



ANALYSING DATA ON THE ETIOLOGY, CLASSIFICATION AND PROGRESSION FACTORS OF CHRONIC KIDNEY DISEASE IN CHILDHOOD

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Received 20th Nov 2023,
Accepted 21st Dec 2023,
Online 9th Jan 2024

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Abstract: Chronic kidney disease is defined as kidney damage or decline in kidney function for three months or more regardless of nosological diagnosis. The concept of chronic kidney disease and the classification of CKD stages has been used in modern nephrology since 2002 by the NKF-K/DOQI initiative. In 2003, the term was proposed for use in paediatric nephrology. Kidney disease in childhood continues to progress into adolescence and adulthood, leading to their chronic disease and terminal stage.

Key words: Chronic kidney disease, children, clinic, treatment, prevention.

Introduction. The definition of chronic kidney disease and classification by stage in children is currently not different from that in adults. It is currently known that genetic, endogenous, demographic (sex, age) and a complex of exogenous factors contribute to the development of chronic kidney disease in children. Hypodiagnosis is an actual problem. The course of early stages of chronic kidney disease is variable and often unpredictable.

Determination of risk factors for the development and progression of chronic kidney disease, etiological, structural and functional approach to the diagnosis of renal damage is promising for optimising the diagnosis and treatment of nephropathy in children.

Currently, late diagnosis of chronic kidney disease remains a problem, as well as difficulties

in implementing new approaches to classification, severity assessment, and diagnosis, which are based on new data on the morphofunctional state of the kidneys [2, 6,9]. One of the promising directions of optimisation of diagnostics and treatment of this pathology is awareness of regional features of chronic kidney disease [5]. The study of regional peculiarities of pathology formation in children is the key to effective population health management.

The criterion for chronic kidney disease is the presence of structural and/or functional changes detected by imaging or morphological studies, as well as by abnormalities in urine and/or blood tests.

Objective to study modern data on etiology, classification and factors of progression of chronic kidney disease in childhood.

Material and methods. The literature review devoted to the problem of chronic kidney disease development in children was carried out. The data of domestic and foreign studies were studied.

The most authoritative studies of the criteria of CKD belong to the WHO expert group in the NEONORICA study. The NKE KDOQI guidelines recommend that if CKD is suspected, blood creatinine level should be investigated with calculation of the glomerular filtration rate (rSCF), urine analysis should be tested for microalbuminuria, albumin/protein ratio should be determined. The main criterion is considered to be the rSCF /ml/min/1.73 m² (Schwartz formula is used for children).

CKD is verified when the RGFR is less than 90 ml/min or an equivalent increase in blood creatinine. In children, the criterion used is a decrease in ammoniogenesis, acidogenesis, relative urine density and other indices of tubular function that persist for 3 or more years.

paediatrics

Hypodiagnosis of CKD in children is relevant. The incidence of CKD in different populations is much higher than diagnosed (1%) and ranges from 10 to 12% of the population [5, 10]. In the UK population, the prevalence of CKD ranges from 5.3% (stage 1) - 15.4% (stage 2) - 4.2% (stage 3) to 0.21% (stage 4-5). B.T. Bikbov and N.A. Tomilina [11] consider that the annual increase in dialysis CPN (CKD 5th stage) in adults is about 100 patients per 1 million population, ranging from 60 to 150 patients per 1 million population in different regions.

The prevalence of tCPD in children is 4-5 cases per 1 million children per year in Russia [7, 8, 12, 4, 13], in Europe - 4-6 cases per 1 million children per year (EDTA, 2002) [14, 15, 16]; in the USA - 11 cases per 1 million children per year (US Renal Data Systems, 2002). [17, 18, 19].

It is now known that the development of CKD in children is promoted by genetic, endogenous, demographic (sex, age) and a complex of exogenous factors [20, 21].

In nephrology, there are 4 groups of risk factors that influence the development and course of CKD:

I. Factors influencing the development of CKD:

- Increasing age of the patient;

Stages of chronic kidney disease with regard to glomerular filtration rate

Stages of CKD according to rCKF [^]V/etwork

Stages Description of rSCF (ml/min/1.73t2)

1. Kidney damage* with normal or T rSCF >90
2. Mild 4 rSCF 60-89
3. Moderate 4 pSCF 30-59
4. Severe 4 pSCF 15-29
5. Renal failure <15 or dialysis

Kidney damage is defined by the NKF as 'pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies'

Adapted from NKF K/DOQI Clinical Practice Guidelines 2002: Am J Kidney Dis 2002; 39 (2 Suppl 1): S17-S31

- Aggravated family history of relatives with CKD;
- reduced kidney size and volume;
- low birth weight or prematurity (final maturation of the number of nephrons occurs at 38 weeks of fetal development);
- Low material income (social status) and educational level of the family.

II. Risk factors that initiate CKD:

- Urinary system infections on the background of PMR, urolithiasis, urinary tract obstruction, NIDDM, presence of type 1 and type 2 diabetes mellitus;
- GUS;
- genetic;
- hypertension;
- autoimmune diseases;

➤ Toxic effects of medications.

