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RISK FACTORS FOR CONGENITAL HEART DEFECTS IN CHILDREN OF THE REPUBLIC OF SAKHA (YAKUTIA)

Summary. The aim of the study was to examine the association between the risk of congenital heart defects in children and some perinatal factors, health status and ethnicity of parents. According to the Perinatal Center of the National Center for Medicine for the periods 2001-2003 and 2013-2015 diagnosis of congenital heart defects was more common in children of native parents. The presence of congenital heart disease in parents was associated with a greater frequency of confirmed defects in children. No statistically significant associations were established between the studied perinatal factors and the incidence of congenital heart defects in children. Probably, genetic factors should be considered as one of the main causes of the development of congenital heart defects in the population of Yakutia.

Key words: congenital malformations, congenital heart defects, native peoples of the North, Yakutia, risk factors for congenital heart defects.

Introduction. Congenital heart defects are one of the main problems of modern pediatrics. In the regions of the Russian Federation, congenital heart defects occupy a leading position in prevalence compared to other developmental defects in children and remain the leading cause of their death.

Cardiovascular lesions according to the national register of degenerate malformations have the largest specific gravity, occupying 18,1%. In different regions of the Russian Federation, the incidence rates and structure of congenital heart defects differ significantly from each other. Since 2000, a regional register has been operating in the Republic of Sakha (Yakutia), which includes data on the birth of children with developmental defects, including those with congenital heart defects. Data from this register are the basis for research and statistical work on congenital heart defects. In 2011, in the Republic of Sakha (Yakutia), the incidence of congenital heart defects amounted to 29,1 cases per 100 thousand children. The number of congenital heart defects detected increases steadily over the years and heart defects for a long time occupy the second place in the structure of infant mortality.

In the genesis of congenital heart defects, we should talk about a combination of social, hereditary, medical, as well as environmental factors. Very often, these effects can be combined. Genetic factors are considered as one of the main reasons for the development of degenerate heart defects (chromosomal mutations and deletion, fresh mutations). In isolated populations (for example, in places of compact residence of native people), genetic manifestations can arise as a result of homolocal and national marriages. According to the Yakutsk Republican Medical Information Center for the period 2002-2006,congenital heart defects were the second most common cause of death of patients under the age of 14 among evenks, evens, dolgans and yukagirs. For the period from 1995-2012, the maximum incidence of congenital heart defects was recorded in the Olekminsky, Ust-Maysky and Nizhnekolymsky districts of the Republic of Sakha (Yakutia). When analyzing the incidence of congenital heart defects in various zones of the Republic of Sakha, Yakutia, significant growth is described in the industrial, Arctic and Vilyu groups of regions.

In the structure of congenital heart defects in Yakutia, the most common are the defects of the so-called “big six”: a defect in the interventricular septum, an open arterial duct, transposition of main vessels, a defect in the intervertebral septum, tetralogy of fallot, aortic coarctation.

Due to the high significance of the problem of congenital heart defects, the aim of the study was to study the association between the risk of developing congenital heart disease and some factors of the period, the state of health and ethnicity of parents.

Materials and methods. A retrospective clinical trial was conducted on the basis of the perinatal center of the national center of medicine. The analysis included all cases of congenital heart defects (n=1824) among newborns born alive for periods of 2001-2003, and 2013-2015. The primary documentation was statistical maps of the inpatient (form №066/y-02) and inpatient journals (form №010). All cases were divided into 2 groups (confirmed and unconfirmed congenital heart defects).

In all patients with complex congenital heart defects, except for echocardiographic methods, the diagnosis was confirmed by computed tomography with contrasting vascular amplification, aortography, selective coronaroangiography.

The nationality of parents was determined by self-identification. Representative of the indigenous peoples of Yakutia included Yakuts and indigenous small peoples of the North – evens, evenks, dolgans, yukagirs, chukchi. For the analysis, 2 approaches were used, the first – with the unification of one group of children, one or both of whose parents, were representatives of the indigenous peoples of the Republic of Sakha (Yakutia) – yakuts or natives (n=1319). In the second approach, this group was divided into 2 subgroups – 1246 cases, where both parents were representatives of the native peoples of Yakutia and 73 cases where one parent was a representative of the native peoples of Yakutia. In 503 cases, parents were from other ethnic groups (Russian, peoples of Central Asia (Kyrgyz, Tajiks, Uzbeks); peoples of the Caucasus (Chechens, Ingush, Armenians); representatives of other nation-

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alities (Kumyks, Khakass, Ukrainians, Poles, Germans, Tatars, Buryats)).

