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EPIDEMIOLOGY OF CONGENITAL DYSFUNCTION OF THE ADRENAL CORTEX IN THE REPUBLIC OF SAKHA (YAKUTIA)

DOI 10.25789/YMJ.2023.82.16

УДК 159.91, 612.172.2

In the article the results of the long-term monitoring of the incidence of new cases and prevalence of congenital adrenal cortical hyperplasia in children of the Republic of Sakha (Yakutia) are presented. The Republic of Sakha (Yakutia) is one of those model regions where epidemiological studies of the incidence of hereditary diseases can be carried out in view of the relative constancy of the population and low migration. The results of the neonatal screening and the register of the endocrinology department of the Pediatric Center of the Republican Hospital No.1-NCM showed an increased incidence and prevalence of congenital hyperplasia of the adrenal cortex in children of the Republic of Sakha (Yakutia). Epidemiological studies should become the basis for conducting in-depth molecular genetic studies in view of the high prevalence of severe forms of congenital hyperplasia of the adrenal cortex in children of the Republic of Sakha (Yakutia).

Keywords: Congenital hyperplasia of the adrenal cortex, adrenogenital syndrome, congenital adrenal hyperplasia, Yakutia, epidemiology, frequency, prevalence.

Introduction. Congenital adrenal hyperplasia (CAH) (adrenogenital syndrome, congenital adrenal hyperplasia) is a group of diseases with autosomal recessive type of inheritance, caused by mutations in the genes encoding enzymes involved in cortisol biosynthesis. Depending on the type and severity of the enzyme deficiency, this can lead to impaired biosynthesis of glucocorticoids, mineralocorticoids and sex hormone production [1, 2, 5, 6]. The most common disorder is 21-hydroxylase deficiency, which occurs in up to 95% of cases as a result of mutations or deletions in the CYP21A2 gene. Enzyme deficiency leads to impaired production of cortisol, aldosterone, and an excess of androgens [5, 7].

Congenital adrenal hyperplasia is one of the most common autosomal recessive diseases. Active introduction of neonatal screening has revealed the frequency of congenital adrenal cortical hyperplasia in various populations [1,2]. According to findings of Pang S. Y. et al., the incidence of the classic form of CAH due to 21-hydroxylase deficiency was 1 case per 14199 live births for homozygous subjects and 1 in 60 for heterozygous subjects, respectively, between 1980 and 1988 [8].

A systematic review including results from 58 studies from 31 countries (for the period 1969-2017) showed an average incidence of CAH of 1:9498 (95% confidence interval: 1:9089- 1:9945). The highest incidence was detected in Eastern Mediterranean and Southeast Asian countries; the lowest incidence was registered in Asia-Pacific countries [7]. According to the results of neonatal screening in the Russian Federation, the incidence of classical forms of 21-hydroxylase deficiency is 1 case per 9638 live births [1]. The incidence is highest in the Ural Federal District (1:6749) and lowest in the Northwestern Federal District (1:14876) [1].

Timely diagnosis and prescription of adequate treatment of CAH are urgent tasks of modern endocrinology and pediatrics. Despite a number of profound scientific and clinical achievements in recent years, the data on the frequency, prevalence and molecular genetic features of the disease in different populations require updating.

The aim of the study is to estimate the incidence of new cases and prevalence of congenital adrenal cortical hyperplasia in children in the Republic of Sakha (Yakutia).

Materials and Methods. The data from neonatal screening in the period 2006-2020 were analyzed to estimate the incidence of new cases of congenital adrenal hyperplasia in the Republic of Sakha (Yakutia). To estimate the prevalence of CAH, a registry of children with congenital hyperplasia of the adrenal cortex was compiled according to the endocrinology department of the Pediatric Center of the State Budgetary Institution of the Republic of Sakha (Yakutia), the Republican Hospital No.1-NCM, as the head institution for diagnosing this disease.

The study protocol was approved by the Ethical Committee of the Federal State Budgetary Institution Yakutian Re-

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Table 1

The results of the neonatal screening of newborns for adrenogenital syndrome in the Republic of Sakha (Yakutia) in 2006-2020

Year	The number of newborns in the Republic of Sakha (Yakutia) according to the Yakutian Republican Medical Information and Analytical Center	Examined for adrenogenital syndrome	Coverage. %	The number of ill ones	Frequency (1 case per total number of the surveyed ones)
2006	13623	5559	40.8	0	0
2007	15152	14931	98.5	1	14931
2008	15254	10746	70.4	2	5373
2009	15783	15468	98.0	0	0
2010	15877	15662	98.6	0	0
2006-2010	75689	62366	82.4	3	20788.7
2011	16173	16092	99.5	1	16092
2012	16922	16832	99.5	4	4208
2013	16611	16546	99.6	1	16546
2014	16964	16946	99.9	2	8473
2015	16469	16459	99.9	0	0
2011-2015	83139	82875	99.7	8	10359.4
2016	15418	15385	99.8	0	0
2017	13710	13693	99.9	0	0
2018	13472	13456	99.9	1	13456
2019	12713	7720	60.7	1	7720
2020	13034	6465	49.6	1	6465
2016-2020	68347	56719	83.0	3	18906.3
2006-2020	**227175**	**201960**	**88.9**	**14**	**14425.7**

search Center of Complex Medical Problems (Report No.52 dated January 28, 2021, Resolution No.1).

