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RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN THE ARCTIC ZONE OF THE REPUBLIC OF SAKHA (YAKUTIA)

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To date, there is a worldwide trend of increasing morbidity and mortality in patients with chronic kidney disease. Given the secondary nature of kidney damage, prevention and early detection of risk factors are the main priority of modern medicine.

The purpose of our work was to conduct a screening study of the population of the Momsky district (5 settlements) of the Republic of Sakha (Yakutia) for early detection of damage and decreased kidney function.

Results. The study involved 222 people, of whom 14 (6,3%) had chronic kidney disease (GFR less than 60 ml/min/1.73 m2). An early predictor of the development of chronic kidney disease, albuminuria was found in 70 (31.5%) of the examined patients. The main risk factors affecting the development of chronic kidney disease were hypertension (54.3%), burden of cardiovascular diseases (50%) and obesity (37.1%), burden of kidney diseases were in 11 (15.7%) of the examined patients.

Keywords: chronic kidney disease, Arctic zones, albuminuria, glomerular filtration rate, risk factors.

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Introduction. Currently, it can be stated that the global burden of chronic kidney disease (CKD) is only increasing [2,12]. Being one of the most common pathologies of non-infectious nature, CKD causes not only social, but also economic damage to the medical field. The prevalence of CKD increases exponentially, being the consequences of diseases such as diabetes mellitus and cardiovascular diseases. In the epidemiological study of GBD Chronic Kidney Disease Collaboration, The Lancet, by 2017, the number of patients with various stages of CKD reached almost 700 million, while if the mortality rate at the diagnosis of CKD led to 1.2 million deaths in 2017, the number of which is projected to grow to 2.2 million by 2040 at best and up to 4.0 million in the worst case [12].

Data on the prevalence of CKD differ in countries with a higher standard of living, depend on income and public awareness of the outcomes of cardiometabolic diseases. In addition to regional peculiarities, the formation of CKD is influenced by age, gender, impaired plasma glucose levels, hypertension, high body mass index, high sodium content in food [2,5,12].

In Russia, general population studies of the prevalence of CKD at the predialysis stages have not been conducted, but the results of individual epidemiological studies confirm the high prevalence of pathology [1,2].

Thus, according to the All-Russian register as of 31.12.2020, the number of patients with stage 5 CKD and receiving renal replacement therapy was 60,547 [1]. In addition to epidemiological problems, the cost of treatment in this group of patients should also be attributed, since the costs of renal replacement therapy make up a significant part (2-5%) of health budgets in developed countries, while the proportion of patients is no more than 0.7% of the total number of patients [6]. Although the diagnosis of CKD is quite simple, there is insufficient detectability at the outpatient level, namely the difficulty of registering albuminuria, albumin-creatinine ratio, glomerular filtration rate (GFR) [8].

In the multicenter observational study "CKD screening" conducted in 12 regions of Russia, the aim was to study the prevalence of CKD in patients who visited primary health care institutions who had not previously been diagnosed with CKD [3]. It was found that among the 1.2 million patients who presented to primary health care facilities, 13.2% had previously undiagnosed CKD, 72% of whom had C3a-C3b CKD. At the same time, the main causes of CKD were arterial hypertension, chronic heart failure and obesity.

Considering that the majority of CKD is secondary nephropathies on the background of diabetes mellitus and cardiovascular diseases, the relevance of diagnosis, treatment and, most importantly, prevention of CKD has become an interdisciplinary therapeutic problem.

Thus, considering the impact on the quality of medical care for patients with CKD of such factors as the availability of laboratory methods, awareness of the population, the influence of "urbanized" risk factors on the formation of kidney pathology, we have begun a study of the adult population of remote Arctic regions of the Republic of Sakha (Yakutia).

