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PATHOLOGY OF PREGNANCY IN MOTHERS IS A RISK FACTOR FOR THE DEVELOPMENT OF ALPORT SYNDROME IN CHILDREN

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ANNOTATION

In order to study the influence of maternal pregnancy pathology on the development of Alport syndrome in children, the data of 168 case histories of children aged 1 to 14 years with a diagnosis of glomerulonephritis (acute-130 and chronic-38) for 2017-2021, who received inpatient treatment at the children's multidisciplinary clinic of ASMI, were analyzed. It was revealed that the course of Alport syndrome in children has the following clinical and geneological features: the incidence ratio in boys and girls is 3:1, the maximum incidence rate is 6-10 and 11-14 years. These signs are considered criteria for identifying such patients. The occurrence of Alport syndrome in children depends on the age of the mother and the pathology of the pregnancy period (toxicosis of pregnant women, complications of childbirth, renal, cardiovascular and endocrine diseases), consanguineous marriage, concomitant diseases in the child (acute and chronic pyelonephritis, metabolic nephropathy) and the incidence of the child (4-6 times) during the year. These indicators serve as a factor in the early diagnosis of the progression of renal insufficiency in such patients. Dysembriogenetic stigmas in Alport syndrome in children: flattened occiput, pronounced brow arches, hypertelorism of the eyes and nipples, Gothic palate, anomalies of the location of the ears, sandal-shaped gap between 1-2 fingers of the hands and feet, chest deformity and clinodactyly have a high frequency of registration and are considered criteria for clinical diagnosis.

Key words: Alport syndrome, mothers, children, genetics, glomerulonephritis.

INTRODUCTION

Currently, Alport syndrome in children accounts for about 6-8% of the total number of patients with kidney pathology [1,2,3,4]. One of the causes of hereditary and congenital nephritis, including Alport syndrome, are hereditary diseases in parents, related marriages, various pathologies in the mother, teratogenic effect of various drugs during the first trimester of pregnancy, which often occur in the form of various nephropathies with the stigma of dysembriogenesis [5,6,7,8,9]. Therefore, to date, the study of the influence of pregnancy pathology on the development of Alport syndrome in children is one of the urgent problems of medicine.

The purpose of the study is to study the influence of maternal pregnancy pathology on the development of Alport syndrome in children.

Materials and methods

We analyzed data from 168 case histories of children aged 1 to 14 years with a diagnosis of glomerulonephritis (GN) (acute-130 and chronic-38) for 2017-2021, who received inpatient treatment at the children's multidisciplinary clinic of ASMI.

Catalyst Research Volume 23, Issue 2, October 2023 Pp. 2131-2136

As a control group, 30 children aged 1-14 years suffering from non-hereditary kidney diseases were taken.

Of the examined children: nephritic variant of AGN- 84 (61.8%), nephrotic variant – 22 (16.2%) and in 30 children (22.1%) - nephrotic syndrome with hematuria and hypertension.

Nephrotic form of CGN-31 (65.6%), mixed form – 7 (21.4%), hematuric form - 4 (11.5%). Children with hereditary nephritis (persistent hematuria, hearing loss, eye damage, impaired kidney function in at least one family member) were selected from among children with acute glomerulonephritis (in 8 cases) and 4 among chronic forms of glomerulonephritis.

The total number of children with hereditary nephritis accounted for all cases of acute glomerulonephritis 6.2% and for chronic forms of this disease – 12.5%.

And so hereditary nephritis is most common among chronic kidney diseases mainly among patients with chronic glomerulonephritis (Table.1).

Table 1

Age-sex characteristics in Alport syndrome in children (%)

№	Age	Boys		Girl		Total	
		ABC.	%	ABC.	%	ABC.	%
1.	1-5 years	1	8,5	-	-	1	8,5
2.	6-10 years	6	50	-	-	6	50
3.	11-14 years	2	16,7	3	25	5	41,7
	Total	9	75	3	25	12	100

As the data show (Table.1), boys predominate among the examined children (75%), which significantly exceeds (3:1) the proportion of girls (25%, $p<0.01$). The largest number of examined children were aged 6-10 years -6 children (50%) and 11-14 years (41.7%), the smallest for the age period up to 5 years (8.3%).

