AlQalam
Alq J Med App Sci
https://journal.utripoli.edu.ly/index.php/Alqalam/index eISSN 2707-7179

Original article

Association Between Primary Open Angle Glaucoma and Type II Diabetes Mellitus in Benghazi, Libya

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ARTICLE INFO

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Received*: 16-5-2024*
Accepted*: 25-5-2024*
Published*: 28-05-2024*

Keywords*. Open Angle Glaucoma, Diabetes Mellitus, Visual Acuity, Intraocular Pressure.*

ABSTRACT

Glaucoma, a leading cause of permanent blindness in the world, primarily affects older adults and is classified into four types, with diabetes mellitus potentially influencing the condition. The study aims to identify the link between Diabetes mellitus type two and Primary open angle Glaucoma. Subject and method A case-control study at Benghazi Educational Eye Hospital from December 2023 to February 2024. examined diabetic patients with and without glaucoma. Participants underwent ophthalmic examinations, including visual acuity, and gonioscopy. Patients with history of type two diabetes were included. The mean age of cases was significantly higher than controls [P=0.001]. There were significant differences in best corrected visual acuity between the two groups [P=0.035], Participants with high a [HbA1c] were more likely to have an advanced primary open angle glaucoma type. Participants with uncontrolled diabetes mellitus had higher intraocular pressure levels compared to the control group, [p=0.013]. There was a statistically significant difference in Retinal nerve fibers layers thickness in right eye, and Retinal nerve fibers layer thickness in left eye, between the case and control groups, [P= 0.041, 0.005 respectively. The age 66-75 years had a significantly higher risk of primary open angle glaucoma. A negative correlation between the duration of diabetes and Pattern standard deviation in left eye [P = 0.051], as well as Visual Field left [P = 0.002]. The study reveals a significant link between diabetes mellitus type two and primary open angle glaucoma, with factors like higher intraocular pressure and older age causing higher incidence. early detection and management of risk factors could prevent or delay glaucoma onset.

Cite this article. *Emgory T, Anwar G. Association Between Primary Open Angle Glaucoma and Type II Diabetes Mellitus in Benghazi, Libya. Alq J Med App Sci. 2024;7(2):369-376. https://doi.org/10.54361/ajmas.2472024*

INTRODUCTION

Glaucoma, a global cause of permanent blindness, primarily affects older adults and is divided into four types: primary open-angle glaucoma, acute angle-closure glaucoma, secondary glaucoma, and normal or low-tension type glaucoma [1-3]. Primary open angle glaucoma [POAG] is a persistent, and irreversible optic neuropathy that is distinguished by the presence of an open angle in the anterior chamber, alterations in the optic nerve head, loss of peripheral visual field and later on loss of the central visual field [VF] [3].

POAG affects 70 million people, with 74% in the US. Bilateral blindness affects 5.9 million in 2020. Prevalence is highest in African American and Latin American populations. Women are disproportionately affected. Longitudinal factors contribute to glaucoma epidemiology. Longitudinal factors, including women and developed countries, contribute to glaucoma epidemiology[4,5].

POAG is influenced by factors like age, race, family history, IOP, myopia, Type 2 diabetes, and population rate. African-American, Afro-Caribbean, and West African patients have a four-fold increased risk [6–8]. Diabetes mellitus type two (T2DM) is a global health issue causing severe complications and impacting quality of life. It is also a potential risk factor for POAG, but the relationship between DM and POAG remains controversial. A 2004 meta-analysis showed a positive correlation between DM and POAG susceptibility. [9–11].

A previous meta-analysis conducted in 2004 demonstrated a positive correlation between DM and heightened susceptibility to developing POAG [12]. Nevertheless, the epidemiological investigations examining the association between T2DM and POAG have yielded inconsistent and equivocal findings. Notably, two research have found incongruous outcomes [13,14]. Hence, through this analysis aimed to provide clarity and insight into the association between T2DM and POAG, ultimately improving our understanding of these complex diseases.

METHODS

Study design and setting.

A case-control was conducted in Benghazi Educational Eye Hospital outpatient glaucoma clinic. In the period from December 2023 to February 2024.

