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Intraocular Pressure in the Adult Population of Arkhangelsk and Its Associations with Socio-Demographic Characteristics, Lifestyle, and General Health Status

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ABSTRACT

BACKGROUND: Glaucoma is considered one of the leading causes of disability. Intraocular pressure is a key risk factor for the development of glaucoma, which underscores the importance of its assessment and control. The pneumotonometric method for measuring intraocular pressure is being widely used in glaucoma screening diagnostics.

AIM: The work aimed to determine population-based reference values and age-related changes in intraocular pressure among adults in the European North of Russia and to examine associations between intraocular pressure and socio-demographic characteristics, lifestyle factors, and health indicators.

METHODS: A random sample of Arkhangelsk residents aged 45–74 years (n=1223) was examined, including an ophthalmologic assessment and pneumotonometry. Socio-demographic and lifestyle data were collected via face-to-face interviews, and health characteristics were obtained through clinical examinations. Intraocular pressure reference values were defined using the 5th and 95th percentiles. Associations between intraocular pressure and other studied variables were assessed using multivariable linear regressions and presented as B coefficients with 95% confidence intervals (CI).

RESULTS: The mean intraocular pressure was 14.2 mmHg overall, 13.9 mmHg in men, and 14.4 mmHg in women. Population-based reference ranges for true intraocular pressure were identified as follows: low-normal (9–12 mmHg), mid-normal (12–16 mmHg), and high-normal (16–20 mmHg). Intraocular pressure levels showed a downward trend with increasing age in both women (p=0.007) and men (p=0.011). Inverse associations were found between intraocular pressure and male sex (B=–0.56; 95% CI: –0.94 to –0.18), being a native resident of the Arkhangelsk region (B=–0.50; 95% CI: –0.83 to –0.16), and higher education (B=–0.40; 95% CI: –0.73 to –0.06). Among health-related variables, intraocular pressure was associated with hypertension (B=0.56; 95% CI: 0.17 to 0.94), diabetes mellitus (B=0.46; 95% CI: 0.03 to 0.89), dyslipidemia (B=0.36; 95% CI: 0.01 to 0.71), abdominal obesity (B=0.39; 95% CI: 0.31 to 0.98), thyroid dysfunction (B=0.42; 95% CI: 0.07 to 0.77), vitamin D deficiency (B=0.76; 95% CI: 0.30 to 1.22), and low total serum protein (B=–0.76; 95% CI: –1.43 to –0.09).

CONCLUSION: This study established normal intraocular pressure ranges for residents of the European North of Russia aged 45–74 years. A decrease in intraocular pressure with age was observed, along with lower intraocular pressure levels in men, native residents of the Arkhangelsk Region, and individuals with low serum protein. Elevated intraocular pressure levels were associated with hypertension, diabetes mellitus, dyslipidemia, obesity, thyroid dysfunction, and vitamin D deficiency.

Keywords: intraocular pressure; pneumotonometry; hypertension; diabetes mellitus; dyslipidemia; obesity; thyroid dysfunction; vitamin D deficiency.

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Внутриглазное давление у взрослого населения г. Архангельска и его связи с социально-демографическими характеристиками, образом жизни и общим состоянием здоровья

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АННОТАЦИЯ

Обоснование. Глаукома считается одной из основных причин инвалидизации населения. Ключевым фактором риска развития глаукомы является внутриглазное давление (ВГД), что обуславливает важность его оценки и контроля. Широкое применение в скрининговой диагностике глаукомы приобретает пневмотонометрический метод измерения ВГД.

Цель. Определить популяционные нормы и возрастные изменения ВГД у взрослого населения Европейского Севера России, изучить связи ВГД с социально-демографическими признаками, факторами образа жизни и характеристиками здоровья.

Методы. Обследована случайная выборка жителей г. Архангельска в возрасте 45–74 лет (n=1223), включая осмотр офтальмологом и пневмотонометрию. Данные о социально-демографических характеристиках и образе жизни получены методом устного интервью, о характеристиках здоровья — посредством медицинского обследования. Референсные значения ВГД получены на основании значений 5–95-го процентилей. Связи ВГД с рассматриваемыми переменными оценены с помощью многомерных линейных регрессий и представлены в виде коэффициентов B с 95% доверительными интервалами (ДИ).

Результаты. Среднее значение ВГД составило 14,2 мм рт. ст., у мужчин — 13,9 мм рт. ст., у женщин — 14,4 мм рт. ст. Определены популяционные уровни низкой нормы, средней нормы и высокой нормы истинного ВГД, которые составили от 9 до 12 мм рт. ст., от 12 до 16 мм рт. ст. и от 16 до 20 мм рт. ст. соответственно. Значения ВГД имели нисходящие тренды с увеличением возраста женщин (p=0,007) и мужчин (p=0,011). Установлены отрицательные связи между ВГД и принадлежностью к мужскому полу (B –0,56; 95% ДИ –0,94; –0,18), принадлежностью к коренному населению Архангельской области (B –0,50; 95% ДИ –0,83; –0,16) и наличием высшего образования (B –0,40; 95% ДИ –0,73; –0,06). Из анализируемых характеристик здоровья связи с ВГД имели артериальная гипертензия (B 0,56; 95% ДИ 0,17; 0,94), сахарный диабет (B 0,46; 95% ДИ 0,03; 0,89), дислипидемия (B 0,36; 95% ДИ 0,01; 0,71), абдоминальное ожирение (B 0,39; 95% ДИ 0,31; 0,98), нарушение функции щитовидной железы (B 0,42; 95% ДИ 0,07; 0,77), недостаточность витамина D (B 0,76; 95% ДИ 0,30; 1,22) и снижение уровня общего белка (B –0,76; 95% ДИ –1,43; –0,09).