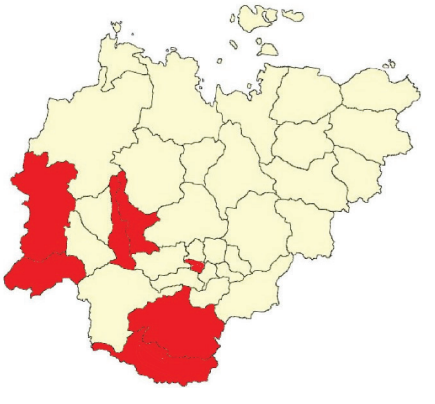
Results and Discussion. Neonatal screening for adrenogenital syndrome in the Republic of Sakha (Yakutia) has been performed since 2006 at the Medical Genetics Center of the Republic of Sakha (Yakutia), the Republican Hospital №1-NCM (head, candidate of medical sciences Sukhomyasova A.L.). A total of 201960 newborns were examined in 2006-2020 (Table 1). During this period 14 children with adrenogenital syndrome were identified. Thus, the incidence of adrenogenital syndrome for 2006-2020 in the population of newborns of the Republic of Sakha (Yakutia) according to neonatal screening was 1 case per14426 studies (14:201960). When divided into 5-year periods, it was found that the frequency of CAH detection was maximal in 2011-2015. For the most recent time interval (2016-2020), the incidence of new cases was 1 case per 18906 neonates examined. Thus, according to neonatal screening, an increase in the frequency of congenital hyperplasia of the adrenal cortex in newborns in the Republic of Sakha (Yakutia) has been observed over the 15-year period.

To assess the dynamics of CAH prevalence, a comparative analysis of the data for 2007 and 2020 (Table 2) according to the register of children with congenital adrenal hyperplasia of the endocrinology department of the Pediatric Center of the State Budgetary Institution of the Republic of Sakha (Yakutia) "Republican Hospital No.1-NCM" was performed. In 2007 there were 11 children with CAH under observation at the endocrinology department of the State Budgetary Institution of the Republic of Sakha (Yakutia), the Republican Hospital No.1-NCM, with a rate of 5.3 per 100,000 of the total child population of the republic. At the end of 2020 there were 21 children with congenital dysfunction of the adrenal cortex (7.9 per 100,000 of the child population). The increase in the prevalence of CAH also indicates an improvement in the results of treatment of the disease.

Table 2

Prevalence of classical CAH in children of the Republic of Sakha (Yakutia) according to the data of the registry

Registry		
Год	Number	Per 100 000 infant population
2007	11 cases per 207405 child population	5.3
2020	21 cases per 264141 child population	7.9



Distribution of patients with CAH by administrative districts of the Republic of Sakha (Yakutia).

Thus, the incidence of congenital dysfunction of the adrenal cortex in the Republic of Sakha (Yakutia) is comparable with the world data [8]. At the same time, studies conducted earlier in the republic have shown that the incidence of mutations associated with the disease in the child population is rather wide and varies in individual ethnic groups [3,4].

As of 2022, there were 23 children with a confirmed diagnosis of congen-

ital adrenal cortical hyperplasia in the Republic of Sakha (Yakutia). Picture 1 shows the areas of residence of patients with the disease.

Of the total number of patients, there are fourteen in Yakutsk and Zhatai, three in Neryungri District, two in Verkhnevilyuisky District, two in Aikhal and Udachny, Mirny District, and one each in the cities of Lensk and Aldan. The ethnic composition of patients with CAH is as follows: 10 children were Sakha, there were 12 Russian and one was of Evenk ethnicity. Among them there are 13 girls and 10 boys. It should be noted that there are 2 orphans among the total number of patients with CAH, half-siblings, from different fathers, living in the City Baby Home of Yakutsk.

Among the children enrolled in the registry of patients with CAH, 95.5% (or 21 in absolute numbers) of children have the solteric form of the disease. Their age ranges from 4 months to 16 years. Ethnic composition of patients with the solterian form is as follows: 11 Russians, 9 Sakha, and 1 Evenk. Gender structure - 11 girls, 10 boys.

Conclusion. The incidence of CAH among children in the Republic of Sakha (Yakutia) according to neonatal screening for the period 2006-2020 is 1 case per 14,426 newborns. Since 2006 the incidence of hereditary pathology has tended upwards (from 1 case per 20789 children in 2006-2010 to 18906 in 2016-2020 respectively). The prevalence of CAH according to the register at the beginning of 2021 was 7.9 cases per 100,000 children. In dynamics, the prevalence of CAH tends to increase, which reflects the accumulation of cases against the background of increasing frequency and improving treatment of the disease. The most common form of CAH among children in the Republic of Sakha (Yakutia) is the solenteric form, the most severe in its course. This fact indicates a high prevalence of severe mutations of groups 0 and A, leading to complete cessation of 21-hydroxylase activity. It is necessary to further investigate the frequency of mutations leading to the deficiency of enzymes involved in cortisol biosynthesis in Yakutia population.

The research was executed within the research theme "Physical development and health of the child population in the Far North (with the example of Yakutia)" (state registration number: 1021062411641-9-3.2.3), within the state assignment of Ministry of Science and Education of the Russian Federation (FSRG-2023-0003, FSRG-2020-0014).

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