

INNOVATIVE SIGNIFICANCE OF INDICATORS OF PARTIAL RENAL FUNCTIONS IN CHRONIC TUBULOINTERSTITIAL NEPHRITIS IN CHILDREN

*Akhmedzhanov I.A.¹, Akhmedzhanova N.I.¹, Izomiddinova M.K.¹
Samarkand State Medical University, Samarkand, Uzbekistan*

Annotation. Despite the progress achieved in the diagnosis and treatment of nephropathies, in almost 25% of patients this pathology continues to progress, which leads to a deterioration in the quality of life of patients.

Purpose of the study: To identify the features of indicators of partial renal functions in chronic tubulointerstitial nephritis in children (taking into account the form of the disease).

Material and research methods. Depending on the clinical form of renal pathology, all patients (120 children) were divided into 2 groups: group 1 - 52 children (43.3%) with recurrent CTIN, group 2 - 68 sick children (56.7%) with latent CTIN.

Research results. Of the calculated weighting coefficients, the most significant in the impairment of renal function were the indicators of acidogenesis and ammoniogenesis, daily proteinuria.

Discussion. It should be noted that in patients with CTIN, more significant disturbances in indicators of acidogenesis and ammoniogenesis, daily proteinuria were revealed, compared with glomerular function (GFR), daily diuresis, which confirms the role of an aseptic inflammatory process of tubular origin.

Conclusion. The condition of the distal tubules in patients with CTIN was characterized by the predominance of dysfunction of ammonia acidogenesis, and the condition of the proximal tubules by an increase in daily proteinuria.

Key words: *partial kidney functions, chronic kidney pathology.*

Relevance. Despite the progress achieved in the diagnosis and treatment of nephropathies, in almost 25% of patients this pathology continues to progress, which leads to a deterioration in the quality of life of patients [1]. The development of a pathological process in the tubulointerstitial tissue (TIT) of the kidneys is caused by heterogeneous specific and nonspecific etiological factors [2, 3]. The center of inflammatory changes in chronic tubulointerstitial nephritis (CTIN) is the interstitial tissue of the kidneys, involving the tubules, blood and lymphatic vessels of the renal stroma in the pathological process [4, 5].

Data on comparative clinical and laboratory assessment of certain types of tubulointerstitial nephritis are also lacking, and the pathogenetic role of the relationship between disorders of tubular functions in patients with various forms of CTIN has not

been sufficiently studied [6, 7]. The task set in our work was to determine the importance of a method for determining indicators of endogenous intoxication in CTIN in children, aimed at preventing their progression and development of chronic renal failure [8, 9, 10].

Purpose of the study: To identify the features of indicators of partial renal functions in chronic tubulointerstitial nephritis in children (taking into account the form of the disease).

Material and research methods. Depending on the clinical form of renal pathology, all patients (120 children) were divided into 2 groups: group 1 - 52 children (43.3%) with recurrent CTIN, group 2 - 68 sick children (56.7%) with latent CTIN. The duration of the chronic form of the disease ranged from 1 year to 9 years. The average duration of CTIN was 4.2 ± 0.5 years. In children with latent CTIN, it was determined from the moment of detection of urinary syndrome according to form No. 112. The frequency of relapses was 2-3 times a year. At the beginning of the study, at the Department of 2-Pediatrics of SamMI (head of the department - Doctor of Medical Sciences, Associate Professor N.I. Akhmedzhanova), an individual observation card for the patient was compiled, including data on the patient's life history and illness, genealogical and medical data. biological history, results of clinical, paraclinical, instrumental examination of the child.

The clinical diagnosis of CTIN was made according to the diagnostic criteria proposed in the classification by N.A. Korovina, I.N. Zakharova (2003), where special attention was paid to the characteristics of the pedigree history: determination of IMS, TIN, ICD, metabolic disorders at an early age, which were symptoms of exudative-catarrhal diathesis, dysuric disorders against the background of crystalluria.

All patients with CTIN were characterized by the absence of complaints and the occasional detection of urinary syndrome during clinical examination or examination in connection with the disease of one of the family members. Features of the clinical characteristics of the latent variant of CTIN (85.2% (58/68)) - random determination of isolated urinary syndrome, in 88.2% (60/68) cases in combination with signs of endogenous intoxication, a tendency to hypotension in 58, 8% of cases (40/68). The constant persistence of urinary syndrome in these patients did not allow us to clearly distinguish between the stages of CTIN.