Заключение. В исследовании определены нормальные диапазоны ВГД для жителей Европейского Севера России 45–74 лет. Отмечено снижение уровня ВГД с возрастом, пониженные его значения у мужчин, у коренных жителей Архангельской области, а также при низком уровне общего белка в крови. Повышенные уровни ВГД ассоциировались с наличием артериальной гипертензии, сахарного диабета, дислипидемии, ожирения, с дисфункцией щитовидной железы, недостаточностью витамина D.

Ключевые слова: внутриглазное давление; пневмотонометрия; артериальная гипертензия; сахарный диабет; дислипидемия; ожирение; дисфункция щитовидной железы; недостаточность витамина D.

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Arkhangelsk市成年居民的眼压水平及其与社会人口学特征、生活方式和健康状况的关系

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摘要

论证。青光眼是导致人群致残的主要原因之一。眼内压 (intraocular pressure, IOP) 是青光眼发展的关键危险因素，因此对眼压的评估和监测具有重要意义。在青光眼筛查中，广泛采用气动眼压计法 (pneumotonometry) 进行IOP测量。

目的。明确俄罗斯欧洲北部地区成年居民的群体IOP参考值及其不同年龄段的变化，研究眼压与社会人口学特征、生活方式因素和健康指标之间的关系。

方法。对Arkhangelsk市45－74岁居民的随机样本（n=1223）进行检查，包括由眼科医生进行的检查和气动眼压测量。通过面对面访谈收集社会人口学和生活方式资料，通过医学检查收集健康状况数据。IOP参考值依据第5－95百分位数确定。IOP与各变量之间的关系通过多元线性回归进行评估，结果以回归系数B及其95%置信区间（CI）的形式呈现。

结果。总体人群的平均IOP为14.2 mmHg，其中男性为13.9 mmHg，女性为14.4 mmHg。明确了群体IOP的低正常（9－12 mmHg）、中等正常（12－16 mmHg）和高正常（16－20 mmHg）三个范围。IOP随年龄增长呈下降趋势，女性（*p*=0.007），男性（*p*=0.011）。IOP与男性性别（B=0.56；95% CI －0.94, －0.18）、为 Arkhangelsk Region 原住民身份（B=0.50；95% CI －0.83, －0.16）以及高等教育水平（B=0.40；95% CI －0.73, －0.06）呈负相关。在所分析的健康指标中，以下因素与IOP存在关联：高血压（B=0.56；95% CI 0.17, 0.94）、糖尿病（B=0.46；95% CI 0.03, 0.89）、血脂异常（B=0.36；95% CI 0.01, 0.71）、腹型肥胖（B=0.39；95% CI 0.31, 0.98）、甲状腺功能异常（B=0.42；95% CI 0.07, 0.77）、维生素D缺乏（B=0.76；95% CI 0.30, 1.22）以及血清总蛋白水平下降（B=－0.76；95% CI －1.43, －0.09）。

结论。本研究明确了俄罗斯欧洲北部45－74岁人群的IOP正常范围。研究发现，IOP水平随年龄增长而下降，男性、Arkhangelsk Region 原住民以及血清总蛋白水平较低者的眼压较低。而高血压、糖尿病、血脂异常、肥胖、甲状腺功能异常和维生素D缺乏则与IOP升高有关。

关键词：眼内压；气动眼压计法；高血压；糖尿病；血脂异常；肥胖；甲状腺功能异常；维生素D缺乏。

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BACKGROUND

Glaucoma is the leading cause of irreversible blindness in the world. In 2013, glaucoma was diagnosed in 64.3 million people aged 40–80 years worldwide. The number of cases increased to 76.0 million in 2020 and is estimated to reach 111.8 million in 2040 [1].

Intraocular pressure (IOP) is the most important and the only modifiable risk factor for glaucoma [2, 3]. IOP directly affects the long-term prognosis of maintaining visual function, therefore its assessment and timely correction are the actual tasks of practical ophthalmology. The ability to see is one of the constituents of the sensory domain of the intrinsic capacity and plays an important role in ensuring healthy aging[1], which, in turn, is one of the priorities of national healthcare.

Screening of the population for signs of glaucoma is primarily based on tonometry tests. Elevated IOP is an indication for further diagnosis. Recently, a simple, non-contact, and available method called pneumotonometry has become widespread in screening examinations.

Individual IOP normal ranges are extremely variable and depend not only on patient's characteristics, but also on race and even ethnicity. Currently, African and Asian patients are known to have higher average IOP than Caucasian people [4]; and IOP in the Japanese population is lower than in the Chinese and Indian population [5–7]. Although several population-based studies have been performed [8, 9], reference IOP values of the population of specific regions are still unknown. The nature of age-related changes in IOP may also depend on race. Thus, studies in the European and American populations have shown an increase in IOP with age [10, 11] compared with a decrease in the Asian population [5, 12, 13].

In addition to age, sex, and race, epidemiological studies have determined other factors associated with IOP such as elevated blood pressure, glucose levels, obesity, smoking, alcohol and coffee consumption, physical activity, central corneal thickness, iris color, nuclear cataract, and myopia [14–16]. There have been no studies of IOP in the population of the European North of Russia, and the IOP association with socio-demographic factors, lifestyle, and general health statushas not been studied.

AIM

The work aimed to determine population-based reference values, describe age-related changes in IOP among adults in the European North of Russia, and to examine associations between IOP and socio-demographic characteristics, lifestyle factors, and health characteristics.