Inclusion and exclusion criteria

The study included two groups diabetic patients type two with glaucoma and diabetic patients type two without glaucoma. All patients 45-75 years old, patients who had type two diabetes mellitus [T2DM] for more than 5 years, the patients who had a primary open angle glaucoma [POAG] included in the study. Patients younger than 45 and older than 75, Patients who have type one diabetes mellitus [T1DM], and patients with secondary open angle glaucoma [SOAG].

Data collection and ophthalmic examination

An interviewer-administered questionnaire was used to assess ocular and medical histories, diabetes duration and laboratory testing was performed to obtain HBA1C. Participants underwent a comprehensive ophthalmic examination, including visual acuity, slit-lamp examination, intraocular pressure measurements, maximal dilation, posterior segment examination, and fundus photography. Gonioscopy was performed for both eyes to exclude closed or narrow angle glaucoma. Ocular coherence tomography (OCT) was used to assess vertical and horizontal cup-to-disc ratios, and peripapillary nerve fiber layer. The Humphrey Automated Field Analyzer was used for visual field testing twice in each eye. If the results were normal, no further testing was conducted. However, if the initial results were unreliable or abnormal, a repeat test was conducted. The criteria for diagnosing glaucoma in the LALES include a wide anterior chamber angle, evidence of glaucomatous optic disc damage on stereo fundus photography in at least one eye, and a characteristic or compatible glaucomatous visual field abnormality [15].

Ethical approval

The study was approved by the Institutional Review Board at our institution. All participants provided informed consent before participating in the study.

Statistical analysis

The study used SPSS software for statistical analysis, including descriptive and logistic regression analyses to assess the association between risk factors and POAG. A multivariate Poisson regression analysis was conducted to compare OAG incidence rates in the at-risk population. Tests were conducted at a $\leqslant 0.05$ significance level.

RESULTS

Results the mean age of the participants was 65 years. The mean age of participants with glaucoma was significantly higher than those without the condition [mean age for case = 63.85+7., for control = 57.92+5.6., P=0.001], participants with cases were more likely to have lower visual acuity in their right eye [0.885+1.07] compared controls. there were significant differences in BCVA between the two groups [P=0.035], The duration of diabetes mellitus did not significantly differ between the cases and controls, participants with higher HbA1c levels were more likely to have a

longer duration of glaucoma. participants with diabetes mellitus had higher [IOP] levels compared to the control group, with a statistically significant difference [p=0.013]. There was a significant difference in BCVAL and CDRVR values between the case and control groups (P<0.005). There was a statistically significant difference in RNFLTR and RNFLTL between the case and control groups, with p-values of 0.041 and 0.005 respectively [Table 1].

Table 1. Basic characteristics of the study participants

Character	Case	Control	P value
Male	15[55.6%]	8[29.6%]	0.049*
Female	12[44.4%]	19[70.4%]	
Mean age	63.85±7	57.92±5.6	0.001*
45-55	3[11.1%]	11[40.7%]	0.004*
56-65	13[48.1%]	14[51.9%]	
66-75	11[40.7%]	2[7.4%]	
Mean Visual acuity right	0.885±1.07	0.711±0.67	0.480
Mean BCVA right	0.688± 0.987	0.622± 0.484	0.754
Mild **Moderate** **Severe** **Blindness**	18[66.7%] 4[14.8%] 1[3.7%] 4[14.8%]	16[59.3%] 4[14.8%] 7[25.9%] 0	0.035*
Mean Visual acuity left	0.829±0.909	0.615±0.553	0.304
Mean BCVA Left	0.488± 0.487	0.581±0.348	0.425
Mild **Moderate** **Severe** **Blindness**	17[63.0%] 4[14.8%] 5[18.5%] 1[3.7%]	14[53.8%] 8[30.8%] 4[15.4%] 0	0.437
Duration of DM	11.4±6.4	13±6.2	0.372
HBA1C	8.14± 1.16	26.07±31.95	0.005*
IOPR	16.92±3.8	14.59±2.6	0.013*
IOPL	17.51±5.09	14.81±2.8	0.019*
BCVA Rt	0.688±0.98736	0.622±0.484	0.243
BCVA Lt	0.488± 0.487	0.581± 0.348	0.425
CDRVR	10.11± 20.23	4.11± 1.31	0.130
CDRVL	5.72±2.3	4.13±1.3	0.004*
RNFLTR	81.74±26.31	93.77±13.38	0.041*
RNFLTL	80.85±24.8	97.29±13.8	0.005*

The study also revealed that older age groups, had a significantly higher risk of primary. Additionally, there was no significant association between the duration of diabetes mellitus and the risk of glaucoma. Similarly, HBA1C levels did not show a significant correlation with glaucoma risk (Table 2).

