the study at any time.

### Clinical and Biochemical Data Collection

Demographic and clinical data (age, sex, BMI, smoking, hypertension, diabetes duration, and vitamin D usage (as an observational, self-reported variable)) were obtained via structured interviews and confirmed with medical records. Fasting venous blood samples were collected to measure HbA1c, total cholesterol, and 25(OH)D. All samples were analyzed in 1 certified laboratory: HbA1c and cholesterol using standard enzymatic and immunoturbidimetric assays, and 25(OH)D using chemiluminescent immunoassay via HISCL-800 (Sysmex Corporation, Japan). Internal quality control procedures were followed using 2 levels of commercial controls with each run.

### Assessment of Diabetic Retinopathy

All patients underwent a full ophthalmologic assessment by a retina specialist blinded to clinical data. After pupillary dilation, fundus examination included slit-lamp biomicroscopy, indirect ophthalmoscopy, and fundus photography. DR was graded as NPDR or PDR using the international severity scale, with the more severely affected eye classified in bilateral cases.

### Statistical Analyses

Analyses were performed with SPSS v26.0 (IBM Corp., Armonk, NY). Continuous variables are expressed as mean ± SD, and categorical data as frequencies (%). Independent-samples *t*-tests compared continuous parameters between groups, and chi-square tests explored categorical associations. Independent predictors of DR were identified using 2 logistic regression models: one with continuous variables (age, BMI, diabetes duration, HbA1c, cholesterol, vitamin D, hypertension) and another with binary predictors (sex, smoking, vitamin D supplementation, blood pressure, treatment type). Odds ratios (OR) with 95% CI were reported.

## Results

### Comparison of Clinical and Biochemical Parameters by Retinopathy Status

Independent-samples *t*-tests were conducted to compare key clinical and biochemical variables between patients with and without diabetic retinopathy. Patients with retinopathy (n = 80) had a significantly longer duration of diabetes (19.21 ± 9.44 years) compared to those without retinopathy (n = 40; 11.20 ± 8.94 years; $P < .001$). Mean HbA1c was also higher in the retinopathy group (8.56% ± 1.29%) than in the non-retinopathy group (7.58% ± 1.06%; $P < .001$), indicating poorer glycemic control. Cholesterol levels were significantly elevated in the retinopathy group (216.94 ± 45.89 mg/dL) compared to those without retinopathy (193.80 ± 50.21 mg/dL; $P = .013$). Additionally, vitamin D levels were markedly lower in patients with retinopathy (19.43 ± 4.50 ng/mL) compared to those without (26.48 ± 8.99 ng/mL; $P < .001$). There were no significant differences between groups in age (62.01 ± 11.36 vs. 58.98 ± 12.83 years; $P = .189$) or BMI (26.90 ± 4.06 vs. 26.98 ± 3.93 kg/m$^2$; $P = .890$) (Table 1). As expected, the results confirm a highly significant difference in mean vitamin D levels between patients reporting supplement use (27.80 ± 7.09 ng/mL) and non-users (17.18 ± 1.67 ng/mL) ($P < .001$).

### Comparison of Clinical and Biochemical Variables Between Proliferative and Non-Proliferative Diabetic Retinopathy

To compare patients with PDR and NPDR, independent-samples *t*-tests were conducted across 6 clinical and biochemical parameters. A significant difference in diabetes duration was observed, with patients in the PDR group having a longer disease history (22.03 ± 9.61 years) than those in the NPDR group (16.40 ± 8.14 years; $P = .007$). Cholesterol levels were also significantly higher in the PDR group (229.37 ± 35.94 mg/dL) than in the NPDR group (204.50 ± 51.54 mg/dL; $P = .014$). No statistically significant differences were observed

