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PREVALENCE OF NORMAL-TENSION GLAUCOMA IN KAZAKHSTAN: RESULTS OF STATE SCREENING PROGRAM

Resume: To assess the prevalence of normal-tension glaucoma in Kazakhstan using the results of the State Screening program.
Materials and methods. 1 806 876 participants aged 40-70 years underwent screening examinations for the detection of glaucoma. Also, the measurement of intraocular pressure (IOP) using applanation tonometry employing a Maklakov tonometer under topical anaesthesia was carried out with the other ophthalmologic examinations: visometry, autorefractometry, computerized examination of the visual field, slit-lamp observation of the anterior and posterior eye segments and evaluation of the optic disc using direct ophthalmoscopy.
Results. The prevalence of various types of glaucoma, including primary open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG) and normal-tension glaucoma (NTG) were investigated, with the particular focus on the latter. NTG was detected in 10 711 respondents, which is 0.6% of all participants with normal or lower IOP.
Conclusion. The study of NTG prevalence was demonstrated in this paper and more than 10 thousand people were diagnosed with normal or low tension glaucoma according to the outcomes of the State Screening program.
Keywords: glaucoma, intraocular pressure, screening, tonometry, Kazakhstan

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РАСПРОСТРАНЕННОСТЬ ГЛАУКОМЫ НОРМАЛЬНОГО НАПРЯЖЕНИЯ В КАЗАХСТАНЕ: РЕЗУЛЬТАТЫ ГОСУДАРСТВЕННОЙ ПРОГРАММЫ СКРИНИНГА

Резюме: Оценить распространенность глаукомы нормального напряжения в Казахстане с использованием результатов Государственной программы скрининга.
Материалы и методы. 1 806 876 участников в возрасте 40-70 лет прошли скрининговые обследования на предмет выявления глаукомы. Кроме того, измерение внутриглазного давления (ВГД) с помощью аппланационной тонометрии с использованием тонометра Маклакова под местной анестезией проводилось вместе с другими офтальмологическими исследованиями: визометрией, авторефрактометрией, компьютерным исследованием поля зрения, наблюдением переднего и заднего сегментов глаза при щелевой лампе и оценкой диска зрительного нерва с помощью прямой офтальмоскопии.
Результаты. Была исследована распространенность различных типов глаукомы, включая первичную открытоугольную глаукому (POUG), первичную закрытоугольную глаукому (PACG) и глаукому нормального напряжения (NTG), с особым акцентом на последнем. НТГ был обнаружен у 10 711 респондентов, что составляет 0,6% от всех участников с нормальным или более низким ВГД.
Выводы. В этой статье было продемонстрировано исследование распространенности НТГ, и более чем у 10 тысяч человек была диагностирована глаукома нормального или низкого напряжения в соответствии с результатами Государственной программы скрининга.
Ключевые слова: глаукома, внутриглазное давление, скрининг, тонометрия, Казахстан

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ҚАЗАҚСТАНДА ҚАЛЫПТЫ КЕРНЕУ ГЛАУКОМАСЫНЫҢ ТАРАЛУЫ: МЕМЛЕКЕТТІК СКРИНИНГ БАҒДАРЛАМАСЫНЫҢ НӘТИЖЕЛЕРІ

Түйін: мемлекеттік скрининг бағдарламасының нәтижелерін пайдалана отырып, Қазақстанда қалыпты кернеу глаукомасының таралуын бағалау.
Материалдар мен әдістер. 40-70 жас аралығындағы 1 806 876 қатысушылар глаукоманы анықтау үшін скринингтік тексеруден өтті. Сонымен қатар, жергілікті анестезиямен Маклаков тонометрін қолдана отырып, аппланациялық тонометрия көмегімен көзішілік қысымды өлшеу басқа офтальмологиялық зерттеулермен бірге жүргізілді: визометрия, авторефрактометрия, көру өрісін компьютерлік зерттеу, саңылаулы шаммен көздің алдыңғы және артқы сегменттерін байқау және тікелей офтальмоскопия арқылы оптикалық нерв дискісін бағалау.