[1] Decade of healthy ageing: baseline report. Summary. WHO, 2021. Available from: https://apps.who.int/iris/handle/10665/338677

METHODS

Study Design

A population-based, cross-sectional study of intrinsic capacity biomarkers in residents of the European North of Russia was performed at the consultative and diagnostic outpatient clinic of the Northern State Medical University (Arkhangelsk) from May 2023 through June 2024. The study enrolled 1,223 Arkhangelsk residents aged 45–74 years who had lived in the Arkhangelsk Region (AR) for at least 10 years.

Eligibility Criteria

For the purposes of this study, the analysis included eligible individuals.

Inclusion criteria:

- Healthy screened volunteers (without glaucoma) of both sexes aged 45–74 years;
- Clinical refraction of ±3.0 D and astigmatism of ±1.5 D;
- Corrected visual acuity of ⩾0.5;
- Caucasians.

Exclusion criteria:

- Ametropia and/or astigmatism greater than those specified in the inclusion criteria;
- Ocular condition (glaucoma, corneal, retinal, or choroidal abnormality, or mature cataract);
- History of keratorefractive surgery;
- History of ophthalmic surgery (including intravitreal administration of angiogenesis inhibitors), ocular trauma, or uveitis;
- A decompensated somatic pathology;
- Systemic diseases requiring hormone therapy.

Study Setting

Ophthalmic examination. Ophthalmic examination was performed in all participants in the morning (09:00 to 12:00) and included measurement of uncorrected visual acuity (UCVA) ranging from 0 to 1.0 arbitrary units according to the Golovin-Sivtsev charts (Golovin S.S., Sivtsev D.A., 1928), and the parameters of best corrected visual acuity (BCVA) were determined. Clinical refractive error was determined using automated refractometry. The diagnosis was based on the ophthalmic examination data (primary ophthalmic examination, Appendix to Form 025/u approved by Order No. 834n of the Ministry of Health of the Russian Federation, December 15, 2014) in accordance with the International Classification of Diseases 10th revision (ICD-10). The participants also underwent pneumotonometry using a TX-10 automated pneumotonometer (Canon, Japan). True IOP (P_0) was recorded in examination cards.

Interview. Data on socio-demographic characteristics (sex, age, indigenous status in the Arkhangelsk region, marital status, higher education, employment, and financial constraints) and lifestyle factors (smoking and hazardous alcohol use) were collected using a standardized oral interview.

Participants who had at least two previous generations on their father's and mother's sides born in the Arkhangelsk Region were considered native residents [17]. Employment was defined as a full- or part-time job, marital status included such options as a civil marriage or living with a partner, and financial constraints meant financial difficulties buying food or clothes. The smoking factor was considered present only if a participant was a smoker at screening, and hazardous drinking was defined as a score of 8 or more on the Alcohol Use Disorders Identification Test (AUDIT) [18].

Measurements. Health characteristics analyzed for the association with IOP were collected during a medical examination, including medical history (conditions and medications), a range of instrumental measurements, and blood analysis.

The following instruments were used for measurements: a Seca® 217 stadiometer (Seca Limited) for body height (cm), TANITA BC-418MA body composition analyzer (TANITA EUROPE GmbH) for body weight (kg), and Seca®201 measuring tape (Seca Limited) for waist and hip circumference (cm). Brachial artery systolic and diastolic blood pressure (SBP and DBP, mmHg) and heart rate (HR, bpm) were measured using an OMRON M2 Basic (OMRON Healthcare) automated blood pressure monitor three times after 5-minute rest, with 2 minute intervals. The means of the second and third measurements were included in the analysis.

Laboratory tests. Fasting blood samples were taken from a cubital vein into vacuum systems with ethylenediaminetetraacetic acid (EDTA) anticoagulant. On the day of blood sampling, glycated hemoglobin (HbA_{1c}) was measured in whole-blood hemolysate using a Random Access A-15 automated biochemical analyzer (BioSystems, Spain) and BioSystems reagent kits (Spain). To obtain the serum, vacutainers with blood were centrifuged at 3000 rpm in a refrigerated centrifuge no later than 2 hours after sampling. The obtained serum samples were frozen at −20˚C until analysed. Total cholesterol (TH), triglycerides (TG), high-density lipoproteins (HDL), serum iron and total protein were measured using the Random Access A-15 automated biochemical analyzer (BioSystems, Spain) using BioSystems reagent kits (Spain). Low-density lipoproteins (LDL) were calculated using the Friedewald equation: LDL=TH–(HDL–TG)/2.2. Triiodothyronine (T3), free thyroxine (T4), and thyroid-stimulating hormone (TSH) were determined by an enzyme linked immunosorbent assay (ELISA) using a Stratec Biomedical Gemini automated enzyme immunoassay analyzer (Stratec, Germany) and Vector-Best reagent kits (Russia). Ferritin was measured by ELISA using a Multiskan FC semi-automated analyzer (Thermo Scientific, USA) and Vector-Best reagent kits (Russia). To quantify vitamin D, serum total 25-OH vitamin D was determined using 25OH Vitamin D Total ELISA reagent kit (DRG, USA) designed to quantify 25-hydroxyvitamin D2 and D3 (25OH-D2 and 25OH-D3) in human serum samples by ELISA using the Stratec Biomedical Gemini automated analyzer (Stratec, Germany).

