New Day in Medicine
Новый День в Медицине
NDM

TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal

AVICENNA-MED.UZ

ISSN 2181-712X.
EiSSN 2181-2187

9 (71) 2024

ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал

УЧРЕДИТЕЛИ:

БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»

Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского является генеральным научно-практическим консультантом редакции

Журнал был включен в список журнальных изданий, рецензируемых Высшей Аттестационной Комиссией Республики Узбекистан (Протокол № 201/03 от 30.12.2013 г.)

9 (71)

2024

сентябрь

www.bsmi.uz
https://newdaymedicine.com E: ndmuz@mail.ru
Тел: +99890 8061882

Received: 20.08.2024, Accepted: 02.09.2024, Published: 10.09.2024

UDC 617.741-004.1-067-07-08:577.21

GENETIC STRUCTURE OF HEREDITARY EYE DISEASES IN SURKHANDARYA POPULATION

[1]*Bilalov E.N.* https://orcid.org/0000-0002-3484-1225
[1]*Narzikulova K.I.* https://orcid.org/0000-0001-6395-0730
[2]*Ochildiev M.B.* https://0009-0005-4002-4730
[1]*Orolov B.A. Email:* Orolovbekhruz@mail.ru

[1]Tashkent Medical Academy (TMA) Uzbekistan, 100109, Tashkent, Almazar district, st. Farobi 2, phone: +99878 1507825, E-mail: info@tma.uz
[2]Termez branch of the Tashkent Medical Academy Surkhandarya region Termez city, I. Karimov street No. 64 Tel: +998 (76) 223-47-20 E-mail: info@ttatf.uz

✓ ***Resume***

Most congenital eye diseases occur more often in children whose parents are closely related, and cases of repeated incidence of these pathologies are observed in the 3rd-4th generation of families.
The purpose of the research. It consists in studying the genetic frequency of certain types of hereditary eye diseases in Surkhandarya population. Material and methods. Genetic and epidemiological survey of the population of the Surkhandarya region was carried out in 15 districts, with a total population of 2.8 million. Based on the screening analysis, 385 patients with various hereditary eye diseases were identified. There are 208 men and 177 women among them.The main contingent percentage was made up of patients under the age of 26 years. According to the results of segregation analysis, 97 patients with hereditary eye diseases were identified: 38 of them had autosomal recessive, 53 - autosomal dominant and 6 patients X-linked type of inheritance).The cause of morbidity in all cases was closely related marriages. Results and conclusion.Analysis of the results of the study showed that the most common hereditary ophthalmopathologies were diseases of the retina and choroid (18.5%), congenital cataracts (15.5%), and high myopia (12%). The study of the dependence of all characteristics of the load of hereditary ophthalmopathologies on the genetic structure of the population conducted in 13 districts of the Surkhanadaryo region showed, that the highest values of the random component of inbreeding (F_{ST}) were found in the rural population of the Kumkurgan and Muzrabad districts, which, in our opinion, is associated with the highest frequency of closely related marriages in the studied areas.

Keywords: hereditary ophthalmopathology, autosomal dominant, autosomal recessive, congenital diseases

ИРСИЙ КЎЗ КАСАЛЛИКЛАРИНИНГ СУРХОНДАРЁ ПОПУЛЯЦИСИДАГИ ГЕНЕТИК ТУЗИЛИШИ

[1]*Билалов Э.Н.* https://orcid.org/0000-0002-3484-1225
[1]*Нарзикулова К.И.* https://orcid.org/0000-0001-6395-0730
[2]*Очилдиев М.Б.* https://0009-0005-4002-4730
[1]*Оролов Б.А. Email:* Orolovbekhruz@mail.ru

[1]Тошкент тиббиёт академияси. Ўзбекистон, 100109, Тошкент, Олмазор тумани, Фароби кўчаси 2, тел: +99878 1507825, E-mail: info@tma.uz
[2]Тошкент тиббиёт академияси Термиз филиали Сурхондарё вилояти Термиз шаҳри, И.Каримов кўчаси 64-уй Тел: +998 (76) 223-47-20 E-mail: info@ttatf.uz

