·Investigation·

Epidemiology of primary open angle glaucoma in a rural population in Shaanxi Province of China

Zhi-Lan Bai [1,2], Bai-Chao Ren [2], Yuan He [2,3], Jian-Gang Yang [2], Li Chen [2,4], Nai-Xue Sun [2]

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[1]Department of Image, the Second Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China

[2] The Group of Ophthalmologic Epidemiological Study, the Second Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China

[3]Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510060, Guangdong Province, China

[4]Department of Ophthalmology, the Fourth Hospital of Xi'an City, Xi'an 710004, Shaanxi Province, China

Correspondence to: Zhi-Lan Bai. Department of Image, the Second Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China. rbc369@yahoo.com.cn

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Abstract

• AIM: To assess the prevalence and related risk factors of primary open angle glaucoma (POAG) in a rural population in Shaanxi Province.

• METHODS: By using a stratified, cluster-based, random sampling technique, 8 500 persons of all ages were selected randomly, from the North, the South and the Middle of Shaanxi Province from July to December in 2006. All participants had an interview with a standard questionnaire and those questions related to glaucoma of previous diagnosis and treatment, family history and outbreak history. Then a detailed and relative eye examination was performed, including logarithm of the minimum angle of resolution visual acuity, external eye examination with slit-lamp biomicroscopy and fundus examination. The intraocular pressure (IOP) was measured with Perkins applanation tonometry to those persons aged 50 years old or more and those with suspected increased IOP. A further examination was performed to those persons with suspicious glaucoma, including repeated tonometric examination, gonioscopy, dark room test, automated visual field testing, *et al*.

• RESULTS: A total of 6 815 among the eligible 8 500 persons of all ages were interviewed and examined from July to December in 2006, a response rate of 80.18%. Nine participants were found to have POAG, with the prevalence of 0.13%, age ranging from 38 to 80 years (mean year: 62.0). In those aged 30 years old or more, the prevalence of the disease was 0.23%, 0.28% and 0.39% for those more than 40 and 50 years old, respectively. The rate of suspicious POAG was 0.18% (12 cases) with age ranging from 35 to 77 years (mean year: 54.7). With multiple logistic analyses, the prevalence increased significantly with age (P=0.023).Other than increasing age, myopia was also a strong risk factor for POAG. Of 9 participants with POAG, only 2 cases (22.22%) had been previously diagnosed. No one with POAG was received any treatment previously. 66.67%(6 cases) participants with POAG suffered from visual impairment in various degrees secondary to POAG. The percentage of blindness in either eye was 33.33%.

• CONCLUSION: The prevalence of POAG is close to that from other Chinese populations, increasing with age. A majority of glaucoma was undiagnosed and untreated previously.

• KEYWORDS: primary open angle glaucoma; prevalence; related risk factors

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INTRODUCTION

Glaucoma is the second leading cause of blindness around the world [1]. It is estimated that there will be 66.8 million people with glaucoma and that 6.7 million of these people will have blindness as the result of glaucoma[2]. Because of the slow progression of glaucoma, almost 50% of people with glaucoma are unaware that they have the disease[3-8]. Moreover, the progression of primary open angle glaucoma (POAG) is much slow without any symptom until a significant visual loss. Therefore, POAG patients suffer visual impairment more easily. POAG is more common in the white and the black than in Asian population, and 4.2%-8.8% [4,11,12] reported in previously published studies for African population, whereas 1.1%-3% for white population [3-10].

Recently, data on the epidemiology of POAG depended on population-based study is relatively limited in China. With the aging of Chinese population, the prevalence of agerelated eye disease, including POAG, also increased. To effectively prevent and control the morbidity resulting from POAG, one of the important things is to know the prevalence, distribution, features and relative risk factors of POAG. From July to December 2006, we launched such a population-based survey in rural population of Shaanxi Province, China, to assess the prevalence, features and risk factors of eye diseases, the causes of blindness and visual impairment, the problems on eye care services perceived by the local people. This paper mainly reported the prevalence and risk factors of POAG in rural population of Shaanxi Province, China.

MATERIALS AND METHODS

Shaanxi Province is located in the western China, with the north region Loess Plateau, the south region Qinba Mountainous area and Middle region Wei River Plain, constituting the special landform of this province. The area of Shaanxi Province is approximately 206 000 km^2, and the total population is 34.82 million.