With the undulating course of CTIN, in 100% of cases the symptoms of endogenous intoxication predominated, as well as weight loss, anorexia, fatigue, and arterial hypotension. Dysuric symptoms occurred in 40.0% (20/52), pain in the abdomen and lumbar region - 78.8% (41/52), skin rashes in 5/52 patients, low-grade fever - in 38.4% (20/52) .

Urinary syndrome was characterized by leukocyturia (up to 5-10 cells in the subsection), microhematuria (up to 25 or more red blood cells in the subsection).

Cylindruria (54/120) in the form of hyaline cylinders (no more than 2-3 in the p/z). Proteinuria up to 1.05 g/l in a single amount of urine. In all examined children, bacteriuria in single portions and three-fold bacteriological urine culture were negative. According to the Nechiporenko test, the average number of leukocytes is 4016.13 cells per 1 ml. Erythrocyturia from 640.0 to maximum - 8450.0 cells per 1 ml. We noted the following variants of TIN with a chronic course: circulatory TIN often occurred against the background of anomalies of the renal vessels (7 (13.4%)), kidney rotation, and nephroptosis. Dysmetabolic TIN was characteristic of patients with secondary oxalate crystalluria (29 (55.7%)); against the background of dysembryogenesis (anomalies of the urinary system with impaired urodynamics) - 6 (11.5%). One child (1.9%) had an autoimmune nature of the disease. The manifest onset of the disease, established in 52 children (43%), subsequently took on a wave-like character. The latent variant of the chronic course occurred in 68 patients (57%). Among them there were 65 boys (54%), 55 girls (46%).

Noteworthy is the family history of kidney disease and metabolic disorders (urolithiasis, cholelithiasis), amounting to 82% of cases. The parents of 4 patients (3.3%) reported occupational hazards (chemical factors).

Unfavorable antenatal history was one of the development factors in 57 cases (47.5%). Pathological course of pregnancy with a predominance of early gestosis in mothers of observed children (19), acute perinatal gestosis (3) and intrauterine infection (1). Perinatal encephalopathy was observed in 4.1% of cases (5 children). A short period of breastfeeding was noted in 84 (70%) children.

Intercurrent diseases were noted in 81 (67.5%) children, in connection with which 24 patients (46.1%) used various medications (antibacterial) drugs up to several courses per year (5). Chronic foci of infection were found in 71 (59.1%) patients in the form of carious teeth, adenoiditis, and tonsillitis.

It is important to point out that 60 children (50%) had a burdened history of allergies (in the form of atopic dermatitis, acute urticaria, allergies to medications and food allergens).

Indicators of glomerular function in patients with CTIN indicated the absence of its impairment. The tubular part of the nephron was characterized by a relative decrease in the reabsorption function of the proximal tubules. The parameters of amino nitrogen in the blood (6.66 ± 0.36 mg/%) corresponded to the norm, the level of aminoaciduria did not approach negative values. Daily excretion of titratable acids is 45.3 ± 0.45 μ g/day and ammonia 41.0 ± 0.52 μ g/day in recurrent CTIN.

There were no significant changes in daily diuresis. Daily diuresis ranged from 710 ml/day to 1670 ml/day, depending on age. Of the calculated weighting coefficients, the most significant in the impairment of renal function were the indicators of acidogenesis and ammoniogenesis, daily proteinuria. In patients with

recurrent CTIN in the acute stage, changes in the functional state of the kidneys are more pronounced in terms of daily proteinuria and urine osmolarity, while the level of acidogenesis and ammoniaogenesis was most impaired in the latent course of CTIN, which we associate with a more pronounced tendency to metabolic acidosis due to untimely diagnosis and treatment of the latent course of CTIN.

We determined that a common cause of exacerbation of TIN in the children we observed were adverse reactions and complications of drug therapy, acute respiratory viral infections and bacterial infections. This is due to the fact that most drugs and their metabolites are excreted from the body by the kidneys. Kidney damage can be caused by the direct toxic effect of medications and mediated through immunopathological reactions.

