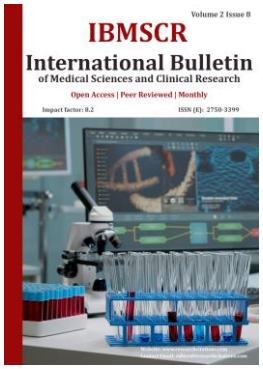

ANALYSIS OF THE KIDNEY CONDITION IN NEWBORNS FROM MOTHERS WITH CYTOMEGALOVIRUS INFECTION

Khazratkulova Mashkhura Ismatovna
Basic doctoral student in the course of neonatology, Faculty of Postgraduate Education , Samarkand State Medical University, Samarkand, Uzbekistan.
Email: mashhuraxazratkulova@gmail.com
Dilmuradova Clara Ravshanovna
- Doctor of Medical Sciences, Associate Professor, Head of the Neonatology Course at the Faculty of Postgraduate Education of Samarkand State Medical University, Samarkand, Uzbekistan.
Email: vmofneonatologiya.km@mail.ru
ORSID: https://orsid.org/0000-0002-8408-0233
Samarkand State Medical University, Samarkand, Uzbekistan
https://doi.org/10.5281/zenodo.10259327

ANNOTATION

One of the causes of kidney damage that occurs during pregnancy and childbirth is fetal infections, among which cytomegalovirus infection takes one of the leading places. 50 babies born in 2022-2023 were observed in the Samarkand Regional Perinatal Center and maternity complex No. 1, 30 of them were born to mothers with cytomegalovirus infection, and 20 were compared with healthy babies born to mothers with no MVI infection was studied. From the results of the examination, it was found that the increase of the NGAL biomarker in urine and blood serum can increase the risk of urinary tract inflammation in the later periods of the baby's life.

Key words : C MVI, NGAL, babies, infection, kidneys

Introduction: CMV has the highest proportion among congenital infections [7]. A significant factor in its spread is the asymptomatic course in most adults and low awareness of the dangers that infection of the fetus and newborn child entails. CMV infection is detected, according to various sources, in 0.18–2.5% of newborns [2].

Recently, great importance has been attached to the study of herpesvirus infections. One of the significant pathogens in the herpesvirus family is cytomegalovirus (CMV). According to the authors [13,15], in recent years, CMV infection in children has increased by 30.3%, and among newborns it has increased by 2.1 times. The number of cases of intrauterine infection has increased 5 times. They not only lead to a high mortality rate, especially in the perinatal period, but in some cases they also cause profound disability caused by congenital malformations and chronic diseases [13,15].

CMV infection is characterized by its widespread prevalence both among adults (40-95%) and children (20-60%). Congenital CMV is the most common intrauterine infection (IUI) and occupies one of the leading places in the structure of perinatal morbidity and mortality. Every year in the world, congenital CMV infection is detected in 0.5-6.1% of living newborns. The variety of clinical manifestations of the disease is determined by the ability of CMV to infect the fetus at any stage of pregnancy [2].

In terms of teratogenic ability, cytomegalovirus (CMV) ranks second after the causative agent of rubella. The ability of CMV to persist and multiply in different cells of the human body

suggests that it is pantropic, and the pronounced immunosuppressive effect of CMV is second only to HIV infection [9].

When studying kidney pathology in children with congenital CVMI, it was found that the formation of anomalies of the urinary system is possible. Anomalies of kidney development are represented by duplication, polycystic disease, hypoplasia, horseshoe kidney, and urinary tract obstruction. Congenital CVMI occurs, accompanied by clinical symptoms of interstitial nephritis, including the development of nephrotic syndrome, dysmetabolic nephropathy, and accompanying urinary tract infection [3,5].

Kidney damage during cytomegalovirus infection can manifest itself in the form of interstitial nephritis, malformations, often complicated by severe recurrent secondary pyelonephritis, and very rarely - in the form of nephrotic syndrome [3,14,16].

It can be assumed that newborn children with developmental anomalies of the pyelourethral segment should be examined for CMV infection, which, in the presence of an infectious process, will allow specific therapy to be carried out in a specialized department and to prevent the progression of congenital pyelectasia [4].