Table 2. Crude and adjusted adds of the primary open-angle glaucoma

Factor	Unadjusted OR [95% CI]	P value	Adjusted OR [95% CI]	P value
Model 1				
56-65	3.41 [0.77-15]	0.105	2.701 [0.561-13]	0.215
66-75	20.16 [2.8-145.3]	0.003	12.28 [1.591-94.8]	0.016*
Duration of DM	0.961 [0.88-1.05]	0.366	0.984 [0.892-1.087]	0.757
HBA1C	0.93 [0.83-1.04]	0.202	0.939 [0.842-1.047]	0.255
Model 2				
Mean Age	1.159 [1.05-1.28]	0.004*	1.130 [1.0-1.27]	0.051*
Duration of DM	0.961 [0.88-1.05]	0.366	0.873 [0.734-1.03]	0.126
HBA1C	0.93 [0.83-1.04]	0.202	0.950 [0.846-1.06]	0.390
IOPR	1.25 [1.03-1.51]	0.021*	1.373 [0.948-1.98]	0.094
IOPL	1.25 [1.03-1.52]	0.024*	1.074 [0.779-1.48]	0.665
CDRVL	1.619 [1.12-2.33]	0.010*	1.703 [1.051-2.75]	0.031*
RNFLTR	0.972 [0.95-1]	0.046*	1.017 [0.947-1.09]	0.642
RNFLTL	0.96 [0.93-0.99]	0.009*	0.948 [0.879-1.02]	0.171

The results of the study showed that there were significant associations between certain factors and primary open angle glaucoma 2.701 [0.561-13] there was no significant difference. Specifically, in model2 for unadjusted odds., age, intraocular pressure in the right eye, cup-to-disc ratio in the left eye, and retinal nerve fiber layer thickness in the right eye were all found to have a significant impact on the development of the condition P value = [0.004, 0.021, 0.024, 0.010, 0.046, 0.009] respectively. However, after adjusting for other variables such as duration of diabetes mellitus and glycated hemoglobin levels, some of these associations became less significant. For example, the association between age and glaucoma remained significant even after adjustment [P < 0.05] (Table 2 & figure 1).

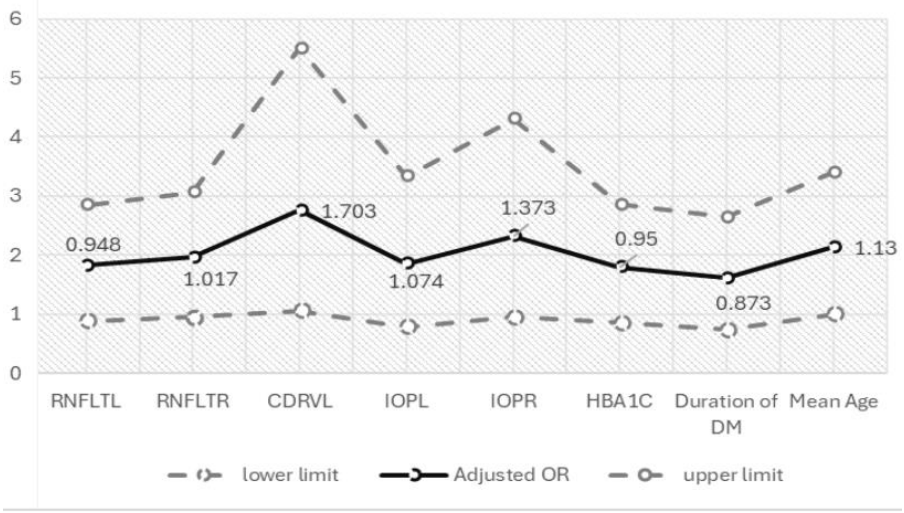

Figure 1. Relationship between various factors and the primary open-angle glaucoma, risk-adjusted for age, duration of diabetes mellitus, HBA1C, intra-ocular pressure, CDRVL, and retinal fiber thickness.
The y-axis denotes the rate of the risk in percentage. The dotted lines correspond to the 95% confidence interval.

