Early predictors and prognostication of children chronic kidney disease in the conditions of environmental disability

Pronósticos tempranos y pronóstico de niños con enfermedad renal crónica en condiciones de discapacidad ambiental

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Abstract

The kidneys do not have a direct connection with external agents, but the elimination of a variety of harmful environmental substances from the human body mainly occurs through this organ. At the same time, the kidneys experience a significant functional load, which can be realized in the clinical course, and in the occurrence of kidney disease. The goal of our study was to identify early predictors of diagnosis and prediction of children chronic kidney disease (CKD) in conditions of environmental distress. The frequency, clinical and laboratory characteristics of chronic kidney disease were studied among 460 children from the industrial zone, between the ages of birth and 18 years old (girls - 258 and boys - 202). All children were treated in the nephrology department of the regional children's clinical hospital in the period from 2015 to 2017. We have identified three risk groups for the development of children CKD in conditions of environmental distress: the "high risk" group is an unfavorable prognosis group, the "medium risk" group is "attention group" and the "minimal risk" group. The revealed features of children CKD of the main region indicate pronounced functional disorders and changes in the structure of the renal tissue, which is caused by prolonged contact with polymetallic dust. The nature of the revealed features of children CKD of the main region indicates the intensity of the process of adaptation of the organism to adverse environmental factors and the predominant latent and low manifestation course of the disease.

Keywords: children, chronic kidney disease, area of ecological trouble, early predictors, prognostication.

Resumen

Los riñones no tienen una conexión directa con agentes externos, pero la eliminación de una variedad de sustancias ambientales nocivas del cuerpo humano ocurre principalmente a través de este órgano. Al mismo tiempo, los riñones experimentan una carga funcional significativa, que puede realizarse en el curso clínico y en la aparición de la enfermedad renal. El objetivo de nuestro estudio fue identificar los predictores tempranos del diagnóstico y la predicción de los niños con enfermedad renal crónica (ERC) en condiciones de malestar ambiental. La frecuencia, las características clínicas y de laboratorio de la enfermedad renal crónica se estudiaron entre 460 niños de la zona industrial, entre las edades de nacimiento y los 18 años (niñas - 258 y niños - 202). Todos los niños fueron tratados en el departamento de nefrología del hospital clínico infantil regional en el período de 2015 a 2017. Hemos identificado tres grupos de riesgo para el desarrollo de niños con ERC en condiciones de estrés ambiental: el grupo de "alto riesgo" es un pronóstico desfavorable grupo, el grupo de "riesgo medio" es el "grupo de atención" y el grupo de "riesgo mínimo". Las características reveladas de los niños con ERC de la región principal indican trastornos funcionales pronunciados y cambios en la estructura del tejido renal, que es causado por el contacto prolongado con el polvo polimetálico. La naturaleza de las características reveladas de los niños con ERC de la región principal indica la intensidad del proceso de adaptación del organismo a los factores ambientales adversos y el curso predominante latente y de baja manifestación de la enfermedad.

Palabras clave: niños, enfermedad renal crónica, área de problemas ecológicos, predictores tempranos, pronóstico.

Introduction

Health and illness are not a simple reflection of a person's environment. Human, on the one hand, has a certain biological constitution, acquired as a result of evolutionary development, and is subject to the influence of natural factors. On the other hand, it is formed under the influence of socio-economic factors that are constantly being improved. The transformation of the environment affects the socio-hygienic and psycho-physiological working conditions, life and leisure of a person, which in turn determine the mechanisms of morbidity, the level of development of people's intellectual abilities.

The kidneys do not have a direct connection with external agents, but the elimination of a variety of harmful environmental substances from the human body mainly occurs through this organ. At the same time, the kidneys experience a significant functional load, which can be realized in the clinical course, and in the occurrence of kidney disease (Vecchio, Bonerba, Palmer, Craig, Ruospo, Samuels, Molony, Schena & Strippoli, 2015; Levey, Eckardt, Tsukamoto, et al., 2005; Hogg, Furth, Lemley, et al., 2003).

For Kazakhstan, which has several climatic-geographical zones with different levels of environmental pollution and the formation of technogenic biogeochemical regions, it is important to study the role of environmental factors in the prevalence of chronic kidney disease (Scheplyagina, 2008; Kanatbaeva & Kabulbaev, 2009; Glance, 1998; Shukurov et al., 2016).

