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The Relation between High Myopia and Diabetic Retinopathy

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Abstract

Background: The prevalence of myopia is growing worldwide, and myopia is becoming a major epidemiological problem. A higher prevalence of myopia has been observed in people with diabetes compared with people without diabetes and poorer glycaemic control considered to be a risk factor.

Aim of Study: To determine the relation between High Myopia and Diabetic Retinopathy and to detect whether high Myopes are self-protected against diabetic changes and diabetic retinopathy or not.

Patients and Methods: The study included 140 eyes from 96 diabetic patients recruited from National Institute of Diabetes and Endocrinology in the Ophthalmic Clinic. They were classified according to the refractive status into four groups: Emmetropia (0.00 to –0.50 {DS}), Low Myopia (–0.50 DS to –3.0 DS), Moderate Myopia (3.00 DS to –5.00 DS) and High Myopia (more than –5.00 DS). High myopia (70 eyes of 41 patients), moderate myopia (10 eyes of 7 patients), low myopia (39 eyes of 29 patients) and emmetropia (21 eyes of 19 patients).

Results: Total male patients represent 52.08% and females 46.92% in our study. There were statistically significant difference between groups as regard mean of refraction. Mean of refraction represented by Spherical equivalent among groups (Emmetrope, high myope, mild myope and moderate myope) was (2.08±0.495, 14.94±3.73, 3.23±0.642, 5.505±0.41) respectively. From our results the frequency of NPDR totally was 70 eyes (50%) and no DR was 70 eyes (50%). All high myopic eyes (70 eyes) showed no DR and all eyes of other groups which are totally (70 eyes) showed DR with its different grades. All high myopic eyes (70 eyes of 41 patients) had no DR in their fundus photograph while (low myopic, moderate myopic eyes and emmetropic eyes (39, 10, 21 eyes) respectively showed DR with its different grades: Low myopic eyes (39 eyes of 29 patients) showed moderate NPDR, the moderate myopic eyes (10 eyes of 7 patients) showed mild NPDR and the emmetropic eyes (21 eyes of 19 patients) showed severe NPDR. There were statistically significant difference between groups as regard severity of diabetes in which p-value <0.005. From our results as the degree of myopia increases the severity of DR decreases.

Conclusion: There is a protective role for high myopia against DR.

Key Words: *Myopia – Diabetic retinopathy.*

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Introduction

MYOPIA has been identified as a leading cause of visual impairment and blindness **[1]**. It has many classifications; one of them is by etiology. Refractive myopia is caused by the increase of the power of the eye either by increased curvature of refractive media of the eye as cornea and lens or index myopia caused by increase in the index of the refractive media as in nuclear sclerosis of the lens **[2]**.

Another classification is by degree into: Low from –0.25 to –3.00 Diopters (D), medium from 3.00 to –6.00 D and high more than –6.00 D **[3]**.

In high myopia, near vision is also affected as objects must be extremely close to the eyes to see clearly **[4]**.

Myopic eyes with a spherical equivalent more myopic than –6.00 (D) or an axial length longer than 26mm are defined as high myopia **[2]**.

High myopia associated with posterior staphyloma and degenerative changes (eg, progressive chorioretinal atrophy) is characterized as Pathologic Myopia (PM) or degenerative myopia. PM is associated with pathologic features (eg, tessellated fundus, diffuse or patchy chorioretinal atrophy, macular atrophy, lacquer crack, Fuchs spot, choroidal neovascularization, posterior staphyloma **[4]**.

There is an increasing evidence that myopia has a protective association with Diabetic Retinopathy (DR). Researchers have hypothesized that this is due to axial elongation of the myopic eye, leading to decreased blood flow and reduced metabolic demands, thus decreasing the impact of diabetes induced microvasculature changes. How-

ever, it is still unclear whether the protective association of myopia with DR reported in earlier studies is related to the axial dimensions of the eye or to other refractive components of myopia, such as Corneal Curvature (CC), some studies has investigated the impact of myopia and ocular biometric parameters on Diabetic Macular Edema (DME), which can occur at any stage of DR [5].

Diabetes is one of the serious diseases worldwide. It occurs when excess sugar builds up in the blood either because not enough amount of insulin is produced by the pancreas or the body does not use the insulin it produces correctly [6].

