RISK FACTORS FOR THE DEVELOPMENT OF HEREDITARY NEPHRITIS IN CHILDREN

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Annotation. In order to identify clinical and genetic risk factors for the development of hereditary nephritis in children, data from 168 medical histories of children aged 1 to 14 years with a diagnosis of glomerulonephritis (acute-130 and chronic-38) for 2017-2021 were analyzed. Who received inpatient treatment in the children's multidisciplinary clinic of Andijan State Medical Institute. It was revealed that in the conditions of the Fergana Valley there is a tendency to increase the number of patients with urinary tract infection and dysmetabolic nephropathies of familial genesis. The incidence of hereditary nephritis is higher among patients with chronic glomerulonephritis than with acute glomerulonephritis and pyelonephritis. Algorithms for early diagnosis of hereditary nephritis in children include combined damage to the organs of hearing and vision, kidney diseases in several family members or among relatives.

Key words: hereditary nephritis, risk, factor, children

Introduction

Currently, the problem of nephropathies developing with a genetic predisposition is complex [1,2,4,10]. Hereditary nephritis according to the nephrological department of pediatrics and pediatric surgery of the Ministry of Health of the Republic of Uzbekistan, according to long-term observations, accounts for 6-8% of the total number of patients with kidney pathology in different years. In the Fergana Valley, one of the causes of hereditary and congenital nephritis is related to marriages, hereditary diseases in parents, relatives, infectious diseases of the mother, as well as the teratogenic effect of various drugs during the first trimester of

pregnancy. Clinical observationsof scientists confirm that a number of congenital or hereditary diseases of the urinary system are characterized by stigmas of connective tissue disembryogenesis, and not only external, somatic, but also, in particular, organs of the urinary system associated with hereditary transmission of diseases or a condition called "from organ to organ" [3,5,6,7,11]. In this regard, in recent years, it is imperative to study genetic the basis of kidney disease, clinically manifested by nephropathy.

The purpose of the study was to study the clinical and genetic risk factors for the development of hereditary nephritis in children in the conditions of the Fergana Valley.

Materials and methods

We analyzed the data of 168 medical histories of children aged 1 to 14 years with a diagnosis of glomerulonephritis (GN) (acute-130 and chronic-38) for 2015-2021, who received inpatient treatment in the children's multidisciplinary clinic of Andijan State Medical Institute. Of these: nephritic variant of AGN- 84 (65%), nephrotic variant - 32 (25%) and in 14 children (10%) - nephrotic syndrome with hematuria and hypertension. Nephrotic form of CGN-27 (71%), mixed form - 7 (18,5%), hematuria form - 4 (10.5%). Children with hereditary nephritis (persistent hematuria, hearing loss, eye damage, impaired renal function in at least one family member) were selected from children with acute glomerulonephritis (in 8 cases) and in 4 among chronic forms of glomerulonephritis (Table 1).

Table 1

Structural characteristics of various forms of glomerulonephritis

Acute glomerulonephritis						Chronic glomerulonephritis					
Nephrotic syndrome		Nephritic syndrome		Nephrotic syndrome with hematuria and hypertension		Nephrotic form		Hematuria form		Mixed form	
Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%
32	25	84	65	14	10	27	71	4	10,5	7	18,5

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 often found among patients with chronic glomerulonephritis (Table 2).

Table 2

Resource requirements by component
Age-sex characteristics of children with hereditary nephritis (%)

№	Age of examined patients	Boys		Girls		Summary	
		Abs.	%	Abs.	%	Abs.	%
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
	Altogether	9	75	3	25	12	100

As the data show (Table 2), boys (75%) predominate among the examined children, which significantly exceeds (3: 1) the proportion of girls (25%, $p<0.01$). The largest number of those examined was at the age *of 6-10 years* - 6 children (50%) and *11-14 years* (41.7%), the lowest for the period *up to 5 years* (8,5 %). The predominance of boys among the examined children with hereditary nephritis in our studies indicates adhesion to the X recessive inheritance. As a control group, 30 children aged 1-14 years suffered from non-hereditary kidney diseases were taken.