Criteria for health disorders. The criterion for abdominal obesity was the ratio of waist circumference to height of >0.5. Hypertension was defined as SAD ⩾130 mmHg and/or DBP ⩾85 mmHg and/or reported antihypertensive medication. Type 2 diabetes mellitus was defined as HbA_{1c} ⩾6.5% and/or reported antidiabetic medication and/or the reported diagnosed disease with the identified type. Dyslipidemia was determined as TH ⩾5.2 mmol/L, TG >1.7 mmol/L, and/or LDL >3.0 mmol/L and/or HDL <1.0 mmol/L for men or <1.2 mmol/L for women [19] and/or reported lipid-lowering medication. Thyroid dysfunction was defined as blood TSH outside the range of 0.3–4.0 mIU/mL and/or $_{T3}$ outside the range of 4.0–8.6 pmol/L, and/or $_{T4}$ outside the range of 10.3–24.5 pmol/L. Low blood iron concentration was defined as serum iron <9.0 mmol/L and/or ferritin <20 ng/mL for men or <10 ng/mL for women. Total protein level of <64 g/L was considered low. Vitamin D deficiency was determined at <30 ng/mL. Oncological diseases defined using medical history.

Subgroups

For the data analysis, the participants were divided by sex and categorized by age into the following six groups: participants aged 45–49 years (group 1), 50–54 (group 2), 55–59 (group 3), 60–64 (group 4), 65–69 (group 5), and 70–74 (group 6).

Statistical Analysis

Categorical variables are represented as absolute values (n) and percentages (%). The normal distribution of continuous quantitative variables was assessed visually and using asymmetry (skewness) and kurtosis (peakedness) tests. Based on the results, the quantitative variables were described as the median (Me) with the first and third quartiles (Q1–Q3). The groups were compared by categorical variales using the Pearson chi-square test (χ^2) and by quantitative criteria using the Mann–Whitney test.

The reference (normal) IOP values for the analyzed age group and subgroups were obtained based on the analysis of the examination results of individual participants' eyes and are presented in the range of the 5th–95th percentiles (P5–P95). To describe the reference IOP values and trends in IOP change with age, the means (M) and standard deviations (SD) are also presented. Differences in the IOP percentiles in male and female eyes without age subgrouping and in the matching age groups were assessed using quantile regressions. The trends in IOP changes in men and women with age were assessed using the Jonckheere–Terpstra test.

Multidimensional linear regression analysis was used to consistently assess the associations of IOP with socio-demographic characteristics and lifestyle factors (Stage 1) and with the health characteristics (Stage 2). At each stage, the obtained data were first adjusted by sex and age (Model 1) and then additionally adjusted by other variables assessed at the corresponding stage (Model 2) and variables with determined associations with IOP at the previous stage.

The regression analysis results are presented as regression coefficients B with 95% confidence intervals (CI) for binary independent variables, reflecting adjusted differences in IOP means in the corresponding groups. Additionally, standardized β-coefficients are shown to compare the strength of the associations between the analyzed parameters and IOP. Applicability of linear models was determined using distribution analysis of residuals.

The differences between the groups and the associations between the variables were considered statistically significant at $p < 0.05$. Statistical analysis was performed using Stata 18.0 (StataCorp, USA, Texas, College Station).

Ethics Approval

The study was approved by the Local Ethics Committee of the Northern State Medical University (Arkhangelsk) of the Ministry of Health of the Russian Federation (Protocol No. 03/04-23, April 26, 2023). All participants provided written informed consent voluntarily.

RESULTS

A total of 1223 residents of Arkhangelsk aged 45–74 years were examined; examination data of 1620 eyes (66.2%) out of 2446 were included in the analysis. The analysis excluded 413 participants with at least one eye meeting the exclusion criteria. Accordingly, the examination results of 826 eyes were excluded, as 596 of them had refractive error outside the acceptable range; 118 had an ocular condition (glaucoma, corneal, retinal, or choroidal abnormality, mature cataract); 54 had a history of keratorefractive surgery; 32 had best corrected visual acuity below 0.5; 20 had systemic diseases requiring glucocorticosteroid therapy; examination and IOP data were missing for 6 eyes.

After applying the exclusion criteria, 1024 female (512 women) and 596 male (298 men) eyes were included in the study. The analyzed female (Me 58, Q1–Q3: 51-65) and male (Me 58, Q1–Q3: 51–65) eyes had no significant age differences ($p = 0.295$). Age subgrouping was the following: 312 eyes in group 1 (45–49 years), 306 in group 2 (50–54), 280 in group 3 (55–59), 304 in group 4 (60–64), 224 in group 5 (65–69), 194 in group 6 (70–74).

Compared with women, more men were married (82.2% vs. 51.8%), smoked (27.5% vs. 11.3%), had higher hazardous drinking score (31.9% vs. 2.3%), or kept unhealthy diet (7.6% vs. 4.1%) (Table 1). Women were more likely to report financial difficulties compared with men (7.8% vs. 4.0%).

The IOP distribution of male and female eyes in the study population was similar to the Gaussian distribution (Fig. 1), but was slightly left-skewed (the asymmetry coefficient was 0.15 [p=0.039] for women and 0.22 [p=0.027] for men) and highly peaked (the coefficient of kurtosis was 2.45 [p <0.001] for women and 2.54 [$p < 0.001$] for men).

In the analyzed group of participants aged 45–74 years, mean IOP was 14.2 mmHg, 13.9 mmHg for men, 14.4 mmHg for women (Table 2). IOP median for the analyzed group and for men and women subgroups was 14.0 mmHg, the total range of the 5th–95th percentiles for men and women was 9–20 mmHg. However, P75, P90, and P95 values for female eyes (17.0, 19.0, and 20.0 mmHg) were higher than those for male eyes (16.0, 18.0, and 19.0 mmHg, respectively). In five-year age groups, IOP in female eyes compared with male eyes had higher P10–P50 values in the 44–49 years group and higher P5-P25 and P75 values in the 70–74 years group. At the age of 60–64 years, male eyes had higher P5 values, whereas female eyes had higher P25 values.