Population Sampling According to the special geographical location, three counties were selected randomly from the North, South and Middle of Shaanxi Province. The population of these three counties are totally 1.466 million and a majority of them belongs to Han nationality, mainly living on farming. In order to obtain a representative sample from the rural population, we used a stratified, cluster-based, random sampling technique to divide all nature villages in these three countries into basic sampling units. The whole village would be regarded as a basic sampling unit if its population was close to 1 000; The whole village would be merged with other villages or divided into parts to make the population close to 1 000 to be a basic sampling unit according to the production groups' in the village if its population was significantly less or more than 1 000. According to the method mentioned above, 10 basic sampling units were randomly and systematically selected out, corresponding to 8 500 people of all ages as the total sample, of which 3 500 were 40 years of age or older. Participants were interviewed and examined based on documentary evidence. If the residents had left out for more than half past year, they would not be regarded as participants, whereas those who did not belong to the local population would be regarded as participants if they had lived in the place for more than half past year. The composition of the sample together with the participants rates according to age, gender and education level achieved was in accordance with the proportion of local population. Therefore, the sample of this rural population was representative.

Organization of the Survey The investigation was performed from July to December 2006 by a special equipped staff, mainly including five ophthalmologists and five ophthalmic assistants. All members of the team were trained 2 weeks before the formal survey in order to make agreement in the diagnosis criterions of eye diseases among the ophthalmologists. The pre-survey was also performed in anther place which did not belong to the three counties mentioned above before formal investigation, and data obtained from it did not count into the formal available data, only being regarded as reference and gist for quality control.

Ocular Examination The elementary schools at local places were set up as temporary clinic centres for interview and eye examination. All participants had a verbal consent after explanations of nature and possible consequence of the study. The participants were interviewed by local interviewers speaking dialect according to the standard questionnaires, including information on participants demographic characteristics, education status, profession,incoming, smoking habits, alcohol intake, family history of cardiovascular diseases, diabetes, and any therapies implemented as well as current visual symptoms, and a family history of glaucoma, outbreak history of glaucoma, previous diagnosis and treatment of glaucoma. Two blood pressure readings in the sitting position were taken. Detailed eye examinations were completed by trained research staff using a standard protocol. Distance and near visual acuity, present visual acuity (with current refraction correction if often; or else naked eye visual acuity was performed) were measured using logarithm of minimum angle of resolution (log MAR) charts by a trained ophthalmic assistant at 3.8m in ambient illumination, and with a pinhole if the visual acuity less than 20/20. Anterior chamber depth was assessed by using oblique torchor or penlight illumination. External eye examination, conjunctiva, cornea, aqueous fluid, assessment of papillary reaction, peripheral anterior chamber depth (assessing by van Herick method) and lens with slit lamp biomicroscopy were performed. By using direct ophthalmoscope, the fundus was examined to evaluate the vertical and asymmetrical cup-to-disc ratios. In addition, other abnormalities of the optic disc, including cupping or excavation, notching, thinning of the neuroretinal rim, disc haemorrhages and loss of the retinal nerve fibre layer were examined by an experienced ophthalmologist. The intraocular pressure (IOP) was measured three times after the instillation of one drop of oxybuprocaine hydrochloride

(4g/L) in each eye. The measurement was taken with Perkins (HA-2, Kowa, Japan) applanation tonometry by an experienced and trained ophthalmologist. The mean value of the three measurements was used for analysis. If the peripheral chamber was less than one fourth of corneal thickness according to van Herick method, Gonioscopy would be performed with Goldman two-mirror lens. Angle grading was modified from Shaffer system of classification. If more than 10° clock hours were clearly visible up to the spur in each eye, angles were considered open; otherwise, they were judged to be occludable. All participants underwent papillary dilatation with 1% tropicamide except those with occludable angles according to van Herick method. Lenses of those with papillary dilatation were graded at the slit lamp using the lens Opacities classification System III [13].

Screening criteria of POAG: if it fell into one of the followings, the further examination was performed; including repeated tonometric examination, gonioscopy and water drinking test.