According to the International Diabetes Federation, an estimated 415 million adults ended up developing diabetes in 2015, in which more than one third would develop DR [7].

DR is one of the most common diabetic complications, which has become a leading cause for vision loss, mainly because of macular edema and vitreous hemorrhage. DR is categorized into two stages, Non Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR), based on the presence of neovascularization or vitreous hemorrhage [8].

The presence of cotton wool spots in retinal images indicates advancing retinal non profusion and progressive ischemia. Progressive retinal ischemia is the signal to the development of retinal neovascularization, which is one of the most serious cases of PDR and frequently leads to the vision impairment and blindness. Moreover, CWSs are associated not only with DR but also with other diseases such as hypertensive retinopathy, embolism, ischemia, and neoplasticity, as well as connective tissue and infectious diseases. The detection of CWSs is a critical task to grade the severity of DR [9].

In the fundus image, CWSs can appear isolated or with other pathological signs such as hard exudates, microaneurysms, or hemorrhages [10].

The presence of new blood vessels is called neovascularization, it is a sign caused by the later stages of DR, and it may lead to irreversible loss of vision [10].

Aim of the study:

The aim of our study is to determine the relation between high myopia and diabetic retinopathy and to detect whether high myopes are self protected against diabetic changes and diabetic retinopathy or not.

Patients and Methods

The comparative cross sectional study was conducted on diabetic patients recruited from National Institute of Diabetes and Endocrinology in the Ophthalmic Clinic and Ain Shams University Hospital.

Data were collected during the period of January 2019 to December 2019.

Inclusion criteria:

- Diabetic patients (type I on insulin and type II on oral drugs) uncontrolled.
- Age between 40-65 years old.
- Diabetic duration 5-10 years.
- Clear view of the retina.
- Myopic and Emmotropic patients.

Exclusion criteria:

- Eyes with advanced cataract and unclear media.
- Patient with history of any vitreoretinal surgery.
- Patient with history of retinopathy due to any other cause as hypertension or vascular diseases.

For all patients complete ophthalmological examination was done; a detailed history was taken including age, duration of diabetes, type of treatment and any systemic medical or surgical history. Refraction by autorefractometer (TopconRM-8000b, Japan) without cycloplegia. Refraction was converted to Spherical equivalent calculated as the spherical value plus half of astigmatic value and further categorized refractive status into four groups: Emmetropia (0.00 to –0.50 {DS}), Low Myopia (0.50 DS to –3.0 DS), Moderate Myopia (3.00 DS to 5.00 DS) and High Myopia (more than –5.00 DS). Visual acuity was measured using Eye chart (6 Meter Illiterate E Chart). Slit lamp biomicroscopy: Was performed for determination of diseases in anterior segement of the eye and exclude cases of haze cornea or mature cataract. Fundus examination by indirect ophalmoscope and lens +90D. OCT (NIDEK.RS-3000 Advance) was done for all patients to detect the presence or absence of Diabetic Macular Oedema (DMO) in cases of Diabetic Retinopathy. Fundus photographs by (TRC.50DX; TOPCON, Japan) was done for all patients.

All patients were photographed by using optical coherence tomography (Nidek RS –3000 advance) to detect the presence or absence of (DMO) in patients having DR.

The RS-3000 Advance is a SD-OCT instrument. Its wavelengths is 880nm, and the instrument acquires 53,000 A scans per second with an axial resolution of 7 µm, a lateral resolution of 20 µm, and a scan depth of 2.1mm. The current software of the RS-3000 OCT (software version 1.4.2.1).

Fundus photography was done for all patients to detect the presence or absence of DR using.

Retinal camera (TRC. 50DX, TOPCON, made in Japan) and the patients were classified according to International Clinical Diabetic Retinopathy Disease Severity Scale into (no DR, mild NPDR, moderate NPDR, severe NPDR) then the relation between degree of myopia (depending on the refractive error) and DR was assessed.