IOP values in women and men showed significant downward trends with the increasing age groups (Fig. 2).

The analysis of associations of IOP with socio-demographic characteristics and lifestyle factors with age and sex adjustment (Model 1) and with mutual adjustment of

Table 1. Socio-demographic and behavioral characteristics of study participants by sex

Specifications	All participants (n=810)	Women (n=512)	Men (n=298)	p*
	abs (%)			
Native resident of AO[1]	273 (33.7)	165 (32.2)	108 (36.2)	0.244
Higher education	320 (39.5)	199 (38.9)	121 (40.6)	0.626
Full or part-time employment	509 (62.8)	315 (61.5)	194 (65.1)	0.310
Married	510 (63.0)	265 (51.8)	245 (82.2)	<0.001
Financial constraints[2]	51 (6.3)	40 (7.8)	11 (4.0)	0.019
Smoking	140 (17.3)	58 (11.3)	82 (27.5)	<0.001
Hazardous drinking[3]	107 (13.2)	12 (2.3)	95 (31.9)	<0.001
Unhealthy diet[4]	42 (5.4)	20 (4.1)	22 (7.6)	0.034
Physical inactivity[5]	139 (17.2)	92 (18.0)	47 (15.6)	0.424

Notes: [1] At least two previous generations on the father's and mother's sides were born in the Arkhangelsk region; [2] The presence of financial difficulties when buying food or clothing. [3] ⩾8 points on the AUDIT test; [4] Determined using the Dietary Quality Score questionnaire; [5] Determined using the short version of the International Questionnaire for Determining Physical Activity (IPAQ). * Pearson's test χ^2.

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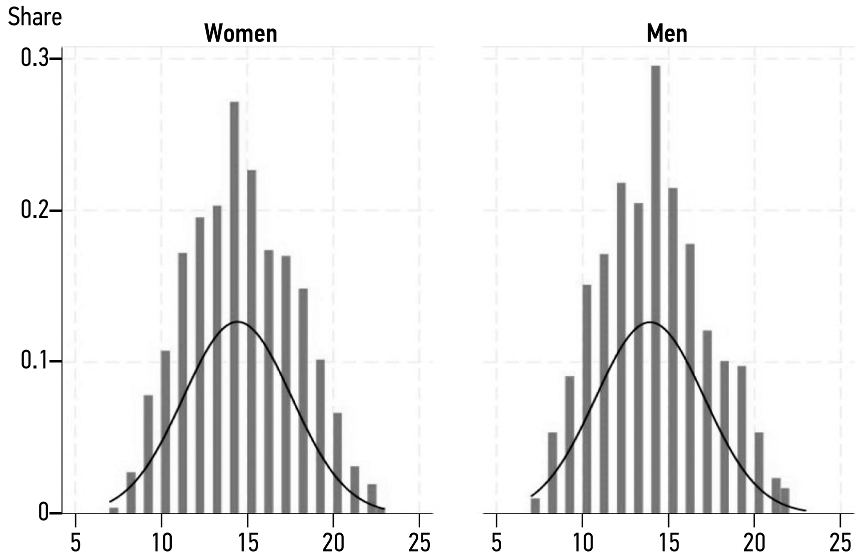

Fig. 1. Distribution of intraocular pressure values (mmHg) in male and female eyes, aged 45–74 years, residents of Arkhangelsk.

all analyzed parameters (Model 2) demonstrated that IOP decreased with age, was significantly lower in men compared with women, in the native residents of AR compared with non-native residents, and in participants with higher education compared with those without it (Table 3). Other socio-demographic characteristics and lifestyle factors had no significant associations with IOP. In Model 2, male sex (β=–0.085), age (β = –0.084), and indigenous status in AR (β=–0.074) had the strongest negative associations with IOP.

The analysis of associations of IOP with the general health characteristics (Table 4) adjusted for sex and age (Model 1) revealed that IOP was significantly higher in individuals with hypertension, diabetes mellitus, dyslipidemia, abdominal obesity, thyroid dysfunction, and vitamin D deficiency compared with those without these conditions. IOP was significantly lower in participants with low total protein, while oncological diseases and low blood iron had no association with IOP. With adjustment for all socio-demographic characteristics and lifestyle factors with significant associations with IOP presented in Table 3 and with all studied health characteristics included in the regression analysis (Model 2), the above associations between health characteristics and IOP were slightly weaker, but remained statistically significant. Vitamin D deficiency (β = 0.079) and hypertension (β=0.077) had the strongest associations with IOP in Model 2.

Table 2. Reference ranges of intraocular pressure (mmHg) in male and female eyes. age 45–74 years. residents of Arkhangelsk

Gender	Age, years	N	M	SD	P5	P10	P25	P50	P75	P90	P95
Both gender	40-74	1620	14.2	3.2	9.0	10.0	12.0	14.0	16.0	19.0	20.0
Womens	40-74	1024	14.4	3.2	9.0	10.0	12.0	14.0	17.0†	19.0†	20.0†
Mens	40-74	596	13.9	3.2	9.0	10.0	12.0	14.0	16.0†	18.0†	19.0†
Women	44-49	186	14.8	3.1	9.0	11.0†	13.0†	15.0†	17.0	19.0	20.0
	50-54	200	14.4	3.4	9.0	10.0	12.0	14.0	17.0	19.0	20.0
	55-59	182	14.7	2.9	10.0	11.0	13.0	14.0	17.0	18.0	19.0
	60-64	180	14.3	3.3	9.0†	10.0	12.0†	14.0	16.0	19.0	20.0
	65-69	138	14.3	3.2	9.0	10.0	12.0	14.0	16.0	19.0	20.0
	70-74	138	13.9	3.0	10.0†	11.0†	12.0†	13.0	17.0†	18.0	19.0
Men	44-49	126	14.0	3.2	10.0	10.0†	11.0†	14.0†	16.0	19.0	20.0
	50-54	106	14.3	3.3	9.0	10.0	12.0	14.0	17.0	19.0	19.0
	55-59	98	14.2	2.8	9.0	11.0	13.0	14.0	16.0	18.0	19.0
	60-64	124	14.1	3.1	10.0†	10.0	11.0†	14.0	16.0	18.0	20.0
	65-69	86	13.3	3.3	8.0	9.0	11.0	13.0	15.0	18.0	20.0
	70-74	56	12.9	3.0	8.0†	9.0†	10.5†	13.0	15.0†	16.0	19.0