**Table 1. Comparison of Clinical and Biochemical Characteristics Between Patients with and Without Diabetic Retinopathy**

| | Retinopathy (means ± SDs) | | |
|---|---|---|---|
| **Variables** | **No (n = 40)** | **Yes (n = 80)** | ***P*** |
| Age (years) | 58.98 ± 12.83 | 62.01 ± 11.36 | .189 |
| BMI (kg/m$^2$) | 26.98 ± 3.93 | 26.90 ± 4.06 | .890 |
| Diabetes duration (years) | 11.20 ± 8.94 | 19.21 ± 9.44 | <.001 |
| HbA1c (%) | 7.58 ± 1.06 | 8.56 ± 1.29 | <.001 |
| Cholesterol (mg/dL) | 193.80 ± 50.21 | 216.94 ± 45.89 | .013 |
| Vitamin D level (ng/mL) | 26.48 ± 8.99 | 19.43 ± 4.50 | <.001 |

## MAIN POINTS

- Patients with type 2 diabetes who have diabetic retinopathy (DR) show significantly lower vitamin D levels than those without retinopathy.
- Low vitamin D levels are independently linked with a higher risk and greater severity of DR.
- Each small increase in vitamin D concentration lowers the likelihood of developing retinopathy, even after accounting for blood sugar control and diabetes duration.
- Regular vitamin D supplementation is less common among patients with severe forms of retinopathy.
- Maintaining adequate vitamin D may protect the retina and represent a straightforward, modifiable intervention to lower retinopathy risk in patients with type 2 diabetes.

**Table 2. Clinical and Metabolic Profile According to Type of Diabetic Retinopathy**

| Variables | Type of Retinopathy (Means ± SDs) Proliferative (n = 40) | Non-Proliferative (n = 40) | *P* |
|---|---|---|---|
| Age (years) | 63.13 ± 8.96 | 60.90 ± 13.36 | .384 |
| BMI (kg/m$^2$) | 26.91 ± 3.32 | 26.88 ± 4.73 | .973 |
| Diabetes duration (years) | 22.03 ± 9.61 | 16.40 ± 8.14 | .007 |
| HbA1c (%) | 8.75 ± 1.10 | 8.38 ± 1.46 | .199 |
| Cholesterol (mg/dL) | 229.37 ± 35.94 | 204.50 ± 51.54 | .014 |
| Vitamin D level (ng/mL) | 19.10 ± 4.14 | 19.76 ± 4.86 | .513 |

between the 2 groups in terms of age (63.13 ± 8.96 vs. 60.90 ± 13.36 years; $P = .384$), BMI (26.91 ± 3.32 vs. 26.88 ± 4.73 kg/m$^2$; $P = .973$), HbA1c (8.75 ± 1.10 vs. 8.38% ± 1.46%; $P = .199$), or vitamin D levels (19.10 ± 4.14 vs. 19.76 ng/mL; $P = .513$) (Table 2, Figure 1).

### *Association of Categorical Risk Factors with Diabetic Retinopathy*

A chi-square analysis was conducted to examine associations between DR status and categorical variables, including diabetes medication type, smoking status, hypertension, and vitamin D use. The only statistically significant association was observed with vitamin D supplementation: patients without DR were significantly more likely to use vitamin D (75.0%) compared to those with DR (27.5%) ($P < .001$). No significant associations were found between DR and diabetes medication type ($P = .171$), smoking status ($P = .271$), or hypertension ($P = .359$). These results suggest that vitamin D supplementation may be inversely associated with diabetic retinopathy, whereas the other categorical clinical variables examined did not show significant differences between the groups (Table 3).

### *Association of Categorical Clinical Variables with Type of Diabetic Retinopathy*

A chi-square analysis was conducted to evaluate the association between DR type (proliferative vs. non-proliferative) and 4 categorical clinical variables: diabetes medication type, smoking status, hypertension, and vitamin D use. Among these, only vitamin D supplementation showed a statistically significant difference between groups. Vitamin D use was reported by a higher proportion of patients with non-proliferative DR (30.0%) than with proliferative DR (25.0%), and this difference was statistically significant ($P < .001$). There were no significant differences between the proliferative and non-proliferative groups in terms of diabetes medication type ($P = .250$), smoking status ($P = .346$), or hypertension ($P = .521$). These results suggest a potential link between vitamin D supplementation and less severe forms of retinopathy, while other categorical clinical variables did not differ significantly between DR subtypes (Table 4).

