ПЕРЕДОВАЯ СТАТЬЯ

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PREVALENCE AND TREATMENT OF ARTERIAL HYPERTENSION IN THE NATIVE RURAL POPULATION OF YAKUTIA

The **objective** of the research was to study the prevalence and characteristics of treatment of arterial hypertension (AH) in the indigenous rural population of the Sakha (Yakutia) Republic.

Epidemiological research was conducted among the population (20 years and older) of 3 districts of the Sakha (Yakutia) Republic, and representatives of indigenous ethnic groups (Yakuts, Evens, and Evenks). The prevalence of AH among the surveyed population was 45.9% (95% CI: 42.5-49.3). There were no statistically significant differences in the frequency of hypertension in men and women (45.3 and 46.2%, respectively, p = 0.805). According to the survey, antihypertensive drugs (AHD) were taken by 51.2% of individuals with hypertension according to research criteria. Among women, the proportion of individuals using AHD was statistically significantly higher than among men (57.6 and 39.2%, respectively, p < 0.001). In 75.4% of cases, patients took one antihypertensive drug. In 52.8% of cases, drug therapy included angiotensin-converting enzyme inhibitors, in 42% of cases – calcium channel blockers, in 13.6% – β-blockers, 8.4% – angiotensin II receptor blockers, and in 3.1% – diuretics. The level of blood pressure corresponded to the "target" in 30.9% of those taking AHD.

Along with improving the diagnosis of hypertension and finding and eliminating risk factors, it is necessary to take measures to increase patient adherence to treatment and control blood pressure levels, as well as to conduct pharmacogenetic studies of the effectiveness of antihypertensive drugs.

Keywords: arterial hypertension, arterial hypertension, prevalence, antihypertensive drugs, treatment efficacy, Yakutia.

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Introduction. Arterial hypertension is a major risk factor for coronary heart disease, chronic renal failure, cerebral stroke and other cardiovascular diseases. According to WHO, in 2015, 22% of the world's population aged 18 years and older had elevated blood pressure [8]. While in high-income countries there is currently a decrease in the prevalence of AH, in low- and middle-income countries the number of AH patients continues to increase. This is caused not only by the aging of the population but also by the presence of such risk factors as overweight or obesity, decreased physical activity, stress, environmental degradation, etc.

In the Russian Federation, according to the multicenter study called Epidemiology of Cardiovascular Diseases in Various Regions of Russia (ECCD), the prevalence of hypertension among the population of 25–64 years old was 44%. The study showed variability in the prevalence rate depending on the region of the participant (from 37.8 to 56.1%) [1].

Sakha (Yakutia) Republic is the largest subject of the Russian Federation, characterized by unfavorable climatic conditions for living and working people. For the period from 2004 to 2018, the prevalence of diseases associated with high blood pressure increased among the adult population of the Republic from 65.0 to 108.4 per 1000 population [2, 5]. At the same time, official statistics probably do not fully reflect the entire situation. Additional research may help to make adjustments to ongoing prevention programs in the region.

The aim of the research was to study the prevalence and characteristics of treatment of hypertension in the indigenous rural population of the Sakha (Yakutia) Republic.

Materials and Methods. A screening survey was conducted in 2017-2018, among the population of 3 districts of the Sakha (Yakutia) Republic aged 20 years and older (Oymyakonsky, Gorny and Tattinsky), who were representatives of indigenous ethnic groups (Yakuts, Evens, and Evenki) The study was conducted subject to the voluntary informed consent of the participants. The survey program included: a survey using a special questionnaire, an anthropometric examination using a standardized method, a threefold measurement of blood pressure (BP), and venous blood sampling after fasting. The content of glucose, total cholesterol (cholesterol), triglycerides, high-density lipoprotein cholesterol (HDL cholesterol) was determined using the express analyzer CardioChek PA, USA. The concentration of low-density lipoprotein cholesterol (LDL cholesterol) was calculated using the Friedewald formula with a blood triglyceride level of less than 4.5 mmol/L. Arterial hypertension (AH) was established by the criteria of ESH/ESC, 2013 [9]. The group with hypertension also included individuals who took antihypertensive drugs (AHD) during the survey or stopped taking them less than 2 weeks before the survey, regardless of the measured blood pressure level. Effective treatment of hypertension was considered the achievement of target values of blood pressure on the back-