When studying partial renal functions, a number of functional methods were used:

Group I - methods that allow quantitative characterization of the state of individual kidney functions:

a) GFR (endogenous creatinine clearance), which was calculated using the Van-Slake formula; the degree of proteinuria was assessed by the amount of daily protein excretion divided by body weight in kilograms.

b) The state of the distal tubules according to the function of osmotic concentration. We used Zimnitsky's test to determine the concentration ability of the kidneys. Additionally, the magnitude of ammoniogenesis and the ability to acidify urine were studied (titratable acids and ammonia were determined in daily urine).

Group II - methods based on the study of certain blood parameters, reflecting the result of the total work of both kidneys (urea, creatinine, electrolytes - potassium, sodium).

Methods of statistical processing. The statistical significance of the obtained results was assessed using parametric Student-Fisher tests with calculation of mean values (M), standard deviation (δ) and error of the arithmetic mean (m). Using the table, Student's t-test was used to determine the probability (p) of a possible error. The result was considered statistically significant at $P < 0.05$. The correlation coefficient (r) between data on the functional state of the kidneys and metabolic changes was determined by Brava-Pearson.

Research results. As the results of the study showed, 100% of patients with CTIN had moderately severe abacterial leukocyturia; in 88.9% of sick children (56 people) - no more than 4016.13 cells in 1 ml (while 2/3 of leukocytes in the urine were lymphocytes), and in healthy children - leukocyturia did not exceed 2000 cells in 1 ml.

A study of glomerular function indicators in patients with CTIN showed unreliable values for impaired glomerular filtration (Table 1).

No bacteriuria was observed in children with CTIN. We found microhematuria of up to 5-6 red blood cells per 1 ml in 90.5% of patients in both groups, macrohematuria in 9.5% of examined children, as a result of damage to interstitial tissue and instability of the basement membrane in children with a dismetabolic variant of CTIN, in which there were up to 19 -20 red blood cells per 1 ml., while in healthy children the number of red blood cells in the urine does not exceed 0-1 cells. in 1 ml.

Table 1.

Indicators of partial renal function in CTIN in children upon admission in the acute period (M±m)

Indicators	Healthy children (n =30)	Recurrent CTIN (n =52)	Latent CTIN (n =68)
GFR , m l/min. m ²	88,6±7,8	82,0±0,25 p≥0,1	83,4±1,23 p≥0,1
Daily diuresis, l/day.	1,7±0,036	1,06±0,015 p=0,03	1,42±0,034 p=0,01
Minute diuresis, ml/min	1,2±0,037	0,61±0,010 p=0,028	0,79±0,02 p=0,041
Daily excretion of titratable acids (µg/day)	51,0±2,8	45,3±0,45 p=0,01	42,3±0,52 p=0,001
Daily ammonia excretion (µg/day)	46,8±1,2	41,0±0,52 p=0,01	39,67±0,58 p=0,001

Note: p-significance of the difference between the indicators in healthy children and children with CTIN.

Determining the titratable acidity of urine (AT) gives a more accurate idea of the excretion of hydrogen ions by the kidneys than urine pH. Comparison with other indicators (amount of NH₃ in urine, urine pH, blood pH) is of great importance for assessing the acid-base balance in the body.

It was found that in patients with latent CTIN before treatment there was a significantly lower content of NH₃, AT in the urine 39.67±0.58 µg/day, 42.3±0.52 µg/day (p=0.001), which indicates a higher tendency to the appearance of acidosis compared to recurrent CTIN 41.0±0.52 mcg/day, 45.3±0.45 mcg/day (p=0.01).

We noted a decrease in the osmotic dilution function in CTIN. Osmoregulation as the process of maintaining the total concentration of ions and molecules in body fluids and maintaining water-ion balance is one of the important aspects of the complex of homeostatic reactions of the body.

Of the calculated weighting coefficients, the most significant in the impairment of renal function were the indicators of acidogenesis and ammoniogenesis, daily proteinuria.

When analyzing the results of biochemical studies before treatment, it was found that in children with CTIN, the protein content in a single amount of urine was up to 1.05 g/l and exceeded the values in healthy children (0.02 g/l) in 76.9% (40) patients, and in children of group 2 in 82.5% (52) of children.

