Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Association Between Low Serum Vitamin A Level and Diabetic Retinopathy in Patients with Type 2 Diabetes: A Hospital-Based Study

Mao-Ju Zhang, Fen Cheng

Department of Ophthalmology, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, Enshi, 445000, People's Republic of China

Correspondence: Fen Cheng, Department of Ophthalmology, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, No. 158 Wuyang Road, Enshi, 445000, People's Republic of China, Email c123903641@163.com

Background: Vitamin A deficiency (VAD) has been shown to be associated with diabetic retinopathy (DR). However, only a small number of studies have examined the association between VAD and DR in patients with type 2 diabetes (T2DM). The aim of this study was therefore to determine the association between serum vitamin A level and DR in T2DM patients.

Methods: From 2019 to 2024, information was retrospectively collected on 470 healthy controls and 1020 patients with T2DM (500 without DR and 520 with DR). Inclusion criteria included those older than 30 years and having undergone retinal examinations for DR severity grading and measurement of serum vitamin A level.

Results: Of the total participants, 44.03% had a deficient serum vitamin A level (<1.0 μmol/L). Vitamin A level in patients with DR was significantly reduced compared to those in healthy controls ($P < 0.001$). Multivariate logistic regression analysis showed that VAD was a predictor for DR in T2DM patients (OR = 0.81, $P = 0.004$, 95% CI 0.26–0.97). After adjustment for all confounders, the DR patients had a 2.21-fold increased risk for having VAD ($P = 0.005$). Stratification of the patients by DR grade showed that decreased vitamin A level was related to the severity of DR. The stratified analysis also showed that the association between vitamin A deficiency and DR was influenced by smoking status or a history of hypertension. In the T2DM patients, vitamin A level correlated negatively with DR severity, indicating a dose-related gradient and a significant risk of developing DR during two years of follow-up (RR = 0.91, $P = 0.042$, 95% CI 0.65–0.96).

Conclusion: This study suggests that low serum levels of vitamin A correlate with the presence and severity of DR. VAD may therefore represent a potential biological vulnerability for DR.

Keywords: vitamin A, type 2 diabetes, diabetic retinopathy

Introduction

Complications may occur over the entire body in patients with type 2 diabetes (T2DM), one of which is the eye disease, diabetic retinopathy (DR).[1] DR is a common microvascular complication of T2DM and is the leading cause globally of preventable blindness. DR is caused by angiogenesis, inflammation, and the formation of fibrous connective tissue.[2] Many researchers have demonstrated that hypertension, higher HbA1c levels, and the duration of T2DM, in combination with other chronic comorbidities, are involved in the pathogenesis of DR.[3] Epidemiological studies have reported that DR develops in 20.9% of patients with a history of diabetes and comorbidities of 6 to 10 years duration and in 66.7% of cases with a disease duration of >15 years.[4] Although DR does not increase the mortality rate, it may reduce the quality-of-life of patients, thereby increasing healthcare expenditure due to the loss of eyesight.[5]

Vitamin A has been shown to be involved in immune system function, cell differentiation, and vision.[6] It has also been reported to inhibit angiogenesis, inflammation, and fibrosis, all of which contribute to the pathogenesis of DR.[7] Vitamin A suppresses angiogenesis by repressing vascular endothelial growth factor, and reduces the inflammatory response by decreasing the levels of cytokines in the blood.[8] In addition, vitamin A has been reported in animal models to

Received: 15 January 2025
Accepted: 23 April 2025
Published: 31 May 2025

inhibit fibrosis by regulating the expression of all fibrosis biomarkers.[9] These actions of vitamin A are thought to have important effects in preventing the development of DR.

Several studies have investigated the association between vitamin A level and DR. Rostamkhani et al showed that increasing serum vitamin A level decreased the risk of DR by 31.1%.[10] However, another study reported that vitamin A supplementation had no significant effect on DR risk, a finding that was possibly due to the detection method used in the study.[11] The association between vitamin A and DR is no consistent conclusion yet. We therefore performed a study to determine, in terms of ocular diagnosis, the association between serum vitamin A level and DR in a relatively large and well-characterized population. Vital confounding factors, including age, sex, education, smoking status, drinking status, BMI (body mass index), vitamin A supplements use, hypertension, insulin usage, HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, and LDL-C, were also taken into account in the analyses. The aims of the study were to compare the serum vitamin A level in T2DM patients with or without DR and healthy controls, and to examine the association between serum vitamin A level and the severity and clinical course of DR.

