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Myopia-diabetic retinopathy relationship

Relación miopía-retinopatía diabética

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ABSTRACT:

Background: Previous studies have suggested an inverse relationship between myopia and diabetic retinopathy (DR) but such protective effect remains inconsistent. This study aimed to further investigate the relationship between myopia and DR.**Methods:** This cross-sectional study included two-hundred and one (221) type 2 diabetic patients (437 eyes). After pupil dilatation, autorefractometry was done to determine the spherical equivalent of refraction. Standard fundus photographs were used to grade diabetic retinopathy. Axial length was measured using Echo scan US-500 (NIDEK). Demographic and clinical information were obtained via interview. A multivariate regression analysis was performed to examine the independent predictors of diabetic retinopathy.**Results:** A total of 221 patients (437 eyes) were included in the final analysis. The prevalence of diabetic retinopathy was 50.3%. Among the eyes with diabetic retinopathy, 12.6% had mild NPD, 9.4% moderate NPD, 16.9% severe NPD, and 11.4% PDR respectively. After adjusting for confounding factors, any diabetic retinopathy was independently associated with myopia (OR, 0.39; 95% CI=0.17-0.91, P= 0.028) and axial length (OR, 0.31; 95% CI, 0.24-0.94; P <0.001. The axial length was inversely and significantly associated with the grade of diabetic retinopathy.

The presence of diabetic retinopathy was independently related to HbA1c, duration of diabetes, and serum cholesterol.

Conclusion: Myopia and longer axial length could protect against the occurrence and severity of diabetic retinopathy.**KEYWORDS:** Autorefractometry, axial length, diabetes mellitus, diabetic retinopathy, myopia.

RESUMEN:

Antecedentes: estudios anteriores han sugerido una relación inversa entre la miopía y la retinopatía diabética (RD), pero dicho efecto protector sigue siendo inconsistente. Este estudio tuvo como objetivo investigar más a fondo la relación entre la miopía y la RD.**Métodos:** Este estudio transversal incluyó a doscientos un (221) pacientes diabéticos tipo 2 (437 ojos). Después de la dilatación de la pupila, se realizó una autorrefracción para determinar el equivalente esférico de refracción. Se utilizaron fotografías estándar del fondo de ojo para clasificar la retinopatía diabética. La longitud axial se midió utilizando Echo scan US-500 (NIDEK). La información demográfica y clínica se obtuvo mediante entrevista. Se realizó un análisis de regresión multivariante para examinar los predictores independientes de retinopatía diabética.**Resultados:** Se incluyó un total de 221 pacientes (437 ojos) en el análisis final. La prevalencia de retinopatía diabética fue del 50,3%. Entre los ojos con retinopatía diabética, el 12,6% tenía NPD leve, el 9,4% NPD moderado, el 16,9% NPD grave y el 11,4% PDR, respectivamente. Después de ajustar por factores de confusión, cualquier retinopatía diabética se asoció de forma independiente con miopía (OR, 0,39; IC del 95% = 0,17-0,91, P = 0,028) y longitud axial (OR, 0,31; IC del 95%, 0,24-0,94; P < 0,001. La longitud axial se asoció inversa y significativamente con el grado de retinopatía diabética.

La presencia de retinopatía diabética se relacionó de forma independiente con HbA1c, la duración de la diabetes y el colesterol sérico.

Conclusión: La miopía y la mayor longitud axial podrían proteger contra la aparición y la gravedad de la retinopatía diabética.**PALABRAS CLAVE:** autorrefracción, longitud axial, diabetes mellitus, retinopatía diabética, miopía.

INTRODUCTION

Diabetic retinopathy (DR) is a widespread and serious diabetic microvascular complication. It raises the risk of avoidable blindness particularly in the early stage of the disease. It was reported to be responsible for 2.6% of global blindness^{1,2}. Previous studies have reported a protective effect of myopia against DR^{3,4}. The exact mechanism behind this protective association is not well known. However, a plausible hypothesis is that increased axial length may contribute to this protective relationship^{3,5-7}. The retinal blood vessels are extended and thinned by such elongation, leading to a decrease in low blood pressure and a decrease in capillary hydrostatic pressure, thus reducing the risk of leakage and rupture^{7,8}.

