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# INDICATORS OF RENAL MEMBRANOLYSIS IN CHILDREN WITH PYELONEPHRITIS DURING THE COVID-19 PANDEMIC

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**Abstract:**
COVID-19 is the biggest challenge facing medicine and scientists in the world in modern times. The highly contagious and severe course of the disease has become a serious test for the global health system**.**
**The purpose of the work:** Determination of correlation between indicators of renal functional status and endogenous intoxication, renal enzymes in urine in children with pyelonephritis during the COVID-19 pandemic.
**Materials and research methods:** -we selected 100 children as research groups. Group I - Main group, Group II - Control group. All patients were examined using clinical, instrumental and laboratory methods.
**Results:** An increase in the activity of NADFN-cytochrome s-reductase is not enough to ensure the limit of cytochrome C output, because it is released from erythrocytes in large quantities, which is confirmed by an increase in the amount of cytochrome C in plasma. At the same time, the increase in the activity of NADFN-cytochrome b5-reductase provides a high pool of cytochrome b5, which exceeds the control values by 28.1% (R<0.002).
**Conclusions:** Children with COVID-19 should be examined according to the following plan for the purpose of early diagnosis and prevention of pyelonephritis, in addition to the generally accepted examination methods: 1. Taking into account the glomerular filtration rate, it is necessary to determine the concentration of creatinine in the blood serum, check the concentration of urea, uric acid, total protein, ALT, AST, GGT, IF and XE, the level of OMP, LPO (MDA and XL). Also, after recovery, it is necessary to check once a month for the first 3 months, then once a year for 3 years; 2. in case of pyelonephritis, attention should be paid to the levels of Cytochrome S, NADFN-cytochrome s-reductase, NADFN-cytochrome b5-reductase, Cytochrome b5, G-6-FDG in erythrocytes and plasma;

**Keywords:** COVID-19, pyelonephritis, protienuria, microhematuria, sarcoiduria, retinol amine.

**Background:**
COVID-19 is the biggest challenge facing medicine and scientists in the world in modern times. The highly contagious and severe course of the disease has become a serious test for the global health system. Unprecedented measures have been taken around the world to limit the spread of the disease, to increase the possibilities of emergency medical care for patients with coronavirus infection, to stop planned operations, to limit inpatient and outpatient care for seriously ill patients, including the conversion of multidisciplinary and specialized clinics to the urological profile. The pathogenesis of kidney damage in SARS-CoV-2 infection is multifactorial. First, SARS-CoV-2 may have a direct cytopathic effect on the kidney. This is confirmed by the detection of coronavirus fragments by polymerase chain reaction in the urine of patients infected with COVID-19. Research data from domestic and foreign authors show that the kidneys are the target organ of the new infection, and their damage ranges from proteinuria and hematuria to acute kidney injury.
In recent years, the most informative diagnostic markers of the inflammatory process are LPO indicators, toxic OMP excreted in urine, and the amount of kidney tissue enzymes.

**Objective:**
To determine the relationship between indicators of renal functional status and endogenous intoxication, renal enzymes in urine in children with pyelonephritis during the COVID-19 pandemic.

**Materials and Methods:**
From March 2021 to 2022, a retrospective analysis of children admitted to the Children's Hospital of Infectious Diseases of Samarkand Region (n=422) with confirmed COVID-19 infection was conducted, combined with transcription polymerase chain reaction. Changes in the kidneys were studied in 50 children with confirmed COVID-19 infection as the main group. 50 patients with pyelonephritis who did not suffer from COVID-19 were taken as a control group. The most informative diagnostic markers of the inflammatory process are LPO indicators, toxic OMP excreted in the urine, and the amount of kidney tissue enzymes.

**Results:**
Determination of these compounds in urine is a convenient non-invasive test method. These examination methods are used for the early detection of organ damage at the level of cellular processes, which is important in predicting the outcome of the disease. We mainly studied the activity of alkaline phosphatase (IF), γ-glutamyltransferase (γ-GGT), cholinesterase (XE), alanine aminotransferase (ALT), aspartate aminotransferase (AST). Because they are located in the epithelium of the proximal part of the nephron and are the most important intracellular enzymes.