Нәтижелері. *Глаукоманың әртүрлі түрлерінің таралуы зерттелді, оның ішінде бастапқы ашық бұрышты глаукома (POUG), бастапқы жабық бұрышты глаукома (PACG) және қалыпты кернеулі глаукома (NTG), соңғысына ерекше назар аударылды. 10 711 респонденттен анықталды, бұл қалыпты немесе төмен деңгейде барлық қатысушылардың 0,6% құрайды.*

Қорытынды. *Бұл мақалада глаукома таралуын зерттеу көрсетілді және 10 мыңнан астам адамға мемлекеттік скринингтік бағдарламаның нәтижелеріне сәйкес қалыпты немесе төмен кернеулі глаукома диагнозы қойылғандығын көрсетеді.*

Түйінді сөздер: *глаукома, көзішілік қысым, скрининг, тонометрия, Қазақстан*

Introduction

Glaucoma is the leading cause of irreversible blindness, which affects 70 million people worldwide [1, 2]. Due to the asymptomatic nature of the disease, there is an assumption that the real prevalence of glaucoma is much greater than the reported values [3].

Normal-tension glaucoma (NTG) is a disease with progressive optic neuropathy and is characterised by a normal range of intraocular pressure (IOP) equalling the IOP of a healthy human (<22 mmHg) [4]. The incidence rate of NTG varies from region to region, majorly depending on the population's geographical area [5].

Multiple factors can cause NTG, and the pathogenesis of the disease remains unclear. Treatment options also vary, but similar procedures of therapy of open-angle glaucoma can be used. However, due to the normal/low IOP of patients with NTG, it is difficult to reach the values of eye pressure, which is not progressing the disease pathogenesis. While the primary management strategy includes the monitoring and prevention of systemic risk factors, the secondary interventions of the standard treatment of NTG are to decrease IOP and improvement of ocular perfusion [4].

Measurement of IOP has been the general method of screening for glaucoma. The sensitivity and specificity of this technique, however, is low, and there is a demand for more extensive detection methods [6]. The Glaucoma State Screening program was one of the main achievements in the organisation of the fight against glaucoma in the Republic of Kazakhstan. The program began in 2011 and was aimed at early detection of glaucoma. The mission of the Kazakhstan State screening program was to identify cases of increased IOP among persons over 40 years of age, followed by an examination for glaucoma in specialised glaucoma cabinets. These specialised glaucoma cabinets with state-of-art glaucoma diagnostic machines were opened as part of the state program "Salamatty Kazakhstan" for health care system development in the Republic of Kazakhstan between 2011–2015. Availability of the retinal tomography and computer perimeters in the regional glaucoma cabinets, therefore, upgraded the quality of disease management and follow-up strategy.

The innovative development of diagnostic ophthalmic equipment has led to improved standards of diagnosis and monitoring of glaucoma. Despite this great implementation, there have been no systematic comparative studies of the prevalence of NTG in Kazakhstan to date. It is thus unclear whether these state programs enhance NTG detection in the country and identify the vulnerable population groups. To address this knowledge gap, we aimed to investigate the prevalence of normal-tension glaucoma in Kazakhstan using the results of the State Screening program.

Materials and methods

Population and Geographic area

The study aimed to investigate the data obtained from the State Screening program [7], where the glaucoma epidemiology of the whole population of Kazakhstan over 40 years of age was investigated. The proportion of this cohort constitutes around 40% of the entire population of the country. Assuming the 2% prevalence of glaucoma according to the outcomes of the State Screening program [7] and a margin of the standard error of 1.5-2%, it has been calculated the number of people with overall glaucoma in 2011 and the participants with the normal IOP, but glaucoma manifestation, or else the number of patients with NTG.

