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Ethnicity as a model for the development of cardiovascular diseases and their risk factors in epidemiological studies

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Abstract

Aim. To assess the indigenous small population of the Shor people in terms of the ethnic-specific development of cardiovascular diseases and their risk factors during the epidemiological studies in the Mountain Shoria.

Methods. The study was carried included the indigenous and non-indigenous population of the Mountain Shoria during two different time periods: the first period (1998–2002) — 1215 people (550 indigenous Shors and 665 non-indigenous people) and the second period (2013–2017) — 1409 people (901 and 508, respectively). The prevalence of cardiovascular risk factors, arterial hypertension (AH) and ischemic heart disease (CHD) was studied. In the second period of the study, the genotype frequencies of the genes *ACE* (I/D, r 4340), *AGT* (c.803T>C, rs699), *AGTR1* (A1166C, rs5186), *ADRB1* (c.145A>G, Ser49Gly, rs1801252), *ADRA2B* (I/D, rs28365031), *MTHFR* (c.677C>T, Ala222Val, rs1801133) and *NOS3* (VNTR, 4b/4a) and their associations with arterial hypertension were identified. There was data on organ damage obtained among patients with high blood pressure (left ventricular myocardial hypertrophia, carotid arteries intima-media complex thickening, albumin level).

Results. The first period of the studies showed that the Shors differed from the incoming population in an extremely low prevalence of lipid metabolism disorders, obesity, and an almost complete absence of diabetes mellitus. At the same time, there was a high prevalence of tobacco smoking and alcohol consumption. The second period of the studies demonstrated significant differences between different ethnic cohorts according to the "genetic passport" towards a more favorable profile among the indigenous people. However, the Shor people with arterial hypertension had a more severe course of hypertensive disease, defined as frequent organ damage. In addition, the "profile" of a patient with coronary heart disease differed depending on the place of residence, in urban or rural. Epidemiological studies contribute to the acquisition of new knowledge about different ethnic groups, their lifestyles and agricultural practices, regions of residence, and the features of candidate gene polymorphism. This provides valuable material for individualizing the prevention and treatment of diseases.

Conclusion. Ethnicity makes adjustments to the patient's profile; understanding the ethnic specificity allows developing targeted preventive measures, thereby preserving the people's health.

Keywords: ethnic group, epidemiological studies, cardiovascular risk factors, target organ damage, polymorphism of candidate genes.

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Background. In the late XX and early XXI centuries, the identification and correction of the diseases of circulatory system qualitatively reached a new level. However, cardiovascular diseases (CVD) continue to rank first globally among the causes of death [1]. The major role in the development and progression of the CVD is assigned to risk factors (RF). One of the main RFs for the development of CV complications is arterial hypertension (AH) which ranks first in terms of its contribution to mortality and disability in the Russian population [2].

Currently, epidemiological studies provide objective information about the causes of the CVD. A survey at the level of population groups reveals a real picture of the prevalence of diseases and their

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RFs, which enables to establish the obvious aspects of the influence of social and natural conditions, and most importantly, to identify cause-and-effect relationships in the development and manifestation of the diseases. Epidemiological research may provide essential information to improve the public health. And since contemporary medicine is, first, patient-oriented, and its main task is to increase the life expectancy and improvement of its quality, epidemiological research makes a significant contribution to its solution.

Individualization of approaches in predicting the complications from the diseases of the circulatory system in real clinical practice is not possible without considering the specific characteristics of a particular patient, including those related to the ethnicity [3]. Ethnicity largely determines the behavioral stereotypes and food preferences. Many of the smaller ethnic groups often live for centuries under specific conditions of climate, air, and geographical latitude. [4].

In this regard, it may be assumed that in different ethnic groups, traditional CVD RFs may have a different distribution, and as a result, value in the disease prevention. Based on this, it could be quite convincing to state that ethnos is a model for the formation of CVDs and their RFs in the epidemiological studies.

Shors, Teleuts, and Kalmaks are considered the most numerous populations among the small indigenous peoples of the Kemerovo region. The Shors are the most representative ethnic group among the small peoples, they belong to the Mongoloid race of the South Siberian type, and their traditional way of life is hunting, harvesting berries, mushrooms, and plants. As early as the XVII century, separate Shor ethnographic groups were appeared, and already in the Soviet period, a single Shor ethnos with its own national and cultural specifics was formed. Today in the Russian Federation, the number of this Turkic-speaking people is about 14 thousand, and about 10.5 thousand people in the Kemerovo region.

It should be noted that the level of CV risk in the different ethnic groups, as a rule, differs. Moreover, there is enough information in the literature that the well-known parameters do not enable to understand the patient completely, since the manifestations of RF largely depend on the time of their influence, the intensity of their influence, and the genetic characteristics of the person [5, 6]. Genetic prerequisites that ensure the unequal susceptibility of the respondents to the effects of RF, and the specificity of the morbidity are also universal for the people of certain nations. In addition, the incidence of genetic factors in a particular disease of the circulatory system is closely related to the specific characteristics of the population and the ethnic group, which determines the distribution of the allelic gene polymorphism and differences between the races [5]. The genetic predisposition to CVD could be assessed long before the appearance of the clinical presentation and symptoms of the disease, which contributes to the timely implementation of the preventive measures, and the postponement of its manifestation.

The study aimed to assess the indigenous small population of Shors from the standpoint of the ethnic individuality of the development of CVDs and their RFs, during an epidemiological study in the mountain called Shoriya.