Patients and Methods

Baseline Characteristics of the Participants

From January 2019 to March 2024, we enrolled 470 healthy controls and 1020 T2DM patients (500 without DR and 520 with DR) in the study. All the participants had a variety of examinations, such as height, weight, blood pressure, laboratory testing (HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, LDL-C), and standardized questionnaires on age, sex, education, smoking status, drinking status, and insulin usage in Department of Ophthalmology, the Central Hospital of Enshi Tujia and Miao Autonomous Prefecture. The questionnaire was adapted from the STEPwise Approach to Surveillance of Noncommunicable Disease Risk Factors of WHO.[12] Serum sample of all participants were collected after enrollment. The levels of vitamin A were measured by LC-MS/MS (AB SCIEX 4500 QTRAP, Foster City, CA) which had 4.82% intra- and 7.42% inter-assay coefficients of variation. Liquid chromatography separation was performed with a flow rate of 0.35 mL/min at 45°C. 50% methanol in milli-Q water with 0.2% formic acid (v/v; solution A) and methanol with 0.2% formic acid (v/v; solution B) were wielded as mobile phases. The gradient was 0–2.5 min 40% B, 2.5–6 min 40–100% B, 6–10 min 100% B, 10–10.1 min 100–40% B, and 10.1–15 min 40% B. The injection volume was 15 μL.[13] A serum vitamin A level <1.0 μmol/L was considered vitamin A deficient (VAD),[14] 1.0–2.0 μmol/L as desirable, and >2.0 μmol/L as adequate.

Inclusion and Exclusion Criteria

All participants met the following criteria: (1) thirty years or older; (2) diagnosed with T2DM; (3) provided informed consent. The exclusion criteria included: (1) unclear diabetes status and missing HbA1c data; (2) unable to provide a blood sample; (3) immunologic or infectious diseases; and (4) hepatic or renal dysfunction, heart failure, or malignant cancer. The fundus was checked using AO scanning laser ophthalmoscopy (SLO) in all patients and graded based on the modified Early Treatment of Diabetic Retinopathy Study (ETDRS) scale.[15] The severity of DR was graded as non-DR, mild non-proliferative DR (NPDR), moderate NPDR, severe NPDR, or proliferative DR (PDR).[16] The study was approved by the ethics committee of the Central Hospital of Enshi Tujia and Miao Autonomous Prefecture (No. KJB2018065).

Statistical Analysis

Continuous variables (age, education, BMI, HbA1c, urea, creatinine, TC, TG, HDL-C, LDL-C, vitamin A) were expressed as means ± s.d. and categorical variables (sex, smoking status, drinking status, vitamin A supplements use, hypertension, insulin usage, albuminuria) as percentages. Differences in the baseline characteristics were analyzed based on DR status using the Chi-square test or analyses of variance, as appropriate. Univariate and multivariate logistic regression analyses were applied to identify the predictors for DR. Multinomial logistic regression was used to analyze the odds for desirable, deficient versus adequate vitamin A level in the DR status groups. Multinomial logistic regressions were also used to assess the association between vitamin A level and the severity of DR and VAD and the different DR

stages (DR, NPDR, and PDR). Stratified analysis was used to evaluate the relationship between vitamin A level and DR, grouped by smoking status, hypertension, and HbA1c. In addition, left-censored regression models were used to determine the association between vitamin A level and the continuous measure of DR duration during the two-year follow-up period. All the tests were performed using SPSS 24.0 (IBM Corp., Armonk, NY, USA). A P-value < 0.05 was considered statistically significant.