The country population who is aged over 40 years to be enrolled on the study was selected on the basis of data provided by the State Statistics Dataset [8] and our recent study [9] as they contained the data of all participants who underwent the screening programs. Each selected participant was invited by the glaucoma cabinet specialists – Ophthalmologists/Optometrists following the simple random sampling. All participants were informed of the study purposes and procedures, signed an informed consent form.

Procedures

The study was conducted in all fourteen regions and two major cities of Kazakhstan, in specially equipped screening centres, so-called glaucoma cabinets. The ophthalmic examinations were performed by trained and tested medical practitioners, who underwent periodical to quality control by the specialists of Kazakh Eye Research Institute. It was important to use the same instruments and devices throughout the entire screening period to be consistent in data collection and avoid deviations in the scanning of the retinal topography, measurement of IOP and visual field. All data obtained from patients were recorded on the record cards – History of Disease.

All procedures performed in studies involving human participants were reviewed and approved by the Institutional Review Board of the Local ethics committee of the Kazakh Eye Research Institute (Almaty, Kazakhstan) prior to the initiation of the study and were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Screening examination

Apart from the medical history survey there was conducted an ophthalmologic examination, which included visometry, autorefractometry, computerized examination of the visual field (not available in all regions), slit-lamp observation of the anterior and posterior eye segments, evaluation of the optic disc using direct ophthalmoscopy and applanation (contact) tonometry utilizing a Maklakov tonometer under topical anaesthesia.

Glaucoma classification

To classify the screening outcomes, the following diagnostic criteria were adopted: ocular hypertension (OH); primary open-angle glaucoma (POAG); primary angle-closure glaucoma (PACG) and normal-tension glaucoma (NTG).

Ocular hypertension manifests with the IOP ≥ 22 mmHg without the damage of the visual field and ONH, with no characteristic symptoms of secondary glaucoma and closure of anterior chamber angle. POAG is characterised by ocular hypertension, glaucomatous ONH and visual field

abnormalities. However, the chamber angle is not occluded, whereas the sing of partly or totally closed anterior chamber angle is closed in PACG. Moreover, PACG is also manifested by the above-mentioned glaucoma signs. The main difference of NTG from OH, POAG and PACG is the normal eye pressure (IOP < 22 mmHg) with other pathognomic symptoms: the damage of the visual field and ONH.

Statistical analysis

The dataset was analysed using the MATLAB application package version R2017b (MathWorks, USA).

Results

An upward trend in the number of patients diagnosed with glaucoma was noted in the detection of the disease in different age groups according to the screening results in the framework of the State Program of the Development of Healthcare (Figure 1). More than 50% of older age groups starting from 64 years of age were identified, reaching 80% in 69-70 years old participants.
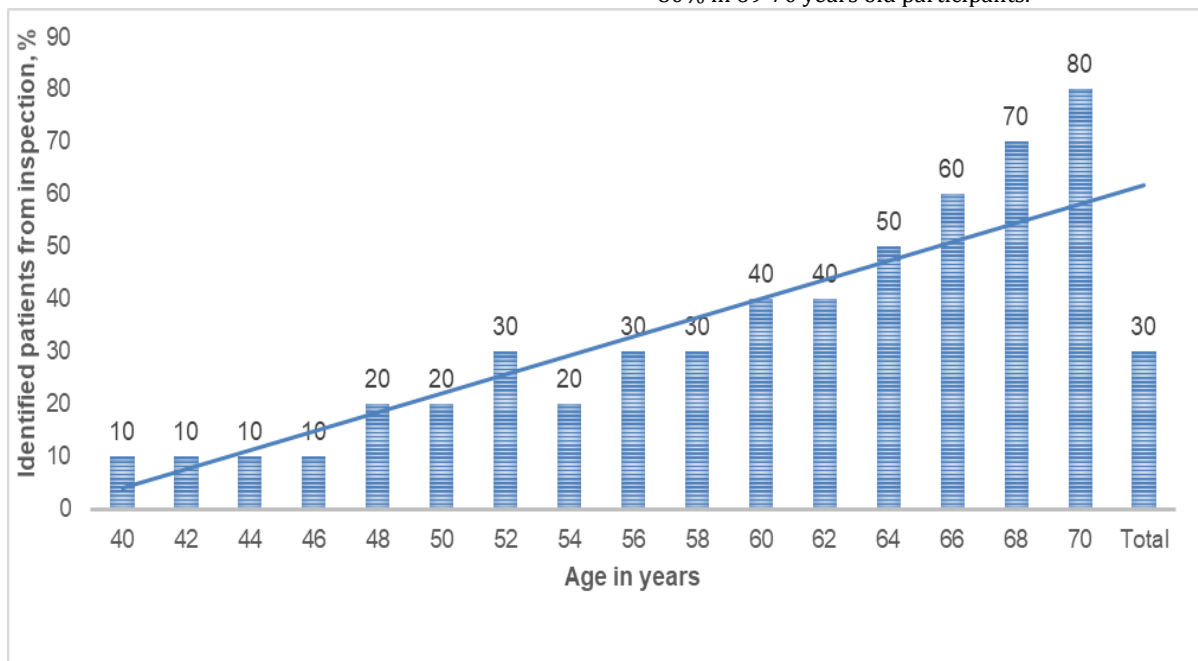
Figure 1 - Glaucoma detection in different age groups according to the screening results in the framework of the State Program of the Development of Healthcare