According to the study, the history of pregnancy, the course of the birth of the mother, the history of the child's life, place of residence, clinical and laboratory indicators were referred to the category of early predictors.

Purpose of the Study

Identification of early predictors and prediction of children chronic kidney disease (CKD) under environmental conditions.

Currently, chronic kidney disease (CKD) is a global medical, economic and social problem (Karimdzanov & Israilova, 2017). Among chronic noncommunicable diseases, CKD occupies a special place because it is widespread, associated with a sharp deterioration in the quality of life, high mortality, and in the terminal stage necessitates the use of expensive replacement therapy methods - dialysis and kidney transplantation (Schaefer & Wühl, 2012; Schieppati & Remuzzi, 2005; Andrew, Levey, Coresh, Kline, et al., 2002).

According to the recommendations of the K / DOQI (Kidney Disease Outcomes Quality Initiative) and the KDIGO (Clinical Practice Guideline for the Kidney Disease), the concept of CKD was formulated, under which all nephropathies characterized by a gradual progressive course with a gradual decrease and loss of kidney functions are combined, with signs of kidney damage, according to laboratory and instrumental studies, and/or a decrease in the filtration functions of the kidneys, persist for 3 months or more and affect health (Andrew, Levey, Coresh, Kline, et al., 2002; Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group, 2013).

In pediatrics, the term "chronic kidney disease" was first used by R.J. Hogg in 2003 is identical to the term used in therapeutic practice. Currently, the definition and classification of children CKD by stages do not differ from those in adults and is widely used in the pediatric clinic and in scientific research (Hogg, Furth, Lemley, et al., 2013; Davooabadi & Aghajani, 2013).

At the same time, CKD in childhood differs in causes and features, including effects on growth, the occurrence of cardiovascular complications, psychological effects on the patient and his family (Harambat, Karlijn, Stralenm, Kim & Tizard, 2012; Vivante & Hildebrandt, 2016; Smith, Stablein, Munoz, Hebert & McDonald, 2007).

Most of the existing data on the epidemiology of children CKD relate to the late stages of renal dysfunction, whereas population studies are not available. According to national registries, impaired renal filtration function is diagnosed in 18.5–58.3 cases per 1 million children. It is considered that the average incidence of terminal chronic renal failure (TCRF) up to 16 years is 1-3 new cases per year per 1 million of the total population. In Russia, the prevalence of children TCRF is 4–5 cases per 1 million children per year, in Europe - 4–6, in the USA - 11 cases (Daminova, 2016; Van Stralen, Verrina, Schaefer & Jager, 2008). According to the European Renal Association — European Dialysis and Transplant Association (ERA-EDTA) register, the annual incidence of TCRF in Europe was 7.1 per 1 million children in 1980–1984 and 9.9 - in the next 15 years (Cannata-Andia, Zoccali & Wanner, 2006).

The development of TCRF depends on age: its prevalence among children 15–19 years old is twice as high as in the age group 10–14 years old, and almost 3 times higher than among children 0–5 years old. According to the Japanese National Registry and the Registry of Australia and New Zealand Dialysis and Transplantation (ANZDATA), the annual incidence of TCRF is 22 per 1 million children, and indigenous children are at higher risk than other children (McDonald & Excell, 2005; Hattori, Yosioka, Honda, Ito, 2002). The median frequency of children renal replacement therapy (RRT) <20 years of age is ~ 9 cases per 1 million children throughout the world, while the prevalence rate is ~ 65 cases (Warady, & Chadha, 2007; Harambat, Bonthuis, Van Stralen, et al. 2014). At the same time, higher incidence and prevalence rates were recorded in the United States, probably due to the fact that the RRT begins earlier and at higher levels of glomerular filtration rate (GFR) compared to other developed countries (Saran,

Li, Robinson, et al. 2015). The prevalence of patients receiving RRT increased from 22.9 in 1980 to 62.1 per 1 million in 2000, which is primarily associated with an increase in the long-term survival of patients (Lagomarsimo, Valenzuela, Cavagnaro, & Solar, 1999; United States Renal Data System, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2005; Siyer et al., 2016).