✓ ***Резюме***

Кўпинча туғма кўз касалликлари ота-оналари яқин қариндош бўлган болаларда тез-тез учрайди ва бу патологияларнинг такрорий касалланиш ҳолатлари оилаларнинг 3-4-авлодларида кузатилади. Тадқиқот мақсади: Сурхондарё популяциясида ирсий кўз касалликларининг айрим турларининг генетик частотасини ўрганишдан иборат. Материаллар ва усуллар. Сурхондарё вилоятида 2,8 миллион аҳоли истиқомат қиладиган 15 та туманда аҳолининг генетик-эпидемиологик текшируви ўтказилди. Скрининг таҳлиллари

асосида турли ирсий кўз касалликлари билан касалланган 385 нафар бемор аниқланди. Беморларнинг ёши ҳаётнинг биринчи ойларидан 78 ёшгача бўлган. Уларнинг 208 нафари эркак, 177 нафарини аёллар ташкил этдилар. Асосий контингент фоизини 26 ёшгача бўлган беморлар ташкил этди. Сегрегация таҳлилига асосан ирсий офтальмопатологияси бўлган 97 нафар бемор аниқланди (шундан 38 беморда аутосома-рецессив, 53 беморда аутосома-доминант мойиллик тури ва 6 беморда Х хромасомага боғланган ирсият шакли бўлган). Барча ҳолатларда касалланишининг сабаби яқин қариндошлик асосидаги никоҳлар билан чамбарчас боғлиқ бўлди. Натижа ва хулоса. Тадқиқот натижаларини таҳлил қилиш шуни кўрсатдики, энг кенг тарқалган ирсий офтальмопатологиялар тўр парда ва хороидеа касалликлари (18,5%), туғма катаракта (15,5%), шунингдек, юқори даражали миопия (12%) учради. Сурхондарё вилоятининг 15 та туман ахолисида ирсий кўз касалликлари юкининг барча хусусиятлари популяциянинг генетик тузилишига боғлиқлигини ўрганиш, наслчиликнинг тасодифий компоненти (F_{ST}) энг юқори кўрсаткичлари аниқланган Кумқўрғон ва Музрабод туманларидаги қишлоқ аҳолисида, яқин қариндошлик асосидаги никоҳларнинг юқорилиги билан боғлиқлигини кўрсатди.

Калит сўзлар: ирсий офтальмопатология, аутосома - доминант, аутосома - рецессив, туғма нуқсонлар.

ГЕНЕТИЧЕСКАЯ СТРУКТУРА НАСЛЕДСТВЕННЫХ ЗАБОЛЕВАНИЙ ГЛАЗ У НАСЕЛЕНИЯ СУРХАНДАРЬИ

[1]Билалов Э.Н. https://orcid.org/0000-0002-3484-1225
[1]Нарзикулова К.И. https://orcid.org/0000-0001-6395-0730
[2]Очилдиев М.Б. https://0009-0005-4002-4730
[1]Оролов Б.А. Email: Orolovbekhruz@mail.ru

[1]Ташкентская Медицинская Академия (ТМА) Узбекистан, 100109, Ташкент, Алмазарский район, ул. Фароби 2, тел: +99878 1507825, E-mail: info@tma.uz
[2]Термезский филиал Ташкентской медицинской академии Сурхандарьинская область город Термез, улица И. Каримова №64 Тел: +998 (76) 223-47-20 E-mail: info@ttatf.uz

✓ ***Резюме***

Большинство врожденных заболеваний глаз чаще возникают у детей, чьи родители находятся в близком родстве, а случаи повторной заболеваемости данными патологиями наблюдаются в 3-4-м поколении семей. Цель исследования. Изучение генетической частоты некоторых видов наследственных заболеваний глаз в популяции Сурхандарьи. Материал и методы. Проведено генетико-эпидемиологическое обследование населения Сурхандарьинской области в 15 районах, с общей численностью 2,8 млн. На основании скринингового анализа выявлено 385 пациентов с различными наследственными заболеваниями глаз. Возраст пациентов варьировал от первых месяцев жизни до 78 лет. Среди них мужчин 208, женщин – 177 человек. Основной контингент процент составили пациенты в возрасте до 26 лет. По результатам сегрегационного анализа выявлено 97 пациентов с наследственными заболеваниями глаз: 38 из них имели аутосомно-рецессивный, 53 - аутосомно-доминантный и 6 пациентов *Х-сцепленный* ***тип наследования). Причиной заболеваемости во всех случаях стали близкородственные браки.Результаты и заключение.Анализ результатов исследования показал, что наиболее часто встречающимися наследственными офтальмопатологиями явились заболевания сетчатки и хориоидеи (18,5%), врожденные катаракты (15,5%), а также миопия высокой степени (12%). Изучение зависимости всех характеристик груза наследственных офтальмопатологий от генетической структуры популяции проведенный в 13 районах Сурханадарьинской области показал, что наибольшие значения случайной составляющей инбридинга (F_{ST}) были выявлены в сельской популяции районов Кумкурган и Музрабад, что, на наш взгляд, связано с наиболее высокой частотой близкородственных браков в изучаемых районах.***