Table 1

Main Characteristics of the Surveyed Indigenous Population of the Sakha (Yakutia) Republic, 20 Years and Older

Indicator	20-43 years n=237	44-59 years n=310	60-74 years n=177	75 year and old n=53	p
Мужчины n=287					
SBP, mm Hg	120.0 (111.8-133.3)	130.0 (116.3-143.0)	141.0 (130.0-160.0)	130.0 (120.0-152.5)	<0.001
DBP, mm Hg	80.0 (70.3-84.3)	80.0 (73.3-90.0)	90.0 (80.0-100.0)	90.0 (80.0-92.5)	<0.001
Height, cm	168.0 (164.1-172.0)	167.0 (163.0-172.0)	162.0 (158.0-165.8)	160.0 (157.0-166.8)	<0.001
Body mass, kg	69.0 (62.0-79.8)	74.0 (64.0-81.0)	66.0 (62.0-76.0)	64.5 (55.8-73.8)	<0.001
Body mass index, kg/m^2	24.1 (21.9-27.3)	26.8 (23.7-29.3)	25.3 (23.1-29.2)	25.1 (22.1-26.7)	0.007
Waist circumference, cm	81.5 (76.3-94.0)	92.0 (84.0-99.8)	92.0 (84.0-97.5)	92.0 (88.0-97.0)	<0.001
Triglycerides, mmol/L	0.9 (0.6-1.2)	1.1 (0.8-1.8)	0.9 (0.6-1.3)	0.8 (0.6-1.4)	0.048
Total cholesterol, mmol/L	4.8 (4.1-5.8)	5.4 (4.3-6.2)	5.0 (4.2-5.7)	4.7 (3.7-5.6)	0.103
HDL cholesterol, mmol/L	1.4 (1.2-1.7)	1.4 (1.2-1.6)	1.5 (1.2-1.6)	1.1 (0.9-1.5)	0.032
LDL cholesterol, mmol/L	2.5 (1.9-3.1)	2.9 (2.2-3.4)	2.8 (2.2-3.7)	2.8 (2.2-3.7)	0.038
Atherogenic index, c.u.	2.4 (1.8-3.3)	2.8 (2.1-3.5)	2.4 (1.9-3.1)	2.7 (2.1-3.9)	0.106
Glucose, mmol/L	4.8 (4.5-5.3)	5.1 (4.6-5.6)	4.9 (4.3-5.5)	4.7 (3.9-5.0)	0.006
Women n=526					
SBP, mm Hg	120.0 (110.0-130.0)	134.0 (120.0-150.0)	140.0 (120.0-165.4)	150.0 (138.5-176.7)	<0.001
DBP, mm Hg	78.5 (70.0-84.2)	85.0 (80.0-94.0)	89.5 (80.0-100.0)	90.0 (80.0-100.0)	<0.001
Height, cm	158.0 (152.9-162.0)	154.0 (150.0-158.0)	150.0 (147.5-154.0)	146.0 (141.5-150.0)	<0.001
Body mass index, kg	61.9 (54.0-72.0)	67.0 (58.2-76.0)	63.0 (55.0-74.0)	58.0 (49.0-69.5)	<0.001
BMI, kg/m^2	24.9 (22.4-28.4)	27.9 (24.9-31.6)	27.9 (24.3-32.3)	27.6 (23.4-32.0)	<0.001
Waist circumference, cm	82.0 (74.0-93.8)	91.0 (83.0-100.0)	94.0 (83.5-103.0)	93.0 (84.3-101.0)	<0.001
Triglycerides, mmol/L	0.8 (0.6-1.1)	1.1 (0.8-1.5)	1.0 (0.7-1.4)	0.9 (0.7-1.1)	<0.001
Total cholesterol, mmol/L	4.6 (3.9-5.3)	5.7 (4.9-6.4)	5.4 (4.7-6.2)	5.4 (4.6-5.9)	<0.001
HDL cholesterol, mmol/L	1.6 (1.3-1.8)	1.5 (1.4-1.7)	1.4 (1.3-1.7)	1.5 (1.2-1.7)	0.253
LDL cholesterol, mmol/L	2.2 (1.8-2.8)	3.1 (2.5-3.8)	3.1 (2.6-3.8)	3.3 (2.5-4.0)	<0.001
Atherogenic index, c.u	2.2 (1.5-2.7)	2.8 (2.2-3.5)	2.7 (2.0-3.5)	2.6 (2.1-3.1)	<0.001
Glucose, mmol/L	4.6 (4.3-5.1)	4.9 (4.5-5.6)	4.6 (4.2-5.4)	4.5 (4.1-4.9)	<0.001