The predominance of the proportion of boys among the examined children with Alport syndrome in our studies indicates the coupling with the sex X chromosome in the recessive type of inheritance.

In the study of family members of sick children, we used an integrated approach: clinical and anamnestic, laboratory (clinical and biochemical) and genealogical studies. Air and bone audimetry of the auditory threshold was also performed on a domestic audiometer. Identification of the stigma of dysembriogenesis was an additional reference method of diagnosis. From general clinical laboratory methods, a general analysis of blood, urine and feces was carried out. When interpreting the indicators of urine analysis, typing of hematuria variants was carried out using the criteria West C.C. 1976, Bragon J. 1977, by Y.Y.Illeka et al. (2000), the severity of erythrocyturia according to the recommendations of T.V.Sergeeva (1976). The digital data were processed by the method of variational statistics with the calculation of the reliability of numerical differences by the Student.

Results and their discussion

Catalyst Research Volume 23, Issue 2, October 2023 Pp. 2131-2136

The study analyzed the pathology of pregnancy and obstetric anamnesis of mothers of patients (Table.2).

Table 2

Pathology of pregnancy of mothers with Alport syndrome in children (M±m)

№	Nosology	Mothers of children with Alport syndrome, n= 18		Mothers of healthy children, n= 30		P
		Абс	%	Абс.	%	
1.	The course of pregnancy:					
	- gestosis of pregnancy;	4	33,3	5	16,7	<0,01
	-bleeding in the 1st half of pregnancy;	2	16,5	1	3,33	<0,001
	--extragenital diseases:					
	a) cardiovascular diseases;					
	b) gastrointestinal diseases;	5	41,7	3	10,0	<0,01
	c) diseases of endocrine genesis;	3	25,0	5	16,7	<0,05
	d)kidney and urinary tract diseases;	5	41,7	6	20,0	<0,01
	e)other: allergic, hematological.	6	50,0	8	26,7	<0,01
		4	33,3	7	23,3	<0,05
2.	Course of labor:					
	-discoordinated labor;	3	25,0	5	16,7	<0,05
	-weakness of labor activity;					
	- placental abruption;	5	41,7	7	23.3	<0,01
	-entanglement of the umbilical cord;	4	33,3	8	26,7	<0,05
	- fetal hypoxia;	3	25,0	4	13,3	<0,01
	-asphyxia of newborns;	6	50,0	10	33,3	<0,05
	-birth of children with low body weight (<2700 g)	7	58,3	12	40,0	<0,05
		5	41,7	6	20,0	<0,01

As can be seen from the data (Table 2), mothers were more likely to suffer from pregnancy toxicities, a history of bleeding was revealed; among extragenital diseases, pathology of the kidneys and urinary tract was more often detected (P<0.01), cardiovascular diseases (P<0.01), diseases of endocrine genesis (P<0.01) than diseases Gastrointestinal tract, hematological and

Catalyst Research Volume 23, Issue 2, October 2023 Pp. 2131-2136

allergological genesis (P<0.05). In mothers, childbirth was more often complicated by discoordinated childbirth - fast and rapid (P<0.05), weakness of labor activity (P<0.01), detachment of the normally located placenta (P<0.05) and entanglement of the umbilical cord (P<0.01), which were the basis for the development of hypoxia in the fetus (P<0.05) and asphyxia of newborns (P<0.05). Among patients with Alport syndrome, children born with low body weight (≤ 2700 gy.) prevailed when compared with the control group (P<0.01).

The study of the frequency of transferred diseases in patients with Alport syndrome showed that they belong to the group of frequently ill children (P<0.01), with repeated infections of the respiratory system (up to 4-6 times a year), suffered from allergies (P<0.01), at an early age often suffered intestinal infections, hepatitis, salmonellosis, as well as in the anamnesis, the frequency of transmitted viral infections is high – measles, rubella, etc. (P<0.01), which had a statistically significant association with the pathologies of pregnancy in the mother (P<0.01).