However, many population-based studies showed controversial and inconsistent results. According to the Singapore Malay Eye Report, eyes with a higher degree of myopia had a lower risk to develop diabetic retinopathy³. The Beijing Eye Research, on the other hand, found no connection between myopia and DR⁹. Man et al reported that the protective relationship between myopia and DR might be due to axial elongation rather than myopia¹⁰. However, Tayyab et al reported that longer axial length of globe has a protective effect on the stage and severity of diabetic retinopathy¹¹. A recent Korean study¹² found that axial myopia and a low HbA1c level could prevent diabetic retinopathy.

A thorough understanding of the association between myopia and DR is crucial for guiding public health policies and providing transparency into DR pathophysiology. The aim of this study was to assess a potential relationship between myopia, axial length and diabetic retinopathy

PATIENTS AND METHODS

Study design and study population

This cross-sectional study was carried out in the Ophthalmology Unit, Al-Sadder Teaching Hospital in Basrah, Iraq from September 2020 to February 2021.

A total of 221 known type 2 diabetic patients consecutively attending the outpatient clinic of the aforementioned hospital were enrolled in this study.

Data collection

An interview was done with standardized questionnaire including information about socio-demographic and clinical characteristics. Body weight and height were measured and body mass index (BMI) was calculated. Blood samples were drawn under fasting conditions to assess blood glucose, HbA1c, and cholesterol concentrations. After 5 minutes of rest, blood pressure was measured with a mercury sphygmomanometer while the patient is in a sitting position.

Ophthalmic examination

The ophthalmic examinations included measurement of visual acuity by autorefractometry (Tomey USA/RC 500). Intraocular pressure was measured by (Tomey USA/automated FT-1000). After pupil dilatation by tropicamide 1%, fundi were examined using Slit Lamp Biomicroscope (Haag streit) and indirect ophthalmoscope then ocular coherent tomography (OCT) type (Optovue/USA) and or ultra-wide field retinal high resolution imaging by (Optos California-Nikon). Axial length was measured by an independent expert optometrist using Echo scan US-500 (NIDEK). Myopia was defined as "a spherical equivalent of -1.00 diopter or less"¹⁴.

DR assessment

According to the "Early Treatment of Diabetic Retinopathy Study (ETDRS) criteria"¹³, diabetic retinopathy was categorized as mild non-proliferative (NDR), moderate NDR, severe NDR, and

proliferative DR. For analytical purposes, the outcome (diabetic retinopathy) was dichotomized into absence or presence of diabetic retinopathy.

Exclusion criteria

Patients with history of other systemic diseases, high intraocular pressure, optic nerve disease, history of any eye surgery, and those diagnosed with retinal abnormalities were excluded from the study¹⁵.

Ethical consideration

The Ethical Committee of College of Medicine approved this study, University of Basrah No. 030407022-2019. Informed consent was achieved from all participants before enrollment in the study.

Statistical analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) version 23, (IBM, Chicago, Illinois, USA). Numbers and percentages were used to describe categorical variables, whereas continuous variables were expressed as means $\pm$ standard deviations. Chi squared test, t-test, and one-way ANOVA were used where applicable. A binary logistic analysis was performed to test the variables that independently affect diabetic retinopathy, including those that were significant at $P < 0.05$ by the univariate analysis.

Odds ratios and 95% CIs were calculated for axial length and DR, axial length and type of DR, and presence or absence of myopia and DR. Multinomial regression analysis was performed to examine the association of axial length with grade (severity) of DR.