①family history of glaucoma; ②IOP≥22mmHg or a difference IOP≥5mmHg between two eyes; ③CDR≥0.6 or a difference between two eyes CDR≥0.2 or vertical CDR> horizontal CDR.

Criteria of glaucomatous optic damage: when fell into two of the followings, it was regarded as optic damage; and if fulfilled only one of them, it was considered to be suspicious optic damage: ①vertical CDR≥0.6;②a difference between two eyes vertical CDR≥0.2; ③nothing; ④thinning of the neuroretinal rim; ⑤disk haemorrhages; ⑥loss of retinal never fibre lager.

Automated visual field were performed with the HQDS-1 visual field analyzer (HQDS-1, Beijing, China), when indicated either suspicious disc damage or higher IOP more than 22mmHg in either eye. If visual field testing was unreliable, it was repeated on another day. All-field test was performed in accordance with a standard protocol by a specially trained ophthalmologic assistant by using machine. Visual field defects were not from glaucoma if media opacification or other intraocular diseases were present and would explain the abnormal visual field. Criteria of abnormal visual field: abnormal glaucoma hemifield test or corrected pattern standard deviation P<0.05. Criteria of unreliable visual field: positive responses≥50%, negative responses≥30%, and fixation losses≥50%.

Other Factors Systemic hypertension: fulfilling one of the following: ①systolic blood pressure >160 mmHg; ②diastolic blood pressure >95mmHg; ③a self- reported history of hypertension.

Diabetes:a self-reported history of diabetes.

High myopia:representation of hyper-myopic retinopathy by direct ophthalmoscopy.

Examination at Home If participants were unable to come to the clinic on account of physical health, they would be examined at home with portable equipments, including hand-held slit lamp and Perkins applanation tonometer. The examination was similar to that at the clinic except gonioscopy and automated visual fields.

Diagnostic Criteria and Definitions Primary open angle glaucoma: an IOP of 22mmHg or more with obvious glaucomatous optic damage and/or visual field loss in the presence of an open angle by gonioscopy. If indicated typical glaucomatous optic damage and/or visual field defects with IOP of 21mmHg or less on presentation, it would be regarded as normal tension glaucoma (NTG).

Suspicious POAG: suspicion of glaucoma disc damage without obvious visual field loss.

According to the criteria of blindness and low vision constituted by World Health Organization, visual impairment was classified into:

Blindness: best corrected visual acuity >20/200 in one or two eyes. Low vision: best corrected visual acuity ≥20/200 and <60/200 in one or two eyes.

Statistical Analysis All the questionnaires and examination data recorded were re-reviewed by a senior ophthalmologist after every participant finished the eye examination. When indicated suspicious information or record, it would be checked again with original participant, even to be re-examined if necessary.

Data were double-entered forms in a customized Epi info (centres for Disease Control and Prevention, Atlanta, GA, USA) database with validation, range and consistency checks. Analysis was performed by using SPSS version 11.0 statistical software (SPSS Inc., Chicago, IL, USA). Confidence intervals of the prevalence estimates were calculated using a Poisson approximation of the binomial distillation. The association of POAG or suspicious POAG with age, gender and education were assessed first with univariate analysis, including the chi-square test for trend in binomial proportions, followed by multiple logistic regression analysis. A multiple logistic regression analysis with possible risk factors was then employed using Forward stepwise model building. Statistical significance was assessed if the associated P values were less than 0.05.

RESULTS

Study Participants Totally, 6 815 of the eligible 8 500 people of all ages were interviewed and examined from July

to December 2006 with a response rate of 81.00%. The ages of these participants ranged from 1 to 91 years (media age: 35.0 years; mean age: 34.4 years). There were 3 833 participants (56.24%) with 30 years of age or older, 2 835 participants (41.60%) with 40 years of age or older, 1 775 participants (26.05%) with 50 years of age or older, and 3 654 participants (53.62%) who were female. Eight hundred and sixty-one (12.63%) participants were illiteracy, and 5 577 (81.83%) were non-illiteracy.

