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ETHNIC AND AGE-RELATED CHARACTERISTICS OF NEUROLOGICAL SYMPTOMS AND FUNCTIONAL STATE OF THE KIDNEYS IN ELDERLY AND SENILE AGE PEOPLE OF YAKUTIA

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The study was conducted in patients of elderly and senile age, representatives of the indigenous and non-indigenous ethnic group. It has been established that the development and progression of chronic cerebral ischemia occurs in parallel with the progression of chronic kidney disease. At the same time, representatives of the non-indigenous population showed more severe neurological symptoms due to structural changes in the cerebral vascular bed due to hypertension and atherosclerosis, as well as severe renal dysfunction. Evens had milder clinical symptoms of chronic cerebral ischemia and lower renal abnormalities.

Keywords: ethnos, elderly and senile age, chronic brain ischemia, chronic kidney disease.

The problem of cerebro-renal interactions in elderly and senile age patients suffering from chronic cerebral ischemia (CCI) in modern medicine is relevant primarily due to the large medical and social significance. This is due to the fact that impaired renal function plays a significant role in accelerating the development and

progression of CCI associated with atherosclerosis and arterial hypertension [1]. The high prevalence of CCI is explained not only by demographic changes in modern society with an increase in the proportion of elderly and senile age people, but also by an increase in the prevalence of risk factors, which include arterial hypertension, atherosclerosis, diabetes and obesity [3]. It is known that each ethnic group of the population determines its own characteristics in the epidemiology of a disease. CCI in combination with chronic kidney disease (CKD) is no exception.

The aim of the study was to research the ethnic and age-related characteristics

of neurological symptoms and functional state of the kidneys in elderly and senile age people of Yakutia.

Materials and research methods.

This study was performed in the confines of the neurological department of the Geriatric Center of the Republican Hospital of Sakha (Yakutia) "Republican Hospital №3". 522 patients from 60 to 89 years, of comparable age and sex, were examined. CCI was diagnosed according to the Classification of Vascular Brain Lesions of the Institute of Neurology, Russian Academy of Medical Sciences (1985), the diagnosis was worded in accordance with ICD-10. The criterion for the diagnosis was instrumentally con-

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firmed lesion of cerebral vessels with the corresponding clinical picture of the stages of CCI in accordance with the classification of E.V. Schmidt (1985) - patients with chronic cerebral ischemia stage I (CCI I) and patients with chronic cerebral ischemia stage II (CCI II).

The following diseases were excluded:

- identified malignant neoplasms or operations for such pathology in the patient's medical history;

- diseases of the blood system, including anemia;

- angina pectoris of the 4th FC, as well as acute myocardial infarction (up to 40 days), the presence of congestive heart failure of the 3rd and more functional class (NYHA, New York, 1964);

- Alzheimer's disease and vascular dementia;

- chronic renal failure >3rd stage according to M.A. Ratner;

- acute inflammatory pathology of the articular apparatus;

- chronic obstructive diseases of the bronchopulmonary apparatus with respiratory failure (RF) stage II-III and manifestations of chronic pulmonary heart disease;

- obliterating arteriopathy of the lower limbs stages III-IV according to Fontaine.

Strict elimination criteria are justified by the fact that the clinical manifestations of the diseases listed above come to the forefront, changing the clinical picture and the course of chronic cerebral ischemia.

All patients were divided into three ethnic groups:

1st group - 174 patients of the Even nationality (representatives of small indigenous peoples of the North), living in the Arctic zone. 87 people were in the subgroup of CCI I, CCI II - 87.

2nd group - 177 patients of the Yakut nationality (CCI I - 90, CCI II - 87),

3rd group - 171 patients of the Russian nationality (CCI I - 86, CCI II - 85).

The age of the examined patients ranged from 60 to 89 years; the average age of the examined was 72.7 ± 7.2 years, for men - 72.9 ± 7.2 , for women - 72.6 ± 7.2 years. The age groups were formed based on the WHO classification: early elderly people - 60-74 years, late elderly people - 75-89 years.