Statistical calculations were performed using IBM SPSS Statistics 17 (IBM, USA) software. The Pearson X2 and Mann-Whitney criteria were used to compare the groups. The critical value of the significance level in testing statistical hypotheses was taken to be 5%.

Results and discussions. The diagnosis of congenital heart disease was confirmed in 625 out of 1822 children (34,3%). Statistically significant more often these were children of parents of native people (Table 1). These differences persisted when dividing the native group into subgroups.

Of the children with confirmed congenital heart defects 549 (87,8%) had a simple heart defect, and 76 (12,2%) – complex. When comparing the structures of confirmed congenital heart defects, no statistically significant differences were found in the proportion of simple and complex defects in children of different nationalities (Table 2).

Differences in congenital heart disease rates between native and non-native ethnos may have been due to differences in parental age, lower health quality, presence of adverse factors during pregnancy, higher incidence of genetic disorders, etc. To test these hypotheses, a comparative analysis was consistently conducted in 2 groups.

Comparison of groups by age of parents and ordinal number of pregnancy revealed no statistically significant differences (Table 3).

When studying history, it was found that in the general group in 3,8% of cases, one of the parents had a congenital heart defect. At the same time, this factor was somewhat more often noted in the group of parents of native people, the level of significance was close to critical. When dividing natives into 2 subgroups, in the group where both parents are natives, the incidence of congenital heart defects in parents was 4,4% (Table 4).

The presence of congenital heart disease in parents was associated with a greater frequency of confirmed heart defects in children. Moreover, these differences were more clearly traced in native children. The chances of having this risk factor were 2,9 times higher in children with congenital heart defects (Table 5).

All perinatal factors studied were grouped into 5 modules. Module 1 – aggravated obstetric anamnesis, module 2 – pathology of pregnancy, module 3 – harmful environmental factors, module 4 – maternal health disorders, 5 – harmful maternal habits. When comparing groups

Table 1

Incidence of confirmed congenital heart defects in different ethnic groups, n (%)

Groups	Confirmed vice		p
	No (n=1197)	Yes (n=625)	
1 approach			
Коренные (n=1319)	836 (63.4)	483 (36.6)	0.001
Некоренные (n=503)	361 (71.8)	142 (28.2)	
2 approach			
Both parents is a native (n=1246)	785 (63.0)	461 (37.0)	0.002
One of the parents is a native (n=73)	51 (69.9)	22 (30.1)	
Parents of a different nationality (n=503)	361 (71.8)	142 (28.2)	

Note: p – level of significance achieved when comparing groups (Pearson test χ2).

Table 2

Structure of confirmed congenital heart defects, n (%)

Groups	Simple (n=549)	Complex (n=76)	p
1 approach			
Native (n=483)	422 (87.4)	61 (12.6)	0.508
Non-native (n=142)	127 (89.4)	15 (10.6)	
2 approach			
Both parents is a native (n=461)	403 (87.4)	58 (12.6)	0.794
One of the parents is a native (n=22)	19 (86.4)	3 (13.6)	
Parents of a different nationality (n=142)	127 (89.4)	15 (10.6)	

Note: p – level of significance achieved when comparing groups (Pearson test χ2).

Table 3

Comparison of groups by age of parents and ordinal number of pregnancy

Indicator	Group	N	Me (Q1-Q3)	p
Mothers age, years	Non-native	142	28 (23-34)	0.262
	Native	481	27 (23-32)	
Fathers age, years	Non-native	125	30 (26-35)	0.055
	native	435	29 (25-35)	
Pregnancy sequence number	Non-native	142	2 (1-4)	0.490
	Native	482	2 (1-4)	

Note: p – level of significance achieved when comparing groups (Mann-Whitney test).

Table 4

Rate of congenital heart defects in parents, n (%)

Group of children	Congenital heart desease in parents		p
	non (n=1753)	yeah (n=69)	
1 approach			
Native (n=1319)	1262 (95.7)	57 (4.3)	0.053
Non-native (n=503)	491 (97.6)	12 (2.4)	
2 approach			
Both parents are native	1191 (95.6)	55 (4.4)	0.118
One of the parents of the native	71 (97.3)	2 (2.7)	
Parents of a different nationality	491 (97.6)	12 (2.4)	

Note: p – level of significance achieved when comparing groups (Pearson test χ2).