Results

A total of 470 healthy controls and 1020 patients with T2DM (500 without DR and 520 with DR) were enrolled in the study. Table 1 shows the baseline characteristics of the study cohort. The mean age of the participants was 59.81 (±10.57) years and 48.19% were male. T2DM patients were more often female, were smokers, and had a higher BMI, higher proportion of hypertension and insulin usage, and higher levels of HbA1c, urea, creatinine, and albuminuria than healthy controls. Patients with DR had poor lifestyle and health indicators and clinical characteristics. Only 5.30% of participants had received vitamin A supplements.

The results in Table 2 showed that sex, smoking status, BMI, hypertension, albuminuria, HbA1c, and vitamin A were associated with DR in T2DM patients. Multivariate analysis demonstrated that smoking status (OR = 0.51, P = 0.043, 95% CI 0.22–0.99), hypertension (OR = 1.50, P = 0.041, 95% CI 1.07–3.43), HbA1c (OR = 0.76, P = 0.047, 95% CI 0.32–0.99), and vitamin A (OR = 0.81, P = 0.004, 95% CI 0.26–0.97) were predictors for DR in T2DM patients.

Table 1 Baseline Characteristics of Participants

Variables	Healthy Controls (n = 470)	T2DM		*P*
		Non-DR (n = 500)	DR (n = 520)	
Sociodemographic				
Age (years)	59.07±10.84	59.49±11.06	60.78±9.85	0.174
Sex (male, %)	279 (59.36%)	211 (42.20%)	228 (43.85%)	0.044
Education (years)	12.74±4.51	13.82±4.31	12.92±3.97	0.518
Lifestyle and health indicators				
Smoking status (%)				<0.001
Non smoker	177 (37.66%)	127 (25.40%)	143 (27.50%)	
Former smoker	168 (35.74%)	178 (35.60%)	136 (26.15%)	
Current smoker	125 (26.60%)	195 (39.00%)	241 (46.35%)	
Drinking status (%)				0.184
Ex-drinker	155 (32.98%)	179 (35.80%)	167 (32.12%)	
Sometime	300 (63.83%)	315 (63.00%)	351 (67.50%)	
Everyday	15 (3.19%)	6 (1.20%)	2 (0.38%)	
BMI (mean, SD)	21.52±4.13	26.49±4.22	27.82±4.31	0.015
Vitamin A supplements use (%)	26 (5.53%)	24 (4.80%)	29 (5.58%)	0.725
Clinical characteristics				
Hypertension (%)	0 (%)	226 (45.20%)	265 (50.96%)	0.018
Insulin usage (%)	0 (%)	172 (34.40%)	248 (47.69%)	<0.001
HbA1c (%)	5.31±1.34	7.31±0.97	7.70±0.85	0.003
Serum urea (mg/dL)	22.92±13.54	28.89±11.26	31.52±12.42	0.009
Serum creatinine (mg/dL)	0.59±0.25	0.90±0.37	1.07±0.52	0.026
Albuminuria (%)	21 (4.47%)	154 (30.80%)	242 (46.54%)	<0.001
TC (mmol/L)	3.99±0.46	4.22±0.51	4.23±0.48	0.076
TG (mmol/L)	1.34±0.43	1.37±0.39	1.36±0.41	0.105
HDL-C (mmol/L)	1.25±0.32	1.25±0.34	1.23±0.36	0.437
LDL-C (mmol/L)	2.03±0.49	2.05±0.57	2.07±0.52	0.519
Serum vitamin A (μmol/L)	2.07±0.52	1.24±0.42	0.99±0.38	<0.001

https://doi.org/10.2147/JIR.S514127

Table 2 Univariate and Multivariate Logistic Regression Analysis with Predictors of DR