POAG Prevalence The media age of participants with POAG was 64.0 (range: 38-80)years, and the mean age was 62.0 years. There were totally 9 participants to be found to have POAG in our study, and its prevalence was 0.13% (95% CI, 0.06, 0.26). In those aged 30 years old, the prevalence of POAG was 0.23% (95%CI, 0.11, 0.46), and 0.28% (95% CI, 0.13, 0.58) for 40-year-old people, and 0.39% (95%CI, 0.17, 0.85) for 50-year-old people.

The rate of suspicious POAG was 0.18%, and 12 cases with age ranging from 35 to 77 years were found in this population. Corresponding rates for those more than 30, 40 and 50 years old were 0.31%, 0.38%, 0.56%, respectively.

Table 1 shows the distribution of POAG and suspicious POAG in age, gender and education level achieved. By using multiple logistic regression analysis (Enter), we found the prevalence of POAG increased significantly only with increasing age(P=0.023), whereas no significant association was found between suspicious POAG and age (P=0.477), though it increased from 0.1% in 30-years bracket of age to 0.95% in 70-year bracket (Table 2).

Table 3 shows a multiple logistic regression analysis with possible risk factors was then employed using Forward stepwise conditional model building. Age and high myopia entered the logistic model at last; indicated increasing age and high myopia were independent risk factors of POAG. Education level achieved possibly associated with POAG (odds ratio: 7.36, 95%CI, 0.84, 64.21), though its P value was 0.035, which was more than 0.05. No associations were found with gender, smoking, drinking, hypertension, diabetic and cataract operation.

Of the 9 participants with POAG,only 2 (22.22%) were diagnosed previously, and the other 7 cases (77.78%) without previous diagnosis also had not an ocular consultation within 5 years before our study. No one with POAG received any treatment previously. Six of the 9 participants with POAG (66.67%) suffered visual impairment in various degrees secondary to POAG, of which 33.33% for blindness in one eye, none in both eyes, and the other 3 (33.33%) for low vision in one or both eyes. Seven participants (33.33%) with POAG were with blindness or low vision in one or two eyes as a result of POAG. Four of those 7 participants (57.14%) who were not diagnosed previously suffered visual impairment, of which blindness in one eye accounted for 14.29% and the remain (42.86%) for low vision in one or two eyes.

Table 1 Distribution of POAG and suspicious POAG in age, gender and education level achieved in people aged 30 or older *n* (%)

	n	POAG	Suspicious POAG	Total
Age (yr)	*[1]	*[2]	*[3]	
30~	998	1(0.10)	1(0.10)	2(0.20)
40~	1060	1(0.09)	2(0.19)	3(0.28)
50~	861	1(0.12)	3(0.35)	4(0.46)
60~	598	3(0.50)	3(0.50)	6(1.00)
≥70	316	3(0.95)	3(0.95)	6(1.90)
Gender	†[1]	†[2]	†[3]	
Male	1618	5(0.31)	8(0.49)	13(0.80)
Female	2215	4(0.18)	4(0.18)	8(0.36)
Education	‡[1]	‡[2]	‡[3]	
Illiteracy	835	1(0.12)	4(0.48)	5(0.60)
Non-Illiteracy	2998	8(0.27)	8(0.27)	16(0.53)
Total	3833	9 (0.23)	12(0.31)	21(0.55)

[1]Chi-square=10.888,P=0.028;[2]Chi-square=6.790,P=0.147;*[3]Chi-quare= 16.546,P=0.002;†[1]Chi-square=0.658, P=0.417;†[2]Chi-square= 2.951,P=0.086; †[3]Chi-square=3.357,P=0.067; ‡[1]Chi-square= 0.594, P=0.441;‡[2]Chi-square=0.962,P=0.327;‡[3]Chi-square=0.056,P=0.812

Of the 9 participants with POAG, 3 (33.33%) had an IOP less than 21mmHg in both eyes, of which only one case had larger vertical cup-to-disc ratio more than 0.6 with a difference of IOP between two eyes more than 3mmHg; the other 6 had an IOP more than 22mmHg at least in one eye, of which an IOP higher by 3mmHg or more between two eyes was presented in 3 people.

Twelve participants with suspicious POAG all presented suspicious disc damage with no visual field defects, and all of them had an IOP less than 21mmHg in both eyes.