Materials and methods of research. In Mountain Shoriya, located in the south of the Kemerovo region, a clinical and epidemiological single-center single-stage comparative study was performed in a 15-year time interval. The indigenous (Shors) and non-indigenous (95% of them Russians) adults were included by the continuous method. The study was conducted over two time periods. The period-1 (1998–2002) included an examination of the rural residents, a total of 1,215 people (550 Shors and 665 representatives of non-indigenous ethnicity). The period-2 (2013–2017) included an examination of the rural and urban residents, a total of 1,409 people (901 Shors, 508 non-indigenous residents).

The national groups included in the study were comparable in gender and the age. In both ethnic cohorts, the proportion of the surveyed male and female population did not differ significantly, and amounted to 31.5% of the Shor men and 30.1% of non-indigenous men ($p = 0.585$), as well as 68.5% of Shor women and 69.9% of non-indigenous women ($p = 0.585$). Each participant invited to the examination signed an informed consent and received his/her own number in the study, which was approved by the Ethics Committee of the Research Institute for Complex Problems of CVD (Kemerovo; protocol No. 10 dated 06/10/2015).

All the people included in the study underwent a clinical examination with an assessment of the history, complaints, and the objective status. Blood pressure (BP) and anthropometric parameters (height, body weight, and waist circumference) were measured. During the period-1 of the study, BP was assessed according to the recommendations of the WHO[1]/ISH[2] (1999), and according to the methodology of the WHO/RMSAH[1] (2010)

[1] WHO — World Health Organization.

[2] ISH — International Society of Hypertension.

[3] RMSAH — Russian Medical Society for Arterial Hypertension.

during the period-2. In both periods, the criteria for diagnosing the AH was by observing the level of systolic BP of 140 mm Hg., and higher, diastolic BP of 90 mm Hg and higher, and/or by taking the antihypertensive drugs, the criterion for obesity was a body mass index of 30.0 kg/m^2 and above. In 1998–2002, abdominal obesity was diagnosed by the waist-hip index (>0.90 for men, >0.85 for women), in 2013–2017, it was diagnosed by the waist circumference (≥102 cm for men, ≥ 88 cm for women). The main components of the metabolic syndrome were interpreted according to the criteria of the WHO (1999) and the International Diabetes Federation (2005).

Alcohol consumption was assessed in all the patients included in the study by the frequency, volume, and the type of alcoholic beverages consumed. People who took more than 12 g of ethanol per day (women) and 24 g of ethanol per day (men) were classified as alcohol abusers. People who smoked at least one cigarette a day were smokers.

In the morning in fasting blood was taken from all the patients examined for further biochemical studies. After centrifugation of the blood, the serum was frozen, and stored at a negative temperature.

In the period-1, laboratory tests were used to determine lipid profile (total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, and triglycerides), fasting plasma glucose, and after exercise, the polymorphism of the *apolipoprotein-E* gene.

In the period-2, in addition to the activities performed in the period-1, nitrogenous slags, cystatin C, urine albumin, and gene polymorphism *ACE* (I/D, rs4340), *AGT* (c.803T>C, rs699), $AGTR_1$ (A1166C, rs5186), $ADRB_1$ (c.145A>G, Ser49Gly, rs1801252), $ADRA_2B$ (I/D, rs28365031), *MTHFR* (c.677C>T, Ala222Val, rs1801133), and NOS_3 (VNTR, 4b/4a) were determined. These polymorphisms were tested in a real time using the TaqMan technology with the use of polymerase chain reaction. To assess the renal function, the glomerular filtration rate (GFR) was calculated using the CKD-EPI (chronic kidney disease epidemiology collaboration) equation. Renal dysfunction was diagnosed at a GFR standardized to the body surface area < 90 ml/min/1.73 m^2.

An electrocardiogram (ECG) was recorded on the SCHILLER A6 AT-6 electrocardiograph in 1998–2002 studies; and the SCHILLER CARDIOVIT AT-2 electrocardiograph was used in 2013–2017 to record ECG in 12 leads, with a tape speed of 25 mm/s. ECG analysis of all the study participants was performed using the Minnesota Code.

The diagnosis of coronary heart disease (CHD) was established if the respondent had one of three epidemiological criteria, namely "definite" and "possible" CHD according to the Minnesota code, CHD according to the Rose questionnaire, and a history of myocardial infarction.

In the period-2, all the patients, in addition to the ECG recording, underwent echocardiography, and color duplex scanning of the extracranial sections of the brachiocephalic arteries. The left ventricular myocardial mass index, and the thickness of the intima-media complex of the carotid artery wall were evaluated. According to the RMSAH recommendations (2013), the criteria for left ventricular myocardial hypertrophy were the left ventricular myocardial mass index > 115 g/m^2 in men and >95 g/m^2 in women; and thickening of the intima-media complex was the size of the vessel wall of 0.9 mm or greater and/or the presence of a plaque.

The results were processed using the statistical package Statistica 6.0 (StatSoft Inc., USA). The Kolmogorov–Smirnov test was used to test the normal distribution of the sample. Using the descriptive statistics, quantitative variables were presented as mean and standard deviation (M ± SD); qualitative variables were summarized in contingency tables. When comparing the quantitative indicators, Student's t-test for unrelated samples (parametric) and Mann–Whitney test (nonparametric) were used; and Pearson's χ^2 test was used when comparing the qualitative parameters.