Notes: † Significant differences (p <0.050) in percentile values between men and women of the corresponding age.

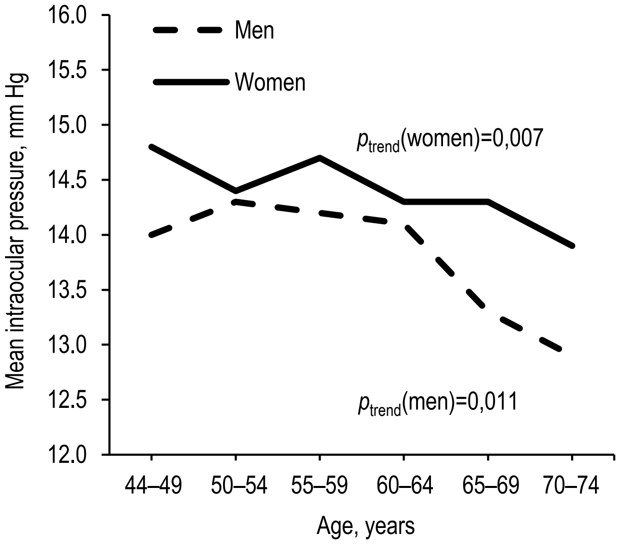

Fig. 2. Mean intraocular pressure in men and women across 5-year age groups within the 45–74-year range, residents of Arkhangelsk (1552 eyes).

DISCUSSION

The Federal Clinical Guidelines on primary open-angle glaucoma[2] state that true IOP of up to 21 mmHg is considered the upper limit of normal. The national guidelines provide the following three ranges of normal for IOP determined using tonometry: low norm of 15–18 mmHg, medium norm of 19–22 mmHg, and high norm of 23–25 mmHg [3]. Our study showed that IOP normal ranges for Arkhangelsk residents aged 45–74 years, defined by the 5th–95th IOP percentile range, was 9–20 mmHg, the low norm (5th–25th percentile) was 9–12 mmHg, the medium norm (25th–75th percentile) was 12–16 mmHg, and the high norm (75th–95th percentile) was 16–20 mmHg. Therefore, our empirical upper limit of normal for residents of the European North of Russia aged 45–74 years corresponds to the current clinical guidelines, whereas the ranges of low, medium, and high norms are lower than those suggested in the clinical guidelines.

As mentioned above, prior population-based studies in the Volga region using the Maklakov tonometer have demonstrated higher IOP compared with our results [20–24]. In our study, mean IOP values are 2 mmHg lower than those obtained by Egorov et al. in Central Russia, Belarus, Ukraine, Moldova, Tajikistan, and Kazakhstan [25, 26]. This may be explained by age differences between the study samples. In addition, our study did not include patients with early glaucoma, which affected the results obtained. Also, the authors in other studies used tonometry method, which overestimates aqueous pressure on the eye membranes compared with true IOP in our study measured using pneumotonometry [27].

[2] Clinical guidelines on primary open-angle glaucoma (approved by the Ministry of Health of the Russian Federation, 2024). Age group: adults. Available at: https://legalacts.ru/doc/klinicheskie-rekomendatsii-glaukoma-pervichnaja-otkrytougolnaja-odobreny-minzdravom-rossii/ Accessed on: February 26, 2025.

Mean IOP in our study is lower than in studies conducted in the South Chinese population, in Barbados, the USA and the UK [9, 28–30], but higher compared with the results of population-based studies performed in Bashkortostan, Iran, South Korea, Central Australia, and Taiwan [11, 12, 31–34]. This confirms the association of IOP with race and ethnicity. Moreover, we found that native residents of the Arkhangelsk region, who had at least two previous generations on their father's and mother's sides born in the region, had lower IOP compared with non-native residents. This indicates a genetic cause of decreased IOP, which may be explained by adaptation to uncomfortable climatic and geographical conditions of the North. Several authors believe that IOP is affected not only by climatic conditions, such as the average annual temperature, sunlight, humidity, wind speed, and trace elements in soil and water, but also by anatomical features of the eye in certain races and ethnicities [35–37].

Our study demonstrates a negative association of IOP with age. Publications show various age-related trends in IOP. Some large population-based studies among the American and African populations revealed a positive correlation of IOP and age [9, 29, 38]. However, studies performed in Asia show a reverse association [14, 28–30]. IOP decrease with age may be associated with a lower body mass index (BMI) and blood pressure in the old and advanced age [31]. It is known that obesity and uncontrolled hypertension are risk factors for cardiovascular death [39]. For this reason, there are fewer people with increased BMI and BP in the elderly and geriatric group, and the survivors in these groups may have lower IOP [12, 13, 29].