In the study of family members of sick children, we used an integrated approach: clinical-anamnesis, laboratory (clinical and biochemical) and genealogical studies. Air and bone audimetry of the auditory threshold was also performed on the domestic audiometer. Detection of stigmas of disembryogenesis was an additional reference method of diagnosis. Of the general clinical laboratory methods, it was mandatory to conduct a clinical analysis of blood, urine and feces. When interpreting the indicators of urine analysis, hematuria variants were typed using the criteria west C.C. 1976, Bragon J. 1977, po Y.Y. Illek et al. (2000), the severity of erythrocyturia according to the recommendations of T.V. Sergeeva (1976). Assessment of the state of the cardiovascular system was carried out by measuring blood pressure, calculating the cardiac index, specific and minute volume of the heart, ECG. The numerical data were processed by the method of variational

statistics with the calculation of the reliability of numerical differences according to the Student.

Results and discussion

In the course of our research, we studied the structure of kidney diseases (2015-2018) according to the nephrology department of the clinic (Table 3).

Table 3

Nosologically structure of kidney disease (% of the total number of patients)

№	Name of diseases	2015 year		2016 year		2017 year		Total, p<0,01	
		Abs.	%	Abs.	%	Abs.	%	Abs.	%
1.	Acute pyelonephritis	95	20,9	117	20,9	159	27,2	371	23,2
2.	Chronic pyelonephritis	48	10,5	77	13,8	82	14,04	207	12,9
3.	Acute glomerulonephritis	146	32,1	159	28,4	102	17,3	407	25,47
4.	Chronic glomerulonephritis	109	23,9	104	18,6	73	12,4	286	17,9
5.	Dysmetabolic nephropathy	39	8,57	64	11,45	99	17,47	202	12,64
6.	Urinary tract infections - cystitis	9	1,98	17	3,04	45	7,70	71	4,44
7.	Tubulopathy	1	0,22	2	0,36	1	0,17	4	0,25
8.	Congenital nephrotic syndrome	2	0,44	10	1,79	9	1,54	21	1,31
9.	Chronic renal failure	2	0,44	4	0,72	6	1,03	12	0,75
10.	Hereditary nephritis: Alport syndrome, Lowe and Fanconi syndrome	4	0,88	5	0,89	8	1,37	17	1,06
	Summary	455	100	559	100	584	100	1598	100

As can be seen from the data (Table. 3), among nephrological patients, the proportion of children with acute and chronic forms of pyelonephritis increases year after year, acute forms increased from 20.95 in 2015 to 27.0% in 2017, while chronic forms from 10.5% to 14.04%. The total number of pyelonephritis in the structure of

nephrological diseases over the study years was 36.1%. On the contrary, the proportion of glomerulonephritis in the structure of nephrological diseases decreased - acute from 32.1% to 17.3%, and chronic from 23.9% to 12.4%. The total proportion of glomerulonephritis over the years was 43.4%, which exceeds the total share of pyelonephritis (36.1%), ($p<0.01$). Our studies have shown that in the general structure of kidney disease nosology, the proportion of urinary tract infections was also increased (from 1.98% in 2015 to 7.7% in 2017).

Data analysis (Table. 3) showed that in the structure of nephrological diseases, the proportion of dysmetabolic nephropathies is also increasing from 8.57% in 2015 to 17.47% in 2017, i.e. almost twice. Our attention is drawn to the fact that dysmetabolic nephropathy in our studies was due to family, environmental and hereditary factors, i.e. similar symptoms were noted in parents, siblings and they can be attributed to familial forms of nephropathy. If we take into account, that many secondary forms of pyelonephritis are more often caused by familial dysmetabolic nephropathies, familial or hereditary nephropathies in the Fergana Valley region account for 25.2% of all kidney diseases over the past years.