Using the multivariate analysis, the associations of candidate gene polymorphisms with AH were established. To eliminate the possible modifying effect, the variables "age" and "gender" were introduced. The odds ratio (OR) and 95% confidence interval (CI) were assessed in five inheritance models (codominant, dominant, recessive, over-dominant, and log-additive). The critical level of significance was taken $p < 0.05$ when testing the statistical hypotheses in the study.

Results. The period-1 of the epidemiological study in the Mountain Shoriya demonstrated the prevalence of AH in the indigenous population at the level of 47.4% (53.6% in women and 40.6% in men), which was higher than in Russia at that time, according to the S.A. Shalnova (2006) [6], namely 40.1% (41.1% among women and 39.2% among men). CHD was registered in this population in 6.2% of the cases (5.2% among women and 7.3% among men), while in the Russian Federation, its prevalence was 13.5% (13.0% among women and 14.3% among men) [7].

A study conducted 15 years ago showed that the Shors differed from the non-indigenous population in a lower frequency of various disorders of lipid

metabolism (10.6% vs. 24.5% among women, 3.2% vs. 5.5% among men), obesity (13.3% vs. 44.4% among women, 3.4% vs. 5.3% among men), including the abdominal type (14.3% vs. 54.5% among women, 4.4% vs. 9.5% among men), and almost complete absence of diabetes mellitus (0.5% vs. 6.5% among women, 0.3% vs. 5.8% among men). At the same time, a high frequency of smoking and alcohol abuse was noted.

In the period 1998−2002, the frequencies of the genotypes of the *apolipoprotein-E* gene were determined in the indigenous people. It was revealed that the most widespread was the *E3/E3* genotype, which was found in more than half of the people examined. Allele $ApoE_2$ within different genotypes ($ApoE_2/_4$, $ApoE_2/_3$) was detected in 15% of Shors. Allele $ApoE_4$ in different genotypes ($ApoE_2/_4$, $ApoE_3/_4$, and $ApoE_4/_4$) was registered in 34.6% of the cases. The levels of total cholesterol, low density lipoprotein cholesterol, and atherogenic index were higher in carriers of the $ApoE_4/_4$ genotype compared to $ApoE_3/_3$ (7.84 mmol/L vs. 4.71 mmol/L; 5.89 mmol/L vs. 2.76 mmol/l, and 5.62 vs. 2.47, respectively), which is consistent with the literature data regarding the effect of this genotype on the risk of atherosclerosis.

In the recent decades, the living conditions of the population of the Mountain Shoriya have changed significantly. The Shors abandoned their national eating habits, methods of obtaining food, and reduced physical activity, which affected the state of health of the circulatory system organs. In this regard, we studied changes in the incidence and severity of CV RF in representatives of the indigenous and non-indigenous ethnic group over a time.

During the period analyzed (from 1998–2002 to 2013–2017), the residents of the Mountain Shoriya experienced the unfavorable changes in the incidence of the main RFs, expressed in changes in body mass index indicators, deterioration of the metabolic indicators. For 15 years, indigenous women had negative dynamics in the lipid metabolism and body mass index. In both women and men in all the age groups, the level of fasting glycemia and the index of waist/hip circumference increased.

During the period analyzed, representatives of non-indigenous nationas experienced the similar unfavorable changes, noted to a greater extent in women than in men. Metabolic syndrome in 2013–2017 was established in 40.2% of the cases, namely 12.4% among male Shors and 47.8% among male representatives of a non-indigenous ethnic group ($p = 0.0001$); and among 36.8% and 60.7% women, respectively ($p = 0.0001$).

In the both ethnic cohorts, the following combinations were the most frequent manifestations of the metabolic syndrome:

a) abdominal obesity, AH, pathology of carbohydrate metabolism.

b) abdominal obesity, pathology of carbohydrate metabolism, AH, low level of high density lipoprotein cholesterol.

A high frequency of smoking was registered in the population of this region, namely in female population, in 27.7% of the cases among the indigenous ethnic group and in 31.3% of the cases among the non-indigenous ethnic group ($p = 0.625$); and in 46.1% and 50.7% of the cases of the male population, respectively ($p = 0.435$). At the same time, the proportion of the smokers among women in both national groups during the analyzed time increased to 44.3% among the female Shors and 39.5% among women of the non-indigenous ethnicity.

The period-2 of the epidemiological study in the Mountain Shoriya showed a comparable incidence of AH among Shors and representatives of the non-indigenous ethnic group, namely 40.7% and 45.3% ($p = 0.098$). However, among men, increased BP was less common among the indigenous people (34.9%) compared with the non-indigenous people (44.4%, $p = 0.049$). The proportion of people with various modifiable RFs was lower among the Shors than the non-indigenous people (Table 1).

A similar pattern was noted in relation to the renal dysfunction, which was less common among the Shors, namely 13.7% vs. 34.6% ($p = 0.0001$). In this category of patients, albuminuria was detected in 15.9% of the indigenous and 32.5% of the non-indigenous patients examined ($p = 0.0001$), and cystatin C was revealed in 86.7% and 81.2% of cases ($p = 0.182$), respectively.

A rather important aspect of the stage-2 of the study should be emphasized, as significant differences were found between the ethnic cohorts according to the "genetic passport" (Fig. 1).

The genotypes known in the literature as minor, or prognostically unfavorable, were less common in the Shor group. Thus, the frequencies of the mutant genotypes' D/D rs4340 of the *ACE* gene, C/C rs5186 of the $AGTR_1$ gene, T/T rs1801133 of the *MTHFR* gene, 4a/4a VNTR of the NOS_3 gene, and A/A rs1801252 of the $ADRB_1$ gene were found to be lower in indigenous representatives compared with the non-indigenous ones.