Note: p is the achieved level of statistical significance of differences when comparing age groups by gender (Kruskal–Wallis test).

ground of antihypertensive therapy [9].

Statistical data analysis was carried out in the IBM SPSS STATISTICS 22 package. When comparing groups depending on the type of data, Kruskal-Wallis criteria were used, as well as Pearson's chi-squared test (χ^2). The critical value of the level of statistical significance of differences (p) was taken to be 5%. Descriptive statistics of quantitative data are presented as median (Me) and interquartile range (Q1-Q2). AH prevalence rates are presented with a 95% confidence interval (95% CI).

Results and Discussion. During the epidemiological study in 3 districts of Yakutia, 813 men and women aged 20 years and older were examined. Men and women were comparable in age, the average age of the men surveyed was 49.3 (15.9) years, women – 50.9 (15.3) years (p = 0.138).

Analysis of the main anthropometric and metabolic indicators of the sample showed that, in general, the indigenous rural population is characterized by increased body weight, waist circumference, and a fairly favorable lipid profile (Table 1). At the same time, from the age of 44, the upper quartile of the distribution of systolic and diastolic blood pressures is in the range corresponding to the criterion of AH. These features were noted by us in previous studies [4, 6, 7].

Table 2

Prevalence of hypertension among the indigenous population of Yakutia, n (%)

Age, years	Men n=287	Women n=526	Both genders n=813	p
20-43	29 (26.6)	35 (21.3)	64 (23.4)	0.315
44-59	38 (41.80)	115 (52.5)	153 (49.4)	0.085
60-74	51 (71.80)	63 (59.4)	114 (64.4)	0.091
75 and older	12 (75.0)	30 (81.1)	42 (79.2)	0.616
All	130 (45.3)	243 (46.2)	373 (45.9)	0.805

Note: p is the achieved level of statistical significance of differences when comparing groups by gender (Pearson's test χ^2).

The prevalence of AH among the surveyed population was 45.9% (95% CI: 42.5-49.3). Among the male population, the figures were 45.3% (95% CI: 39.5-51.2), and among women 46.2% (95% CI: 41.9-51.5), respectively. With an increase in the age of the examined, the frequency of hypertension increased significantly (Table 2). There are no statistically significant differences in the prevalence of hypertension among men and women, both in general and in each age group separately. These data are close to the results of the ECCD study in 9 regions involving 15,300 people, where the prevalence of AH was on average 44%. The prevalence rates of hypertension in 8 regions were higher for men than for women. In the Tyumen Region, which also belongs to the northern territories, there are also no significant differences between women and men in the frequency of hypertension [1].

Evaluation of antihypertensive therapy was carried out according to the patients' self-reports, which makes possible the presence of a systematic error associated with a "memory error". Some patients could not specify all drugs that were taken in connection with high blood pressure. At the same time, it is closer to the actual practice of taking the drugs by the patients themselves. Conducting a future study with simultaneous evaluation of the doctor's prescriptions and patient self-report could help eliminate these shortcomings and objectively assess the patients' adherence to treatment, as well as the treatment tactics used by the medical staff.
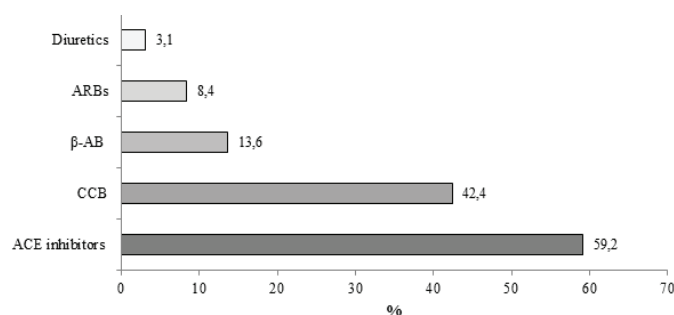
Fig. 1. Frequency of use of different groups of antihypertensive drugs: ACE inhibitors – inhibitors of the angiotensin-converting enzyme; CCB – calcium channel blockers; β-AB – beta blockers; ARBs – angiotensin II receptor blockers.