Ключевые слова: наследственные офтальмопатологии, аутосомно- доминантный, аутосомно- рецессивный, врожденные заболевания.

Relevance

Past 25y have witnessed an exponential increase in knowledge and understanding of ocular diseases and their respective genetic underpinnings. As a result, scientists have mapped many genes and their variants that can influence vision and health of our eyes [4,5].

Among infants, more than 60 percent of cases where blindness has occurred are caused by inherited eye diseases such as congenital (present at birth) cataracts, congenital glaucoma, retinal degeneration, optic atrophy and eye malformations. Additionally, up to 40% of children and infants with certain types of strabismus (misalignment of one eye in relation to the other) have a family history of the disease.

The ophthalmologist's role in the management and diagnosis of genetic disorders can be critical for patients, families and referring providers in the steadily advancing field of genetics [2]. Genetic testing can be a useful medical tool in ophthalmology to help confirm or rule out a suspected inherited ocular disorder, provide important information of inheritance patterns and risk of recurrences for families, and help guide clinical management, appropriate referral and surveillance decisions. Furthermore, genetic testing may also provide a societal benefit in improv. Based on these findings, it is becoming clear that an early diagnosis employing genetic testing can help evaluate patients' conditions for instituting treatment plan and follow-up care to avoid vision complications later. For example, knowing family history becomes crucial for inherited eye diseases as it can benefit members in family who may have similar eye diseases or predispositions, the understanding of genes, genetic diseases, and future treatments [3]. Therefore, gathering information from an elaborate examination along with complete assessment of past medical illness by ophthalmologists followed by consultation with geneticists can help create a roadmap for making diagnosis and treatment precise and beneficial [1,2,4,5].

Purpose of the research. To study the occurrence of certain types of hereditary eye diseases in the Surkhandarya region.

Material and methods

A genetic and epidemiological survey was carried out in population of 15 districts of the Surkhandarya region numbering 209597 people, which was aimed to identifying hereditary ophthalmopathologies (HOP) in the period from 2022-2023.To determine the possible change in the burden of HOP and its nosological spectrum, the population of Kumkurkan, Muzrabad and Jarkurgan districts was examined twice. The ethnic composition of the population represented by Uzbeksin 89%.

Information data on patients with HOP was obtained from the following sources: from general practitioners in rural medical centers, city polyclinics, ophthalmologists from the central districtspolyclinics (by using a questionnaire), as well as from the register of disabled people of the Bureau of Medical and Social Expertise.

Patients underwent general ophthalmological research methods, including visometry, skiascopy in conditions of drug mydriasis, the study of reflex motor reactions (pupillary and "tracking" reactions) in children under 3 years of age,study of color perception, keratometry, biomicroscopy of the anterior segment of the eye, as well as ophthalmoscopy.Some patients, according to indications, underwent perimetry, tonometry and gonioscopy. In order to accurately verify the diagnosis, the patients were examined at the Termez branch of the Republican Specialized Scientific and Practical Center for Eye Microsurgery, where they underwent special ophthalmological examination methods.

We also used a number of mathematical methods for statistical processing of the obtained material, including segregation analysis, uniformity of the distribution of hereditary pathology of the organ of vision by region, comparison of prevalence using the Student's t-test, analysis of the distribution of surnames by the isonymy method to assess random F_{ST} inbreeding.