### *Predicting Retinopathy from Continuous Predictors*

A binary logistic regression was performed to assess the ability of age, BMI, diabetes duration, hypertension status, HbA1c, cholesterol, and vitamin D level to predict the presence of retinopathy. The overall model was significant, $\chi^2(7) = 45.37$, $P < .001$, and explained between 31.5% (Cox & Snell $R^2$) and 43.7% (Nagelkerke $R^2$) of the variance in retinopathy status. The −2 log-likelihood of the model was 107.39.

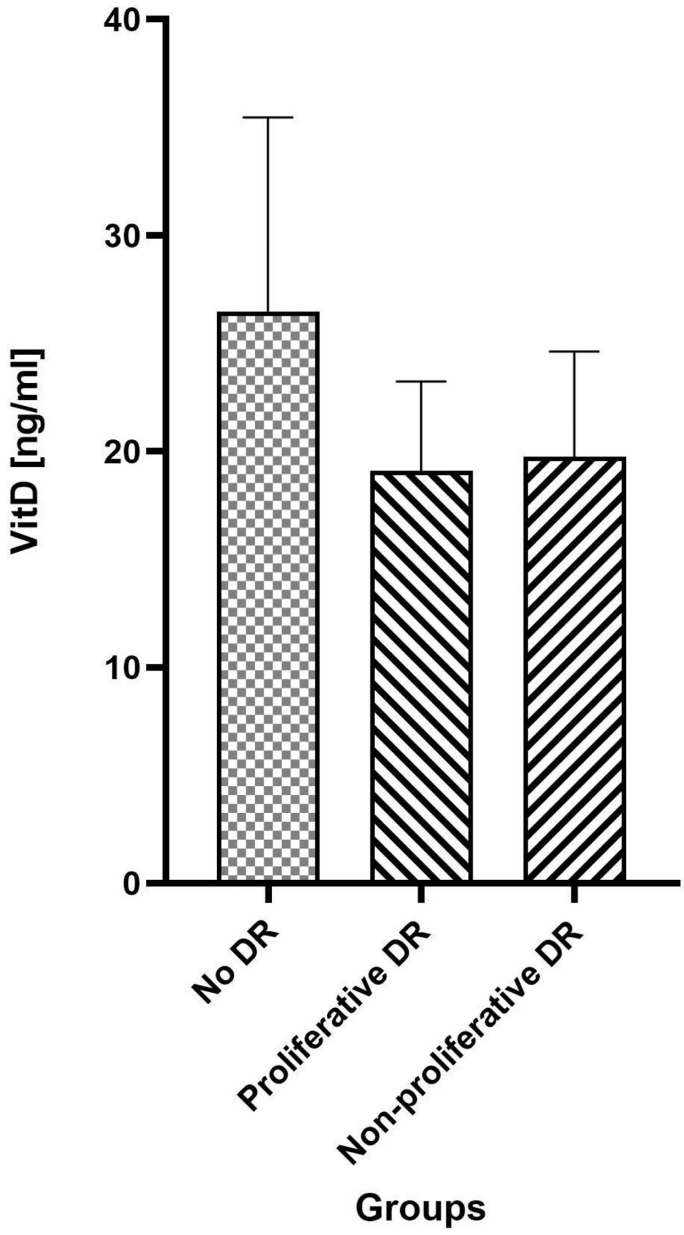


**Figure 1. Distribution of serum 25-hydroxyvitamin D (25(OH)D) levels in patients with type 2 diabetes, stratified by diabetic retinopathy status. The box plot displays the median, interquartile range, and full range of 25(OH)D concentrations for patients with no retinopathy (No DR), non-proliferative diabetic retinopathy (Non-proliferative DR), and proliferative diabetic retinopathy (Proliferative DR). Units are ng/mL.**

Among the individual predictors, longer diabetes duration was associated with higher odds of retinopathy (B = 0.063, SE = 0.030, Wald = 4.37, $P = .036$; OR = 1.065, 95% CI [1.004, 1.129]). Higher vitamin D levels were associated with lower odds of retinopathy (B = −0.135, SE = 0.045, Wald = 9.01, $P = .003$; OR = 0.873, 95% CI [0.797, 0.956]). The effects of age (OR = 1.023, $P = .341$), BMI (OR = 0.957, $P = .473$), hypertension (OR = 1.335, $P = .575$), HbA1c (OR = 1.626, $P = .054$), and cholesterol (OR = 1.005, $P = .374$) were not statistically significant (Table 5).