DISCUSSION

Demographic projections reflects the fact that the Chinese population is aging and therefore conditions that are associated with older population, such as glaucoma increase in prevalence. To prevent and control visual impairment, particularly blindness secondary to glaucoma, the principal thing is to know the prevalence, distribution, features and relative risk factors for the disease. In the article we reported the prevalence and risk factors for POAG.

In the rural population that we studied, the prevalence of

Table 2 Effect of age, gender and education on prevalence of POAG and suspicious POAG with multiple logistic regression

	POAG Odds Ratio (95%CI)	*P*	Suspicious POAG Odds Ratio (95%CI)	*P*	POAG or Suspicious POAG Odds Ratio (95%CI)	*P*
Age (a)						
30~	1.00		1.00		1.00	
40~	0.97 (0.06,15.57)		1.79 (0.16,19.81)		1.396 (0.23,8.38)	
50~	1.41(0.09,22.72)		3.18(0.33,30.86)		2.408 (0.44,13.28)	
60~	7.57(0.75, 76.31)		4.11(0.41,41.61)		5.457 (1.06,28.08)	
⩾70	18.91(1.81,197.48)	0.023	7.41(0.68,80.95)	0.477	11.552 (2.14,62.36)	0.012
Gender						
Male	1.00		1.00		1.00	
Female	1.02 (0.26,4.06)	0.978	0.37(0.10,1.31)	0.122	0.57 (0.23,1.46)	0.242
Education						
Illiteracy	1.00		1.00		1.00	
Non-illiteracy	6.42 (0.71,57.95)	0.098	0.74(0.18,2.96)	0.667	1.68 (0.54,5.22)	0.368

POAG= primary open angle glaucoma; CI= confidence interval

Table 3 Multiple logistic regression (Forward stepwise) for risk factors of POAG

Age (a)	Odds ratio	(95%CI)	*P*
30~	1.00		0.035
40~	0.93	(0.06,14.85)	
50~	1.25	(0.08,20.25)	
60~	5.79	(0.51,58.40)	
⩾70	15.77	(1.53,162.08)	
High myopia			
No	1.00		0.009
Yes	9.17	(1.76,47.88)	
Education			
Illiteracy	1.00		
Non-illiteracy	7.36	(0.84,64.21)	0.071

POAG = primary open angle glaucoma; CI = confidence interval

POAG of all ages was 0.13% (95% CI, 0.06, 0.26). In those aged 30 years old, the prevalence of POAG was 0.23% (95% CI, 0.11, 0.46), and 0.28% (95% CI, 0.13, 0.58) for 40-year-old people, and 0.39% (95% CI, 0.17, 0.85) for 50-year-old people. This result was close to that reported in Chinese population of Beijing and Mongolian population[14]; less than that reported from Singaporeans [15], Japanese [16], Thailand [17], Indian [18] and African [4,11], confirmed that the prevalence of POAG was lower in Chinese population.

As other studies which reported a strong increase in the prevalence of POAG with age [4,8,10,11,18], we found the similar results in this population: with multivariate analysis for association of definite POAG with some demographic variables, significant association of definite POAG was found with age increasing (P= 0.023) and that POAG is uncommon among people younger than 50 years old. In our population-based study we found that participants aged 70 years and older were six times more likely to have definite POAG or suspected POAG than those less than 50 years of age, whereas Indians aged 70 years or older were five times more [18]. The similar phenomena have also been found in other studies, which suggests one of the strongest demography risk factors of POAG is older age (>70 years).

Other than advanced age and race which have been reported as risk factors of POAG [3-23], other possible determinations such as gender, diet habits, smoking, drinking, hypertension, diabetic and high myopia were also reported to have association with POAG probably in some studies. In several studies a higher prevalence of POAG has also been identified in males [20-23], whereas other investigations found a similar prevalence of POAG in both sexes[3, 4,18]. In our study, no significant association between POAG and gender was found. Smoking and drinking were also assumed to probably effect POAG prevalence, whereas were not identified by other studies [23-25]. Myopia was regarded as to have strong relationship with POAG. According to the Blue Mountain Eye Study in Australian[26], myopia people had a high risk of glaucoma two or three times as much as that without myopia. In a Japanese glaucoma survey [27], the strength of myopic refraction was positively associated with having glaucoma. And until recently, the association of POAG with hypertension and diabetes was also controversial. In another Blue Mountain Eye Study in Australian [28], the authors reported a positive ion between POAG and diabetes, and this association was also found in Beaver Eye Study [29], whereas was not reported in Baltimore Eye Study [30].Tielsch *et al* [31] and Dielemans *et al* [32] reported POAG associated