Results and discussion

Screening analysis identified 385 patients with various eye diseases. The age of patients ranged from the first months of life to 78 years. Men made up 54%, women - 46%. The largest percentage was made up of patients under the age of 26 years (38%).After a comprehensive examination of all selected people, were identified patients with a presumably hereditary eye pathology (112 people).The conducted segregation analysis in families with presumably autosomal recessive (AR) and autosomal dominant (AD) pathology of the eye showed compliance with a certain type of inheritanceand

compiled for a group of families witheye diseases with AR type of inheritance 0.17, for a group of families with an autosomal dominant pathology of the eye - 0.32, which indicates that the risk of having a sick child in burdened families with an autosomal recessive type of inheritance is 20-25%, with autosomal dominant - 45-50%. The segregation analysis revealed 97 patients withhereditary ophthalmopathologies (38 of patients had an autosomal recessive, 53 patients had an autosomal dominant type of inheritance, and 6 patients had an X-linked inheritance pattern).In all cases, closely related marriages became the cause of morbidity.

The most common hereditary ophthalmopathologies were diseases of the retina and choroid (18.5%), congenital cataracts (15.5%), and high myopia (12%).Was studied interpopulation, interfamily, clinical and genetic polymorphism.In all patients, the prenatal anamnesis and anamnesis of life were not burdened, concomitant pathology of the eye and other organs and systems was not revealed.

The largest contingent consisted of patients with a mixed form of retinal-pigmented tapetoretinalabiotrophy - 11 probands from 11 families, aged 32 to 58 years. At the same time, changes were detected only in men. Such symptoms of the disease as: deterioration in dark adaptation and day blindness with excessive illumination, which later turned into nyctalopia and narrowing of the visual field, were observed mainly at the age of 9 to 24 years. At an older age (25-40 years) there was a significant decrease in vision severity (0.09 and below) and the appearance of peripheral scotomas. The anterior segment of the eyes in this group of patients was not changed. At the age of 41-58 years, dystrophic changes in the retina were observed with damage of the eye vessels, the development of complicated cataract and clouding of the vitreous body, which led to the appearance of "tunnel vision" with very low visual acuity, as well as hemeralopia and impaired color perception.In all patients, ophthalmoscopy revealed symmetrical changes in both eyes.

The peripheral form of pigmented tapetoretinalabiotrophy was detected in 5 women. In 3 of themwas noted an autosomal dominant type, in 2 - an autosomal recessive type of inheritance. The initial symptoms of the disease manifested themselves at the age of 11-28 years in the form of hemeralopia and narrowing of the visual fields. Visual acuity indicators were 0.4 and below. The oldest patient had complicated cataract. Typical, symmetrical changes were observed in the fundus.

Franceschetti-type retinal abiotrophy was detected in 2 male patients from different families at the age of 40 and 43 years. The initial symptoms of the disease appeared at the age of 18 and 26 years in the form of a decrease in visual acuity from 0.7 to 0.05, depending on the duration of the disease, narrowing of the visual fields with the determination of relative and absolute scotomas. Ophthalmoscopy revealed changes typical for this disease.

Axenfeld-Rigger syndrome was detected in 3 patients from 2 families. All patients had such clinical symptoms as complete aniridia, incomplete cataract and secondary glaucoma.

Marfan's syndrome was diagnosed in 4 patients from different families aged 16 to 21 years. At the same time, men suffered with the same frequency as women. All patients had typical systemic changes in the connective tissue and heart. There were myopic changes in the vision organ, lens subluxation was observed in 2 patients.

Hereditary cataracts occurred in 16 patients from 12 families. The age of the patients ranged from 6 months to 25 years. The distribution of patients by gender did not differ significantly. In the majority of patients (75%), clouding of the lens was noted already in the first year of life. Cataract progression was not observed in this group of patients. In the remaining patients (25%), clouding of the lens was noted at the age of 5 years and older (in examining the relatives of the proband). Decrease in visual acuity to 0.5-0.7 was observed in 2 patients, 0.2-0.4 - in 6 patients (37.5%) and in 8 patients (50%) visual acuity was 0.1 or lower. The highest frequency was in patients with capsular cataracts (9 patients), 4 patients had polar cataracts and 3 patients had complete cataracts.