Significant importance in our research was given to the problem of hereditary nephritis (HN). We diagnosed HN if the child has persistent hematuria (macro- or microhematuria) in combination with vision loss, hearing appratus, as well as the identification among family members (parents, siblings) of at least one patient with kidney disease of similar genesis. As can be seen from the results of our studies, HN tends to increase (4 cases in 2015 and 12 cases in 2017). After retrospective analysis which includes audiometric and genealogical studies, we found over the past 3 years 18 children with hearing and vision problems which accounted for 3.17% of all hospitalized (1598 children). The diagnosis of HN was established in 8 cases among children with glomerulonephritis - in 2 cases with their acute course and initial treatment, in 6 cases with chronic course of pathology; in 4 cases in children with pyelonephritis with the dysmetabolic nephropathy, in 5 children hospitalized in various stages of. CRF when contacting specialists with vision and hearing problems.

The latter fact indicates a belated diagnosis of HN, their relatively hidden debut, which shortens the terms of possible conservative therapy for this category of patients and causes a relatively rapid death. Our analysis of a sample of children with HN showed that they mainly consisted of rural regions (Shakhrikhan, Kurgantepa) - 11 than urban (Andijan) - 7. The difficulties of diagnosing HN are also evidenced by the fact that from among children with HN in 8 cases they were long (up to 6 years), observed in local clinics, children's hospitals under the diagnosis of "glomerulonephritis", "nephrotic syndrome" , "secondary pyelonephritis", "urinary tract infections" and did not use additional (genetic, audiometric) research methods. The age of children with HN was predominantly up to 8 years (58.3%) than 12 years and older (41.7%) and among them male children (75%) than girls (25%) and the ratio of boys to girls was 3: 1.

Table 4

Obstetric history of mothers of sick children with hereditary nephritis (%)

№	List of nosological units	Mothers of children with HN n= 18		Mothers of healthy children n= 30		p
		Abs	%	Abs.	%	
Course of pregnancy:						
	gestosis of pregnancy;	4	22,2	5	16,7	<0,0 1
	bleeding in the 1st half of pregnancy;	2	11,1	1	3,33	<0,001
	extragenic diseases: cardiovascular diseases;	5	27,7	3	10,0	<0,0 1
	gastrointestinal diseases;	3	16,6	5	16,7	<0,0 1
	diseases of endocrine genesis;	5	27,7	6	20,0	<0,0 5
	kidney and urinary tract diseases;	6	33,3	8	26,7	<0,0 1
	other: allergology, hematological.	4	22,2	7	23,3	<0,0 5
Course of labor:						

	discordinated labor;	3	16,6	5	16,7	<0,0 5
	weakness of labor;	5	27,7	7	23,3	<0,0 1
	placental abruption;	4	22,2	8	26,7	<0,0 5
	cord entanglement;	3	16,6	4	13,3	<0,0 1
	fetal hypoxia;	6	33,3	10	33,3	<0,0 5
	asphyxia of newborns;	7	39,0	12	40,0	<0,0 5
	birth of children with low body weight (<2700 g)	5	27,7	6	20,0	<0,0 5

As can be seen from the data (Table. 4), the characteristics of the obstetric history of mothers of sick children with HN showed that mothers more often suffered from toxicosis of pregnancy, hemorrhage after labor in the anamnesis was detected; 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 genesisa ($p<0.01$) than diseases of the gastrointestinal tract, hematological and allergic genesis ($p<0.05$). In mothers, childbirth was more often complicated by discordinate labor – very fast labor ($p<0.05$), weakness of labor ($p<0.01$), abruption of a normally located placenta ($p<0.05$) and cord entanglement ($p<0.01$) and was the basis for the development of fetal hypoxia ($p<0.05$) and asphyxia of newborns ($p<0.01$). Among the children with HN, children born with an initially low body weight prevailed ($\leq$ 2700 grams) ($p<0.01$) than the children of the mothers of the control group.

The study of the frequency of transferred diseases in children of HN showed that they belong to the group of frequently ill children ($p<0.01$), with repeated infections of the respiratory system (up to 4-5 times a year), suffered from various forms of food and drug allergies ($p<0.01$), in early childhood often suffered from intestinal infections (hepatitis, salmonellosis, intestinal coli infections, etc.), they have a history of high frequency of viral infections - measles, rubella, etc. ($p<0.01$).