Male sex [IRR 1.048, CI 0.751–1.463] and older age [10-year increment] were associated with a higher incidence of OAG [IRR 1.364, CI 0.843–2.205]. longer duration of diabetes associated with a longer duration of OAG [IRR 1.023, CI 0.999–1.047] (Table 3).

Table 3. Incidence rate ratios of open-angle glaucoma duration

Factors	IRR	95% CI	P value
Male	1.048	[0.751-1.463]	0.782
Age 55-65 years	1.110	[0.807-1.527]	0.206
66-75 years	1.364	[0.843-2.205]	0.521
Diabetes duration	1.023	[0.999-1.047]	0.062

The results of the bivariate analysis revealed a statistically significant association between glaucoma [POAG] and [RNFLT]. On the right side, the mean difference in RNFLT between POAG patients and controls was -12.037, with a t-value of -2.118 and a p-value of 0.041. Similarly, on the left side, the mean difference was -16.44, with a t-value of -3.002 and a p-value of 0.005. These suggest a significant relationship between POAG and changes in RNFLT (Table 4).

Table 4. Association between primary open-angle glaucoma and retinal fiber layer thickness

RNFLT	POAG patient	Control	Mean deference	T	P
Right side	-81.74±26.3-	-93.77±13.3-	-12.037-	-2.118-	0.041*
Left side	-80.85±24.8-	-97.29±13.8-	-16.44-	-3.002-	0.005

In table 5, the study found a negative correlation between diabetes duration and visual field defects in both eyes, with a statistically significant correlation for left eye (PSDL)(P=0.051) The correlation was stronger in left eye, as indicated by a higher negative Spearman Rho value for MD Lt (P=0.002).

Table 5. correlation of diabetes duration and Visual Field right

Duration of diabetes	Spearman Rho	P- value
PSDR	-0.288-	0.145
PSDL	-0.379-	0.051*
MD Rt	-0.243-	0.222
MD Lt	-0.563-	0.002*

In table 6, there appears to be a significant negative correlation between the duration of diabetes and PSDL [Spearman Rho = -0.379, P = 0.051*], as well as Visual Field left [Spearman Rho = -0.563, P = 0.002*]. These findings suggest that as the duration of diabetes increases, there is a corresponding decrease in both PSDL and Visual Field left. However, no significant correlations.

Table 6. correlation of glaucoma duration and Visual Field

Duration of glaucoma	Spearman Rho	P- value
PSDR	-0.471-	0.013*
PSDL	-0.430-	0.025*
MD Rt	-0.431-	0.025*
MD Lt	-0.433-	0.024*

DISCUSSION

Diabetes may exacerbate primary open-angle glaucoma in patients, causing higher intraocular pressure. Understanding this relationship could aid in developing better treatment strategies and provide insights into the mechanisms underlying glaucoma development in diabetic patients, affecting the optic nerve and blood vessels [16].

A meta-analysis of 13 studies revealed that individuals with diabetes have a 1.4-fold increased risk of developing POAG compared to non-diabetic individuals. In case-control studies, the odds were 49% higher for DM. The association was significant across all subgroups [11]. Several hypotheses suggest biological links between diabetes mellitus (DM) and polycystic adipose gynecomastia (POAG), including long-standing hyperglycemia, lipid anomalies, reduced blood flow regulation, and optic nerve head tissue remodeling [17–22]. Along these lines, we found that there is a correlation between OAG duration and diabetes duration [IRR 1.023, CI 0.999-1.047].

The study found significant differences in age, visual acuity, intraocular pressure, and retinal nerve fiber layer thickness between participants with and without glaucoma, with older participants being more likely to have glaucoma. [RR 1.364, CI 0.843-2.205]. The study indicates a potentially intricate link between glaucoma, diabetes, age, and one-sex individuals [IRR 1.048, CI 0.751-1.463].

The study found that glaucoma significantly increases with aging in a 40-64-year-old Iranian population, with a prevalence of 3.52% among diabetics and 1.71% in non-diabetic individuals, and highest prevalence among adults aged 65-80.[23], with POAG prevalence three to four times higher among these groups. High intraocular pressure, thin central cornea, and corneal hysteresis are also risk factors. The prevalence increases with age, rising to 9.4% for whites 75 or older, while 23.2% for Blacks in the same age group [24].