In order to study the functional state of the kidneys and assess the severity of chronic kidney disease (stage) in patients with different stages of CCI, depending on ethnicity, the level of glomerular filtration rate was calculated, the parameter most correctly (in the form of one specific numerical value) reflecting global kidney function. The speed of the glomerular fil-

Distribution of patients with chronic cerebral ischemia by ethnicity and age groups

Age group	Evens n=174		Yakuts n=177		Russians n=171	
	n	%	n	%	n	%
CCI I						
60-74 years	42	48.3	61	67.8	54	62.8
75-89 years	45	51.7	29	32.2	32	37.2
CCI II						
60-74 years	46	52.9	58	66.7	40	47.1
75-89 years	41	47.1	29	33.3	45	52.9

tration rate was determined by two computational methods with the subsequent determination of the stages of chronic kidney disease:

Cockcroft&Gault

$GFR (ml/min) = \frac{(140-age) \times body\ weight\ (kg)}{720} \times E\ blood\ creatinine\ (\mu mol/l)$,
where E-1,23 for men and 1,04 for women

MDRD:

$GFR (ml/min/1.73\ m^2) = 186 \times (serum\ creatinine\ (mg/dL))^{-1.154} \times (age)^{-0.203} \times (0.742\ for\ women)$.

The stages of chronic kidney disease were determined in accordance with the classification of the National Kidney Foundation of the USA [4].

Statistical processing of the research results was performed using the SPSS 19.0 software package. To describe the quantitative data, an average value with a standard deviation was calculated. Qualitative attributes are presented in the form of frequency tables containing absolute values and the relative share of the attribute (percentage). Verification of the laws of distribution of quantitative traits for compliance with the normal law was performed using the Kolmogorov-Smirnov test. The test results showed that the distribution of the studied parameters differs from the normal distribution. The Mann-Whitney paired test was used to compare the average values of the studied parameters. In all statistical criteria used, the value of $p < 0.05$ was taken as the threshold level of significance.

Results and discussion. The main objective of our work was to study the functional state of the kidneys, which was determined by the decrease in the glomerular filtration rate, a parameter that most correctly (as one specific numerical value) reflects global kidney function, and an assessment of the severity of chronic kidney disease (stage) by the glomerular filtration rate [2]. The value was determined by two computational methods with subsequent determination of the stages of chronic kidney disease.

As shown in table 2, manifestations of renal dysfunction with glomerular filtration rate from 58.78 to 77.87 are observed in all patients with CCI, a more pronounced decrease in renal function is observed in the representatives of the 3rd group in both computational formulas. In patients of the 1st group, the glomerular filtration rate is higher than in patients of the 2nd and 3rd

Table 2

The average value of glomerular filtration rate by calculation formulas (unit)

Formula	Subgroup	Evens		Yakuts		Russians		P_{e-r}	P_{e-ya}	P_{ya-r}
		M	m	M	m	M	m			
Cockcroft&Gault	CCI I	74.21	2.34	72.19	2.26	72.64	2.57	0.652	0.536	0.895
		77.97	2.48	72.54	2.23	73.93	2.63	0.991	0.669	0.687
Cockcroft&Gault	CCI II	70.06	2.31	65.05	2.22	58.78	2.25	0.001	0.121	0.005
		77.87	7.17	66.52	2.29	67.87	10.00	0.416	0.194	0.895

Note: M - average value, m - standard error of the mean

Table 3

The average values of glomerular filtration rate, depending on age and ethnicity

	Calculation formula	Evens		Yakuts		Russians		P _{e-ya}	P _{e-r}	P _{ya-r}
		M	m	M	m	M	m			
CCI I	60-74 years									
	Cockcroft&Gault	91.81	2	81.72	2.29	86.54	2.08	0.002	0.078	0.127
	MDRD	90.25	2.96	81.89	2.25	85.87	2.29	0.025	0.521	0.66
	75-89 years									
	Cockcroft&Gault	57.79	2.15	53.13	2.40	49.18	2.81	0.092	0.016	0.434
	MDRD	58.78	2.19	52.88	2.41	50.40	2.71	0.083	0.018	0.501
CCI II	60-74 years									
	Cockcroft&Gault	78.10	2.86	70.67	2.57	70.79	2.96	0.057	0.81	0.976
	MDRD	78.27	2.89	74.44	2.68	69.9	20.65	0.145	0.552	0.319
	75-89 years									
	Cockcroft&Gault	61.04	3.21	53.80	3.44	48.10	2.43	0.136	0.002	0.169
	MDRD	77.42	14.97	54.88	3.43	48.29	2.42	0.213	0.048	0.123

groups. Statistically significant differences were observed in patients with CCI II in Evens and Yakuts compared with Russians.

