

MODIFIED APPROACH TO THE DIAGNOSIS OF PYELONEPHRITIS IN CHILDREN

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Abstract

Pyelonephritis is the second most common disease in children after acute respiratory infections, between which there is a clear and close relationship. Objective. Determination of clinical and laboratory features of early diagnosis of pyelonephritis in children who have had COVID-19. Methods. A cohort retrospective clinical follow-up of 121 children with pyelonephritis was carried out. Results and discussion. An analysis of changes in the partial function of the kidneys in all patients with pyelonephritis was carried out. The results of the study indicate that in patients of groups 1 and 3, all the studied clinical and laboratory parameters were significantly impaired compared to group 2. These changes confirm the possibility of their different severity depending on the causes of the disease (etiological factors). Conclusion. In patients with pyelonephritis who had COVID-19, damage was found not only to the proximal (proteinuria increased by 11 times compared to healthy children) and distal tubules (ammoniogenesis function decreased by 34%) of the renal nephrons, but also to the glomeruli (GFR decreased by 38% compared to healthy children), which is atypical for pyelonephritis in children without a history of COVID-19.

Keywords: COVID-19, acute pyelonephritis, CMM-1, β 2-microglobulin level.

Introduction

Pyelonephritis is the second most common disease in children after acute respiratory infections, and there is a clear and close relationship between them. In pediatric urology, every fourth case of pyelonephritis is described as a complication of acute respiratory infections. Pyelonephritis is most common in preschool children [1, 2].

A new COVID-19 disease caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) first emerged in Wuhan, China, in December 2019 [4, 6]. Soon after, the World Health Organization (WHO) declared a global pandemic. COVID-19 is a major challenge facing modern medicine and science. The high contagiousness and severity of the disease have become a serious challenge for the world's healthcare systems [5, 7].

According to international medical statistics for 2020, children and adolescents accounted for 2-10% of patients infected with COVID-19 in the initial phase of the pandemic. In children, the disease is less pronounced and is characterized by a milder clinical picture than in adults. Mortality rates among children are also significantly lower than among adults [8].

However, the epidemiological situation has deteriorated sharply with the emergence of new strains of SARS-CoV-2. By the end of November 2021, more than 12,000 children and adolescents had died from COVID-19 worldwide.



Determination of biomarkers such as γ -GT, β 2M, NGAL and KIM-1 in urine is an effective non-invasive method for early and accurate diagnosis of pyelonephritis. Elevated levels of these biomarkers in the urine are indicative of the extent of damage and inflammation in the kidney tissue. The use of these biomarkers in clinical practice is of great importance for predicting the outcome of the disease and reducing the economic burden on the healthcare system [3].

Objective

Determination of clinical and laboratory features of early diagnosis of pyelonephritis in children who have had COVID-19.

Material and methods of research

The study included 121 children examined in 2020-2022, who were divided into three groups. The first group included children with acute pyelonephritis (n=50) with a history of COVID-19, the second group included children with acute pyelonephritis (n=50) with negative COVID-19 test results (PCR, ELISA) in anamnesis, and the third group included patients with chronic pyelonephritis (n=21) with a history of COVID-19. admission to the hospital.

All patients were included in the study during the clinically active period of acute pyelonephritis and during the period of relapse of chronic pyelonephritis. Clinical diagnostics according to the classification proposed by Korovina N.A. (2002), was carried out on the basis of diagnostic criteria. The work uses general clinical, biochemical, microbiological, instrumental and statistical research methods. The following methods were used to analyze the partial functions of the kidneys:

- Methods that determine the state of nephron structures: GFR; proximal tubules – diurnal proteinuria; distal tubules – the level of ammonia and titratable acid in the urine, the pH of the urine;
- Methods for assessing the total activity of the nephron: determination of the concentration of creatinine and urea in the blood serum.

For the purpose of early detection of the pathological state of the renal tissue and assessment of the severity of pyelonephritis, pathobiochemical studies of urine were carried out: the levels of KIM-1, β 2-microglobulin were determined.

In addition, all patients underwent renal ultrasound to assess urinary function, blood pressure, and renal hemodynamics.

Results

An analysis of changes in the partial functions of the kidneys in all patients with pyelonephritis was carried out. The results of the study indicate that in patients of groups 1 and 3, all the studied clinical and laboratory parameters were significantly impaired compared to group 2. These changes confirm the possibility of their different severity depending on the causes of the disease (etiological factors). The results of the study showed that in patients of the 2nd group in the active stage of the disease, GFR (86.3 ± 0.4 ml/min/1.73 m²) remained within the level of healthy children (97.6 ± 2.1 ml/min/1.73 m²). At the same time, patients in groups 1 (64.5 ± 0.30 ml/min/1.73 m²; $p \leq 0.001$) and 3 (61.62 ± 0.28 ml/min/1.73 m²; $p \leq 0.001$) showed a statistically significant decrease in glomerular filtration.



In the study groups, a decrease in the excretion of titratable acidity was revealed (group 1 – 23.23 ± 0.64 mmol/24 h, $p \leq 0.01$; group 2 – 32.04 ± 0.24 mmol/24 h; group 3 – 22.12 ± 0.18 mmol/24 h, $p \leq 0.01$), which indicates significant dysfunction of the distal tubules in children of groups 1 and 3.