The study found significant differences in visual acuity and retinal nerve fiber thickness between glaucoma and control groups. A strong positive association was found between the duration of glaucoma and the thickness of the retinal nerve fiber layer (RTFLT). Primary open-angle glaucoma (POAG) was also linked to changes in RNFLT, suggesting that changes in RNFLT may serve as a predictive biomarker for early detection and monitoring. Diabetes duration also had a significant negative correlation with the left eye's Pattern of Standard Deviation (PSD) and Visual Field (VFL), suggesting a decline in these visual parameters as diabetes persists over time. No significant correlations were found between diabetes duration and PSDR or Visual Field right.

Diabetes mellitus duration doesn't significantly differ between cases and controls. High HbA1c levels lead to longer glaucoma duration and higher intraocular pressure. Visual acuity in glaucomatous eyes is correlated with VF and OCT parameters, with moderate and severe stages showing significant decrease [30]. Previous reports suggest that some glaucoma patients may experience a decrease in VF sensitivity or ganglion cell-inner plexiform layer thickness [25,26]. The rate of RNFL thickness changes is linked to baseline RNFL thickness, with a higher baseline measurement indicating faster progression in early glaucoma. OCT RNFL measurement is superior for early glaucoma detection due to standard deviation differences. The RNFLD angle can assess VF progression independently of subjective methods,

with 85.7% of eyes showing a widening RNFL progression pattern. Average RNFL thickness is a reliable diagnostic tool for glaucoma. [27–31].

Increased retinal vascular permeability in diabetic patients may lead to leakage of serum proteins and lipids in the intraretinal space, resulting in higher values of retinal parameters [32]. Studies have shown that mean RNFL and superior and inferior ganglion cell layer [GCL] are thicker in diabetic patients and thinner in diabetic patients with retinopathy [32]. Garcia-Martin et al [33], reported less GCL thickness in diabetic patients compared to healthy controls, but the RNFL was thinner only in the outer inferior quadrant. Serum Hb1Ac levels have a significant negative correlation with RNFL thickness [34], but not with other parameters like average macular GCL and average macular thickness. Some authors suggest that thinning of the inner retina may be seen in patients with diabetes even before changes suggestive of diabetic retinopathy. However, this study found no significant association between diabetes, RNFL, or diabetic and ocular parameters. No significant differences were found between controls and diabetic patients, or between patients with glaucoma with or without diabetes [34,35].

A study found significant relationships between age, intraocular pressure, cup-to-disc ratio, and retinal nerve fiber layer thickness with primary open-angle glaucoma. However, these relationships lost significance after controlling for confounders like diabetes mellitus and glycated hemoglobin levels. Age is a strong predictor of glaucoma development, but other factors like diabetes mellitus duration and glycated hemoglobin levels may also play a role. The cup-to-disc ratio in the left eye may be influenced by these variables, highlighting the complex nature of the disease.

Spaide's research [36] examined the neurovascular characteristics of the retina in three groups: healthy controls, people with diabetes, and those with glaucoma. Results showed that glaucoma patients had thicker RNFLs and larger GCLs than healthy controls. The thickness of RNFL decreased linearly with the severity of visual field abnormalities in glaucoma patients. However, the study found no significant differences in retinal metrics between healthy controls, glaucoma patients, and those with both glaucoma and diabetes [37–39]

The study found a positive correlation between glaucoma duration and cup-to-disc ratio [CDR], indicating an increase in CDR as the disease progresses. The study emphasizes the importance of early detection and management of glaucoma to prevent irreversible damage to the optic nerve and preserve visual function. The size of the optic disc significantly influences the relationship between RGCs and CDRs [40,41].

This study was limited to a very short period resulting in a small sample size, which exposes the study to a type II error. This may have affected the statistical power of the results. Additionally, Future research could benefit from a larger and more diverse sample size, as well as considering additional variables that may impact the findings.