Characteristics	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	0.75	0.44–1.13	0.537			
Sex	0.55	0.14–0.97	0.045	0.62	0.22–1.09	0.107
Education	1.47	0.69–2.53	0.711			
Smoking status	0.49	0.18–0.85	0.015	0.51	0.22–0.99	0.043
Drinking status	2.42	0.83–6.81	0.724			
BMI	1.22	1.05–3.59	0.041	1.36	0.89–3.21	0.094
Vitamin A supplements use	0.73	0.49–1.51	0.328			
Hypertension	1.42	1.07–3.51	0.006	1.50	1.07–3.43	0.041
Insulin usage	1.12	0.84–2.37	0.316			
HbA1c	0.72	0.31–0.96	0.027	0.76	0.32–0.99	0.047
Urea	1.06	0.73–2.41	0.422			
Creatinine	1.32	0.83–1.88	0.279			
Albuminuria	0.77	0.31–0.97	0.048	0.83	0.36–1.10	0.106
TC	0.55	0.23–1.17	0.158			
TG	0.71	0.42–1.27	0.352			
HDL-C	1.13	0.54–1.89	0.417			
LDL-C	1.09	0.77–1.78	0.362			
Vitamin A	0.78	0.21–0.94	<0.001	0.81	0.26–0.97	0.004

Table 3 shows the odds of desirable and deficient vitamin A serum levels assessed by multinomial logistic regression in which adequate status (>2.0 μmol/L) was set as the reference category. In the partially adjusted models, compared with healthy controls, patients without DR had a 1.57-fold ($P = 0.014$) increased risk for deficient vitamin A level, while those with DR had a 1.48-fold ($P = 0.016$) and 2.45-fold ($P < 0.001$) increased risk for desirable and deficient vitamin A level, respectively. In the fully adjusted models, compared with controls, patients with DR had a 1.39-fold ($P = 0.027$) and 2.21-fold ($P = 0.005$) increased risk for desirable and deficient vitamin A level, respectively.

Three models were constructed to examine the association between VAD and DR (Table 4). In model 1, the nominal presence of VAD was related significantly to DR. Models 2 and 3 showed a relationship between VAD and the severity of DR, indicating that the presence of VAD increased the risk of severe non-proliferative diabetic retinopathy (NPDR) (OR = 1.24, $P = 0.015$, 95% CI 1.04–1.79) and PDR (OR = 2.01, $P < 0.001$, 95% CI 1.42–3.16).

Table 3 Adjusted Association Among DR Status of Serum Vitamin A Level

DR Status	Serum Vitamin A Level						
	Adequate (n = 368)	Desirable (n = 466)			Deficient (n = 656)		
		OR	95% CI	*P*	OR	95% CI	*P*
Model 1							
Healthy controls	Reference category	1.00			1.00		
Non-DR		1.31	(1.09–1.89)	0.042	1.57	(1.08–3.06)	0.014
DR		1.48	(1.11–1.97)	0.016	2.45	(1.46–3.65)	<0.001
Model 2							
Healthy controls	Reference category	1.00			1.00		
Non-DR		1.26	(0.96–1.86)	0.064	1.45	(0.89–2.68)	0.107
DR		1.39	(1.06–1.83)	0.027	2.21	(1.18–3.55)	0.005

Notes: Model 1: adjusted for age, sex, education, smoking status, drinking status. Model 2: adjusted for age, sex, education, smoking status, drinking status, BMI, vitamin A supplements use, hypertension, insulin usage, HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, and LDL-C.

Table 4 Logistic Regression Models Evaluating Association Among Vitamin A Deficient (VAD) and DR Presence and Severity

	VAD Prevalence (n, %)	Multivariate	
		OR (95% CI)	*P*
Model 1			
Non-DR (n = 500)	287 (57.40%)	Reference	
DR (n = 520)	319 (61.35%)	1.12 (1.06–1.38)	0.046
Model 2			
Non-DR (n = 500)	287 (57.40%)	Reference	
Mild NPDR (n = 197)	112 (56.85%)	0.86 (0.73–1.06)	0.217
Moderate NPDR (n = 174)	106 (60.92%)	1.09 (0.92–1.18)	0.068
Severe NPDR (n = 95)	60 (63.16%)	1.24 (1.04–1.79)	0.015
PDR (n = 54)	41 (75.93%)	2.01 (1.42–3.16)	<0.001
Model 3			
Non-DR (n = 500)	287 (57.40%)	Reference	
NPDR (n = 466)	278 (59.66%)	1.06 (0.98–1.20)	0.217
PDR (n = 54)	41 (75.93%)	2.06 (1.45–3.18)	<0.001

Note: Multivariate models for DR status as predicted by age, sex, education, smoking status, drinking status, BMI, vitamin A supplements use, hypertension, insulin usage, HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, and LDL-C.