III. Risk factors that lead to progression of CKD:

- Genetic;
- impaired urodynamics;
- high degree of proteinuria or (and) hypertension;
- Inadequate control of hyperglycaemia, involvement of metabolic factors (lipiduria, POL, lepti-nemia, etc.).

IV. Risk factors for end-stage CKD:

- low dialysis dose;
- temporary vascular access;
- Anaemia;
- low albumin levels;
- Late initiation of renal replacement therapy.

In childhood it is possible to reverse the development of chronic kidney damage and restore the function of the organ, so early detection, timely treatment of kidney disease is an important prerequisite to prevent or distance from its fatal outcome [5, 22].

Currently in Bukhara region 92 children are on dispensary registration with CKD, including 53 children and adolescents with chronic renal failure (CRF): 6 patients under 17 years of age are on haemodialysis. At the pre-dialysis stage of CKD 42 children are on dispensary registration.

The causes of CKD in children are tubulointerstitial kidney damage - TIPP (91.1%) against the background of congenital obstructive uropathies, vesicoureteral reflux, urolithiasis complicated by pyelonephritis, TIPP against the background of GUS; hereditary nephropathies (renal hypo- and dysplasia, polycystic kidney disease, nephronophthisis, cystinosis, etc.), glomerulopathies - 8.9%, including nephrotic syndrome with FSGS.), glomerulopathies - 8.9%, including nephrotic syndrome with FSGS.

Structure of chronic kidney disease in children of Bukhara region

Experience of observation of patients with renal pathology shows that persistent deterioration of renal function in patients with nephrolithiasis, diabetic nephropathy, reflux uropathy, dys-metabolic (urate) nephropathy, as well as in patients in the general population is associated with the development of TIPP, characteristic features of which are tubulointerstitial fibrosis and tubule atrophy.

It is generally accepted that TIPP is a heterogeneous group of diseases with different etiologies, progression of proliferative processes in the interstitium, dystrophy of tubular sections of the non-fronton with the outcome in interstitial fibrosis, tubular atrophy and secondary shrinkage of glomeruli. Tubulointerstitial renal lesions associated with urodynamic, haemodynamic, metabolic disorders, exposure to essential hypertension, infectious, drug, environmental and other factors are of paramount importance in the development of progressive renal pathology [21]. The existing opinion about the distinction between microbial and abacterial TIPP has been replaced by the idea about the stages of tubulointerstitial inflammation development [5, 4, 13]. When a patient is diagnosed with TIPP signs, a specific nosological form, etiological factor determination and pathogenetic mechanism of tubulointerstitial fibrosis and tubule atrophy development are envisaged. All this makes it relevant to search for methods of early diagnosis of tubulointerstitial diseases based on etiological approach and clinical analysis, the use of which allows to prevent or delay the progression of tubulointerstitial fibrosis, which often determines the outcome of renal damage of different etiology and different mechanisms of its development.

Conditions that increase the risk of developing CKD in children:

- Polycystic kidney disease or other genetic kidney disease in family history
- Low birth weight
- Acute renal failure due to perinatal hypoxaemia or other acute kidney injury
- Renal dysplasia or hypoplasia

- Urological anomalies, especially obstructive uropathies
- Vesicoureteral reflux associated with recurrent urinary tract infections and renal scarring
- History of acute nephritis or nephrotic syndrome
- History of haemolytic-uremic syndrome
- History of Schoenlein-Genoch disease
- Diabetes mellitus
- Systemic lupus erythematosus
- A history of hypertension, particularly as a result of renal artery or renal vein thrombosis in the perinatal period.

The risks of developing CKD, early hypertension and a more severe course of acquired kidney disease are:

- prematurity;
- extremely low body weight;
- Fetal ESRD and low birth weight.

A prospective observational study and examination of 1250 children aged 0 to 15 years at risk for CKD was carried out with the aim of early detection of nephropathies with TIPP: patients with obstructive uropathies, urolithiasis, PMR complicated by pyelonephritis (570 patients), patients with renal hypoplasia (75 children), who had suffered GUS (35 children), OPN (75 children), systemic microthrombovasculitis (43 children), as well as 452 children of the risk group (polycystic kidney disease in the family, low birth weight), 50 children of the control group (conditionally healthy children).

During long-term (more than 10 years) observation of children who developed TIPP, different variants of the course of the renal process were identified, depending on the nature of combinations of endogenous (including hereditary) factors and environmental (including infectious) influences: persistent endogenous (including hereditary) factors and environmental (including infectious) influences. infectious influences: persistent abacterial stage of tubulointerstitial inflammation (15%), long-term

(more than 5 years) clinical and laboratory remission of bacterial TIPP (in 20% of patients) and recurrent course with alternation of abacterial and bacterial stages of tubulointerstitial inflammation (65% of observed patients).