Statistical package and data analysis: The collected data were revised, coded, tabulated and analyzed using the statistical package program for Social Science (SPSS version 25 Software for Windows). Pearson Chi-Square and Phi test were used to measure the relationship between degree of myopia and diabetic retinopathy and then followed by Kruskal-Wallis test. Kruskal-Wallis test is a non-parametric alternative for a one Way Analysis of Variance (ANOVA) was used to compare between groups of study i.e. High Myope Diabetic, Emmtrope Diabetic, Low Myope Diabetic and Moderate Myope Diabetic. Qualitative data was presented as number and percentage. Quantitative data were described using range (minimum-maximum), mean, standard deviation. Analysis of variance (ANOVA) was used to assess statistically significance of the difference between more than two study groups. Chi-square test was used to examine the relationship between two qualitative variables. *p*-value <0.05 was considered statistically significant.

Ethical considerations: The study was approved from Ethical Committee, Faculty of Medicine, Ain Shams University and informed consent was taken from patients.

Results

The comparison between studied groups regarding mean age among the study shows that there is no statistically significant difference between groups as shown in (Table 1).

Table (1): Comparison between studied groups regarding age.

Myope/Emmetrope	Age	F	*p*
High myope	54.16±8.54	1.222	0.304
Moderate myope	52.3±4.95		
Low myope	51.6667±5.054		
Emmetrope	52.2381±4.78		

Table (2): Comparison between studied groups as regards duration of diabetes.

Myope/Emmetrope	Duration of diabetes in years (mean ± SD)	N	F	*p*
High myope	8.54±2.15	70	0.183	0.908
Moderate myope	8.7±1.06	10		
Low myope	8.72±1.50	39		
Emmetrope	8.86±1.71	21		

The comparison between studied groups as regards mean duration of diabetes represented in years as seen in (Table 2) shows that there is no statistically significant difference between all groups since *p*-value >0.05.

Table (3): Number of subjects in each group.

Myope/Emmetrope diabetics				
	Frequency	Percent	Valid percent	Cumulative percent
Valid:				
High myope diabetic	70	50.0	50.0	50.0
Moderate myope diabetic	10	7.1	7.1	100.0
Low myope diabetic	39	27.9	27.9	92.9
Emmtrope diabetic	21	15.0	15.0	65.0
Total	140	100.0	100.0	

The following tables shows that high myopic patients has no DR in their fundus photograph, this indicates that high myopia has a protective effect for diabetic patients against DR.

Table (4): Chi-square tests.

Chi-square tests	Value	df	Asymptotic significance (2-sided)
Pearson chi-square	140.000a	3	<0.001
Likelihood ratio	194.081	3	<0.001
Linear-by-linear association	111.534	1	<0.001
N of valid cases	140		

The most important in this test is Pearson Chi-Square Asymptotic Significance (2-sided) result which is <0.000 and this is less than 0.05. So this indicates that there is a relation between myopia and DR as seen in (Table 4).

Table (5): Both Phi and Cramer's tests.

Symmetric measures		
	Value	Approximate significance
Nominal by nominal:		
Phi	1.000	<0.001
Cramer's V	1.000	<0.001
N of valid cases	140	

This (Table 5) shows that the value of significance of both Phi and Cramer's is less than 0.05, this also indicates that there is a relation between myopia and DR.

All the previous tests chi-square, Phi and Cramer's show that there is a relation between myopia and DR, but to know which type of myopia, Kruskal-Wallis H test is done.

Mean Rank of high myope diabetics is more than that of the other three groups,and this indicates that the high myope diabetics does not have any DR in their fundus photograph.

This indicates that high myopia has a protective role.

The relation between high myopia and the absence of DR is highly significant in which the Asymptotic Significance is <0.000 which is less than 0.05 as shown in (Table 6).

Table (6): Kruskal-Wallis H-test.

Ranks		
Myope diabetics	N	Mean Rank
High Myope diabetic	70	105.50
Emmtrope diabetic	21	35.50
Low Myope diabetic	39	35.50
Moderate Myope diabetic	10	35.50
Total	140	

Test statistics[a,b]	
	OCT
Kruskal-Wallis H	139.000
Df	3
Asymp. sig.	<0.001

a: Kruskal Wallis Test
b: Grouping Variable: Myope Diabetes.

Table (7): Frequency of DR in high myopic, moderate myopic, low myopic and emmetropic eyes of diabetic patients.