The rate of CKD development depends on the prevalence of damage to the glomerular apparatus of the kidneys or tubulointerstitial tissue and the severity of dysplastic processes. The nature of the renal pathology causing CKD varies with age. Among young children, hereditary and congenital nephropathy most often lead to the development of CKD. In the thoracic and preschool years, the same spectrum of congenital diseases is observed, and the effects of the pathology (hemolytic-uremic syndrome, tubular necrosis, renal vein thrombosis, etc.) are added. Among children older than 5 years, acquired renal diseases play a major role: various forms of glomerulonephritis and hereditary diseases (familial juvenile hyperuricemic nephropathy, Alport syndrome), chronic renal failure caused by metabolic disorders (cystinosis, hyperoxaluria), some inherited diseases (polycystic kidney disease), which may occur among children of any age (Vivante & Hildebrandt, 2016; Warady & Chadha, 2007).

Chronic kidney disease, even in its early stages, is a condition that, if left untreated, is highly likely to result in TCRF. Diagnostic and therapeutic approaches to CKD should be aimed at preventing, early detection and aggressive treatment of nephropathy in order to prevent the development of TCRF (Papayan, & Savenkova, 2008). In the modified stratification of the stages of chronic kidney disease (KDIGO, 2013), 5 stages of the disease are distinguished - from I – III (IIIa - IIIb - moderate and significant decrease, respectively) to IV – V (TCRF) - depending on the GFR (Table 1) (KDIGO, 2013). In children, GFR varies with age, gender, body size, and reaches the level of adults by about 2 years. Stage I – II chronic kidney disease includes any chronic disease with damage to the kidney parenchyma and intact or slightly reduced glomerular filtration (chronic glomerulonephritis, chronic recurrent pyelonephritis, tubulointerstitial nephritis, obstructive nephropathy, early stages of diabetic nephropathy, etc.). At these stages that the adequate specific treatment of a specific disease (for example, immunosuppressive therapy for glomerulonephritis, strict glycemia control in diabetic nephropathy, prevention of pyelonephritis recurrence) can completely prevent the development of renal failure (Mak, 2007; Smirnov, Shilov, Dobronravov, et al. 2012). When CRF occurs, as a rule, its progression to the terminal stage is inevitable. Therapeutic tactics in stage III – V CKD is less dependent on the nature of the originally noted pathology and should be aimed at slowing the progression of CRF, preventing cardiovascular pathology and ensuring the normal growth and development of the child (Mitsnefes, 2008; Loimann, Tsygin, Sargsyan, 2010).

Prognosis Among Children with CKD

When predicting CKD outcomes, the following factors need to be established: the cause of CKD, GFR and albuminuria indicators, other risk factors and comorbidities. According to the recommendations of KDIGO (2012), albuminuria in CKD is determined by albumin excretion per day: normal or slightly increased - <30 mg, moderately increased - 30–300 mg, significantly increased -> 300 mg. The risk of progression of children CKD depends on the degree of impairment of GFR and the severity of albuminuria. At stage I – II of CKD, with normal or initial decrease in GFR, normal and elevated albuminuria, the risk of progression is low, with the same stage of CKD with a moderate and significant decrease in GFR, with a moderate and sharp increase in albuminuria, the risk of progression increases and becomes high. At stages III – V of CKD with a moderate, pronounced decrease in GFR and TCRF and a slight, moderate and pronounced increase in albuminuria, the risk of CKD progression increases from moderate to high and very high, respectively (KDIGO, 2013). Although over the past 40 years there has been a significant increase in the long-term survival of children and adolescents with TCRF, in developed countries the total (on dialysis and after transplantation) 10-year survival reaches only 80% and mortality by age is still 30–150 times higher than among healthy children. General principles of diagnosis of children CKD is based on data from the history of the disease (duration of proteinuria, the presence of hypertension, physical developmental delay, kidney disease, kidney transplantation), family history (congenital anomalies of the kidneys, urinary tract, hereditary nephropathy, systemic connective diseases tissue), physical examination (underweight, skeletal deformity, anemia, hearing loss, etc.), clinical and laboratory tests (clinical and biochemical analyzes of blood and urine with the determination of protein, albumin, creatinine, the ratio of albumin/creatinine in urine, electrolytes, erythrocytes and urine cylinders, GFR), nephron biopsy, ultrasound, computerized, magnetic resonance imaging, angiography, as well as isotope diagnostic methods (KDIGO, 2013). Depending on the disease that caused the irreversible death of nephrons, CKD can be diagnosed both in the early (I – II stage) and late (III – V stage) stages. GFR is an integral indicator of the functional status of the kidneys. In pediatric practice, the definition of GF is widespread in determining SCF. Schwartz as an accurate and convenient way to evaluate GFR (Schwartz, Muñoz, Schneider, et al. 2009).