Old age and CCI increasing severity decreases GFR in all ethnic groups (table 3). In Yakuts and Russians with CCI I and CCI II of all age groups GFR is lower compared with the Evens. Significant differences were noted in patients with CCI I of the Yakut nationality compared

with Evens in the elderly (60-74 y/o) age group and in Russians compared with the Evens in the senile (75-89 y/o) age group according to the two computational formulas. In patients with CCI II, statistically significant differences were noted only in Russians aged 75-89 years compared with the Evens in the same group. Decrease in GFR, depending on the stage

of CCI, is less pronounced in Evens, more in Russians, Yakuts occupy an intermediate position.

Evaluation of the functional state of the kidneys in patients using the computational formulas revealed a high incidence of the formation of chronic kidney disease in patients with CCI. In our opinion, the cause of such relationships may be the parallelism of atherogenesis processes.

Thus, in patients with CCI, both in stage I and stage II, in the elderly and the senile, the best indicators of kidney function are observed in Evens rather than in Yakuts and Russians. Moreover, with age, the severity of chronic kidney disease increases in parallel with the stage of chronic cerebral ischemia in each ethnic group.

We also carried out a comparative analysis of the dependence of the neurological symptoms of chronic cerebral ischemia on the mean value of the glomerular filtration rate in the elderly and senile, taking into account national identity and age group (Table 4). We have

Table 4

Neurological symptoms in the studied patients by age depending on the magnitude of the glomerular filtration rate

Neurological symptoms	Evens		Yakuts		Russians		P _{e-ya}	P _{e-r}	P _{ya-r}
	M	m	M	m	M	m			
60-74 years									
Vestibulopathy	74.81	4.26	70.83	3.63	71.83	3.54	0.083	0.595	0.844
CCF	82.28	2.29	76.04	1.91	78.53	2.05	0.039	0.225	0.377
Extrapyramidal syndrome	85.95	9.47	65.86	9.45	51.56	11.34	0.19	0.083	0.381
MCI	76.11	4.55	71.10	3.39	71.50	4.17	0.384	0.462	0.941
POR	41.04	2.96	39.09	4.83	54.45	17.87	0.753	0.589	0.544
Ataxia	77.62	4.03	73.30	3.67	72.52	4.18	0.432	0.385	0.889
Pyramidal syndrome	77.32	4.19	71.79	3.23	71.95	3.52	0.303	0.334	0.973
Pathological reflexes	50.00	9.12	36.77	2.20	43.32	3.65	0.282	0.552	0.209
Vegetative symptoms	84.07	3.92	78.20	5.04	82.87	2.48	0.368	0.798	0.418
Sensory disorders	85.04	5.14	76.45	4.99	80.01	3.86	0.238	0.441	0.575
Reflex asymmetry	89.35	5.51	85.24	3.70	85.48	3.78	0.544	0.570	0.965
Vestibular-ataxic disorders	95.55	4.31	85.57	3.21	92.50	3.74	0.078	0.60	0.172
Changes in muscle tone	102.09	5.50	86.95	7.56	84.66	5.04	0.141	0.044	0.807
75-89 years									
Vestibulopathy	59.87	4.36	54.78	7.64	47.78	2.71	0.576	0.026	0.417
CCF	59.20	2.39	53.13	2.26	49.71	1.95	0.069	0.003	0.256
Extrapyramidal syndrome	79.85	6.69	37.28	1.05	52.29	5.27	0.125	0.235	0.035
MCI	60.47	6.31	55.02	4.14	48.75	3.41	0.408	0.124	0.250
POR	41.41	2.29	38.79	6.04	54.83	6.77	0.742	0.101	0.152
Ataxia	56.33	4.74	52.92	4.08	48.10	3.23	0.590	0.161	0.361
Pyramidal syndrome	62.93	4.52	54.34	5.50	44.89	2.41	0.239	0.001	0.134
Pathological reflexes	39.29	1.25	38.23	1.43	40.97	2.29	0.588	0.537	0.335
Vegetative symptoms	54.54	4.23	50.07	4.12	41.93	3.02	0.457	0.022	0.429
Sensory disorders	61.68	5.93	51.54	4.61	49.69	3.50	0.192	0.098	0.751
Reflex asymmetry	56.81	6.23	52.44	3.15	51.38	5.95	0.547	0.540	0.879
Vestibular-ataxic disorders	54.05	5.20	53.47	3.33	55.20	4.36	0.926	0.818	0.756
Changes in muscle tone	49.55	4.21	50.24	1.87	45.66	8.78	0.809	0.846	0.657

identified changes in the clinical picture, neurological status. Persons of Russian nationality had more pronounced changes in the clinical picture of neurological symptoms.