Emmetrope/ degree of myopia	DR	Eyes No. (%)	Patient No. (%)
High Myopia	No DR	70 (50.00)	41 (42.71)
Moderate Myopia	Mild DR	10 (7.14)	7 (7.29)
Low Myopia	Moderate DR	39 (27.86)	29 (30.21)
Emmetrope	Severe DR	21 (15.00)	19 (19.79)
Total		140	96

All high myopic eyes (70 eyes of 41 patients) had no DR in their fundus photograph while (low myopic, moderate myopic eyes and emmetropic eyes (39, 10, 21 eyes) respectively showed DR with its different grades in their fundus photograph: The low myopic eyes (39 eyes of 29 patients) showed moderate NPDR, the moderate myopic eyes (10 eyes of 7 patients) showed mild NPDR and the emmetropic eyes (21 eyes of 19 patients) showed severe NPDR in their fundus photograph seen in (Tables 8,9).

Table (8): Relation between groups of study.

Myope/ Emmetrope	Female	Male	Chi square	*p*-value	Odd Ratio
High Myopia	30	40	2.857	0.09	0.5625
Moderate Myopia	6	4			
Low Myopia	19	20			
Emmetrope	15	6			

Table (9): Comparison bteween studied groups as regard refraction represented by (SQ) and its relation with the presence or absence of DR which is detected by fundus photograph.

Myope/Emmetrope	SQ spherical equivalent (diopter)	F	*p*
High Myopia (no DR)	12.6±3.33	182.705	<0.001
Moderate Myopia (mild DR)	5.505±0.41		
Low Myopia (moderate DR)	3.2308±0.64		
Emmetrope (severe DR)	2.0833±0.50		

The comparison between studied groups as regard mean of refraction represented by (SQ) as seen in (Table 9) shows that there is statistically significant difference between all groups. In our results all high myopic eyes (70 eyes of 41 patients) had no DR in their fundus photograph while (low, moderate myopic eyes and emmetropic eyes (39, 10, 21 eyes) respectively showed DR with its different grades in their fundus photograph: The low myopic eyes (39 eyes of 29 patients) showed moderate DR, the moderate myopic eyes (10 eyes of 7 pstients) showed mild DR and the emmetropic eyes (21 eyes of 19 patients) showed severe DR in their fundus photograph, *p*-value is 0.000 (*p* <0.001) which indicates that there is statistically high significant differences between all groups.

This indicates that as the degree of myopia increases the severity of DR decreases which means that there is a protective relation between high myopia and DR.

Table (10): Post hoc test between groups of study.

Groups	SE
High Myope	12.600±3.33 **a**
Moderate Myope	5.5050±0.41 **b**
Low Myope	3.2308±0.64 **c**
Emmetrope	2.0833±0.50 **c**
F	182.705
p	<0.001

Followed the one-way ANOVA test by post hoc test using Duncan test to make multiple comparisons between averages of different groups. The means followed by the same letter in each column are not significantly different from each other at the 5 percent probability level (Duncan's multiple range test).

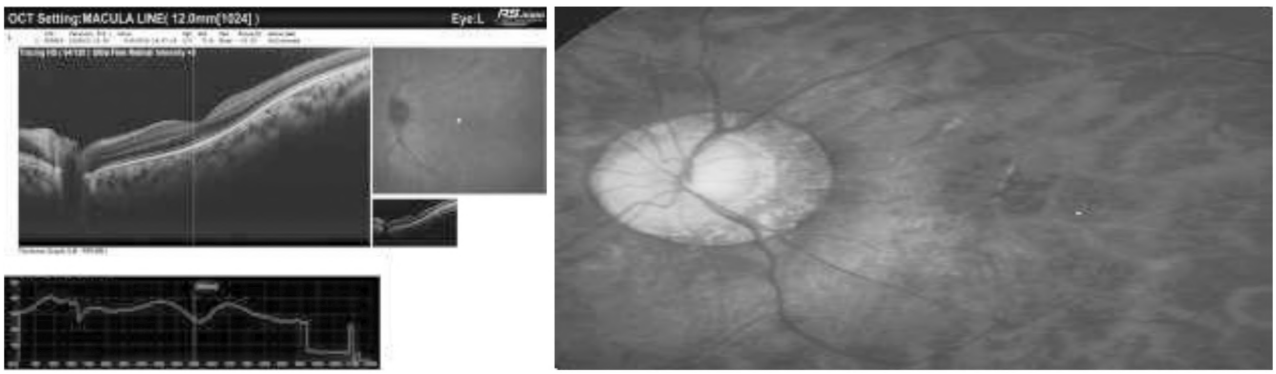

Fig. (1): OCT and fundus photograph of high myopic patient (–15)D.