Carriage of the C/C genotype of the $AGTR_1$ gene determined a high risk of developing the AH according to the recessive mode of inheritance in both Shors (OR 10.02; 95% CI 1.08–93.36; $p = 0.017$) and non-indigenous people (OR 26, 77;

Table 1. Prevalence of cardiovascular risk factors in the population of the Mountain Shoriya, taking into account ethnicity (period-2 of the study).

Risk factors	Indigenous population			Non-indigenous population			p
	Number of patients examined	Incidence of risk factors		Number of patients examined	Incidence of risk factors		
		n	%		n	%	
Male gender	901	284	31.5	508	153	30.1	0.585
Age (≥ 55 years in men)	284	99	34.9	153	67	43.8	0.067
Age (≥ 65 years in men)	617	82	13.3	355	60	16.9	0.125
Family history of early CVD	901	295	32.7	508	215	42.3	0.0003
Smoking	901	296	32.9	508	166	32.7	0.946
HCS	767	473	61.7	423	290	68.6	0.018
↑ LDL-CS	629	316	50.2	343	207	60.4	0.003
↓ HDL-CS	625	154	24.6	340	135	39.7	0.0001
HTG	768	202	26.3	424	188	44.3	0.0001
DLP	768	561	73.1	424	352	83.0	0.0001
↑ Fasting plasma glucose	652	97	14.9	375	65	17.3	0.299
IGT	652	27	4.1	375	24	6.4	0.109
Obesity	901	162	18.0	508	195	38.4	0.0001
Abdominal obesity	901	238	26.4	508	217	42.7	0.0001

Notes: CVD — cardiovascular disease; HCS — hypercholesterolemia; LDL-CS — low density lipoprotein cholesterol; HDL-CS — high density lipoprotein cholesterol; HTG — hypertriglyceridemia; DLP — dyslipidemia; IGT — impaired glucose tolerance.

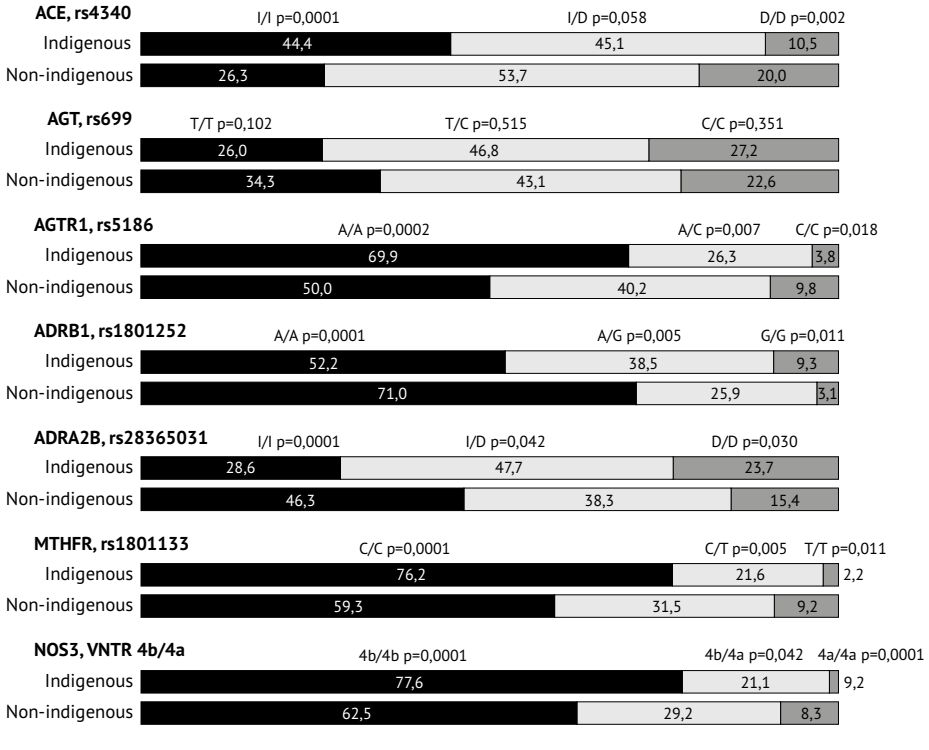

Fig. 1. Frequency of genotypes of candidate genes for arterial hypertension in the population of Mountain Shoriya, depending on the ethnicity.

Table 2. Characteristics of patients with coronary heart disease among the indigenous population of Mountain Shoriya, depending on the place of residence.