According to the survey, 191 people from among 373 persons diagnosed with AH by screening (51.2%) were taking AHD. Among women, the proportion of drug users was statistically significantly higher than among men (57.6 and 39.2%, respectively, p <0.001). According to the results of the ECCD study, on average in Russia 60.9% of women and 39.5% of men with hypertension took AHD [1]. Thus, the attitude of patients to the treatment of hypertension in Russia has common features, regardless of the region.

The most commonly used drugs were angiotensin-converting enzyme inhibitors (ACE inhibitors), which were used as monotherapy or were part of combination therapy in 59% of treatment cases. In 42% of cases, calcium channel block-ers (CCB) were used, in 13.6% – β-blockers (β-АБ), 8.4% – angiotensin II receptor block-ers (ARBs), 3.1% – diuretics (Fig. 1). According to the research of ECCD, ACE inhibitors were also the most frequently used drugs in other territories of the Russian Federation [1]. But in Yakutia, in contrast to the regions studied, the second in use are CCBs. The proportion of people receiving CCB was 18.8% in the Russian study, against 42% in Yakutia. The proportion of β-AB, diuretics and ARBs was significantly lower. The revealed features require additional studies, since the high frequency of prescribing CCBs may be due to their high efficiency in this ethnic group.

144 (75.4%) respondents taking AHD indicated using 1 drug. In 52.8% of cases, these were ACE inhibitors, in 31.9% – calcium antagonists, in 9% – β-AB. Of the 47 patients taking 2 or more drugs, 22 (46.8%) indicated that an ACE inhibitor was taken in combination with CCB. The second in frequency (14.9%) was a combination of an ACE inhibitor with β-AB. 6 respondents noted the use of 3 drugs, of which in 4 cases it was a combination of an ACE inhibitor + CCB + ARBs.

When measured in 59 out of 191 (30.9%) respondents taking AHD, the level of blood pressure corresponded to the "target". In women, the proportion of people with a normal level of blood pressure on the background of drug intake was slightly higher, but the differences did not reach a statistically significant level (32.1 and 27.5%, respectively, p = 0.535). According to the results of the ECCD study, the treatment efficiency was 53.5% among women and 41.4% among men, which is much higher than our data [1].

Thus, the results of the study showed a high incidence of hypertension among the indigenous population of Yakutia (45.9%). AHD was taken by 57.6% of women and 39.2% of men with hypertension according to the research criteria. At the same time, target blood pressure was achieved only in 30.9% of patients. Along with improving the diagnosis of hypertension, finding and eliminating risk factors, measures are needed to increase patient adherence to treatment and controlling blood pressure levels, as well as pharmacogenetic studies of the effectiveness of antihypertensive drugs in this ethnic group.

Table 3

Range of used groups of antihypertensive drugs

Group of drugs	Drug intake n=191 (100%)		Monotherapy n=144 (75.4%)		Combined therapy n=47 (24.6%)	
	n	%	n	%	n	%
ACE inhibitors	76	39.8	76	52.8		
CCB	46	24.1	46	31.9		
β-АБ	13	6.8	13	9.0		
ARBs	5	2.6	5	3.5		
Alpha adrenomimetics	2	1.0	2	1.4		
Diuretics	2	1.0	2	1.4		
ACE inhibitors + CCB	22	11.5			22	46.8
ACE inhibitors + β-AB	7	3.7			7	14.9
CCB + β-AB	4	2.1			4	8.5
ACE inhibitors + AV + ARBs	4	2.1			4	8.5
CCB + ARBs	3	1.6			3	6.4
ACE inhibitors + ARBs	2	1.0			2	4.3
CCB + Diuretics	1	0.5			1	2.1
ARBs + Diuretics	1	0.5			1	2.1
β-AB + ARBs	1	0.5			1	2.1
ACE inhibitors + CCB + Diuretics	1	0.5			1	2.1
ACE inhibitors + β-AB + Diuretics	1	0.5			1	2.1

Note: ACE inhibitors – inhibitors of the angiotensin-converting enzyme; CCB – calcium channel blockers; β-AB – beta blockers; ARBs – angiotensin II receptor blockers.