Original formula by G.J. Schwartz:

GHR, ml/min/1,73 m2 = k • L/ serum creatinine concentration, mmol / l

Where:

L — height (cm);

k — coefficient depending on age and gender: — 0,33 — for premature babies, — 0,45 — for newborns, — 0,55

— for children under 12 and teenage girls, — 0,7 — for teenage boys over 12 years old.

Thus, children CKD is an urgent problem of pediatrics, which determines the need for measures to reduce the risk of its development, early diagnosis and etiotropic treatment of the underlying disease, detection, prevention and treatment of systemic complications of renal dysfunction.

Despite the success of theoretical and practical nephrology, renal morbidity remains high with a tendency to increase, remaining the second most frequent pathology of childhood in the world and in Russia (Vishnevskiy, 1996; Erman & Martsulevich, 2000). Diseases, previously first manifested or developing in adolescence, are currently detected in young children and even in newborns.

Currently, there are only a few works on the prevalence and structure of nephrological pathology in our country, based on a population approach using epidemiological studies.

No less important is the study of the clinical features and pathogenetic mechanisms of the development of kidney diseases. Given the propensity for the chronic course of diseases of the urinary system, the unfavorable prognosis of most of them, their study is necessary, which has medico-demographic, social and climatic features.

The development of preventive measures to prevent complications (arterial hypertension, chronic renal failure) requires the search for the most significant factors for the formation and progress of nephropathy (Ni, 2000).

Materials and Methods: At the first stage - with the hygienic characteristics of the industrial zone for the period from 2010 to 2015, the complex load on the city districts was taken into account, which allowed us to rank the territories according to the intensity of anthropogenic impact. The city of Temirtau is presented in the paper as a model of an industrial city (main district). As control, we took the corresponding data from the south-eastern region of Karaganda, which is considered relatively clean from an environmental point of view (conditionally clean area). The city of Temirtau and the south-eastern region of Karaganda are identical in ethnic composition, characteristics of housing and everyday life, national traditions, children resided at this address. The ecological situation in the main territory, as in most of Kazakhstan's industrial areas, is unfavorable.

Based on the integrated characteristics of the two territories, various polluted areas were identified, which differed in the level and nature of anthropogenic pollution and were designated by us as the main area and conditionally clean area, which is a necessary condition for the phased solution of the tasks of this work.

We compared early predictors of chronic kidney disease in 460 children from the industrial zone - the main area, from birth to 18 years old (girls - 258, boys - 202); all children were treated in the nephrology department of the regional children's clinical hospital (RCCH) in the period from 2015 to 2017 and the control group consisted of 175 children from conditionally clean area, the children were also examined in the RCCH. Informed parental consent and approval of the ethical commission of the NAO "Medical University of Karaganda" was obtained. Diagnosis of chronic kidney disease (CKD) was carried out in accordance with existing criteria and their classification (Hogg, Furth, Lemley, et al. 2003; Scheplyagina, 2008; Kanatbaeva & Kabulbaev, 2009; Glance, 1998). The following criteria are used to make a diagnosis in the outpatient setting for chronic kidney disease (Dusenova, 2017; Becker, Wheeler, & Zeeuw, 2012; Foster, McCauley, & Mak, 2012; James, Oparil, Carter, et al. 2014; Albaramki, Hodson, Craig & Webster, 2012; Aslam, Higgins, Sinha, & Southern, 2017; Cooper, Heathcote, Anderson, Grégoire, Ljungman & Eccleston, 2017; Hahn, Hodson & Craig, 2015):

Table 1. Stages of chronic kidney disease, depending on the glomerular filtration rate.

CKD Stages	Description	GFR ml/ min/1.73m^3
0	Risk factors	>=90
1	Kidney damage with N or↑GFR	>=90
2	Mild reduction GFR	60-89
3	Average reduction GFR	30-59
4	Severe reduction GFR	15-29
5	Chronic renal failure	<15

A) kidney damage structural or functional, with or without a decrease in glomerular filtration rate of more than 6 months with one of the following pathological findings:

- Pathological urinalysis;

- changes in the kidneys with visual methods of research.