Endogenous causes and risk factors for the development of TIPP have been established:

- genetic;
- developmental anomalies of the urinary system organs (including SAKIT syndrome), renal hypoplasia, vesicoureteral reflux, URTIs and their combinations with urodynamic disorders;
- metabolic disorders (urolithiasis on the background of hyperoxaluria, uraturia);
- hypoxia, systemic membranopathological processes.

The special role of maternal kidney disease as a risk factor for the development of TIPP in the child has been confirmed [21].

A high frequency of perinatal factors, including the influence of hypoxia caused by abnormal pregnancy and labour in their mothers, was detected in all children with advanced TIPP. Children with the bacterial stage of TIPP were 5-10 times more likely than children with predisposing conditions to have a maternal history of pregnancy complications (threat of termination of pregnancy, pyelonephritis of pregnancy or exacerbation of chronic pyelonephritis, acute respiratory viral infections and influenza in the 2nd half of pregnancy, toxicosis in the 1st-11th halves).

The high frequency of TIPP formation in children with predisposing conditions requires prospective dispensary observation of them

with systematic monitoring of renal function, microalbuminuria, beta-lysinuria, as well as ultrasound monitoring of the kidneys, monitoring of indicators of anti-infective defence and metabolic disorders for their timely correction to prevent the occurrence and progression of tubulointerstitial process.

Exogenous causes:

- the impact of viruses, bacteria, drugs;

- Influence of environmental factors (heavy metals), etc.

Among the factors etiologically associated with the development of TIPP, a special place is given to the role of viral infection.

In children with TIPP, a direct dependence of the course of the disease on viral influence has been established. Viral involvement of the urinary tract has been detected both in the abacterial and bacterial stages of TIPP. The presence of viruses predominantly (89.1%) of the Cocksackie A and B groups was detected (by immunofluorescent method and serological blood tests) in 36.8% of patients and persisted in the inactive stage in 51.1% of children with TIPP. In the bacterial stage, persistence of viruses in association with bacterial infection was established in 82.1% of patients. The possibility of forming the bacterial stage of TIN under the influence of a combination of coxsackievirus and persistent bacterial infection has been proved, given the incompleteness of nonspecific anti-infection mechanisms, prolonged increase in lipid peroxidation processes and inhibition of antioxidant function.

In children with predisposing conditions, as well as in patients with developed TIN, differences of POL processes and insufficiency of antioxidant functions were revealed: from adaptive level of changes to persistent excessive activation of lipid peroxidation processes. Formation of tubulointerstitial inflammation in children is associated with excessive activation of POL processes.

In the progressive course of abacterial TIPP in 99.2% of patients there was revealed oppression of anti-infective defence, which is characterized by a decrease in the level of B1dA, completion of phagocytosis by neutrophils, dysimmunoglobulinemia, combined with infection of the urinary system with viral-bacterial or bacterial pathogens capable of persistence, which was documented by the isolation of Cocksackie viruses and intracellularly parasitic bacteria with high persistence properties from urine sediment cells.

Progression of tubulointerstitial process, alternation of bacterial and abacterial stages is observed in patients with persistence of viral-bacterial infection, reduced anti-infective defence, impaired intrarenal hemodynamics, microalbuminuria, increased free-radical oxidation processes, which makes it reasonable to use preventive therapy.

The prognostic signs of unfavourable clinical course of the disease with layering of bacterial tubulointerstitial process are the decrease of tubular functions, microalbuminuria, persistent p-lysinuria, stable high level of POL indicators, suppression of antioxidant protection enzymes, decrease of free-radical oxidation processes, decrease of free-radical oxidation, decrease of free-radical oxidation processes.

Diagnostic algorithm of chronic kidney disease in children

Infection resistance factors in combination with persistence of coxsackie viruses and intracellularly parasitic *Escherichia coli* with high ability to inactivate lysozyme.

The high frequency of TIPP formation in children with predisposing conditions requires prospective dispensary observation with systematic monitoring of renal function, microalbuminuria, p-lysinuria, renal ultrasound monitoring with evaluation of intrarenal haemodynamics for timely correction and prevention of tubulointerstitial disease progression.

Conclusions: Thus, chronic kidney disease in children is a stage process, which is formed under the influence of a complex of interdependent factors involved in the progression of renal damage with the formation of nephrosclerosis. Currently, the pathogenetic mechanisms of development and progression of CKD in children are being clarified. Prevention of unfavourable outcome and early diagnosis (1-11 stages) of CKD in children is one of the urgent problems of paediatric nephrology. The introduction of a three-stage system of nephrological care for children, antenatal and early postnatal diagnosis of congenital malformations of the urinary system, identification of risk factors (CKD), monitoring of children's nephrological health,

introduction of an algorithm for early diagnosis of CKD and timely non-protective therapy can prevent the progression of the renal process and reduce the disability of children due to CKD.

Due to the fact that in childhood it is possible to reverse the development of chronic kidney damage and restore the function of the organ, early detection, and timely treatment of kidney disease is an important prerequisite for preventing or distancing from its unfavourable outcome.

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