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ORIGINAL RESEARCHES

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LIPOPROTEIN LIPASE GENE POLYMORPHISM rs320 AND METABOLIC SYNDROME IN NATIVE PEOPLE OF YAKUTIA

The **aim** of the study was investigation the relationship of allelic variants and genotypes of the rs 320 polymorphism of the LPL gene with the metabolic syndrome and its components in adult population of the Yakut ethnic group. In the studied group, it was not possible to establish a direct connection between the allelic variants, the genotypes of the LPL rs320 gene with the metabolic syndrome and its components. However, it is important to note individuals with the TT genotype had somewhat higher level of triglycerides in the blood. It may be associated with a small sample size. We assume that the T allele is associated with low enzyme activity in this population, and plays a key role in the development of diseases associated with metabolic disorders.

Keywords: obesity, metabolic syndrome, multiple metabolic risk factors, population, genetics, rs320 polymorphism of the LPL gene, dyslipidemia, indigenous population, Yakutia, North.

One of the variants of the LPL gene, which encodes the enzyme lipoprotein lipase, is the replacement of thymine (T) by guanine (G) at position 495 in intron 8. The Hind III (rs320) polymorphism changes the recognition site of the Hind III restriction enzyme and affects the activity of the enzyme. In recent studies, it was shown that the polymorphism rs320 of the LPL gene has a significant effect on the structure of the precursor RNA [9]. The frequency of minor G allele in different world populations varies from 24 to 38%, the highest frequency is observed among the population of Saudi Arabia (37,6%) [3, 5]. The literature presents conflicting data on the role of Hind III (rs320) polymorphism in the development of diseases associated with lipid metabolism disorders. In some studies, the presence of a minor allele was associated with a lower risk of diseases associated with impaired lipid metabolism [4, 10, 12, 16], in other studies the presence of this polymorphism was a risk factor for the development of metabolic disorders and related diseases [7, 13].

In early studies the significant association between LPL rs320 with type 2 diabetes in the Yakut population has shown [1, 2, 3]. However, the mechanism of the influence of polymorphism on the development of metabolic disorders has not been studied enough. It is known that the inhabitants of the North from time immemorial adapted to a diet rich in fats. Currently, there is an intensive increase in the incidence of metabolic disorders in the Yakut population. In this regard, the study of the mechanisms of the influence of the LPL gene on the metabolism of indigenous peoples is a very interesting.

The purpose of this study was to estimate of the allele and genotype frequency of LPL gene rs 320 polymorphism and its association with metabolic parameters and components of the metabolic syndrome in the adult population of Yakut nationality living in Central Yakutia.

Materials and methods: The genotype frequency of the LPL gene rs320 was estimated among the unorganized population of the Central region (Gorny ulus, village Berdigestyakh) of the Sakha Republic (Yakutia). The research project was approved by the local bioethics committee of the Yakut Scientific Center for Complex Medical Problems (Protocol No. 39 dated June 26, 2014). Participation in the study was completely voluntary. Obtained clinically useful information was available to study participants. The initial participant's selection was based on household lists. The study included persons of the Yakut nationality (by self-determination) at the age of 18 and older, regardless of whether they have any somatic disease (n = 363).

Analyze of rs320 polymorphism was performed in 189 representatives (142 women and 47 men aged 18 years and older) who gave voluntary informational consent to conduct genetic studies. The average age was 52.7 (13.7) years. All participants were examined by a single program, including anthropometric examination by the standard method, analysis of body composition for bio-impedance analysis "Tanita" (Japan) SSC 330, twofold blood pressure measurement (BP), fasting venous blood sampling. The content of glucose, total cholesterol (cholesterol), triglycerides, high density lipoproteins (HDL cholesterol) was determined on the express analyzer Cardiochek PA, USA. The concentration of low-density lipoprotein cholesterol (LDL cholesterol)