CONCLUSION

The study found a significant link between diabetes and glaucoma, with factors like higher intraocular pressure and older age causing higher open-angle glaucoma incidence. Sex did not significantly affect OAG incidence, but higher HbA1c levels were linked to longer glaucoma duration. The study also found a negative correlation between diabetes duration and visual parameters, suggesting a decline in visual function as glaucoma progresses.

Recommendation

The study emphasizes the importance of diabetic patients monitoring their glaucoma development and the impact of glycemic control on the disease's progression. Indicators like BCVAL, CDRVR, RNFLTR, and RNFLTL could be useful for diagnosing and monitoring glaucoma progression. Early detection and management could potentially prevent or delay glaucoma onset in diabetic patients.

Acknowledgments

We thank Sara Momamed. A. M. Bogazia, assistant lecturer (Department of Oral Biology, Ajdabiya University, Ajdabiya, Libya), for providing the data analysis and for the valuable English language editing of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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العلاقة بين الجلوكوما ذات الزاوية المفتوحة الأولية ومرض السكري من النوع الثاني في بنغازي، ليبيا

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المستخلص

الجلوكوما، وهو السبب الرئيسي للعمى الدائم في العالم، يؤثر في المقام الأول على كبار السن ويتم تصنيفه إلى أربعة أنواع، مع احتمال تأثير داء السكري على الحالة. تهدف الدراسة إلى الكشف عن العلاقة بين مرض السكري من النوع الثاني [T2DM] والمياه الزرقاء ذات الزاوية المفتوحة [POAG]. من خلال فهم العلاقة بين مرض السكري و المياه الزرقاء، يمكن لمقدمي الرعاية الصحية تصميم خطط علاجية أفضل للمرضى الذين يعانون من كلتا الحالتين، مما قد يقلل من خطر فقدان البصر الدائم. هذه الدراسة لديها القدرة على تقديم نظرة ثاقبة لإدارة والوقاية من والمياه الزرقاء لدى الأفراد المصابين بالسكري. أجريت الدراسة في مستشفى بنغازي التعليمي للعيون في الفترة من ديسمبر 2023 إلى فبراير 2024. وشملت الدراسة مرضى المياه الزرقاء وأولئك الذين لا يعانون من المياه الزرقاء. خضع المشاركون لفحص كامل للعين، بما في ذلك حدة البصر تنظير الزوايا. وشملت معايير التشخيص التاريخ المبلغ عنه ذاتيا لمرض السكري، ومستوى الهيموجلوبين السكرى ، والجلوكوز في الدم العشوائي. كان متوسط العمر 65 عامًا، وكان متوسط عمر الحالات أعلى بكثير من الضوابط [الحالة = 63.85+7.، التحكم = 57.92+5.6.، P=0.001]. كانت هناك اختلافات كبيرة في أفضل حدة البصر المصححة بين المجموعتين [P = 0.035]، ولم تختلف مدة داء السكري بشكل كبير بين الحالات والضوابط، وكان المشاركون الذين لديهم مستويات أعلى من HbA1c أكثر عرضة للإصابة ب و المياه الزرقاء لمدة أطول. . كان لدى المشاركين المصابين بداء السكري مستويات أعلى من ضغط العين [IOP] مقارنة بالمجموعة الضابطة [ع = 0.013]. كان هناك اختلاف كبير في قيم BCVAL وCDRVR بين مجموعات الحالة الضوابط [P <0.05]. كان هناك فرق ذو دلالة إحصائية في RNFLTR وRNFLTL بين مجموعات الحالة الضوابط، [P = 0.041، 0.005 على التوالي. وكان عمر 66-75 سنة، أكثر عرضة لخطر الإصابة با المياه الزرقاء ذات الزاوية المفتوحة الأولية. وكان هناك ارتباط سلبي بين مدة العلاج مرض السكري وPSDL [P = 0.051]، وكذلك المجال البصري الأيسر [P = 0.002]. تكشف الدراسة عن وجود صلة كبيرة بين مرض السكري و المياه الزرقاء ، حيث تسبب عوامل مثل ارتفاع الضغط والتقدم في السن ارتفاع معدل الإصابة. ويشير إلى أن الاكتشاف المبكر وإدارة عوامل الخطر يمكن أن يمنع أو يؤخر ظهور والمياه الزرقاء.

الكلمات الدالة. الجلوكوما، مرض السكري، المياه الزرقاء، بنغازي.