with hypertension, but it was not suggested in a case-control study conducted by Kaimbo [33], in which the authors reported that family history, increasing age, BMI, hyperopia, Mongo ethnic group and consumption of rice conferred a significantly greater risk of POAG. In this rural population of Shaanxi Province in western China, by using a multiple logistic regression analysis (Forward stepwise conditional model building) with possible risk factors, increasing age and high myopia strongly associated with POAG, in accordance with that reported in studies mentioned above [26, 27, 31, 32]. No association was found with gender, smoking, drinking, hypertension, diabetes and cataract operation. On account of some self-reported information such as smoking, drinking and history of diseases, there would be recall and report bias.

The prevalence of POAG may have been underestimated because visual field testing was not performed for every participant. Limited sampling size and asymptomatic participants with early presentation of POAG also contributed to the underestimated rate. From data in our study, we also found that the mean age of suspicious POAG was seven years lower than that of POAG in this population. Because the prevalence of POAG increased with age, it could be speculated that some of these suspicious POAG would present typical clinical symptom of POAG and progress to show visual field loss. Prospective data would be needed to determine how many of these show signs of POAG later.

In our investigation we also found that among those with POAG, a majority of participants (77.78%) had not been previously diagnosed and no one had received treatment, as a result of which many of them suffered visual impairment secondary to POAG. The available data shows that POAG is a major cause of visual impairment, especially for blindness, in rural population of Shaanxi Province, despite the low prevalence of the disease. This form of glaucoma with no acute attack is more insidious and often asymmetrical, therefore patients with POAG did not know they had the disease until significant loss of visual field was caused. Poor understanding or awareness of the disease, incomprehensive application of early detection method of POAG and inappropriate treatment in rural population of Shaanxi Province in China possibly contributed to high prevalence of visual impairment secondary to POAG. However, POAG-related visual impairment could be prevented if detected early or treated appropriately. Therefore, early diagnosis and treatment of POAG is crucial for the prevention of the disease development and conserving the available visual acuity of POAG patients. The commonly accepted treatment for POAG is reduction of IOP [33,38]. The role of IOP in the progression of POAG has been demonstrated in our study: the prevalence of POAG increased with elevated IOP. Our finding showed that a majority of those with POAG (66.67%) had an IOP more than 22mmHg at least in one eye with larger cup-to-disc ratios, and indicated that in this group population with POAG would reduce the risk of glaucomatous damage and visual impairment. Of the 9 participants with POAG, 3 (33.33%) had an IOP less than 21mmHg in both eyes and all of them suffered visual impairment in different degree, suggesting that other factors other than IOP may also play a significant role in glaucomatous damage. Therefore, other forms of treatment would also have to be applied [39,40]. Though treatment of reducing IOP would possibly prevent and control the progression of glaucomatous damage to those with an IOP more than 22mmHg, it would be also important to pay more attention to those suspicious POAG with an IOP less than 21mmHg, and it needed more information on the nature history and appropriate treatment to those who presented suspicion of glaucomatous disc damage.

On account of majority of POAG without any symptoms until the late stage of the disease, we speculate that a number of people with this disease would have not been diagnosed in rural population of Shaanxi Province. The following examination had better to be performed as routine ocular examination in rural population-based study in China: enhancing the rudimental knowledge related to glaucoma, encouraging rural adults, especially those older people, to undergo a comprehensive eye examination regularly, widespread using and introduction of visual field testing, regular ophthalmic intercommunication. Visual field testing is the most veracious tool to assess glaucomatous damage, and should be performed as a routine part of the ophthalmic examination in rural Shaanxi Province with might and main. Visual impairment as a result of POAG has been a significant eye health problem in rural population of Shaanxi Province of Western China, despite the lower prevalence of the disease. On account of early diagnosis and treatment that would reduce and prevent visual impairment, including blindness, the importance of early detection and NTG should not be ignored.

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