The main clinical symptoms of HN were pallor, pastosity, cyanosis under the eyes, fatigue, headaches, symptoms of intoxication, arterial hypotension, external stigmas of dysembryogenesis, renal stigmas, hearing loss, vision abnormalities.

The level of blood pressure in patients with HN was SBP (90.0±5.6 mm Hg), DBP (54.0±1.76 mm Hg) and often revealed arterial hypotension - 66.7% compared

with children of the control group (23.3% and 56.7%) (p<0.001). Edematous syndrome was observed at the terminal stage of CRF in children with HN. Urinary syndrome was manifested by persistent proteinuria - 3.57±0.71% in urine portions and showed a daily loss of 1.65 grams of protein in urine in sick children with HN (808±69.5 ml). Moderate hematuria was also detected, that is, erythrocytosis was 3-4 unchanged and 6-8 altered erythrocytes, and leukocytes 7-8 in the field of view. The proportion of urine of sick children with HN averaged 1012±2.59.

Thus, HN in the region of the Fergana Valley proceeds with a predominance of hypotensive, edematous manifestations of disorder than urinary and intoxication symptoms. Hematuria syndrome in HN is most often caused by a violation of glomerular permeability. However, our detection of cases of HN among patients with pyelonephritis (4th case) indicates the development of interstitial nephritis with the dysmetabolic nephropathy and does not exclude tubular genesis of hematuria due to oxaluria and uraturia.

To confirm the diagnosis of HN, it was especially important to identify stigmas and disembryogenesis. In our studies, the most distinctive stigmas of disembryogenesis were hypertelorism of the bridge of the nose and from the scoops (p<0,001) (Table 5).

It is known that the characteristic signs of HN are a decrease in the threshold of hearing (Alport syndrome), which is most often associated with neuritis of the auditory nerve.

In our studies, audiometric evidence of hearing loss - hearing loss of I-II degree was detected in 6 cases (30%), in 7 cases - clinical hearing loss in children with HN, i.e. clinical and instrumental hearing loss in patients was 72.0%, which is consistent with the literature (50-60%). It means 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 stigmatization of disembryogenesis prevailed in children with Alport syndrome and hearing loss.

Table 5

The frequency of disembryogenesis stigma in children with hereditary nephritis (%)

№	Stigma	Children with HN (n = 12)		Control group (n = 30)		p
		Abs.	%	Abs.	%	
I. Skull anomalies						
1	Brachy- and dolichocephalous)	1	8,3	-	-	-
2.	Flattened back of the head	2	16,7	2	6,7	< 0.01
3.	Pronounced eyebrow arches	2	16,7	1	3,3	< 0.01
II. Facial anomalies						
1	Saddle-shaped nose, flattened nose	1	8,3	3	10,0	< 0,05
2.	Hypertelorism	3	25,0	1	3,3	< 0,001
3.	Epicanthus	4	33,3	3	10,0	< 0,05
4.	High gothic palate	2	16,7	1	3,3	< 0,05
5.	Anomalies in 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.	Sandalwood slit between 1-2 fingers and feet	2	16,7	1	3,3	< 0.01
2.	Nipple hypertelorism	3	25	2	6,7	< 0,001
3.	Chest deformity	4	33,3	1	3,3	< 0,001
4.	Clinodactyly	2	16,7	3	10,0	< 0,05

Conclusion:

1. In the Fergana Valley, in the structure of nosological forms of kidney and urinary tract diseases, there is a tendency to increase the number of patients with urinary tract infection and dysmetabolic nephropathies of hereditary genesis.
2. The incidence of hereditary nephritis is higher among patients with chronic glomerulonephritis than with acute glomerulonephritis and pyelonephritis and organ-specific stigmas (anomaly of the kidneys and urinary tract) are more common compared to external somatic stigmas.
3. Algorithms for the early diagnosis of hereditary nephritis in children include combined damage to the organs of hearing and vision, the detection of renal diseases in several family members or among relatives.

4. For early diagnosis of hereditary nephritis among children, it is necessary to include a genealogical method for studying heredity in acute and chronic kidney diseases.

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