The study of the dependence of all characteristics of the load of hereditary ophthalmopathologies on the genetic structure of the population conducted in 13 districts of the Surkhanadaryo region showed, that the highest values of the random component of inbreeding (F_{ST}) were found in the rural population of the Kumkurgan and Muzrabad districts, which, in our opinion, is associated with the highest frequency of closely related marriages in the studied areas.

The coefficient of linear correlation between the prevalence of autosomal recessive hereditary eye diseases and the values of random inbreeding F_{ST} was 0.63+28 (Spearman's rank correlation r=0.78); between F_{St} and the prevalence of autosomal dominant pathology of the organ of vision - 0.44±36

(rank correlation according to Spearman r=0.58); between total hereditary ophthalmopathology, including dominant, recessive and X-linked forms of ophthalmopathology, and F_{ST} values by region - 0.69±32 (Spearman's ranking r=0.66). The correlation coefficient between the variety of nosological forms of hereditary eye diseases and the values of random inbreeding was 0.81.

The obtained correlation coefficients show that the differences between the F_{ST} values and the total prevalence, as well as the severity of autosomal recessive and autosomal dominant eye diseases and the diversity of hereditary pathology of the eye, are explained by the different level of separation of the studied populations.

Conclusions

1. It was established that the most common hereditary ophthalmopathologies in the Surkhandarya region as a result of closely related marriages were diseases of the retina and choroid (18.5%), congenital cataracts (15.5%), high myopia (12%), Marfan syndrome (3.8%) and Axenfeld-Rigger syndrome (2.9%).

2. It was revealed that the highest values of the random component of inbreeding were noted in the rural population in the Muzrabad and Kumkurgan districts of the Surkhandarya region, which is associated with the highest frequency of closely related marriages in this area. The correlation coefficient between the total hereditary ophthalmopathology and the values of random inbreeding by regions was 0.69, between the diversity of the spectrum of hereditary eye pathology and random inbreeding - 0.81.

LIST OF REFERENCES:

1. Билалов Э.Н., Нарзикулова К.И., Очилдиев М.Б., Назирова С.Х.,Распространенность некоторых видов наследственных заболеваний глаз Сурхандарьинской области //Передовая офтальмология 2023; С.36-40. [1. Bilalov E.N., Narzikulova K.I., Ochildiev M.B., NazirovaS.Kh., The prevalence of some types of hereditary eye diseases in the Surkhandarya region //Advanced ophthalmology 2023; P.36-40.] DOI:https://doi.org/10/57231/j.ao.2023/1.1.008
2. Киреева О.Л., Хлебникова О.В., Амалина С.С., Ельчинова Г.И., Зинченко Р.А., Кадышев В.В., Гинтер Е.К. Нозологический спектр и распространенность наследственной офтальмопатологии среди детского населения 12 районов Ростовской области // Офтальмология. 2012;9(4):8-13. [Kireeva O.L., Khlebnikova O.V., Amalina S.S., Elchinova G.I., Zinchenko R.A., Kadyshev V.V., Ginter E.K. Nosological spectrum and prevalence of hereditary ophthalmopathology among children in 12 districts of the Rostov region // Ophthalmology. 2012;9(4):8-13. (In Russ.).].https://doi.org/10.18008/1816-5095-2012-4
3. Шурыгина М.Ф., Хотеева А.М. Диагностика наследственных дистрофий сетчатки с позиции генной терапии. Вестникофтальмологии. 2021;137(4):145-151. [Shurygina MF, Khoteeva A.M. Diagnostics of inherited retinal degenerations by gene therapy. VestnikOftalmologii. 2021;137(4):145-151. In Russ.)]. https://doi.org/10.17116/oftalma2021137041145
4. Na H.J., Kim K.H., KimS. Han P., KimH.J, Hann H.S. Ahn. Prevalence, age at diagnosis, mortality and cause of death in retinitis pigmentosa in Korea - a nationwide population-based study //Am. J. Ophthalmol. 2017;176:157-165. https://doi.org/10.1016/j.ajo.2017.01.014
5. Nangia V., Jonas J.B, Khare A., Sinha A. Prevalence of retinitis pigmentosa in India: the Central India eye and medical study //Acta Ophthalmol. 2012;90:649-650. https://doi.org10.1111/j.1755-3768.2012.02396.x

Entered 20.08.2024