**Table 3. Comparison of Diabetes-Related Clinical Characteristics in Patients with and Without Diabetic Retinopathy**

| | Diabetic Retinopathy Status | | | | |
|---|---|---|---|---|---|
| Variables | With DR (n = 80) | % | Without DR (n = 40) | % | *P* |
| Diabetes medication type | | | | | |
| Insulin | 30 | 37.5 | 10 | 25.0 | .171 |
| Oral | 50 | 62.5 | 30 | 75.0 | |
| Smoking | | | | | |
| Yes | 6 | 7.5 | 1 | 2.5 | .271 |
| No | 74 | 92.5 | 39 | 97.5 | |
| Blood pressure | | | | | |
| Yes | 49 | 61.3 | 21 | 52.5 | .359 |
| No | 31 | 38.7 | 19 | 47.5 | |
| Vitamin D usage | | | | | |
| Yes | 22 | 27.5 | 30 | 75.0 | **<.001*** |
| No | 58 | 72.5 | 10 | 25.0 | |

### *Predicting Retinopathy from Categorical Predictors*

A second binary logistic regression evaluated whether smoking status, hypertension, sex, vitamin D supplementation, and diabetes treatment type predicted retinopathy. This model was also significant, $\chi^2(4) = 12.27$, $P = .015$, accounting for 9.7% (Cox & Snell) to 13.5% (Nagelkerke) of the variance (−2LL = 28.20).

Smoking was associated with reduced odds of retinopathy (B = −2.634, SE = 0.999, Wald = 6.95, $P = .008$; OR = 0.072, 95% CI [0.010, 0.509]), whereas none of the other categorical predictors reached significance: hypertension (OR = 0.710, $P = .439$), sex (male vs. female: OR = 0.353, $P = .060$), vitamin D use (OR = 1.988, $P = .104$), and drug type (insulin vs. oral: OR = 5.966, $P = .100$) (Table 6).

## Discussion

The data shows that vitamin D status was strongly associated with DR. Patients with retinopathy had lower mean 25(OH)D levels than non-DR patients, and the prevalence of deficiency increased with severity. In multivariate analyses, low vitamin D remained an independent predictor of DR, supporting a protective effect of sufficient vitamin D. It was also confirmed that chronic hyperglycemia and diabetes duration were major determinants of DR, while BMI, age, hypertension, and dyslipidemia were not significant. Notably, smoking and insulin therapy were independently linked with DR risk. Together, these results suggest that vitamin D, glycemic control, and disease duration are the most relevant correlates of DR in this cohort.

These findings align with the growing literature linking vitamin D deficiency to DR. Meta-analyses consistently show higher odds of DR in vitamin D-deficient patients, with risk nearly doubling when 25(OH)D < 20 ng/mL.[12] A systemic analysis demonstrated a 27% risk reduction per 10 ng/mL increase in 25(OH)D.[8] Observational studies report progressively lower vitamin D levels with advancing DR severity. Zahedi et al found a mean 25(OH)D of 14.5 ng/mL in DR versus 19.9 ng/mL in non-DR cases.[13] Egyptian and Qatari cohorts similarly reported strong associations.[9,10] The results are consistent with these, supporting the hypothesis that adequate vitamin D may reduce DR risk.

Traditional metabolic factors also emerged as expected. Poor glycemic control and longer diabetes duration are well-established drivers of DR, consistently reported in Middle Eastern and global studies.[6,14] These results suggested that each incremental increase in HbA1c and every additional year of diabetes significantly raised DR prevalence. In contrast, BMI, age, hypertension, and cholesterol were not independent predictors once glycemia was accounted for. This may reflect homogeneity in the cohort (overweight and generally well-controlled blood pressure) or mediation of these factors through glucose and vascular pathways. Thus, while cardiovascular risk factors may contribute indirectly, glycemic control remains central to prevention.

Smoking and insulin therapy were also associated with DR in the study. Evidence for smoking is mixed: some meta-analyses report neutral or even slightly protective associations,[15] but others, particularly in high-smoking populations, demonstrate increased risk.[14] The cohort showed higher DR prevalence among smokers, consistent with known vascular damage from tobacco-induced oxidative stress. Regardless of conflicting epidemiology, smoking cessation remains critical for vascular protection.