Risk factor	Urban population	Rural population	p
Age, years, M±SD	63.7±11.9	72.5±10.5	0.002
Male gender, n (%)	12 (36.4)	9 (24.3)	0.273
Female gender, n (%)	21 (63.6)	28 (75.7)	0.273
Smoking, n (%)	11 (33.3)	8 (21.6)	0.271
BMI, kg/m^2, M±SD	27.4±5.9	23.5±2.8	0.0005
BMI ≥30 kg/m^2, n (%)	10 (30.3)	2 (5.4)	0.006
WC, cm, M±SD	90.9±12.9	78.0±10.4	0.0001
WC ≥80 cm in women and ≥94 cm in men, n (%)	21 (63.6)	7 (18.9)	0.0001
SBP, mm Hg, M±SD	158.5±24.6	168.8±30.4	0.126
DBP, mm Hg, M±SD	91.7±9.9	85.6±10.2	0.013
Arterial hypertension, n (%)	30 (90.9)	35 (94.6)	0.550
Glucose level, mmol/l, M±SD	5.6±1.6	6.2±1.5	0.211
Impaired fasting glucose, n (%)	3 (11.5)	1 (3.2)	0.221
Impaired glucose tolerance, n (%)	0 (0)	2 (6.5)	0.187
Type-2 diabetes mellitus, n (%)	4 (15.4)	13 (41.9)	0.029
TC, mmol/L, M±SD	5.6±0.9	6.2±1.2	0.047
TC > 5.0 mmol/L, n (%)	24 (75.0)	30 (83.3)	0.398
LDL-CS, mmol/L, M±SD	3.7±0.9	3.3±0.8	0.271
LDL-CS > 3.0 mmol/L, n (%)	20 (69.0)	9 (69.2)	0.986
HDL-CS, mmol/L, M±SD	1.4±0.3	1.6±0.4	0.243
HDL-CS < 1.2 mmol/L in women and <1.0 mmol/L in men, n (%)	7 (24.1)	2 (15.4)	0.523
TG, mmol/L, M±SD	1.7±1.4	1.5±0.7	0.550
TG > 1.7 mmol/L, n (%)	11 (34.4)	5 (13.9)	0.047

Notes: BMI — body mass index; WC — waist circumference; SBP — systolic blood pressure; DBP — diastolic blood pressure; TC — total cholesterol; LDL-CS — low density lipoprotein cholesterol; HDL-CS — high density lipoprotein cholesterol; TG — triglycerides.

95% CI 2.14–334.52; $p = 0.001$). The D/D genotype of the *ACE* gene was associated with the increased AH only in the cohort of the indigenous ethnic group (OR 4.39; 95% CI 1.78–10.83; $p = 0.003$). However, even though the Shors showed less expression of RF, and the "genetic passport" was represented by a more favorable spectrum, the damage to target organs in the presence of AH was more pronounced in them than the non-indigenous population. The incidence of left ventricular myocardial hypertrophy and the atherosclerosis of the carotid arteries was higher among the Shors (50.1 and 73.6%) compared with the residents of non-indigenous nationals (41.7%, $p = 0.045$ and 65.3%, $p = 0.047$). This established fact is caused probably by the disruption of the metabolic and adaptive mechanisms that have developed for centuries at the level of the population genotype, during the disease manifestation.

The lifestyle of the representatives of small ethnic groups changes significantly when moving from a village to the urban area. In this regard, among the indigenous people living in the cities, a more pronounced influence of CV RF should be expected than among the rural population.

In our study, in the cohort of Shors, the proportion of people with the obesity and its abdominal type turned out to be higher among urban dwellers than among the rural residents (19.3% vs. 13.6% ($p = 0.018$) and 41.1% vs. 29.3% ($p = 0.0001$), respectively). In men, AH was more common among the city residents than in the villagers (44.2% vs. 30.4%, $p = 0.008$). Differences in the prevalence of CHD were noted, so that this disease was detected in 12.6% of the cases in patients living in the city, and in 8.0% of the cases among the rural residents ($p = 0.048$). At the same time, depending on the place of the residence,

the "portrait" of a CHD patient changed (Table 2).

Urban residents turned out to be younger (63.7 ± 11.9 years vs. 72.5 ± 10.5 years, $p = 0.002$), with a higher body mass index (27.4 ± 5.9 kg/m^2 vs. 23.5 ± 2.8 kg/m^2, $p = 0.0005$) and waist circumference (90.9 ± 12.9 cm vs. 78.0 ± 10.4 cm, $p = 0.0001$), higher diastolic BP (91.7 ± 9.9 mm Hg vs. 85.6 ± 10.2 mm Hg, $p = 0.013$), more often with hypertriglyceridemia (34.4% vs. 13.9%, $p = 0.047$). However, CHD villagers had their own characteristics, namely a higher level of total cholesterol and a higher prevalence of diabetes mellitus.

Discussion. In the recent years, the vector of development of medicine is aimed at the transition to the model of "4P-medicine" (preventive, predictive, personalized, partner), with the personification of the approaches in assessing the risk of diseases, and the implementation of individualized correction programs [3, 8]. Accounting for the ethnicity enables to quickly implement this model and predict the probability of a certain disease in a particular person. Epidemiological, population studies contribute to the timely and effective correction of RF to reduce the disability and mortality from CVD [3, 4].

Epidemiological studies in the Mountain Shoriya, conducted at different time periods, have demonstrated a lower incidence of CV RF in the indigenous Shor population compared to the non-indigenous population.

Many authors studying the ethnic groups have obtained similar results [9–12]. The share of people with the lipid metabolism disorders and obesity among the indigenous people of the Far North was lower than among the non-indigenous population [9]. Similar results were obtained when examining the Dolgans [10] and respondents of Chuvash ethnicity [11]. There was not a single case of obesity among the Khanty [12].

The prevalence of the main RF, AH in the Shor cohort was lower due to the men. Similar data were collected among the indigenous and non-indigenous population of Kyrgyzstan [13]. Similar information was demonstrated by a study by Yu.A. Petrova *et al*. (2016), who showed that the prevalence of this disease among the small indigenous peoples of the North is significantly lower than the non-indigenous population [14]. The assessment of the incidence of metabolic syndrome in Yakutia showed a lower frequency in the indigenous population (43.0%) compared to the non-indigenous population (59.7%, $p = 0.002$), as in the present study in the Mountain Shoriya [15].