It is known that IF and γ-GGT are located in the cytoplasmic membrane of the tubular epithelium of proximal tubules. The presence of these enzymes in the urine is evaluated as a qualitative and quantitative measure of damage to proximal tubule cells [19,28]. ALT and AST enzymes are located in the cell cytosol. The extracellular release of these enzymes indicates that the cytoplasmic membrane of the tubular epithelium has been deeply damaged and cytosolic components have been released into the tubular cavity.

XE activity is determined in the urine to study the state of the kidney glomerular filter, normally it is in the blood and is not excreted in the urine [12,16, 17]. Determining the status of LPO processes is also important. Activation of free radical processes takes place in all pathological processes, including inflammation, and is the main pathogenetic factor in the development of cell alterations. As a result of these breakdowns, primary (XL) and secondary (MDA) LPO products are formed. The dynamics of changes in the amount of OMP in urine indicate the activity of the inflammatory process in the kidney parenchyma, the increase in the amount in the blood - the level of developing endotoxemia.

The above data became the basis for studying the level of these indicators in all children with pyelonephritis against the background of COVID-19. Examination results showed that all patients had fermenturia before treatment: ALT activity increased by 2.42 times, AST – by 2.63 times, IF and γ-GGT – by 2.1 and 1.96 times, compared to the control group. In addition, it was found that MDA in urine increased 2.06 times, XL - 1.80 times, O'MP - 3.76 times compared to the control group (Table 4.3). Determined changes in biochemical indicators in urine indicate the state of the cell membrane in the interstitial tissue of the kidneys.

**Table -1 Biochemical indicators of urine in children with pyelonephritis against the background of COVID-19**

| Indicators | Healthy children | Research groups | |
|---|---|---|---|
| | | 1- group | 2- group |
| ALT ed/l | 2,80±0,07 | 6,77±0,1* | 3,2±0,08** |
| AST, ed/l | 2,73±0,1 | 7,17±0,09* | 4,7±0,1** |
| γ-ГГТ, ed/l | 3,97±0,17 | 7,78±0,12* | 4,37±0,14** |
| alkaline phosphatase, ed/l | 0,89±0,04 | 1,86±0,09* | 0,9±0,02** |
| cholinesterase, ed/l | 60,86±2,18 | 73,4±1,01* | 62,6±3,2** |
| malondialdehyde, мкмоль/л | 5,70±0,14 | 11,7±0,42* | 7,76±0,24** |
| chemiluminescence, imp/s | 31,6±1,2 | 56,88±0,8* | 38,6±1,2** |
| medium molecular weight peptides, g/l | 1,52±0,1 | 5,71±0,5* | 2,03±0,08** |

Note: * - significant difference compared to the indicators of the control group, r<0.05; ** The difference compared to the indicators of the 1st group is significant, r<0.05.

These identified changes indicated that renal parenchymal damage and endotoxemia occur in children with pyelonephritis against the background of COVID-19.
Given that COVID-19 is accompanied by respiratory tract pathology, hypoxia occurs in all organ tissues, including kidney tissue. Hypoxia is caused on the one hand by damage to the respiratory tract, on the other hand by changes in the metabolic and functional activity of erythrocytes. To determine the metabolic activity of erythrocytes, we determined the concentration of cytochrome S, G-6-FDG enzyme, NADFN-cytochrome b5-reductase, NADFN-cytochrome s-reductase, cytochrome b5, which are indicators of activity of the electron transport system in erythrocytes.