Our study showed that IOP was lower in men than in women, and this difference preserved when adjusted for age and other factors. Considering the age of the participants, this result can be explained by an increase in aqueous production in menopausal women associated with hormonal status [29, 32, 40, 41]. Previous studies provided contradictory data on the association between IOP and sex. IOP was higher in men in some population studies [28, 42] and in women in others [31, 43, 44]. This may be explained by the heterogeneous age and ethnicity of the analyzed samples, which, as shown above, is associated with IOP and may change the relationship between IOP and sex.

With adjustments for age and sex, our study demonstrated positive associations of IOP with hypertension, type 2 diabetes mellitus, abdominal obesity, and dyslipidemia. The revealed association of hypertension with relatively higher IOP is consistent with the results of several other studies [45–48]. It is explained by an increase in the aqueous production caused by accelerated ultrafiltration as BP elevates [12]. Other studies have found a positive association between obesity and IOP [9, 13, 29]. Abdominal obesity, type 2 diabetes mellitus, hypertension, and dyslipidemia are medical conditions sharing similar pathogenetic links based on insulin resistance, which reduces glucose utilization in tissues and thereby increases insulin secretion, resulting

Table 3. Association of intraocular pressure with socio-demographic characteristics and lifestyle factors in residents of Arkhangelsk aged 45–74 years (1552 eyes)

Specifications	Model 1ª	Model 2⁶		
	B (95% CI)	B (95% CI)	Standard coefficient β	*p*
Socio-demographic characteristics				
Age, years	–0.03 (–0.05; –0.01)	–0.03 (–0.06; –0.01)	–0.084	0.009
Gender, men	–0.53 (–0.85; –0.22)	–0.56 (–0.94; –0.18)	–0.085	0.004
Native resident of AO[1]	–0.47 (–0.80; –0.15)	–0.50 (–0.83; –0.16)	–0.074	0.003
Higher education	–0.39 (–0.71; –0.07)	–0.40 (–0.73; –0.06)	–0.061	0.020
Full or part-time employment	–0.00 (–0.39; 0.39)	0.07 (–0.34; 0.47)	0.010	0.750
Married	0.11 (–0.23; 0.44)	0.04 (–0.31; 0.39)	0.006	0.817
Financial constraints[2]	0.54 (–0.09; 1.18)	0.39 (–0.28; 1.06)	0.030	0.252
Lifestyle factors				
Smoking	0.14 (–0.28; 0.56)	–0.02 (–0.47; 0.44)	–0.002	0.935
Hazardous drinking[3]	0.11 (–0.40; 0.61)	0.08 (–0.44; 0.61)	0.009	0.752
Unhealthy diet[4]	0.40 (–0.30; 1.10)	0.26 (–0.45; 0.97)	0.018	0.473
Physical inactivity[5]	0.33 (–0.08; 0.75)	0.42 (–0.01; 0.86)	0.050	0.056

Notes: Model 1 – correction for gender and age (for age — only for gender, for gender — only for age); Model 2 — correction for all variables presented in the table. [1] At least two previous generations on the father's and mother's sides were born in the Arkhangelsk region; [2] The presence of financial difficulties when buying food or clothing; [3] ⩾8 points on the AUDIT test; [4] Determined using the Dietary Quality Score questionnaire; [5] Determined using a short version of the international questionnaire to determine physical Activity (IPAQ).

Table 4. Association of intraocular pressure with general health characteristics in residents of Arkhangelsk aged 45–74 years (1618 eyes)

Specifications	Model 1ª	Model 2⁶		
	B (95% CI)	B (95% CI)	Standard coefficient β	*p*
Arterial hypertension [1]	0.89 (0.52; 1.26)	0.56 (0.17; 0.94)	0.077	0.005
Diabetes mellitus 2[2]	0.65 (0.22; 1.07)	0.46 (0.03; 0.89)	0.054	0.035
Dyslipidemia [3]	0.44 (0.10; 0.78)	0.36 (0.01; 0.71)	0.051	0.041
Abdominal obesity [4]	0.64 (0.31; 0.98)	0.39 (0.04; 0.75)	0.059	0.027
Thyroid dysfunction [5]	0.44 (0.08; 0.80)	0.42 (0.07; 0.77)	0.057	0.019
Oncological diseases [6]	0.26 (–0.35; 0.87)	0.25 (–0.35; 0.85)	0.020	0.412
Low blood iron levels [7]	–0.26 (–0.88; 0.35)	–0.19 (–0.80; 0.42)	–0.015	0.543
Low levels of total protein in the blood [8]	–1.01 (–1.68; –0.33)	–0.76 (–1.43; –0.09)	–0.056	0.026
Vitamin D deficiency [9]	0.84 (0.37; 1.30)	0.76 (0.30; 1.22)	0.079	0.001

Notes: Model 1 is a correction for gender and age; Model 2 is a correction for all variables that had significant associations with IOP according to Table 3, and all variables presented in this table. [1]CAP ⩾130 mmHg, DBP ⩾85 mmHg and/ or a report on taking antihypertensive drugs; [2]HbA1c ⩾6.5% and/or a report on taking antidiabetic drugs and/or a report on the presence of a diagnosis indicating the type of diabetes; [3]OX ⩾5.2 mmol/L, triglycerides >1.7 mmol/L and/or LDL >3.0 mmol/L and/or HDL <1.0 mmol/L for men or <1.2 mmol/L for women and/or a message about taking lipid-lowering medications; [4] Ratio of waist circumference to height >0.5; [5]THG outside range 0.3–4.0 mIU/ml and/or T3 outside the range 4.0–8.6 pmol/L and/or T4 outside the range 10.3–24.5 pmol/L; [6] According to medical history; [7] serum iron <9.0 mmol/L and/or ferritin <20 ng/ml for men or <10 ng/ml for women; [8] total protein <64 g/l; 9 vitamin D <30 ng/ml.

in hyperinsulinemia and activation of the sympathoadrenal and renin-angiotensin-aldosterone systems (RAAS) [49–51]. There is a known local system of RAAS components, including in various ocular structures, which help regulate aqueous production [52, 53]. The RAAS increases retinal blood flow and pressure in retinal capillaries, thus elevating IOP [54].