In total, 13 districts belong to the Arctic zone of the republic. According to the data of the Yakut Republican Medical Information and Analytical Center (YARMIAC) on the incidence of the genitourinary system (ICD-10) among the adult population of the Arctic regions of the Sakha Republic (glomerular, tubulointerstitial kidney diseases, other kidney and urinary tract diseases) have a significant tendency to decrease over the past 10 years, which may indicate not only the migration of the population, but also improving the quality of medical care provided. So, in 2013, 649 patients were registered with a newly diagnosed diagnosis for this group of diseases, and in 2022 only 108 people (per 1000 population, this indicator was 13.3 and 2.3, respectively). With respect to renal insufficiency (ICD-10, N18), the total incidence of the adult population in 2013 was 19 people, increasing to 78 by 2022 (0.4 to 1.8 per 1000 population, respectively). As for the primary morbidity, 3 patients were diagnosed with renal insufficiency in 2013, and 15 in 2022 (0.06 and 0.32 per 1000 population, respectively).

In our study, we used screening methods for CKD risk factors among the adult population in one Arctic region – Momsky district.

According to YARMIAC, the total incidence of renal insufficiency in the adult population of Momsky district in 2013 and in 2022 was 2.5 per 1000 population (7 patients each). In 2013, the primary incidence of renal insufficiency was not registered, in 2022 it was diagnosed in 1 person, which was 0.4 per 1000 population.

Material and methods. This study was conducted free of charge based on a screening program designed to identify individuals with an increased risk of kidney disease and to motivate individuals to regular medical examination, as well as correction therapy. Eligible participants in the study were men and women over the age of 18, as far as free circulation. Participants who received regular dialysis treatment or were diagnosed with CKD were excluded from this study.

Data on demographic characteristics of participants, personal and family medical history, as well as health behaviors were collected [4]. Blood and urine samples were collected and processed to determine serum creatinine and urine albumin levels.

Potential risk factors for CKD included age, gender, obesity (body mass index over 30 kg/m2) and nationality. The age was determined by the stated date of birth at the time of screening and was divided into three groups: 18-44, 45-59 and 60 and older according to the criteria of the World Health Organization [6].

The glomerular filtration rate (GFR) was determined using the initial serum creatinine value recalculated by the CKD-EPI formula 2009 [13]. Urine samples were collected and tested for albuminuria using Combilyzer (Human GmbH, Germany). Criteria for CKD were albuminuria > 30 mg/g and/or eGFR < 60 mL/min/1.73 m2 based on the KDIGO 2012 Clinical Guidelines for CKD [13].

The population in the Momsky district in 2022, according to Rosstat, amounted to 3991 people, there is a decrease in the population (in 2021 – 4021 people) [14]. Out of 6 naslegs (settlements) of the Momsky district, the population of 5 settlements and a separate settlement of reindeer herders were examined by a simple screening method. In the Indigir national nasleg (Buor-Sasy village) the total population is 342 people, of whom 40 have been examined; in the Moma national nasleg (Khonu village) - 2295 people, 56 were examined; 255 people live in Sobolokh national nasleg (Sobolokh village), 42 have been examined; in Tebulakh national nasleg (Chumpu-Kytyl village) out of 214 people, 21 were examined; In the Ulakhan-Chistai national nasleg (Sasyr village + reindeer herders' settlement), 63 out of 673 people were examined. The study did not include the Chybagalakh national nasleg (Kulun-Elbut village).

Results. A total of 222 people were screened from February 2023 to May 2023. There were significantly fewer men in the study - 57 (25.7%) than women - 161 (72.5%). The data for the determination of eGFR were available for all 222 (100%) and formed our main research part. CKD (a decrease in eGFR of less than 60 ml/min/m2) was detected in 14 (6.3%) of the studied. Data for the determination of albuminuria among the study population were available for 181 (81.5%) of the total, while high level of albuminuria (A2, A3) was detected in 70 (31.5%) people.

In the age group older than 60 years, 13 (5.9%) showed reduced eGFR, while in the young group (18-44 years) there was no decrease in eGFR (Table 1). We also see a tendency to increase the prevalence and albuminuria with the age of patients (16.2%), but there is a fairly high percentage and in the young age group (13%).

In terms of settlements, most of the participants were in the village of Sasyr with a settlement of reindeer herders, where 63 people were examined, a smaller number of participants in the village of Chumpu-Kytyl were examined 21. At the same time, the percentage of stage 3 CKD (eGFR less than 60 ml/min/m2) among the participants in the localities was the highest among those examined in the village. Buor-Sasy in 5 (12.5%) out of 40 participants and also 5 people (9%) out of 56 in the village of Khonu.