**2-table Indicators of the activity of enzymes of the electron transport system in erythrocytes in children with pyelonephritis against the background of COVID-19**

| Indicators | Healthy children | Research groups | |
|---|---|---|---|
| | | 1- group | 2-group |
| Cytochrome C (er.), nmol/Hb | 6,30±0,28 | 4,28±0,08* | 5,43±0,16** |
| Cytochrome C (pl.), nmol/Hb | 0,18±0,001 | 0,26±0,01* | 0,19±0,02** |
| NADPH-cytochrome c-reductase, nmol/min/Hb | 48,68±1,72 | 64,25±1,02* | 56,4±1,3** |
| NADPH-cytochrome β5-reductase, nmol/min/Hb | 60,89±2,44 | 78,72±1,64* | 64,3±1,5** |
| Cytochrome β5, nmol/Hb | 0,27±0,018 | 0,34±0,02* | 0,28±0,024** |
| G-6-PDG (er.), nmol/min/Hb | 73,36±1,14 | 56,24±0,72* | 69,27±2,16** |

Note: * - significant difference compared to the indicators of the control group, r<0.05; ** The difference compared to the indicators of the 1st group is significant, r<0.05.

The difference in changes in the content of cytochrome S and cytochrome b5 in erythrocytes indicates the tension in the electron transport system in the respiratory chain, which is caused by the disruption of the pentose-phosphate cycle as a result of the decrease in the activity of G-6-FDG and the decrease in the formation of ATF.

At the same time, under conditions of glucose deficiency, the processes aimed at restoring the disturbed physiological balance in erythrocytes are activated, as evidenced by the increase in the activity of NADFN-cytochrome s-reductase and NADFN-cytochrome b5-reductase enzymes [19,28,46].

An increase in the activity of NADFN-cytochrome s-reductase is not enough to ensure the limit of cytochrome C output, because it is released from erythrocytes in large quantities, which is confirmed by an increase in the amount of cytochrome C in plasma. At the same time, the increase in the activity of NADFN-cytochrome b5-reductase provides a high pool of cytochrome b5, which exceeds the control values by 28.1% ($R<0.002$). It is known that NADFN-cytochrome b5-reductase is involved in the mechanism of converting methemoglobin into hemoglobin, which depends on the state of carbohydrate metabolism in erythrocytes. Methaemoglobinemia can be observed in patients with G-6-FDG deficiency, which is one of the important reasons for impaired blood oxygen transport function and the development of polyorgan oxygen deficiency [19,72,84].

At the same time, according to our data, the decrease in G-6-FDG activity leads to a decrease in the function of erythrocytes, the development of hemic hypoxia, and membranolytic changes in organs and tissues, including the kidneys.

Also, on the basis of the obtained data, it can be concluded that the high activity of NADFN-cytochrome b5-reductase is associated with the prevention mechanisms of severe pathological changes in erythrocytes and their respiratory function at a certain stage. At the same time, the release of cytochrome C from erythrocytes indicates the acceleration of apoptosis, which is associated with a decrease in glycolytic processes [12,59,82,102]. Against the background of COVID-19, disruption of glycolysis and respiratory function in erythrocytes aggravates the development of hypoxia in organs and tissues, including kidneys.

**Conclusions and recommendations:**

In order to early diagnose and prevent pyelonephritis, children with COVID-19 should be examined based on the following plan:

1. Taking into account the glomerular filtration rate, it is necessary to determine the concentration of creatinine in the blood serum, check the concentration of urea, uric acid, total protein, ALT, AST, GGT, IF and XE, the level of OMP, LPO (MDA and XL). Also, after recovery, it is necessary to check once a month for the first 3 months, then once a year for 3 years;

2. in case of pyelonephritis, attention should be paid to the levels of Cytochrome S, NADFN-cytochrome s-reductase, NADFN-cytochrome b5-reductase, Cytochrome b5, G-6-FDG in erythrocytes and plasma;

3. The general analysis of blood and urine should be monitored once a month for 3 months, then once a year for 3 years.

4. Daily albuminuria/proteinuria (or albumin/creatinine, protein/creatinine ratio per portion of urine) should be monitored once a month for 3 months, then once a year for 3 years.
4. Urine test according to Zimnitsky 1 time in 1 year.
5. ECG once a year.
6. Kidneys UTT 1 time in 1 year.
7. Scintigraphy according to the instructions.
8. Consultation of a nephrologist and other specialists according to the instructions.

Incomplete recovery of kidney function after COVID-19 infection is a risk factor for pyelonephritis to progress to the terminal stage. Children with COVID-19 infection should be prescribed any medication that takes into account the potential for nephrotoxicity.

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