Table 1 depicts the epidemiology of open-angle glaucoma in Kazakhstan by region. It can be noted that the screening covered 94.83% of adults from 40 to 70 years. Latter is the indicator of the successful accomplishment of

the first mission of the state screening – to maximize the diagnostic coverage throughout the country. On the other hand, not all regions reached the highest degree of screening. For instance, only 67.57% of people attended the screening in the Mangystau region.

Table 1 - Results of the screening examinations of men and women aged 40-70 years for the detection of glaucoma (POAG and PACG)

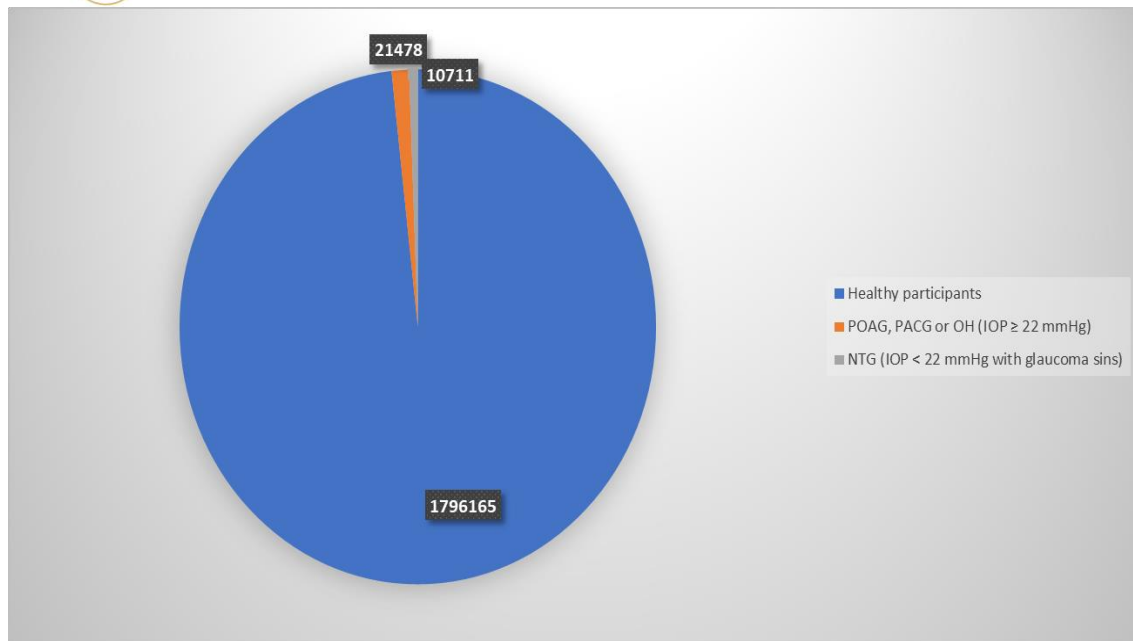| Regions	Subject to screening	Underwent screening		Detected patients	
		Number	Proportion, %	Number	Proportion, %
Akmola region	95 183	88 329	92.8	166	0.19
Aktobe region	88 275	88 275	100	51	0.06
Almaty region	264 410	225 643	85.34	640	0.28
Atyrau region	55 135	51 086	92.66	59	0.12
West-Kazakhstan region	68 871	66 427	96.45	151	0.23
Zhambyl region	124 558	124 591	100	112	0.09
Karagandy region	199 976	190 632	95.33	491	0.26
Kostanai region	122 424	113 369	92.6	71	0.06
Kyzylorda region	131 227	47 752	36.39	128	0.27
Mangystau region	31 969	21 603	67.57	40	0.19
South-Kazakhstan region	264 484	231 201	87.42	1 501	0.65
Pavlodar region	71 376	61 573	86.27	46	0.07