The results of numerous epidemiological studies using the molecular genetic methods have shown that in the specificity of genetic polymorphisms, the ethnicity of a person is of paramount importance. In the Mountain Shoriya, we have revealed the uniqueness of the "genetic apparatus" of the Shor population. The genetic heterogeneity of various national cohorts is demonstrated by the results of Russian and international population genetic studies. Until now, the optimal set of a single nucleotide polymorphisms responsible for the manifestation of a particular phenotypic trait has not been established. At the same time, point gene polymorphisms associated with the expression of a protein involved in the pathogenesis of CVD could be considered as the possible markers of the disease onset and as noted by many authors, have population and racial differences.

Genetic polymorphism of the renin-angiotensin-aldosterone system is widely studied to determine the predisposition to AH. In a particular population, the associative relationship of these candidate genes with an increase in the BP remains controversial. Thus, in the present study, AH in the Shor cohort was associated with mutant alleles D and C of the corresponding genes *ACE* and $AGTR_1$, and only the C allele of the $AGTR_1$ gene in the cohort of the non-indigenous population. A positive relationship between the D/D genotype of the *ACE* gene has been established for the Chinese, Indians, Pakistanis, and Africans [16–19]; as for the C/C genotype of the $AGTR_1$ gene, it has been established only for the population of China and North India [20, 21].

In the Shor population, the *AGT* gene did not increase the risk of AH, while in the populations of Saudi Arabia and India, it confirmed its role in the onset of this disease [22, 23]. The association of AH with genes $ADRB_1$, $ADRA_2B$, *MTHFR*, *e-NOS* was not revealed in both national groups of the Mountain Shoriya. However, K. Xia *et al*. (2017) [24] on the Chinese population and P. Ramu *et al*. (2009) [25] in a cohort of Indians demonstrated the association of the A allele of the $ADRB_1$ gene with AH. S.M. Ghogomu *et al*. (2016) [26] and Z. Tang *et al*. (2017) [27] proved that the minor T/T genotype of the *MTHFR* gene may be an important genetic predictor of high BP in the indigenous population of Cameroon; D.C. Souza-Costa *et al*. (2011) [28] revealed that the mutant genotype 4a/4a of the *e-NOS* gene increased susceptibility to AH.

In the Mountain Shoriya, we have revealed significant differences between representatives of the indigenous ethnic group, as well as between residents of the city and the countryside, in terms of the profile of CV risk and morbidity. On the one hand, in cities, as a rule, the ecological situation is worse, but economic and social opportunities are higher, as well as the availability of medical care. On the other hand, in the village, physical activity

is higher, the consumption of gastronomic products containing salt and fats is less, but the availability of medical care is lower, and this applies to both emergency situations and routine care, and the possibility of consulting qualified specialists [29]. The Shors in the city showed a higher prevalence of RF, including the main one, AH.

The global study PURE (Prospective Urban Rural Epidemiology) demonstrated the similar data. In the rural areas, in general, the RF profile is more favorable, the incidence of CV events and the mortality during their development is lower in the urban residents [29, 30]. Similar results were obtained in Kazakhstan, increased BP was noted in 39.3% of the cases in the urban population, and in 32.2% of the cases in the rural population [31]. Other trends were shown by the ESSE-RF epidemiological study conducted in Russia from 2012–2013, where the prevalence of AH was higher among rural residents than the urban residents, both among men (51.8% vs. 47.5%) and among women (42.9% vs. 40.2%); obesity was also more common among the villagers (33.7% vs. 29.4%) [29].

Epidemiological studies contribute to the acquisition of new knowledge about the population groups differing in ethnic origin, lifestyle characteristics, and methods of economic management, as well as regions of residence, and the peculiarities of candidate gene polymorphism. Understanding the ethnic specifics allows the development of targeted preventive measures, thereby preserving the health of the population.

The patient's profile has its ethnic characteristics. The results of this study have proved that the changes in the habitual way of life in the isolated populations lead to adverse changes in both RFs and the diseases of the circulatory system. During the period analyzed, the incidence of lipid and carbohydrate metabolism disorders increased; the proportion of patients with AH and CHD increased, even though the indigenous small population of Shors was characterized by a more favorable polymorphism profile of candidate genes. Alleles C and D in the homozygous state of the corresponding candidate genes $AGTR_1$ and *ACE* determined a high probability of AH in the Shor cohort (OR 10.02 and OR 4.39), and the homozygous C/C genotype of the $AGTR_1$ gene determined it in representatives of non-indigenous nationalities (OR 26.77).

CONCLUSIONS

1. Epidemiological studies contribute to the acquisition of new knowledge about the population groups differing in ethnic origin, lifestyle characteristics, and the methods of economic management, as well as regions of residence, and the characteristics of candidate gene polymorphism. This provides valuable material for individualizing the prevention and treatment of the diseases.

2. The study enabled to reveal in the indigenous small population of the Mountain Shoriya an increase in the prevalence of CHD from 1998–2001 to 2013–2017, as well as the number of considerable statistically significant differences in the incidence of this pathology among the urban and rural population.

3. The patient's profile has its ethnic characteristics. Understanding the ethnic specifics allows the development of the targeted preventive measures, thereby preserving the health of the population.