Discussion

In this study we found a significant protective role for high myopia against DR in which high myopic eyes were less likely to have DR than emmetropic eyes (OR, 0.562). Although the topic of a possible connection between myopia and DR is not new in the literature, the available data are still conflicting. In 1985, Rand et al. **[11]** defined a significant protective role for myopia against PDR (odds ratio [OR], 10.03) after adjusting for potential confounding factors.

A year later, Baker et al., **[12]** also found similar connection between myopia and NPDR (OR, 6.0) when potential confounding variables such as human leukocyte antigen phenotypes, age, hyperglycemic index, and renal status were adjusted.

In one of the largest series including 2990 adults examined by the Wisconsin Epidemiological study of diabetic retinopathy **[13]** myopia decreased the risk of progression to PDR by 60% only in patients with younger-onset DM (OR, 0.40). In patients with older-onset DM and in either age group, however, such association did not reach a significant statistical level.

In another study in 2010 by the Singapore Malay Eye Study Group **[14]** in 3280 adults, myopic eyes were less likely to have DR after adjusting for potential confounding factors such as age, gender, height, education, cataract, hemoglobin A1c, and accompanying diseases (OR, 0.90).

In a study in 2013 by Pan et al., **[15]** in 3400 Indians aged 40 to 84 years, myopic eyes were also less likely to have DR (OR, 0.68) compared with emmetropic eyes. In two review articles, Fu et al. **[16]** and Wang et al. **[17]** also concluded that myopia significantly decreased the risk of DR (pooled OR,0.75 and 0.80, respectively).

In contrast to these studies and our findings, the Beijing Eye Study **[18]** and Ganesan et al. **[19]** did not report a significant association between myopia and DR. This lack of consensus among studies that examined a relationship between myopia and DR is probably because of variations in employed methodology, quality of studies, and statistical analysis; heterogeneity in the study design such as differences between cross-sectional and longitudinal studies, and using inconsistent classifications for myopia as well as whether refractive myopia (SE) or axial myopia (axial length) were measured **[20]**.

At the same time, it should be noted that examining a possible relationship between myopia and DR is a very complex task, because there are extensive potential confounders in this regard, such as age, duration of DM, human leukocyte antigen phenotypes, hyperglycemic index, renal status, and general health status that make drawing a solid conclusion difficult **[14]**. Controlling the role of all these variables is difficult and almost impossible. For example, the Singapore Malay Eye Study Group, **[14]** the Beijing Eye Study **[18]** and Pierro et al. **[21]** did not adjust for duration of DM in their studies; the Beijing Eye Study (130) and the studies by Yang et al., **[22]** and Pierro et al., **[21]** did not exclude a potential confounding effect of hemoglobin A1c; only the Wisconsin Epidemiological Study excluded patients who had undergone intraocular surgery **[23]**; and only the Singapore Malay Eye Study Group **[14]** and the Beijing Eye Study **[18]** adjusted for socioeconomic factors such as income and education, which have been found in association with myopia **[23]** and the outcome of DR **[24]**.

In this study all patients were diabetic including both type I and type II diabetes, we compared high myopic eyes with the (emmetrope, moderate myopic, low myopic) eyes to evaluate the association between the diagnosis of any diabetic retinopathy and the refractive status. Age, duration of diabetes were adjusted and all eyes included in this study

had clear view of the retina, while eyes with advanced cataract, patients with history of any vitreoretinal surgery, tractional membrane and having retinopathy due to any other cause as hypertension or vascular disease all those were excluded from the study. This study, enabled us to detect an association between high myopia and DR, there were significant differences between all groups in terms of the mean refractive error.

Because of an intimate relationship between refractive errors and ocular biometric parameters, it has been assumed that the association between myopia and DR might be explained in this way **[25]**. It is still unclear whether the refractive component (i.e., corneal curvature, spherical equivalent), the structural component (i.e., axial length), or both the refractive and structural components of myopia play a principal role in connecting myopia and DR **[26]**. For example, Man et al., **[27]** suggested axial length as the only independent variable in association with the risk and severity of DR.