RESULTS

Two-hundred and one (221) type 2 diabetic patients (437 eyes) were enrolled in this study. Of those eyes, 220 eyes 50.3% (95% CI: 45.8%-55.1%) had diabetic retinopathy. Among the eyes with diabetic retinopathy, 12.6% had mild NPD, 9.4% moderate NPD, 16.9% severe NPD, and 11.4% PDR respectively. The mean of axial length was 24.4 ± 1.2 mm (Right eye 24.439 ± 1.23 mm and left eye axial length was 24.36 ± 1.23 mm).

The univariate analysis showed that patients with retinopathy were mainly males, with lower educational level, shorter axial length, increased BMI, higher fasting blood glucose and HbA1c levels, longer duration of diabetes, and higher systolic and diastolic blood pressure. (Table I)

TABLE 1:
Demographic and clinical characteristics of the study population

Table 1: Demographic and clinical characteristics of the study population			
Character	DR* (Positive)	DR (Negative)	P-value
Male sex, No. (%)	63 (55.8)	57 (52.8)	< 0.001
Age (years), Mean $\pm$ SD	63.3 $\pm$ 9.6	54.4 $\pm$ 11.3	< 0.001
Education > 12 years, No. (%)	36 (31.9)	50 (46.3)	< 0.001
Urban residency, No. (%)	61 (53.9)	55 (50.9)	0.636
Current smoker, No. (%)	27 (23.9)	21 (19.4)	0.100
Myopia Positive, No. (%)	41 (36.3)	72 (66.7)	< 0.001
Axial length (mm), Mean $\pm$ SD	23.7 $\pm$ 1.0	25.1 $\pm$ 1.1	< 0.001
BMI [†] (Kg/m ²), Mean $\pm$ SD	29.5 $\pm$ 5.2	28.2 $\pm$ 2.7	0.017
FBG [‡] (mmol/L), Mean $\pm$ SD	8.3 $\pm$ 1.7	7.2 $\pm$ 2.1	< 0.001
HbA1c [§] (%), Mean $\pm$ SD	8.5 $\pm$ 1.7	6.9 $\pm$ 1.4	< 0.001
Duration of DM , Mean $\pm$ SD	12.8 $\pm$ 4.5	9.2 $\pm$ 3.7	< 0.001
SBP (mm Hg), Mean $\pm$ SD	145.8 $\pm$ 17.9	134.3 $\pm$ 11.7	< 0.001
DBP ^{**} (mm Hg), Mean $\pm$ SD	94.1 $\pm$ 12.4	85.4 $\pm$ 8.9	< 0.001
Serum cholesterol (mg/100 ml)	238.4 $\pm$ 39.6	212.3 $\pm$ 35.6	< 0.001

In binary regression analysis, the presence of myopia was inversely associated with diabetic retinopathy (OR, 0.39; 95% CI=0.17-0.91, $P=0.028$). A shorter axial length was significantly related to a higher DR prevalence (OR, 0.31; 95% CI, 0.24-0.94; $P<0.001$). After adjusting for other variables, HbA1c, serum cholesterol, and duration of diabetes were also found to be independent predictors of diabetic retinopathy. (Table 2)

TABLE 2:
Binary logistic regression analysis

Table 2: Binary logistic regression analysis				
Variable	B Coefficient	P-value	Expected B	95% CI of expected B
Myopia	-1.737	0.028	0.39	0.17 - 0.91
Axial length (mm)	-1.188	< 0.001	0.31	0.24 - 0.94
HbA1c*	0.535	< 0.001	1.71	1.35 - 2.17
Duration of DM [†]	0.220	0.007	1.25	1.13 - 1.38
Cholesterol	0.013	0.008	1.10	1.01 - 1.03

Diabetic retinopathy, † Non-proliferative diabetic retinopathy, ‡ Proliferative diabetic retinopathy

The axial length was inversely and significantly associated with grade of diabetic retinopathy. Eyes with longer axial length were less likely to have PDR (OR, 0.16; 95% CI, 0.11-0.25; $P<0.001$), severe NPDR (OR, 0.23; 95% CI, 0.16-0.33; $P<0.001$), moderate NPDR (OR, 0.36; 95% CI, 0.25-0.51; $P<0.001$), and mild NPDR (OR, 0.51; 95% CI, 0.38-0.68; $P<0.001$). (Table 3)