B) GFR less than 60 ml/min x 1.73m^3

GFR (ml / min) = height (cm) x ratio x 88.4 / serum creatinine (μmol / l)

Coefficient deviations:

- 0.45 from 4 months to 2 years;

- 0.55 from 2 years to 13 years for boys and from 2 years to 16 years for girls;

- 0.7 from 13 to 16 for boys.

Static processing

Static processing of the obtained digital results was carried out in the program "Biostatistics 9.0" using the methods of variation statistics in order to establish their reliability and significance of differences between the indicators. By the criterion of Fisher (2007) determined the equality of the variance of the studied parameters. In all groups, normal distribution of indicators and the absence of signifi-

cant differences in variances were observed, which provided grounds for the use of Student's parametric criterion. Also used non-parametric criteria - tests Mann - Whitney and Wilckoxon. The degree of significance of differences between the compared fractions was evaluated by criterion z. Conducted correlation analysis.

For the purpose of clinical prediction of the risk of developing children chronic kidney disease in conditions of environmental distress, the simplest clinical indicators available to institutions at all levels were used. Error of the first kind (false overdiagnosis of CKD) $a = 0{,}1$ (10%), the second kind of error (false diagnosis of CKD absence) $b = 0{,}1$ (10%). Thus, the threshold A (the required minimum amount of points for predicting the risk of developing CKD in the conditions of environmental trouble with a probability of 90%) was $10\lg\frac{1-\alpha}{\beta} = 10\lg\frac{1-0.1}{\beta} = +13$ The threshold B (the required amount of points for rejecting the development of CKD in the conditions of environmental trouble with a probability of 90%) was $10\lg\frac{\alpha}{1-\beta} = 10\lg\frac{0.1}{1-0.1} = -13$. For the selection of the most significant in terms of the development of predicting the risk of CKD in the conditions of environmental distress, the informative value of each trait was determined (Table 1).

Informativeness of each feature ($J(x_j)$) defined as the sum of the informativity of each range (i) of the attribute (j):

$$\sum J(x_j^i)$$

The information content (J) of the range (i) of the sign (j) was determined by the Kullback formula:

$$J(x_j^i) = DK(x_j^i) * \frac{1}{2}\left|P(\frac{x_j^i}{A}) - P(\frac{x_j^i}{B})\right|$$

where DK is the diagnostic coefficient of the range i of the attribute j, determined by the formula: $DK = 10\lg\frac{P(\frac{x_j^i}{A})}{P(\frac{x_j^i}{B})}$, $P(\frac{x_j^i}{A})$

- the frequency of the range i of the trait j in the group of children with cerebral complications A; $P(\frac{x_j^i}{B})$ - the frequency of the range i of the trait j in the group of children with CKD (C).

Results

Analysis of early predictors, results of clinical examination, laboratory and instrumental methods of examination of children with CKD showed:

- high incidence of kidney disease (42% of families) and metabolic pathology (47%) in parents and (or) next of kin;
- Complicated urinary system infection (acute pyelonephritis) prevailed in the nosological structure of children CKD from the main area - 49.2%, the second most common CKD were tubulointerstitial nephritis (TIN) - 35%, in third place are abnormalities of the urinary system (AOMS), their frequency corresponded to 15.8%;
- among children from the risk group, predominantly latent and low manifestation course of the disease;
- prevalence of abdominal syndrome, more often in the group of patients with AOMS;
- the presence of vegetovascular dystonia and (or) isolated urinary syndrome among children with TIN;
- random identification and (or) transient nature of changes in the urine, mainly in the form of minimal urinary syndrome;
- detection of diseases at the stage of microbial - inflammatory or bacterial process in the kidneys, with the development of a complicated urinary system infection (acute pyelonephritis) or TIN;
- the predominance of combined lesions of various organs and systems, which indicates the multiorgan nature of pathological changes.

The more frequent occurrence of children chronic kidney disease in the context of the environmental problems of the Karaganda region, which was established during expert analysis of primary medical records, determines the need for in-depth study of this clinical problem. Prevention of environmentally determined children chronic kidney disease can only be successful if it is possible to predict these complications.

When studying the age of diagnosis CUSI (acute pyelonephritis) revealed that 70.6% of children had the disease diagnosed at preschool age, and in 61.6% up to 3 years.