Abbreviations: DR, Diabetic retinopathy presence; NPDR, Non-proliferative diabetic retinopathy; PDR, Proliferative diabetic retinopathy.

The association between vitamin A and DR remained significant after adjustment for potential confounders and also remained in the majority of subgroup analyses of data stratified by smoking status, hypertension, or HbA1c. In the fully adjusted model, compared with non-DR patients, there were no significant associations in either non-smokers (OR = 1.09, $P = 0.839$, 95% CI 0.65–3.16) or former smokers (OR = 0.55, $P = 0.274$, 95% CI 0.22–1.19). However, in patients who were current smokers, there was a significant association (OR = 0.41, $P = 0.006$, 95% CI 0.11–0.69). When the data were stratified by hypertension, serum vitamin A level was associated closely with DR in patients with hypertension ($P = 0.014$). When stratified by HbA1c, no association between vitamin A level and DR was observed (P all > 0.05, Table 5).

Finally, we assessed whether vitamin A level predicted DR in 100 (10.00%) T2DM patients without DR using data obtained during a two-year follow-up period (Table 6). In the fully adjusted models, each s.d. increase in vitamin A level was related to a 9.00% reduced risk ($P = 0.042$) of having DR at follow-up (33.30% prevalence). Moreover, higher

Table 5 Association Among Serum Vitamin A and DR Stratified by Smoking Status, Hypertension, and HbA1c

	Model 1		Model 2		Model 3	
	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Stratified by smoking stats						
Non smoker	1.34 (0.68–3.92)	0.517	1.17 (0.72–3.49)	0.721	1.09 (0.65–3.16)	0.839
Former smoker	0.63 (0.28–0.97)	0.034	0.59 (0.25–1.09)	0.074	0.55 (0.22–1.19)	0.274
Current smoker	0.49 (0.21–0.87)	<0.001	0.46 (0.18–0.75)	<0.001	0.41 (0.11–0.69)	0.006
Stratified by hypertension						
No	0.48 (0.29–1.17)	0.651	0.43 (0.25–1.14)	0.771	0.39 (0.21–1.07)	0.847
Yes	0.63 (0.31–0.85)	<0.001	0.58 (0.24–0.91)	0.003	0.52 (0.19–0.96)	0.014
HbA1c						
≤7.71%	0.58 (0.22–1.32)	0.417	0.51 (0.19–1.26)	0.526	0.45 (0.14–1.59)	0.742
>7.71%	0.44 (0.27–0.72)	<0.001	0.42 (0.25–0.95)	0.016	0.39 (0.21–1.02)	0.075

Notes: Model 1: no modification variables. Model 2: adjusted for age, sex, education, smoking status, drinking status. Model 3: adjusted for age, sex, education, smoking status, drinking status, BMI, vitamin A supplements use, hypertension, insulin usage, HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, and LDL-C.

Table 6 Multivariate Analysis on Serum Vitamin A Level as a Predictor of DR in Patients with T2DM During the Two-year Follow-up (n = 100)

	Presence (Yes/No) of DR After 2 Years				Time with DR During the 2-Year Follow-up						
					0–2 Years			> 1.5 Years (Highest Quartile)			
	%	RR	95% CI	*P*	Estimate	s.e.	*P*	%	RR	95% CI	*P*
Vitamin A per s.d. increase	33.3	0.91	0.65–0.96	0.042	−0.06	0.02	0.035	19.8	0.84	0.52–0.94	0003
Vitamin A status											
Adequate (n = 32)	26.5	Ref.			Ref.			13.5	Ref.		
Desirable (n = 29)	28.2	1.07	0.67–1.63	0.417	0.04	0.02	0.428	15.2	1.18	0.76–2.62	0.316
Deficient (n = 39)	42.6	1.42	1.07–2.15	0.005	0.06	0.05	0.063	28.4	1.73	1.09–2.57	0.013

Note: Vitamin A per s.d. increase: for each one standard deviation increase in vitamin A levels.
Abbreviations: s.d., standard deviation.

vitamin A level in serum were related to a shorter duration of DR ($P = 0.035$) and a lower risk of having DR in the highest quartile of follow-up duration ($P = 0.003$). Compared to subjects with adequate vitamin A level, patients with deficient levels had a 1.73 ($P = 0.013$, 95% CI: 1.09–2.57) higher risk of having DR in the highest quartile of follow-up duration (Table 6).