According to the results of the study, all patients had a decrease in the relative density of urine, but in patients of groups 1 and 3, the impairment of this parameter was significant compared to the control group (1013.18 ± 0.29 ; 1011.48 ± 0.42 mmol/L; $p \leq 0.01$), which we associate with SARS-COV-2, which exacerbates distal tubular dysfunction.

We studied the level of the kidney injury molecule-1 (KIM-1) in patients. According to the results of the laboratory study, the level of KIM-1 was statistically significantly increased in patients of groups 1 and 3 (5.73 ± 0.03 ng/ml; 6.86 ± 0.02 ng/ml; $p \leq 0.01$), while in patients of group 2 this indicator was 2.97 ± 0.01 ng/ml, and in healthy children – 1.52 ± 0.01 ng/ml (Table 1).

Table 1 Urinary KIM-1 levels in children with pyelonephritis and a history of COVID-19

Indicators	Healthy children n=25	Before treatment		
		Group 1 n=50	Group 2 n = 50	Group 3 n = 21
KIM-1, ng/ml	$1,52 \pm 0,01$	5.73 ± 0.03 $p \leq 0.01$	$2,97 \pm 0,01$ $p \leq 0.05$	6.86 ± 0.02 $R \leq 0.01$

Note: p-significance of differences when comparing the level of CMM-1 in patients with pyelonephritis depending on the history of COVID-19 and healthy children.

In patients of groups 1 and 3, the level of KIM-1 was significantly higher than in patients of group 2. This is due to ischemic and toxic damage to the proximal tubules and increased tubulointerstitial remodeling processes. The level of $\beta 2$ -microglobulin ($\beta 2M$) was also studied in patients included in the study. The $\beta 2M$ protein in the urine is filtered through the glomeruli of the kidneys and then reabsorbed by the proximal tubules. With inflammation in these structures, the level of $\beta 2M$ in the urine increases. It was found that the $\beta 2M$ level in Group 1 was 7.64 times higher (2.37 ± 0.03 mg/L; $p \leq 0.001$) than in healthy children (0.31 ± 0.01 mg/L), and in Group 3 it was 9.16 times higher (2.84 ± 0.03 mg/L; $p \leq 0.001$), while in Group 2 this index was only 3.74 times higher (1.16 ± 0.04 mg/L). This indicates the glomerulotropic course of coronavirus infection.

Discussion

Statistically insignificant differences between the indicators of the functional state of the kidneys in healthy children depending on age were revealed, which served as the basis for combining these indicators into a general group and the subsequent use of average indicators as normative.

An analysis of changes in the partial function of the kidneys in all patients with pyelonephritis was carried out. Thus, patients of groups 1 and 3 had a significant decrease in GFR, NH_3 , AT, and urine concentration capacity compared to patients of group 2, as well as a significant increase in proteinuria, leukocyturia, and microhematuria. This indicated a serious impairment of the filtration, excretory and concentration capacity of the kidneys in patients with pyelonephritis with a history of COVID-19.



The anti-inflammatory activity of KIM-1 is mediated by a complex cascade. This process begins with the absorption of apoptotic cell products from urine by the epithelial cells of the proximal tubules. This leads to the interaction of the molecular domains of kidney injury with the p85 protein, which in turn reduces the activity of the transcription factor NF- κ B, which leads to a decrease in the amount of pro-inflammatory cytokines produced by the cell.

Summarizing the above data, it can be noted that an increase in the concentration of β 2M in urine in patients of groups 1 and 3 ($p \leq 0.001$) is associated with an increase in the permeability of glomerular filtration, a decrease in the ability of tubular cells to reabsorb, vasculopathy and pathological changes in the metabolism of ions and proteins under the influence of SARS-CoV-2. A pronounced direct correlation was found between the level of CMM-1 in the urine and leukocyturia ($r=0.70$; $r=0.64$; $r=0.73$; $p \leq 0.001$), the higher the CMM-1, the more active the pathological process and the higher the level of leukocyturia in the urine. A pronounced inverse correlation between the β 2M level and GFR was revealed ($r=-0.72$; $r=-0.65$; $r=-0.75$; $p \leq 0.001$). The revealed correlations contribute to the development of a therapeutic strategy aimed at normalizing the partial functions of the kidneys and restoring the inflammatory process in the renal tissue, and also indicate the need to improve the treatment of pyelonephritis in children who have had COVID-19.

Conclusion

1. In patients with pyelonephritis who had COVID-19, damage was found not only to the proximal (proteinuria increased 11-fold compared to healthy children) and distal tubules (34-fold decrease in ammoniogenesis function) renal nephrons, but also to the glomeruli (38% decrease in GFR compared to healthy children), which is atypical for pyelonephritis in children without a history of COVID-19.

3. The concentration of KIM-1, β 2M in the urine is directly proportional to the degree of damage to renal tissue. In patients with pyelonephritis who had COVID-19, the level of KIM-1, β 2M was significantly higher compared to patients with pyelonephritis without COVID-19, which indicates the presence of relatively pronounced hypoxia that developed against the background of an inflammatory process in the renal tissue in children with pyelonephritis who had COVID-19.

4. In patients with pyelonephritis who had COVID-19, a high degree of correlation was found between the level of KIM-1 in the urine and leukocyturia ($r = 0.70$; 0.63 ; 0.73 ; $p \leq 0.001$); a high degree of inverse correlation between the level of β 2M and GFR ($r = -0.72$; -0.65 ; -0.75 ; $p \leq 0.001$).

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