In contrast, other more strictly controlled studies indicated that both refraction and axial length are along with a decreased risk of DR in myopic eyes **[17]**. NOOSHIN et al., also found that both more severe myopic refraction and longer axial length were protective against DR and in line with previous studies, **[16]** also they showed that myopic refraction and axial length were significantly associated with the severity of DR.

In our study we found that high myopic refraction was protective against DR and significantly associated with the severity of DR.

Although the exact mechanism(s) underlying the protective effect of high myopia against DR is yet to be defined but some studies shows the protective effect of axial length against DR was due to several hypotheses, one hypothesis is that with axial elongation there is narrowing of blood vessels in the retina leading to reduction in retinal blood flow according to Hagen-Poiseuille law resulting in a decrease in capillary hydrostatic pressure and consequent decreased likelihood of leakage and rupture of compromised retinal capillaries in diabetes (Starling and Laplace's law), **[28]** deformation in the posterior pole, **[20]** increased ocular volume in an elongated eye, **[29]** neurodegeneration, neuron dysfunction, **[30]** thinning of the peripheral retina **[30]** in axially elongated eyes with resultant decreased metabolic demand then could blunt the hypoxic response which is necessary for diabetic retinopathy, **[30]** a reduction in vascular endothelial growth factor concentration in the aqueous associated with increasing axial length, **[31]** an impairment of retinal adaptive circuitry in myopic eyes **[32]** that might be associated with abnormal reduction of inner retinal function **[20]** and the development of posterior vitreous detachment **[33]** that removes the vitreous scaffold for neovascular proliferation and enhances oxygen diffusion across the liquefied vitreous **[17]**.

In the present study we found no statistically significant relation between type of diabetes (I or II) and the presence or absence of DR, and similar associations between myopia and DR in both type I and type II. We also found that the incidence of DR was higher in Type I than in Type II DM. In this study we also concluded that high myopic refraction was protective against DR and significantly associated with the severity of DR.

Conclusion:

From our study there is a protective role for high myopia against DR. Although refraction was found in association with this relationship, but also not focusing on possible underlying mechanism(s) and not measuring axial length and Anterior Chamber Depth (ACD) should be acknowledged as a limitation, so further studies are recommended to show these underlying mechanisms.

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العلاقة بين قصر النظر الشديد وإعتلال الشبكية السكرى

هذه الدراسة تشمل ١٤٠ عين من ٩٦ مريض سكرى من معهد السكر والغدد الصماء. الحالات ذات المرض السكرى تشمل حالات قصر نظر شديد (٧٠ عين من ٤١ مريض) وتشمل حالات ذات قصر نظر متوسط وقصر نظر منخفض وكذلك آسوياء البصر (٧٠ عين من ٥٥ مريض).

آسوياء البصر: (٢١ عين من ١٩ مريض).

حالات قصر نظر متوسط (١٠ عين من ٧ مريض).

حالات قصر نظر منخفض (٣٩ عين من ٢٩ مريض).

تم عمل تصوير قاع العين الفوتوغرافى ملون لجميع الحالات وذلك لتحديد درجة الإعتلال الشبكى السكرى لدى الحالات. آظهرت النتائج آن المجموعات ذات قصر النظر وآسوياء البصر لا يوجد بينهم إختلاف إحصائى من حيث متوسط السن، النوع ذكر آو آنثى، النوع الآول آو النوع الثانى من المرض السكرى، الهيموجلوبين التراكمى. كما وجد آن هناك إختلاف إحصائى من حيث المكافئ الحسابى.

آظهر النتائج آن الحالات ذات قصر النظر العالى ليس لديهم إعتلال شبكى سكرى، الحالات ذات قصر النظر المتوسط لديهم إعتلال شبكى بسيط، الحالات ذات قصر النظر المنخفض لديهم إعتلال شبكى متوسط وآن الآشخاص آسوياء البصر لديهم إعتلال شبكى سكرى شديد.

بذلك يتضح من النتائج آنه كلما زادت درجة قصر النظر كلما قلت شدة الإعتلال الشبكى السكرى وآن قصر النظر الشديد له علاقة وقائية من الإصابة بالإعتلال الشبكى السكرى.