Discussion

This study showed serum vitamin A level correlated positively with a lower risk of developing DR and also with the severity of the condition. In particular, we demonstrated that vitamin A level correlated with a higher risk of DR in patients who either smoked, had hypertension, or HbA1c level >7.71%. Serum vitamin A level >1.0 μmol/L was also shown to significantly reduce the risk of developing DR compared with subjects with VAD. Moreover, in cases with T2DM low serum vitamin A level were associated with a susceptibility to DR over a two-year follow-up period.

Our finding that higher vitamin A level decreased the risk of developing DR can be explained by the mechanism involved in the development of the condition and the mechanism of action for vitamin A. Several mechanisms contribute to the development of DR, such as angiogenesis, the inflammatory response, and fibrosis.[7–9] As a consequence of these three factors, DR may lead to other complications such as NPDR, PDR, vitreous hemorrhage, and traction retinopathy.[17] In contrast, vitamin A has anti-angiogenesis, anti-inflammation, and anti-fibrotic effects, which protect against the onset of DR.[11] Taken together, these findings indicate that vitamin A reduces the risk of DR.

Analysis of our data showed an association between the risk of developing DR, especially with smoking habits, hypertension, and a HbA1c level of >7.71%. Moreover, some researchers have reported that smoking may increase the risk of DR in patients with T2DM.[18] Alcohol intake may also differently affect the DR risk based on the type of diabetes mellitus and adjusted status.[19] Similarly, high BMI may represent potential causal risk factors for diabetic microvascular complications.[20] Several studies have investigated the association between serum vitamin A and DR and showed that serum vitamin A level were reduced significantly in patients with DR compared to those observed in controls, and that higher vitamin A level decreased the risk of developing DR by 31.1%.[21] It has also been reported that lower vitamin A level in the blood correlated most closely with the severity of DR, followed by patients without DR, cases with NPDR, and those with PDR.[10] Our study also showed that after adjustment for confounding factors, including age, sex, education, smoking status, drinking status, BMI, vitamin A supplements use, hypertension, insulin usage, HbA1c, urea, creatinine, albuminuria, TC, TG, HDL-C, and LDL-C, the presence of VAD increased the risk of severe NPDR. In addition, there is evidence that dietary vitamin A intake is decreased significantly in patients with DR compared with those without DR.[22] However, another study was unable to show that high levels of dietary vitamin A were associated with a lower risk of DR.[11] While that study did not indicate that dietary vitamin A level were associated with DR, it was limited by actual measurement of dietary vitamin A intake.

The absorption rate of vitamin A in patients with small intestine disorders, chronic absorption disorders, and reduced pancreatic function can vary due to the fat-solubility of the vitamin.[23] The current study also observed that high levels of serum vitamin A were related to a low risk of developing DR.

Our results provide strong confirmative evidence for a previous study in a large and relatively older population, which was based mainly on a retrospective analysis, that showed an association between vitamin A and DR.[24] Remarkably, we observed that serum vitamin A level in T2DM patients was lower in patients with DR compared to those without DR. Moreover, in T2DM patients without DR those with VAD had an increased risk of developing DR during the follow-up period. However, we are unable to make a definite conclusion on the directionality of the association inferred from our current results. It is possible that VAD may also be a consequence of DR, due to the fact that it affects health-associated lifestyle, including physical activity, diet, and obesity, all of which are known to be associated with serum vitamin A level.[25,26] Our findings therefore need to be confirmed by longitudinal and experimental studies that demonstrate an involvement of vitamin A in the cascade to DR.