Figure 2 - Glaucoma screening results. Here: POAG – primary open-angle glaucoma; OH – ocular hypertension; PACG – primary angle-closure glaucoma; NTG – normal-tension glaucoma

Discussion

Normal-tension glaucoma in Kazakhstan amounts to 0.6% of all population aged 40-70 years, which corresponds to the literature data. For instance, in the study of Bonomi et al., the prevalence of NTG was similar and the proportion of NTG was 0.6%, whereas OH was 2.1%, POAG – 1.4% and PACG – 0.6% [10].

However, it should be noted that in Asia, the prevalence of NTG varies depending on the geographical area and methodology of screening [5, 10, 11]. For example, Japan (3.5%) and Singapore (4.3%) are the countries with the highest incidence of NTG not only in Asia but in the world [12, 13], while the proportion of NTG is lower in the western world. The epidemiological studies in the Netherlands (0.3%) and Italy (0.6%) were elegantly conducted by Klein et al. [14] and Bonomi et al. [10], respectively.

Among other limitations, the screening methods of NTG should be updated and focused on the detection of early subtle retinal signs [15], which can be achieved using high-resolution optical coherence tomography. This may help to detect the neurodegeneration of the retinal ganglion cell body and dendrites before the clinical manifestations of glaucoma and irreversible vision loss. For future investigations, detailed epidemiological studies of NTG and its aetiopathogenesis are needed to construct the strategy of prevention and management of NTG in Kazakhstan.

Although Kazakhstan is recognised as an Asian country, the prevalence of NTG in the country is close to European statistical ranges. Nonetheless, there is a huge concern about the ignorance of NTG as a socially significant eye condition. Hence, further monitoring of NTG is required in terms of the early treatment and preventive measurements of glaucoma.

Recently, in our study, we illustrated the possibilities of early detection of ocular neurodegeneration of retinal diseases in the example of artificial phantoms of the retina [15]. Application of the techniques of machine learning in the interpretation of the outcomes of the optical coherence tomography will place a role in the detection of early signs of retinal ganglion cell apoptosis. This study is the first attempt to calculate the number of normal-tension glaucoma in Kazakhstan, a more hidden and dangerous type of this disease.

All in all, our study and literature data conclude the complexity of the detection of normal-tension glaucoma. The prevalence of NTG in Kazakhstan amounts to more than 10 thousand according to the outcomes of the State Screening program and can be increased if not diagnosed earlier. This disease is a hidden and more dangerous type of POAG, where the signs and symptoms can be detected only in the late stage of the disease. In this situation, irreversible vision loss is inevitable and cannot be treated medically and surgically.

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