From the number of signs presented in table -1 for inclusion in the diagnostic table, only those whose information content was more than 0.50 were selected.

The diagnostic value of the developed table was studied by determining the most important operational characteristics in the study of a diagnostic method, such as sensitivity and specificity (Roderick, Willis, Blakeley, Jones & Tomson, 2007; Zorin, & Vyalkova, 2015).

Table 2. Predicting children chronic kidney disease living in environmental degradation.

Predictors	Gradation factor	Threshold Coefficient (TC)
1. During pregnancy	- no complications;	-8,92
	- preeclampsia 1 and / or 2 halves of pregnancy;	+10,62
	- anemia;	+3,56
	- mother's hypertension;	+9,87
	- Mother's complicated urinary system infection (CUSI) (acute pyelonephritis);	+6,74
	- Father's CUSI (acute pyelonephritis);	-5,0
	- Mother's urolithiasis disease;	-3,4
	- Father's urolithiasis disease;	0
	- threat of interruption;	+2,86
	- Acute respiratory viral infection;	+3,54
	- occupational hazards from the mother.	+3,21
2. Childbirth	- complicated;	+2,99
	- not complicated.	-2,08
3. Artificial feeding	- yes;	-3,45
	- no;	+7,56
4. Nephrological pathology in the first year of life	- present;	+3,58
	- absent;	-2,99
5. Allergic history	- burdened;	+3,65
	- not burdened.	-1,87
6. Belonging to a group of frequently and long-term ills	- belongs;	+4,84
	- don't belong;	-4,18
7. Place of residence	- city center;	+5,04
	- on the outskirts;	-4,36
	- near the enterprise;	+18,1
8. Family composition	- incomplete	+4,74
	- complete.	-5,73
9. Pressure	-normal;	-4,87
	- hypotension	+7,79
	- hypertension;	+3,9
10. The presence of pain	- there is none;	-3,68
	- there is.	+6,12
11. Dysuric syndrome	- there is;	+9,3
	- there is none	-11,4
12. Stigmata dysembryogenesis	- there is;	+9,5
	- there is none	-1.7
13. Edema syndrome	- there is;	+8.5
	- there is none	-2,9
14. Microhematuria	- there is;	+7,2
	- there is none	-11,4

For this purpose, the developed table was used when admitting a young child with CKD to the RCCH. A total of 460 cases of CKD until 2017 were analyzed.

Table 2. Operational characteristics and predictive score for children with CKD.

The results of score evaluation of prognosis	Children with CKD		Predictive results
	From the main district n=50	From conditionally clean area n=50	
> + 13	45	7	PVP=45:(45+7) x100%=86,5%
< + 13	5	43	PVN=43:(5+43)x 100%=89,6%
operating characteristics	Se=45:(45+5) x 100%=90%	Sp=43:(43+7) x100%=86%	

Note: Se - sensitivity; Sp - specificity; PVP is the predictive value of establishing CKD with a score of> + 13; PVN - predictive value of the absence of CKD with a score of <+ 13;

When using the compiled table (table 2) to predict children CKD under environmental conditions, it is necessary to find an algebraic sum for all 14 signs. With a score of +13 and more, with a probability of 90%, CKD can be predicted among children under environmental conditions, with a sum of –13 or less, the prognostication of such CKD can be rejected with the same probability. When receiving the sum of points in the range from -13 to +13, the prognostication for the pathology of the kidney studied remains uncertain, which requires further observation and use of the developed table in the dynamics of the disease.

Prediction of any pathology requires an integrated approach, allowing to take into account the maximum number of risk factors contributing to the occurrence of a particular pathology.

In the available literature, we have not met the work on the prediction of children CKD in conditions of environmental distress. In this regard, we have developed a simple and affordable prognostication method to determine the risk of developing children CKD under environmental conditions.

To select the optimal number of parameters of the "database" of the prognostic system, we studied the material of the case history of 460 children with nephrological pathology depending on the region of residence. The choice of factors contributing to the development of environmentally determined nephropathy among children was based on our own research, as well as on the basis of data from scientific literature. A set of factors is the matrix, which is the basis for the prognostication system. The determination of the most likely complication is reduced to finding the sum of estimates of the detected signs for one of the complications, therefore, with a small number of signs and complications in the case of rounding, the probable complication can be found manually, that is, without the use of computer technology.