**Table 4. Comparison of Categorical Clinical Characteristics Between Proliferative and Non-Proliferative Diabetic Retinopathy Groups**

| | Diabetic Retinopathy Type | | | | |
|---|---|---|---|---|---|
| Variables | Proliferative (n = 40) | % | Non-Proliferative (n = 40) | % | *P* |
| Diabetes medication type | | | | | |
| Insulin | 17 | 42.5 | 13 | 32.5 | .250 |
| Oral | 23 | 57.5 | 27 | 67.5 | |
| Smoking | | | | | |
| Yes | 2 | 5.0 | 4 | 10.0 | .346 |
| No | 38 | 95.0 | 36 | 90.0 | |
| Blood pressure | | | | | |
| Yes | 26 | 65.0 | 23 | 57.5 | .521 |
| No | 14 | 35.0 | 17 | 42.5 | |
| Vitamin D usage | | | | | |
| Yes | 10 | 25.0 | 12 | 30.0 | .616 |
| No | 30 | 75.0 | 28 | 70.0 | |

**Table 5. Binary Logistic Regression Predicting Presence of Diabetic Retinopathy from Continuous Clinical and Biochemical Predictors**

| Predictor | B | SE | Wald $X^2$ | df | *P* | OR (Exp(B)) | 95% CI for OR |
|---|---|---|---|---|---|---|---|
| Age (years) | 0.022 | 0.024 | 0.907 | 1 | .341 | 1.023 | 0.977-1.071 |
| BMI (kg/m$^2$) | −0.044 | 0.062 | 0.515 | 1 | .473 | 0.957 | 0.852-1.075 |
| Diabetes duration (years) | 0.063 | 0.030 | 4.374 | 1 | **.036** | 1.065 | 1.004-1.129 |
| Blood pressure (1 = Yes) | 0.289 | 0.515 | 0.315 | 1 | .575 | 1.335 | 0.491-3.632 |
| HbA1c (%) | 0.486 | 0.252 | 3.718 | 1 | .054 | 1.626 | 0.992-2.665 |
| Cholesterol (mg/dL) | 0.005 | 0.006 | 0.791 | 1 | .374 | 1.005 | 0.993-1.017 |
| Vitamin D (ng/mL) | −0.135 | 0.045 | 9.008 | 1 | **.003** | 0.873 | 0.797-0.956 |

Insulin therapy was another strong correlate. Patients on insulin had higher DR prevalence and severity, consistent with reports from Saudi Arabia[16] and China, where insulin doubled the odds of DR and predicted new cases over 3 years.[17] While this likely reflects indication bias, patients requiring insulin generally have longer or more severe diabetes. The association highlights the need for closer retinal surveillance among insulin users.

The findings also reflect regional trends. In Saudi Arabia, DR prevalence is reported at 30%-40%, with glycemic control and duration as major determinants.[6] Jordanian data identified smoking, insulin use, obesity, hypertension, and nephropathy as correlates.[14] Globally, meta-analyses confirm that metabolic control and disease duration outweigh other risk factors. Importantly, vitamin D deficiency is particularly common in Middle Eastern and South Asian populations,[8] reinforcing the relevance of the results in this context.

Mechanistic evidence strengthens the biologic plausibility of the observations. Vitamin D exerts vascular-protective, anti-inflammatory, and anti-angiogenic effects. In retinal cells, vitamin D3 inhibits ROS/TXNIP/NLRP3 inflammasome activation and NF-κB signaling, thereby reducing pro-inflammatory cytokine production. Calcitriol treatment attenuates oxidative stress and endothelial apoptosis, while downregulating key pathogenic pathways including TGF-β, complement activation, and AGE–RAGE signaling.[18] In animal models, calcitriol suppressed pathological angiogenesis, whereas deletion of the vitamin D receptor produced pro-angiogenic and pro-inflammatory phenotypes.[19] These mechanisms provide a strong rationale for the epidemiological association that was observed.