In the study of an early marker of kidney damage, a high detection rate of albuminuria was observed in 36 out of 63 (57.1%) patients studied in the village of Sasyr with a settlement of reindeer herders, which exceeds the detection rates of albuminuria among the population of the district center of the village of Khonu (34%). At the same time, a decrease in eGFR was detected in only one person in the village of Sasyr.

According to the distribution of patients by categories of CKD (eGFR and albuminuria), the following features were revealed (Table): eGFR ≥90 ml/min/1.73 m2 was detected in 131 patients, of which 44 (33.6%) had albuminuria; eGFR 60-89 ml/min/1.73 m2 in 77 patients, albuminuria in 20 (26%) patients. 13 people had stage 3 CKD (6 patients with albuminuria) and 1 with stage 4 CKD (without albuminuria).

To determine the significance of the influence of risk factors, we assessed age, sex, nationality, obesity, diabetes, hypertension, and smoking, as well as available data on heredity – burden of diabetes, hypertension (cardiovascular diseases) and kidney disease (Table 1).

Patients with diabetes accounted for 31 (14% of the total number studied), and among those who had a eGFR < 60 ml/min/1.73 m2, diabetes was detected in only 3 (9.7)%.

Of all the studied 98 (44.1%) people, arterial hypertension was detected, of which albuminuria was detected in 31 patients (31.6%). The distribution by albuminuria and eGFR is presented in Table.

Obesity (BMI more than 30 kg/m²) was observed in 65 (29.3%) of all patients, among this group of patients, albuminuria with normal eGFR was detected in 14, with eGFR 60-89 ml/min/1.73 m2 in 7, eGFR < 60 ml/min/1.73 m2 in 5.

Among 63 smokers and previous smokers (28.4% of the total number studied), normal eGFR was observed in 61, a decrease in eGFR < 60 ml/min/1.73 m2 in 1, and albuminuria in 21 (9.5% of the total number studied).

A history of diabetes was observed in 32 (14.4%) people according to the questionnaire, while 12 had significant albuminuria. Cardiovascular diseases (CVD), including hypertension, accounted for 101 (45.5%) and albuminuria was detected in 35 in this group. The burden of

Identification of risk factors for CKD in subjects depending on albuminuria and glomerular filtration rate

Criteria	Albuminuria > 30 mg/g in individuals with eGFR ≥ 90 mL/min/1.73 m2 (CKD G1)	Albuminuria > 30 mg/g in individuals with eGFR 60-89 mL/min/1.73 m2 (CKD G2)	eGFR 30-59 mL/min/1.73 m2 *regardless of* albuminuria (CKD G3)	eGFR 15-29 mL/min/1.73 m2 *regardless of* albuminuria (CKD G4)
Albuminuria (> 30mg/g)	44	20	6	0
Age, year old				
18–44	22	7	0	0
45–59	10	2	1	0
Старше 60	12	11	12	1
Gender,				
Men	15	10	1	0
Women	29	10	12	1
Nationality				
Yakuts	27	11	8	1
Evens	14	2	0	0
Evenki	1	2	2	0
Russians	2	3	2	0
Undefined	0	2	0	0
Obesity (BMI 30 kg/m2)	14	7	4	1
Diabetes mellitus	5	1	3	0
Arterial hypertension	17	10	10	1
Smoking	15	5	1	0
History of diabetes mellitus	7	1	3	1
History of cardiovascular disease	23	6	5	1
History of kidney disease	7	2	2	0

kidney disease occurred in 41 (18.5%) of the examined, albuminuria in 11 of them.

It is noteworthy that many of the subjects found it difficult to answer the questionnaire regarding high blood sugar levels and a history of hereditary burden.

In the study of national characteristics, no significant differences were revealed.

Discussion. According to a large epidemiological study [12], CKD is a highly prevalent disease, a burden that has not decreased as much as many other important noncommunicable diseases over the past 27 years.

In our study, 70 (31.5%) of the 222 patients examined had significant albuminuria. 14 (6.3%) had a decrease in eGFR < 60 mL/min/1.73 m2, 93% of whom were in the older age group.