Based on the results of our own research for prognostication, we have compiled a survey map.

After establishing the main set of risk factors, we have chosen the main parameter that will complement the database in the system development process and regarding which the prediction will be carried out. Such a parameter is the risk of developing children CKD in conditions of environmental trouble. This parameter is integral, since the sum and interaction of all other signs characterizing each specific case is displayed by this parameter.

On the basis of a comprehensive clinical assessment of data, taking into account the prognostication, we identified three risk groups for the development of children CKD in the context of environmental problems:

The "high risk" group is a poor prognosis group. It includes children suffering from CKD and living in environmental ill-being, with a PC score of more than 13, and the likelihood of these factors exceeding 90%.

The group of "medium risk" - "attention group" - these include children from the risk group, in whom the sum of PC points for predicting the development of CKD is within 8–13, which corresponds to the probability of these complications occurring in 50–90% of cases.

The "minimal risk" group is a group of children with a PC score for developing CKD less than 8. The possibility of developing children CKD under environmental conditions is less than 50%. The system provides for dynamic analysis, which is an additional criterion for the effectiveness of preventive and therapeutic measures.

For dynamic analysis, it is necessary to note the amounts of PCs in the child's development charts and treatment and preventive measures. Particularly noteworthy is the third group, the so-called "minimal risk", the quality of which is prevented by the quality of treatment and prophylactic measures in the future, depending on the outcome of kidney disease in children.

To determine the dependence of factors in the general list of data of the anamnesis, a one-factor dispersion rank analysis was performed and the prognostic factor significance factor was calculated.

The prognostic factors of each attribute were determined by mathematical calculation using the algorithm of the sequential diagnostic Wald procedure. The table below provides a list of test-early predictors, with each sign expressed by a numerical factor with a positive or negative value. Consideration of the studied factors from the standpoint of ranking consideration allowed to determine them in groups for each specific patient, taking into account his individual characteristics. The table takes into account the biological and socio-hygienic risk factors for CKD and makes it possible to determine the susceptibility of children to the disease. To obtain a predictive conclusion it is necessary to consistently consider all the signs in the order in which they are given in the tables. After consideration of each feature and the corresponding prognostic factor, it is necessary to determine how much the sum of the coefficients of all used features in each case separately approaches the threshold, i.e. allows you to make a conclusion with a pre-selected reliability. Upon reaching the threshold amount, a decision is made (Dusenova, 2017).

Discussion: The authors Foster B.J., McCauley L., Mak R.H., James P.A., Oparil S., Carter B.L., Albaramki J., Hodson E.M., Craig J.C., Webster A.C., Aslam A.A., Higgins C., Sinha I.P., Southern K.W., Cooper T.E., Heathcote L.C., Anderson B., Grégoire M.C., Ljungman G., Eccleston C., Zorin I.V., Vyalkova A.A. in predicting the progression of tubulointerstitial kidney damage among children with reflux nephropathy used an assessment of a complex of immunological, clinical and paraclinical indicators, which allow predicting the progression of reflux nephropathy based on the sum of the contribution of each of them.

We believe that for early prediction of the onset of renal failure, it is advisable to use mathematical models that reflect the approximate timing of the onset of chronic renal failure.

According to Weather P.V. The informative and prognostic significance of biochemical tests of blood and urine of newborns in the diagnosis of ischemic kidney damage (creatinine, lactate, microalbumin, Ma +, K + and carbonic anhydrase) on the basis of calculating their sensitivity and specificity has been proven. A formalized and automated mathematical model and estimated prognostic tables for the allocation of risk groups for the formation of renal pathology in newborns based on prognostically significant clinical and laboratory indicators have also been developed. The presence of correlation with the reliability of prediction is 96%. We used non-invasive early predictors in predicting chronic kidney disease in children.

Conclusion: Prevention of chronic kidney disease among children in conditions of environmental distress can only be successful if it is possible to predict the risk of developing CKD. The basis for creating any prognostication system is always based on several interrelated processes:

• Selection of the optimal number of parameters allowing to sufficiently characterize the process under study;

• the choice of a mathematical apparatus that will allow to combine the selected factors into a general mathematical scheme;

• the effectiveness of the proposed method of prognostication will depend not only on the sufficient choice of information for each clinical case, but also on the capabilities of the software.

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