Our study had some limitations, such as its cross-sectional design, from which causation could not be characterized. Moreover, we could not adjust the detected association for dietary intake of vitamin A, because nutritional data were not available. Although the study was adjusted for the effects of adiposity, liver function, and exogenous vitamin A intake, it is possible that other confounders, such as the duration of T2DM, may have affected the data in unanticipated ways. Furthermore, as stated previously, supplementation of vitamin A was largely absent in the study cohort. In addition, patients with poorly controlled diabetes may also have lower vitamin A levels due to metabolic dysregulation, oxidative stress, and altered hepatic function. Thus, our study does not provide sufficient evidence to establish whether low vitamin A precedes DR or is simply a consequence of advanced diabetes and its complications. Moreover, further interventional studies need to be performed to demonstrate that vitamin A supplementation reduces DR incidence or progression. However, this study had some important strengths, such as its relatively large sample size, clinical diagnosis of DR, and a gold-standard method for measuring vitamin A level. Our findings suggest that low serum levels of vitamin A correlate with the presence and severity of DR. VAD may therefore represent a potential biological vulnerability for DR. Thus, vitamin A should be detected and supplemented to reduce the risk of DR.

Conclusion

In summary, higher serum levels of vitamin A associate with a low risk of developing DR in T2DM patients. In particular, vitamin A correlates with a high risk of developing DR in T2DM patients, more closely in those who are smokers, have hypertension, or have a HbA1c level of >7.71%. However, the observed association is also likely confounded by glycemic control, metabolic status, and dietary factors, making it difficult to attribute an independent role to vitamin A in DR pathogenesis.

Data Sharing Statement

The dataset used in the preparation of this study will be available from the corresponding author upon reasonable request.

Acknowledgments

The authors would like to express their gratitude to EditSprings (https://www.editsprings.cn) for the expert linguistic services provided. The authors confirm that the study complies with the Declaration Helsinki.

Disclosure

The authors declare that they have no conflicts of interest for this work.

References

1. Fung TH, Patel B, Wilmot EG, Amoaku WM. Diabetic retinopathy for the non-ophthalmologist. *Clin Med*. 2022;22(2):112–116. doi:10.7861/clinmed.2021-0792
2. Lin KY, Hsih WH, Lin YB, Wen CY, Chang TJ. Update in the epidemiology, risk factors, screening, and treatment of diabetic retinopathy. *J Diabetes Investig*. 2021;12(8):1322–1325. doi:10.1111/jdi.13480