4. Monitoring of AH and the factors that determine a high risk of its development is one of the best strategies of preventive measures. Considering the markers of predisposition to diseases of the CV system will optimize medical and organizational approaches to the treatment and prophylactic measures.

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REFERENCES

1. Shlyakhto E.V., Baranova E.I. Central directions for reducing cardiovascular mortality: what can be changed today? *Russian Journal of Cardiology*. 2020; 25 (7): 39–83. (In Russ.) DOI: 10.15829/1560-4071-2020-3983.

2. Karpov Yu.A., Gorbunov V.M., Logunova N.A. on behalf of the TRICOLOR research team. Triple fixed-dose combination in the treatment of hypertension: the results of the Russian observational study TRICOLOR. *Russian Journal of Cardiology*. 2020; 25 (10): 4130. (In Russ.) DOI: 10.15829/1560-4071-2020-4130.

3. Brodskaya T.A., Nevzorova V.A., Repina N.I., Bogdanov D.Yu. An issue of cardiovascular risk assessment depending on ethnicity and target organ damage. *Kardiovaskulyarnaya terapiya i profilaktika*. 2017; 16 (4): 93–99. (In Russ.) DOI: 10.15829/1728-8800-2017-4-93-99.

4. Mihalina E.V., Mulerova T.A., Polikutina O.M., Ogarkov M.Yu. Prevalence of coronary artery disease in the indigenous population of Gornaya Shoria (the results of epidemiological studies in 1998–2001 and 2013–2017). *Complex Issues of Cardiovascular Diseases*. 2019; 8 (4S): 15–21. (In Russ.) DOI: 10.17802/2306-1278-2019-8-4S-15-21.

5. Markel A.L. Essential systemic hypertension: genetics, clinics, experiment. *Russian Journal of Cardiology*. 2017; 150 (10): 133–139. (In Russ.) DOI: 10.15829/1560-4071-2017-10-133-139.

6. Shalnova S.A., Balanova Yu.A., Konstantinov V.V., Timofeeva T.N., Ivanov V.M., Kapustina A.V., Deev A.D. Arterial hypertension: prevalence, awareness, antihypertensive pharmaceutical treatment, treatment effectiveness in Russian population. *Russian Journal of Cardiology*. 2006; (4): 45–50. (In Russ.)

7. Shalnova S.A., Deev A.D. Coronary heart disease in Russia: incidence rate and treatment (according to epidemiological data). *Therapeutic archive*. 2011; (1): 7–12. (In Russ.)

8. Flores M., Glusman G., Brogaard K., Price N.D., Hood L. P4 medicine: how systems medicine will transform the healthcare sector and society. *Personification Med*. 2013; 10 (6): 565–576. DOI: 10.2217/pme.13.57.

9. Suplotova L.A., Smetanina S.A., Novakovskaya N.A. The prevalence of metabolic syndrome and its components in women from different ethnic groups. *Ozhirenie i metabolizm*. 2011; (2): 48–51. (In Russ.)

10. Uvarova T.E., Burtseva T.E., Sofronova S.I., Efremova C.D., Golderova A.S. The bloode lipid profile and the lipid metabolizm disorders to indegenious people of the yakutia. *Dal'nevostochnyy meditsinskiy zhurnal*. 2012; (3): 85–88. (In Russ.)

11. Markova T.N., Kichigin V.A., Markov D.S. Age and sexual and ethnic features of prevalence of obesity in the Chuvash Republic. *Vestnik chuvashskogo universiteta*. 2012; (3): 436–440. (In Russ.)

12. Korchina T.Ya. Assessment of risk factors for the development of cardiovascular diseases in residents of the Northern Region. *Nauchnyy meditsinskiy vestnik Yugry*. 2013; (1): 22–26. (In Russ.)

13. Polupanov A.G., Kontsevaya A.V., Khalmatov A.N., Altymysheva A.T., Suvorova E.I., Romanova T.A., Khudyakov M.B., Shalnova S.A., Dzhumagulova A.S. Ethnic features of arterial hypertension prevalence in small town and countryside residents of the Kyrgyz Rebablic: results of the international study Interepid. *Cardiovascular Therapy and Prevention*. 2013; 12 (6): 4–8. (In Russ.) DOI: 10.15829/1728-8800-2013-6-4-8.

14. Petrova Yu.A., Sholomov I.F., Isaev Ya.V., Medvedeva I.V. Prevalence of arterial hypertension according to the clinical examination of the population of the Far North. *Evraziyskiy kardiologicheskiy zhurnal*. 2016; (3): 148. (In Russ.)

15. Sozonova K.K., Tatarinova O.V., Makarenkova K.V., Simonova G.I. Lipids blood profile under conditions of metabolic syndrome at aboriginal and non-aboriginal inhabitants of Yakutia aged 60 years and over. *Ateroskleroz*. 2013; 9 (3–4): 19–23. (In Russ.)

16. Sun F., He N., Zhang K., Wu N., Zhao J., Qiu C. Association of ACE gene A2350G and I/D polymorphisms with essential hypertension in the northernmost province of China. *Clin. Exp. Hypertens*. 2018; 40 (1): 32–38. DOI: 10.1080/10641963.2017.1291659.

17. Rana G., Yadav S., Joshi S., Saraswathy K.N. Association of DD genotype of angiotensin-converting enzyme gene (I/D) polymorphism with hypertension among a North Indian population. *J. Community Genet*. 2018; 9 (1): 51–55. DOI: 10.1007/s12687-017-0321-9.