TABLE 3:
Association of axial length with grade of diabetic retinopathy

Table 3: Association of axial length with grade of diabetic retinopathy				
Grade of DR*	B Coefficient	P-value	Expected B	95% CI of expected B
No DR (Reference)	-	-	1	-
Mild NPDR [†]	-1.737	< 0.001	0.51	0.38 - 0.68
Moderate NPDR	-1.031	< 0.001	0.36	0.25 - 0.51
Severe NPDR	-1.461	< 0.001	0.23	0.16 - 0.33
PDR [‡]	-1.847	< 0.001	0.16	0.11 - 0.25

Diabetic retinopathy, † Non-proliferative diabetic retinopathy, ‡ Proliferative diabetic retinopathy

DISCUSSION

In this study, the prevalence rate of diabetic retinopathy was 50.3%, which is higher than previous results in Baghdad, Iraq (33.1%)¹⁶, and other Asian countries such as India (31.5%)¹⁷, and Jordan (34.1%)¹⁸. However, it is comparable to that reported in some other countries such as China (49.8%)¹⁹, Australia (49.3%)²⁰, Iran (45.1%)²¹, and Saudi Arabia (44.7%)²².

Several studies have indicated a protective, but inconsistent, relation between myopia and a lower risk of diabetic retinopathy. It is indistinct if myopia's structural or refractive elements, or both, play a major role in this protective relationship⁶.

In this study, after adjusting for other risk factors, myopia and DR were found to have a negative relationship (OR=0.39; 95% CI=0.17-0.91, P= 0.028). This association has been found in previous studies of other ethnicities^{10,23,24}. In contrast, Ganesan et al²⁵ found no association between myopia and diabetic retinopathy. The inconsistent results may be due to various definitions or classifications of myopia, fundus photography technique, and diabetic retinopathy definitions, or limited sample size that reduces statistical power to detect a meaningful relationship²⁴.

Furthermore, high prevalence of DR was found to be associated with shorter axial length (OR, 0.31; 95% CI, 0.24-0.94; P<0.001). Such inverse association is in line with that of other population-based studies^{15,26}.

The basic mechanisms of axial length or myopia's protective effect against DR are still unclear¹⁹. Many studies found that as axial length increased, the intraocular concentration of vascular endothelial growth factor²⁷, a factor implicated in the pathogenesis of DR, decreased significantly^{28,29}.

Previous researches^{30,31} have shown that axial myopia causes decreased retinal capillary flow (RCF), which has led to speculation that the weakened retinal capillaries in diabetes are less likely to leak and burst as a result of the reduced flow. Man et al, on the other hand, suggested that decreased RCF might not be a significant factor in the protective relationship between axial elongation and DR²⁰.

Quigley M reported that in axial myopia, the increased length of the arterial tree induces an attenuation of the intraluminal arteriolar pressure, resulting in a lower hydrostatic pressure being presented to the capillary bed. As a result, the protective mechanism of myopia is related to the intraluminal arteriolar pressure rather than the flow despite the fact that the two are frequently related^{32,33}.

Shao et al suggested that the homotetrameric protein transthyretin, which is thought to be produced by retinal pigment epithelial cells in the eye, was observed to be abundant in the vitreous of diabetics with myopia. Transthyretin may control the transcription of key genes in the Tie2 pathway for neovascularization, lowering the risk of DR³⁴.

As in previous researches, this study showed that a higher prevalence of DR was related to higher fasting blood glucose and longer duration of diabetes^{35,36}.

In this study, there are some limitations to be considered. First, rather than a population-based survey, it is a tertiary referral hospital-based study. Second, its cross-sectional nature makes it difficult to establish the causal relationship between exposure and outcome.

CONCLUSION

After adjusting for other risk factors of diabetic retinopathy, myopia and longer axial length were found to be inversely related to the prevalence and severity of DR.

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