At the same time, according to the symptoms, high numbers of GFR are observed in elderly Evens, except for primitive oral reflexes (POR). Yakuts have low GFR, except for extrapyramidal syndrome, ataxia and changes in muscle tone. Russians have a high GFR with POR, a low with extrapyramidal syndrome, ataxia.

Among the senile, the Evens have a more favorable clinical picture, with the exception of POR, pathological reflex, vestibular-ataxic disorders (VAD), changes in muscle tone. Renal dysfunction is expressed in Russians, apart from extrapyramidal syndrome, POR, pathological reflexes, VAD. Late elderly Yakuts occupy an intermediate position, except for the extrapyramidal syndrome, POR, pathological reflexes, VAD, where there are lower rates of GFR.

An interesting fact is that in the elderly the low rate of GFR is observed in representatives of all nationalities with POR and pathological reflexes, which explains the parallelism of the stages of CKD and CCI.

In the senile Evens, GFR is reduced with all objective symptoms of CCI, ex-

cept for the extrapyramidal syndrome, it is mild cognitive impairment (MCI), pyramidal syndrome, and sensory disorders. A more pronounced decrease in GFR is also observed in representatives of all nations with POR, pathological reflexes, in addition, in Evens, with the changes of the muscle tone, in Yakuts with extrapyramidal syndrome, ataxia, in Russians with vestibulopathy, CCF (craniocerebral failure), MCI, ataxia, pyramidal syndrome, and sensitive disorders, change in muscle tone.

Thus, the presence of chronic kidney disease was associated with the most pronounced cognitive and neurological disorders, and a worsening of symptoms with the severity of CCI was noted.

Conclusion. Based on our study, it can be stated that in the studied elderly and senile age patients, the development and progression of chronic cerebral ischemia occurs in parallel with the progression of chronic kidney disease. At the same time, more severe neurological symptoms were discovered in the representatives of the non-indigenous population due to structural changes in the cerebral vascular bed due to arterial hypertension and atherosclerosis, as well as severe renal dysfunction. The Evens, the indigenous inhabitants of the northern regions of Yakutia, who re-

tained a calmer, more traditional lifestyle and nutrition of the peoples of Yakutia, had lighter clinical symptoms of chronic cerebral ischemia and lower renal abnormalities.

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DISTRIBUTION OF CARRIERS OF “INDO-EUROPEAN” HAPLOTYPES OF HLA SYSTEM ON THE TERRITORY OF EURASIA

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The age of the “Indo-European” haplotypes HLA-A1/B17 and HLA-A1/B8 is calculated for different populations of Eurasia. The obtained data are compared with historical events. The results show that the most ancient carriers of the HLA-A1/B17 haplotype are Latvians, and the HLA-A1/B8 haplotype are the Turks. The distribution of the HLA-A1/B17 haplotype in populations is consistent with the migration patterns of Indo-European tribes. This is not observed for HLA-A1/B8; therefore, it has been suggested that the majority of Indo-European tribes did not have this haplotype.

A definition of allele frequencies is proposed by directly counting the number of haplotypes by alleles without using the Bernstein formula.

Keywords: Indo-Europeans, HLA system, haplotype, population, founder effect.

Since the 70-s of the last century, antigens of the HLA system have been widely used for genetic characterization of populations along with other polymorphic systems. On the basis of allele frequencies, similarities or differences between individual populations were identified, and phylogenetic trees were constructed. At the end of the 20th century, a new approach to the study of population genetics appeared, called genetic archeology. The new approach pays great attention

to the study of haplotypes, since it can provide more specific information about some population events.

For the new approach, the HLA system with highly polymorphic and closely linked loci is a very convenient tool for studying the genetic history of populations. From the literature data on the frequencies of alleles and haplotypes of the HLA system from different populations, one can determine the critical moments in their history, the age of expansion of those or other haplotypes, and associate them with a specific historical event.

According to V.V. Fefelova [23] L. Degos and J. Dausset believed that

the *HLA-A1* and *HLA-B8* genes, also *HLA-A1/B8* haplotype are Indo-European, since they appeared in Europe together with Indo-European tribes. At the time, Indo-Europeans in Siberia distributed the haplotype HLA-A1/B17. Therefore, this paper discusses the distribution of haplotypes HLA-A1/B17 and HLA-A1/B8 over the territory Eurasia.

To calculate the age of the haplotype in population, the formula according to [3] is used:

$$S_{1/2} = 1 - p^{1/n},$$

where *S* is the genetic distance between the loci under study, *p* is the level stability (the proportion of chromosomes