Our study demonstrates the association of thyroid dysfunction with increased IOP. However, this has no unequivocal evidence in the available publications, some of which suggest that IOP is associated with endocrine disorders [55–58], and others deny it [59, 60]. This relationship may be typical only for the study population with the higher prevalence of thyroid disorders than in other regions of Russia [61]. The mechanism of an IOP increase in individuals with thyroid dysfunction is not fully understood and should be further studied. High TSH concentrations in patients with hypothyroidism stimulate the production of glycosaminoglycans. They are a part of the trabecular meshwork, extracellular matrix of the optic disc, and lamina cribrosa. Excessive levels of mucopolysaccharides (glycosaminoglycans) in the trabecular meshwork increase the resistance to the aqueous outflow and increase IOP [62]. When thyroid dysfunction is caused by an autoimmune disease, excessive production of autoantibodies to glycosaminoglycans of the trabecular meshwork leads to dysfunction of the latter and increases IOP [63].

We have identified a significant association of elevated IOP with vitamin D deficiency, which is typical for residents of northern regions. These results are comparable with those obtained in other studies [64–66]. Vitamin D is known to be actively involved not only in calcium and phosphate metabolism, but also has many other pleiotropic effects, including the effect on differentiation and apoptosis of eye tissues [67–69]. There are several studies confirming the presence of vitamin D receptors in the eye tissues [70, 71]. Some data show that vitamin D receptors are present in the cells of the corneal endothelium and non-pigmented ciliary epithelium, which contribute the most to the aqueous production [72]. Given this information, vitamin D deficiency may be assumed to negatively affect the function of the eye structures directly involved in the aqueous production, which disrupts the eye hydrodynamics and increases IOP [72–74].

A major strength of our study is examination of a random sample of Arkhangelsk residents aged 45–74 years. As Arkhangelsk is located in the European North of Russia and the Arctic zone, the reference IOP values obtained in this study may be applicable to residents of these regions. Another strength of this study is the statistical power because of the relatively large sample size.

Study Limitations

The study's disadvantage is its cross-sectional design, which limits the determination of the causality of the revealed associations. The study is also constrained by the lack of data on central corneal thickness, which could affect IOP. Data on socio-demographic characteristics, lifestyle, and some health characteristics were reported by the respondents and could be subject to recall or reporting bias. The total number of examined participants (n = 1223) was 61.3% of the total number of invited (n = 1996), which could be a selection bias if the distribution of the studied parameters among the enrolled participants differed from that among those who refused to participate in the study. The sample was limited to urban residents of one region aged 45–74 years, which may hinder the extrapolation to the general population of the European North of Russia including a significant number of rural residents.

CONCLUSION

The study has determined the normal IOP range of 9–20 mmHg for residents of the European North of Russia aged 45–74 years. The low norm is defined as the range 9–12 mmHg, the medium norm is 12–16 mmHg, the high norm is 16–20 mmHg. The trends of an IOP decrease with age in men and women have been revealed. Low IOP was associated with male sex, being the native residents of the Arkhangelsk region, low blood total protein, while the increased IOP was associated with hypertension, diabetes mellitus, dyslipidemia, obesity, thyroid dysfunction, and vitamin D deficiency.

ADDITIONAL INFORMATION

Author contributions: M.A. Sinayskaya: conceptualization, writing—original draft, writing—review & editing; R.N. Zelentsov: conceptualization, investigation, writing—original draft; N.A. Bebyakova: conceptualization, writing—review & editing; N.I. Pechinkina: investigation, writing—review & editing; A.A. Trofimova: writing—review & editing; A.V. Kudryavtsev: conceptualization, formal analysis, funding acquisition, project administration, resources, writing—review & editing. All the authors approved the version of the manuscript to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Ethics approval: The Study Protocol was approved by the Local Ethics Committee of the Northern State Medical University, Ministry of Health of the Russian Federation (Arkhangelsk, Protocol No. 03/04-23 dated April 26, 2023). All participants provided written informed consent prior to enrollment in the study.
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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов: М.А. Синайская — определение концепции, написание черновика рукописи, пересмотр и редактирование рукописи; Р.Н. Зеленцов — определение концепции, проведение исследования, написание черновика рукописи; Н.А. Бебякова — определение концепции, пересмотр и редактирование рукописи; Н.И. Печинкина — проведение исследования, пересмотр и редактирование рукописи; А.А. Трофимова — пересмотр и редактирование рукописи; А.В. Кудрявцев — определение концепции, анализ данных, привлечение финансирования, обеспечение исследования, администрирование проекта, пересмотр и редактирование рукописи. Все авторы одобрили рукопись (версию для публикации), а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой её части.

Этическая экспертиза. Протокол исследования одобрен Локальным этическим комитетом ФГБОУ ВО СГМУ Минздрава России (г. Архангельск, протокол № 03/04-23 от 26.04.2023). Все участники исследования добровольно подписали форму информированного согласия до включения в исследование.

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Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные).

Доступ к данным. Анонимизированные данные, представленные в настоящей статье, доступны по аргументированному запросу к авторскому коллективу.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали два внешних рецензента, член редакционной коллегии и научный редактор издания.

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