The limitations of the study are acknowledged. First, because of the cross-sectional design, causal inferences cannot be made, as either DR or its treatments may have affected vitamin D metabolism. Vitamin D was assessed by a single measurement, not seasonally or longitudinally; some variables (e.g., smoking) relied on self-reports and may have been subject to bias. The cohort was a small sample from a single center and comprised only Middle Eastern patients, which may limit its generalizability. Second, the anomalous finding of an apparently protective effect of smoking against DR (OR: 0.072) starkly contradicts established epidemiological and pathophysiological evidence. This is almost certainly an artifact of the limited sample size, wherein a very small subgroup of smokers (n = 7) may not be representative, highlighting the risk of type I error in underpowered analyses. This result should not be construed as evidence of a protective effect. Insulin therapy as a predictor variable may reflect indication bias despite the adjustments. Lastly, active vitamin D (1,25-dihydroxyvitamin D) was not assessed, nor the various genetic polymorphisms that affect vitamin D metabolism was considered. Also, given the relatively small sample size and consequent limitations in statistical power, particularly for subgroup analyses, this study is best viewed as a pilot or exploratory investigation. The single-center design and specific regional focus further indicate that the findings require confirmation in larger, more diverse cohorts.

Despite the study's limitations, the findings have significant implications. The findings emphasize the importance of glycemic control for DR risk reduction, highlight the additional risk markers of smoking and insulin therapy as contributors, and lend evidence to the notion of vitamin D as a potentially modifiable risk factor. While the observational studies reported here lend support to this association, the next step is to establish whether vitamin D supplementation can reduce the incidence or progression of DR via prospective randomized controlled trials. Longitudinal studies will also clarify whether serum vitamin D improves risk prediction for DR.

## Conclusion

This study provides evidence for a strong association between vitamin D deficiency and the presence and severity of DR in patients with T2DM. In the cohort, low serum 25(OH)D level was an independent risk factor for the presence of diabetic retinopathy, along with longer diabetes duration, poor glycemic control, insulin use, and smoking status. Although vitamin D levels were lower in patients with any DR than in those without, the analysis did not show a statistically significant difference between the NPDR and PDR subgroups. The

**Table 6. Binary Logistic Regression Predicting Retinopathy from Categorical Variables**

| Predictor | Reference | B | SE | Wald $X^2$ | df | *P* | OR (Exp(B)) | 95% CI for OR |
|---|---|---|---|---|---|---|---|---|
| Smoking | No smoking | −2.634 | 0.999 | 6.946 | 1 | **.008** | 0.072 | 0.010-0.509 |
| Hypertension | No hypertensive | −0.342 | 0.442 | 0.599 | 1 | .439 | 0.710 | 0.299-1.688 |
| Sex | Female | −1.041 | 0.553 | 3.542 | 1 | .060 | 0.353 | 0.119-1.044 |
| Vitamin D use | No usage history | 0.687 | 0.422 | 2.650 | 1 | .104 | 1.988 | 0.869-4.545 |
| Drug type | Oral administration | 1.786 | 1.087 | 2.702 | 1 | .100 | 5.966 | 0.744-47.830[1] |

findings are consistent with the literature, both regionally and globally. Vitamin D deficiency should not be viewed only as a marker of poor health, but more as a modifiable risk factor for the development of DR in patients with T2DM. In addition, mechanistic studies support a protective role for vitamin D through anti-inflammatory, anti-angiogenic, and endothelial-stabilizing properties. This leaves the discussion open for interventional studies to determine the effectiveness of vitamin D supplementation as a risk reduction strategy by assessing DR outcomes. Alternatively, until interventional studies are implemented, clinicians need to double down on efforts to improve glycemic control, smoking cessation, and regular eye examinations, and to remember to consider vitamin D deficiency in the comprehensive diabetes care plan.

**Data Availability Statement:** The data that support the findings of this study are available on request from the corresponding author.

**Artificial Intelligence Usage Statement:** The authors declared that no Artificial Intelligence Tool was used in the preparation of the manuscript.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee Babol University of Medical Sciences (Approval no: IR.MUBABOL.REC.1403.103, Date: 26.08.2024).

**Informed Consent:** Written informed consent was obtained from the patients/patient who agreed to take part in the study.

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