The main clinical symptoms of Alport syndrome in children were fatigue, pallor, dry skin, cyanosis under the eyes, pasty, symptoms of intoxication, headaches, hypotension, external stigmas of dysembriogenesis, renal stigmas, hearing loss and visual abnormalities. The blood pressure level in patients with Alport syndrome was SAP (90.0±5.6 mmHg), DAP (54.0±1.76 mmHg) and arterial hypotension was often detected – 66.7% compared with children of the control group (23.3% and 56.7%) (P<0.001).

Edematous syndrome was pronounced in the terminal stage of CRF. Urinary syndrome was manifested by persistent proteinuria – 3.57 ± 0.71%, a decrease in daily diuresis (601 ± 35.2 ml). Moderate hematuria was also detected, that is, erythrocyturia was 3-4 unchanged and 6-8 altered erythrocytes, and leukocytes 7-8 in the field of vision. The specific gravity of urine averaged 1010± 2.65.

It is known that the characteristic signs of Alport syndrome are a decrease in the hearing threshold, which is most often associated with neuritis of the auditory nerve. In our studies, audiometric evidence of hearing loss – grade I-II hearing loss was detected in 6 cases (30%), in 7 cases - clinical hearing loss (72.0%), which is consistent with literature data (50-60%).

It should be taken into account that as the disease progresses, with age there is an increase in the number of sick children with hearing impairment. In 3 cases, cochlear neuritis was confirmed. It is interesting to note that the frequency of dysembriogenesis stigmas prevailed in children with Alport's syndrome and hearing loss. In our studies, the most distinctive stigmas of dysembriogenesis were hypertelorism of the bridge of the nose and nipples (P<0,001) (Table.3).

Table 3

The frequency of dysembriogenesis stigma in Alport syndrome in children (M±m)

№	Stigmas	Children with Alport syndrome (n =12)		Control group (n = 30)		P
		Абс.	%	Абс.	%	

Catalyst Research Volume 23, Issue 2, October 2023 Pp. 2131-2136

I. Skull anomalies						
1	Brachy- and dolichocephaly	1	8,3	-	-	-
2.	Flattened nape	2	16,7	2	6,6	< 0,01
3.	Pronounced brow ridges	2	16,7	1	3,3	< 0,01
II. Anomalies face						
1	Saddle-shaped, flattened nose	1	8,3	3	10,0	< 0,05
2.	Hypertelorism of the eyes	3	25,0	1	3,3	< 0,001
3.	Epicanthus	4	33,3	3	10,0	< 0,05
4.	High Gothic sky	2	16,7	1	3,3	< 0,05
5.	Anomalies of the location of the ears	2	16,7	4	13,3	< 0,05
6.	Dysplastic growth	1	8,3	5	16,7	< 0,05
III. Anomalies of the trunk, limbs						
1.	Sandal-shaped gap between 1-2 fingers of the hands and feet	2	16,7	1	3,3	< 0,01
2.	Nipple hypertelorism	3	15	2	6,6	< 0,001
3.	Chest deformity	4	33,3	1	3,3	< 0,001
4.	Clinodactyly	2	16,7	3	10,0	< 0,05

Conclusions

1. The course of Alport syndrome in children has the following clinical and geneological features: the incidence ratio in boys and girls is 3:1, the maximum incidence rate is 6-10 and 11-14 years. These signs are considered criteria for identifying such patients.
2. The occurrence of Alport syndrome in children depends on the age of the mother and the pathology of the pregnancy period (toxicosis of pregnant women, complications of childbirth, renal, cardiovascular and endocrine diseases), consanguineous marriage, concomitant diseases in the child (acute and chronic pyelonephritis, metabolic nephropathy) and the incidence of the child (4-6 times) during the year. These indicators serve as a factor in the early diagnosis of the progression of renal insufficiency in such patients.
3. Dysembriogenetic stigmas in Alport syndrome in children: flattened occiput, pronounced brow arches, hypertelorism of the eyes and nipples, Gothic palate, anomalies of the location of the ears, sandal-shaped gap between 1-2 fingers of the hands and feet, chest deformity and clinodactyly have a high frequency of registration and are considered criteria for clinical diagnosis.

Catalyst Research Volume 23, Issue 2, October 2023 Pp. 2131-2136

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