Table 5

Incidence of confirmed heart defects in children with heart defects in parents, n (%)

CHD in parents	Confirmed heart disease in a chald		OR (95%CI)	p
	non	year		
The whole group (n=1822)				
non (n=1753)	1169 (66.7)	584 (33.3)	2.9 (1.8-4.8)	<0.001
year (n=69)	28 (40.6)	41 (59.4)		
native (n=1319)				
non (n=1262)	814 (64.5)	448 (35.5)	2.9 (1.7-5.0)	<0.001
year (n=57)	22 (38.6)	35 (61.4)		
Non-native (n=503)				
non (n=491)	355 (72.3)	136 (27.7)	2.6 (0.83-8.2)	0.089
year (n=12)	6 (50.0)	6 (50.0)		

Note: p — level of significance achieved when comparing groups (Pearson test $\chi 2$).
Note: p — level of significance achieved when comparing groups (Pearson test $\chi 2$): OR-odds ratio with 95% Confidence Interval.

Table 6

Maternal risk factors for congenital heart defects in infants, n (%)

	There is no vice	There is a vice	p
Module 1 Aggravated obstetric anamnesis			
Non risk factor	610 (66,7)	305 (33,33)	0,381
There is a risk factor	587 (64,7)	320 (35,3)	
Module 2 Pregnancy pathology			
Non risk factor	80 (65,6)	42 (34,4)	0,976
There is a risk factor	1117 (65,7)	583 (34,3)	
Module 3 Environmental hazards			
Non risk factor	937 (66,1)	480 (33,9)	0,471
There is a risk factor	260 (64,2)	145 (35,8)	
Module 4 Maternal health disorders			
Non risk factor	579 (65)	312 (35)	0,530
There is a risk factor	618 (66,4)	313 (33,6)	
Module 5 Mothers bad habits			
Non risk factor	1106 (66, 2)	564 (33,8)	0,114
There is a risk factor	91 (59,9)	61 (40,1)	

Note: p — level of significance achieved when comparing groups (Pearson test $\chi 2$).

of children without congenital heart disease and with confirmed heart disease, no statistically significant differences in the frequency of risk factors were found (Table 6, p>0,05). Segregation by ethnicity also showed no statistically significant dependence. The health quality of pregnant women was extremely poor regardless of ethnicity.

Genetic syndrome was observed in 24 children, of which in 14 cases the child had a confirmed congenital heart defect (p=0,013). The incidence of genetic syndrome in native children was 15 (1,1%) and 9 (1,8%) in non-native children (p=0,275). In native people, the presence of genetic syndrome was statistically significantly more often associated with the presence of confirmed congenital heart disease (Table 7). It should be noted that the absence of a similar association in non-native people may be due to a small number of observations with genetic syndrome.

No statistically significant differences were found in the incidence of multiple malformations between native and non-native children (5,2% in both groups, p=0,991). In 44 cases out of 94, children with multiple malformations had a confirmed congenital heart defect (p=0.009).

Table 7

Frequency of confirmed congenital heart disease in children with genetic syndrome, n (%)

Group	Genetic syndrome	Confirmed heart disease		p
		non	year	
Non-native (n=494)	non	356 (72.1)	138 (27.9)	0.276
	year	5 (55.6)	4 (44.4)	
Native (n=1304)	non	831 (63.7)	473 (36.3)	0.015
	year	5 (33.3)	10 (66.7)	

Note: p — level of significance achieved when comparing groups (Pearson test $\chi 2$)

Conclusion. Thus, according to the Perinatal Center of the Republican hospital №1 – The National Medicine Center, for the periods 2001-2003 and 2013-2015, the diagnosis of heart disease was statistically significantly more common in children of native parents. The presence of congenital heart disease in parents was associated with a greater frequency of confirmed defects in children. There are no statistically significant differences in the proportion of simple and complex vices in children of different nationalities. The health quality of pregnant women is characterized as “poor” regardless of ethnicity. No statistically significant associations were established between the studied perinatal factors and the incidence of congenital heart defects in children. Probably, genetic factors should be considered as one of the main reasons for the development of congenital heart defects in the native population of Yakutia.

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