18. Hussain M., Awan F.R., Gujjar A., Hafeez S., Islam M. A case control association study of ACE gene polymorphism (I/D) with hypertension in Punjabi population from Faisalabad, Pakistan. *Clin. Exp. Hypertens*. 2018; 40 (2): 186–191. DOI: 10.1080/10641963.2017.1356842.

19. Tchelougou D., Kologo J.K., Karou S.D., Yameogo V.N., Bisseye C., Djigma F.W., Ouermi D., Compaore T.R., Assih M., Pietra V., Zabsonre P., Simpore J. Renin-angiotensin system genes polymorphisms and essential hypertension in Burkina Faso, West Africa. *Int. J. Hypertens*. 2015; 2015: 979631. DOI: 10.1155/2015/979631.

20. Qian X., Guo D., Zhou H., Qiu J., Wang J., Shen C., Guo Z., Xu Y., Dong C. Interactions between PPARG and AGTR1 gene polymorphisms on the risk of hypertension in Chinese Han population. Genet. *Test Mol. Biomarkers*. 2018; 22 (2): 90–97. DOI: 10.1089/gtmb.2017.0141.

21. Sudhir C., Rajiv N., Vishnubhatla S., Bhatia J., Saluja D., Srivastava K. Association of angiotensin II type 1 receptor (A1166C) gene polymorphism and its increased expression in essential hypertension: A case-control study. *PLoS ONE*. 2014; 9 (7): e101502. DOI: 10.1371/journal.pone.0101502.

22. Al-Najai M., Muiya P., Tahir A.I., Elhawari S., Gueco D., Andres E., Mazhar N., Altassan N., Alshahid M., Dzimiri N. Association of the angiotensinogen gene polymorphism with atherosclerosis and its risk traits in the Saudi population. *BMC Cardiovasc. Disord*. 2013; 13: 17. DOI: 10.1186/1471-2261-13-17.

23. Purkait P., Halder K., Thakur S., Roy A.G., Raychaudhuri P., Bhattacharya S., Sarkar B.N., Naidu J.M. Association of angiotensinogen gene SNPs and haplotypes with risk of hypertension in eastern Indian population. *Clin. Hypertens*. 2017; 23: 12. DOI: 10.1186/s40885-017-0069-x.

24. Xia K., Ding R., Zhang Z., Li W., Shang X., Yang X., Wang L., Zhang Q. The association of eight potentially functional polymorphisms in five adrenergic receptor-encoding genes with myocardial infarction risk in Han Chinese. *Gene*. 2017; 624: 43–49. DOI: 10.1016/j.gene.2017.04.045.

25. Ramu P., Rajan S., Shewade D.G., Swaminathan R.P., Dutta T.K., Balachander J., Adithan C. Genetic variants of beta(1)-adrenoceptor gene polymorphisms (Ser49Gly and Arg389Gly) and essential hypertension in a south Indian Tamil population. *Clin. Exp. Pharmacol. Physiol*. 2009; 36 (5–6): 576–582. DOI: 10.1111/j.1440-1681.2008.05117.x.

26. Ghogomu S.M., Ngolle N.E., Mouliom R.N., Asa B.F. Association between the MTHFR C677T gene polymorphism and essential hypertension in South West Cameroon. *Genet. Mol. Res*. 2016; 15 (1): gmr.15017462. DOI: 10.4238/gmr.15017462.

27. Tang Z., Xiao L., Wang J.Q., Zhang T. Analysis of metabolism-related indicators and MTHFR gene polymorphism in patients with H-type hypertension. *Minerva Med*. 2017; 108 (2): 103–107. DOI: 10.23736/S0026-4806.16.04951-X.

28. Souza-Costa D.C., Belo V.A., Silva P.S., Sertorio J.T., Metzger I.F., Lanna C.M., Machado M.A., Tanus-Santos J.E. eNOS haplotype associated with hypertension in obese children and adolescents. *Int. J. Obes. (Lond.)*. 2011; 35 (3): 387–392. DOI: 10.1038/ijo.2010.146.

29. Kontsevaya A.V., Myrzamatova A.O., Kashirin A.K. Cardiovascular risk factors among inhabitants of rural areas by the epidemiological data: review article. *Cardiovascular Therapy and Prevention*. 2016; 15 (6): 66–71. (In Russ.) DOI: 10.15829/1728-8800-2016-6-66-71.

30. Yusuf S., Rangarajan S., Teo K., Islam S., Li W., Liu L., Bo J., Lou Q., Lu F., Liu T., Yu L., Zhang S., Mony P., Swaminathan S., Mohan V., Gupta R., Kumar R., Vijayakumar K., Lear S., Anand S., Wielgosz A., Diaz R., Avezum A., Lopez-Jaramillo P., Lanas F., Yusoff K., Ismail N., Iqbal R., Rahman O., Rosengren A., Yusufali A., Kelishadi R., Kruger A., Puoane T., Szuba A., Chifamba J., Oguz A., McQueen M., McKee M., Dagenais G. (PURE Investigators) Cardiovascular risk and events in 17 low-, middle-, and high-income countries. *N. Engl. J. Med*. 2014; 371 (9): 818–127. DOI: 10.1056/NEJMoa1311890.

31. Turgunova L., Laryushina E., Amirkhanova D., Alina A., Bayesheva T. Prevalence of modifiable risk factors of chronic non infection diseases among urban and rural residents of region. *Georgian Med. News*. 2016; (252): 32–36. PMID: 27119832.