Discussion. It should be noted that in patients with CTIN, more significant disturbances in indicators of acidogenesis and ammoniogenesis, daily proteinuria were revealed, compared with glomerular function (GFR), daily diuresis, which confirms the role of an aseptic inflammatory process of tubular origin.

Consequently, patients with CTIN may experience an exacerbation of the aseptic inflammatory process without visible laboratory manifestations, which may be one of the reasons for late diagnosis and aggravation of the latent course of the disease.

Conclusion. The condition of the distal tubules in patients with CTIN was characterized by the predominance of dysfunction of ammonia acidogenesis, and the condition of the proximal tubules by an increase in daily proteinuria.

References

1. Sigitova O.N., Arkhipov E.V. Tubulointerstitial nephritis. Bulletin of modern clinical medicine. 2010; 3(3): 44-49. [Sigitova ON., Arkhipov EV. Tubulointerstitial nephritis. Vestnik sovremennoy klinicheskoy medicitsiny. 2010; 3(3): 44-49. (In Russ.)].
2. Akhmedzhanova N.I., Akhmedzhanov I.A. Method for treating chronic pyelonephritis in children. Riga: Lap-Lambert. 2018.175 p. [Akhmedzhanova NI., Akhmedzhanov IA. Sposob lecheniya khronicheskogo piyelonefrita u detey. (Method for the treatment of chronic pyelonephritis in children.). Riga: Lap-Lambert. 2018. 175 p. (In Russ.)].
3. Batyushin M.M., Pasechnik D.G. Hematuria: concept, causes and basis of differential diagnosis. Consilium medicum. 2012;1:12-18. [Batyushin MM., Pasechnik DG. Hematuria: concept, causes and bases of differential diagnosis. Konsilium medikum. 2012;1:12-18. (In Russ.)]
4. Alekseev A.V., Gilmanov A.Zh., Gatiyatullina R.S., Rakipov I.G. Modern biomarkers of acute kidney injury. Practical medicine. 2014; 3(79): 22-27. [Alekseev AV, Gilmanov AZ., Gatiyatullina RS, Rakipov IG. Modern biomarkers of acute kidney injury. Prakticheskaya meditsina. 2014; 3(79): 22-27. (In Russ.)]
5. Khlebovets N.I. Tubulointerstitial nephritis in children. Journal of Grodno State Medical University. 2014; 1(14): 92–97. [Khlebovets NI. Tubulointerstitial nephritis

in children. *Jurnal Grodnenskogo gosudarstvennogo meditsinskogo universiteta*. 2014; 1(14):92–97. (In Russ.)]

6. Zorin I.V. Assessing the effectiveness of drug rehabilitation in adolescents with tubulointerstitial kidney damage who have suffered a relapse of renal infection. *Attending doctor*. 2016;6:8–11. [Zorin IV. Evaluation of the effectiveness of medical rehabilitation of adolescents with tubulointerstitial kidney disease who had a relapse of renal infection. *Lechashiy vrach*. 2016;6:8–11. (In Russ.)]

7. Vyalkova A.A. Optimization of diagnosis of secondary tubulointerstitial kidney damage in children. *Pediatrician*. 2011; 2(1):8. [Vyalkova AA. Optimization of the diagnosis of secondary tubulointerstitial kidney damage in children. *Pediatr*. 2011; 2(1):8. (In Russ.)].

8. Batyushin M.M., Pasechnik D.G. Proteinuria: issues of differential diagnosis *Consilium medicum*. 2013;7:48-56. [Batyushin MM., Pasechnik DG. Proteinuria: issues of differential diagnosis. *Konsilium medikum*. 2013;7:48-56. (In Russ.)].

9. Rychkova S.V. Metabolic nephropathies and tubulointerstitial nephritis in pediatric practice. St. Petersburg: RusBlank. 2013. 50 p. [Rychkova SV. *Obmennyye nefropatii i tubulointerstitsial’nyy nefrit v pediatricheskoy praktike*. (Exchange nephropathy and tubulointerstitial nephritis in pediatric practice). St. Petersburg: RusBlank. 2013. 50 p. (In Russ.)]

10. Shutov A.M. Chronic kidney disease is a global problem of the 21st century. *Clinical medicine*. 2014;(92)5:5–10. [Shutov AM. Chronic kidney disease is a global problem of the XXI century. *Clinical medicine*. 2014;92(5):5–10. (In Russ.)]