When analyzing the influence of risk factors on renal injury (patients with albuminuria > 30 mg/g), it was found that 38 (54.3%) had arterial hypertension, 35 (50%) had CVD and hypertension, and 26 (37.1%) had obesity. Among the studied patients in the stage 3-4 CKD group, renal injury is probably more associated with the presence of hypertension (11 patients out of 14) than with diabetes (3 patients). In general, the prevalence of arterial hypertension is quite high - 98 (44.1%), while various forms of diabetes were detected in 31 (14%). Modifiable risk factors have a fairly high prevalence, for example, obesity occurs in about a third of all studied and in 37.1% patients with albuminuria.

In addition, I would like to note the high prevalence of smoking (30%) as a known risk factor for renal damage [17] in the group of patients with albuminuria.

Our study also has some limitations, such as free recourse for examination, there may be an overestimation of the prevalence of albuminuria in a young group of patients (38.6%) who do not have predictors of CKD. In the future, we plan to cover all 13 regions of the Arctic zone of the Republic of Sakha (Yakutia).

It is important to note that slowing the progression of CKD in its early stages provides economic benefits [6, 16] and prevents the development of cardiovascular complications, which are the leading cause of death in patients with CKD. A comprehensive action plan should include effective management of CKD risk factors at the primary health care level, improved detection among at-risk groups, and development of routing (inter-hospital transport, telemedicine technologies) in remote areas for the treatment of patients with confirmed disease.

A characteristic feature of the Arctic regions of the republic is not only a small population, but also a low population density, on the other hand, this can be seen as a positive side. For example, the physician is informed in more detail about the health status of each patient and, knowing the risk factors for the development of CKD, prevention coverage can be of better quality. Thus, according to the YARMIAC, the incidence and primary diagnosis of renal failure has increased, which may indirectly confirm that the diagnosis of CKD in the region has improved.

Further research in the field of prevention and early diagnosis of CKD opens up great prospects for the development of innovative approaches in the prevention, prognosis and treatment of severe socially significant and economically burdened end-stage CKD.

Conclusion. Identification of early predictors of the development of CKD, the introduction of more convenient preclinical diagnosis and documentation of CKD predictors for primary health care, as well as a patient-centered approach considering the inaccessibility of medical care are important to ensure the optimization of population-significant diseases in the residents of the Arctic regions of the Republic of Sakha (Yakutia).

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SCIENTIFIC REVIEWS AND LECTURES

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BIOLOGICAL MARKERS IN PREDICTING THE COURSE OF SPINAL MUSCULAR ATROPHY AND THEIR IMPORTANCE IN ORGANIZING MEDICAL CARE

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A correlation between the levels of blood biomarkers and clinical manifestations of SMA in patients of the main regional healthcare institution of the Samara region was carried out.

Differences in creatinine, creatine phosphokinase, and lactate dehydrogenase levels among patient groups and their association with motor impairment did not show statistical significance. Differences in CPK levels between groups may be related to age, weight, gender, and levels of physical activity of patients. The data obtained from the study of the history of repeated hospitalizations do not provide reliable information due to the limited sample and heterogeneity of the data. The results of this work indicate the ineffectiveness of assessing the levels of creatinine, CPK and LDH in order to monitor and predict the course of SMA, as well as the inappropriateness of repeating these laboratory studies in patients with SMA 5q.

Keywords: creatine phosphokinase, creatinine, neurofilament, neuromuscular diseases, nusinersen, hereditary disease, pathogenetic therapy, risdiplam, spinal muscular atrophy.

Introduction. Spinal muscular atrophy (SMA) is a genetically heterogeneous group of CNS disorders characterized clinically by the loss of motor skills, progressive symmetric peripheral paralysis due to degeneration of motor neurons, and resultant atrophy of striated muscles, which leads to difficulty in swallowing, general paralysis, and respiratory failure. SMA predominantly develops in childhood and is a major hereditary cause of infant mortality (Araujo et al. 2009). The worldwide prevalence of SMA is estimated to be 8.5-10.3 per 100,000 newborns, with carrier frequencies ranging from 1 in 35 to 1 in 60 (Kimizu et al. 2021). SMA is most commonly caused by autosomal inheritance mutations, resulting in a roughly equal distribution among both genders, although the gender frequency differs slightly according to SMA type (Verhaart et al. 2017, Gayduk & Vlasov 2019). The most common forms, known as SMA 5q, have no clear association with cognitive