3. Wang W, Lo ACY. Diabetic retinopathy: pathophysiology and treatments. *Int J Mol Sci*. 2018;19(6):1816. doi:10.3390/ijms19061816
4. Hammoudi J, Bouanani NEH, Chelqi EH, et al. Diabetic retinopathy in the Eastern Morocco: different stage frequencies and associated risk factors. *Saudi J Biol Sci*. 2021;28:775–784. doi:10.1016/j.sjbs.2020.11.010
5. Simó-Servat O, Hernández C, Simó R. Diabetic retinopathy in the context of patients with diabetes. *Ophthalmic Res*. 2019;62(4):211–217. doi:10.1159/000499541
6. Saari JC. Vitamin A and vision. *Subcell Biochem*. 2016;81:231–259. doi:10.1007/978-94-024-0945-1_9
7. Yu X, Ma Y, Luo Y, et al. Neonatal vitamin A administration increases intramuscular fat by promoting angiogenesis and preadipocyte formation. *Meat Sci*. 2022;191:108847. doi:10.1016/j.meatsci.2022.108847
8. Soares MM, Silva MA, Garcia PPC, et al. Efect of vitamin A suplementation: a systematic review. *Cien Saude Colet*. 2019;24(3):827–838.
9. Liu XY, Li D, Li TY, Wu YL, Piao JS, Piao MG. Vitamin A - modified Betulin polymer micelles with hepatic targeting capability for hepatic fibrosis protection. *Eur J Pharm Sci*. 2022;174:106189. doi:10.1016/j.ejps.2022.106189
10. Rostamkhani H, Mellati AA, Tabaei BS, Alavi M, Mousavi SN. Association of serum zinc and vitamin A level with severity of retinopathy in type 2 diabetic patients: a cross-sectional study. *Biol Trace Elem Res*. 2019;192:123–128. doi:10.1007/s12011-019-01664-z
11. Choi YJ, Kwon JW, Jee D. Are dietary intake parameters of vitamin A, carotene, retinol appropriate factors to evaluate the risk of diabetic retinopathy. *Medicine*. 2023;102:e33969. doi:10.1097/MD.0000000000033969
12. Salawu AI, Ajani GO, Soje MO, et al. Diabetes mellitus foot ulcer and associated factors among type 2 diabetes patients in a Tertiary Institution in Southwest Nigeria. *Ann Afr Med*. 2022;21(4):339–347. doi:10.1194/jlr.D087569
13. Le J, Yuan TF, Zhang Y, Wang ST, Li Y. New LC-MS/MS method with single-step pretreatment analyzes fat-soluble vitamins in plasma and amniotic fluid. *J Lipid Res*. 2018;59(9):1783–1790. doi:10.1194/jlr.D087569
14. Wilkinson CP, Ferris FL, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology*. 2003;110(9):1677–1682.
15. Sapiejka E, Krzyżanowska P, Walkowiak D, et al. Vitamin A status and its determinants in patients with cystic fibrosis. *Acta Sci Pol Technol Aliment*. 2017;16(3):345–354. doi:10.17306/J.AFS.0473
16. Patrick PA, Visintainer PF, Shi Q, Weiss IA, Brand DA. Vitamin D and retinopathy in adults with diabetes mellitus. *Arch Ophthalmol*. 2012;130 (6):756–760.
17. Yue T, Shi Y, Luo S, Weng J, Wu Y, Zheng X. The role of inflammation in immune system of diabetic retinopathy: molecular mechanisms, pathogenetic role and therapeutic implications. *Front Immunol*. 2022;13:1055087. doi:10.3389/fimmu.2022.1055087
18. Cai XL, Chen YF, Yang WJ, Gao XY, Han XY, Ji LN. The association of smoking and risk of diabetic retinopathy in patients with type 1 and type 2 diabetes: a meta-analysis. *Endocrine*. 2018;62(2):299–306. doi:10.1016/j.diabres.2023.110975
19. Chen C, Sun Z, Xu W, et al. Associations between alcohol intake and diabetic retinopathy risk: a systematic review and meta-analysis. *BMC Endocr Disord*. 2020;20(1):106. doi:10.1016/j.diabres.2023.110975
20. Huang Y, Zhang X, Li B, et al. Association of BMI and waist circumference with diabetic microvascular complications: a prospective cohort study from the UK Biobank and Mendelian randomization analysis. *Diabet Res Clin Pract*. 2023;205:110975. doi:10.1016/j.diabres.2023.110975
21. Ruamviboonsuk V, Grzybowski A. The roles of vitamins in diabetic retinopathy: a narrative review. *J Clin Med*. 2022;11(21):6490. doi:10.1007/s12011-019-01664-z
22. Zhang C, Li K, Zhang JY, et al. Relationship between retinol and risk of diabetic retinopathy: a case–control study. *Asia Pac J Clin Nutr*. 2019;28:607–613. doi:10.6133/apjcn.201909_28(3).0021
23. Blaner WS, Li Y, Brun PJ, Yuen JJ, Lee SA, Clugston RD. Vitamin A absorption, storage and mobilization. *Subcell Biochem*. 2016;81:95–125. doi:10.1007/978-94-024-0945-1_4
24. Choi YJ, Kwon JW, Jee D. The relationship between blood vitamin A level and diabetic retinopathy: a population-based study. *Sci Rep*. 2024;14 (1):491. doi:10.1038/s41598-023-49937-x
25. Mody N. Alterations in vitamin A/retinoic acid homeostasis in diet-induced obesity and insulin resistance. *Proc Nutr Soc*. 2017;76(4):597–602. doi:10.1017/S0029665117001069
26. Shymotiuk I, Froese N, Werlein C, et al. Vitamin A regulates tissue-specific organ remodeling in diet-induced obesity independent of mitochondrial function. *Front Endocrinol*. 2023;14:1118751. doi:10.2147/JIR.S492115