Previously, it was believed that the main etiological factors in the development of glomerulonephritis are bacteria, primarily nephritogenic strains of group A B-hemolytic streptococcus. However, in recent decades, with the development of new technologies in the study of viral infection, evidence has emerged of the role of viruses in the pathogenesis of glomerulonephritis. According to many authors, various viral infections play a great role in the development and progression of glomerulonephritis [6].

Kidney damage in CMV infection often causes acute glomerular damage with the development of glomerulopathy, membranoproliferative glomerulonephritis (GN), membranous nephropathy, mesangioproliferative GN, IgA nephropathy, TMA [10]. Acute kidney injury is a complex, rapidly progressive (less than 7 days) and potentially reversible condition, accompanied by a decrease in renal excretory function, changes in blood chemistry, as well as a decrease in urine output, or both. AKI is currently considered a clinical syndrome. Modern approaches to the diagnosis of acute kidney injury, regardless of the etiology and pathogenesis of AKI, determine the general links in the formation of damage to renal tissue, the leading of which is considered to be inflammation. An important sign of AKI is a decrease in glomerular filtration (GF). The content of serum creatinine (SC), eliminated from the blood mainly by GF, increases in AKI and still serves as the main diagnostic test for this clinical syndrome. However, in newborns, this indicator reflects the level of creatinine in the mother's blood. Steady-state creatinine concentrations depend on neonatal muscle mass and GFR, which are inversely related to gestational age. In newborns with low birth weight but normal renal function for their gestational age, GFR increases in the first 3 to 5 days of life and then decreases slowly over the next few weeks. These difficulties in interpreting the SC have led to the search for a rapid and sensitive indicator for detecting renal pathology in children, including newborns with low birth weight [11,12].

The most promising biomarkers for early diagnosis of AKI do not reflect HF, but acute damage to the renal parenchyma, cell proliferation, differentiation, apoptosis, disturbances in the immune response and the production of cytokines and chemokines [12.]

In recent years, a marker has been found whose concentration in acute kidney injury increases 1-2 days earlier than the level of creatinine and reflects the severity and severity of kidney damage, neutrophil gelatinase-associated lipocalin-2 (NGAL). NGAL protein with a

molecular weight of 25 kDa is synthesized by epithelial cells, including proximal tubules. Depending on the conditions, lipocalin-2 can be both a cell survival factor and a proapoptotic factor. Urinary and plasma levels correlate if lipocalin-2 synthesis is increased [11].

Purpose of the study : To investigate the characteristics of the kidney condition in newborns from mothers with cytomegalovirus infection

Materials and methods of research : The object of our study is 50 full-term children born in 2022-2023. in the regional perinatal center of Samarkand and in the maternity complex No. 1. The main group included 30 children born to mothers diagnosed with CMV infection. The group of healthy newborns included 20 children born to mothers in whom CMV infection was not detected. The body weight of babies is from 2560 grams to 4200 grams. Of these, 37 (74%) were boys and 13 (26%) girls.

Tests of the observed children were carried out at the SMART DOCTOR clinic: CMV was diagnosed using an enzyme-linked immunosorbent assay on the MindrayMR-96A device, a general blood test on the Mindray BS- 5000 device, and a general biochemical blood test on the Mindray BS-380 device. At the Research Center for Microbiology, Virology, Infectious and Parasitic Diseases named after. L.M. Isaev at Samarkand State Medical University studied the level of acute kidney damage by determining the biomarker INGAL in the urine and blood plasma of a child using the Rayto rt2100c device, CMVI was confirmed by PCR on the BIOER device by examining the blood plasma of the mother and child. Instrumental diagnostic studies were carried out in the radiology department of the multidisciplinary clinic of SamDTU using ultrasound, Doppler and neurosonographic studies of the brain, heart, and kidneys of newborns.

The studies carried out included a general blood test, urine test, biochemical blood test, and special methods (ELISA and PCR studies) were analyzed in umbilical cord blood during childbirth. After discharge, children were examined at the ages of 1 month, 3 months, 6 months and 1 year.

Results . In the main group of newborns, a lower Apgar score was revealed compared to a group of healthy children, slower sucking during the adaptation period, slower response to external influences, respiratory distress syndrome was observed to varying degrees in 9 patients (30%), prolonged jaundice was observed in -10(30%). These clinical indicators were not found in the healthy group. In the general blood test in the main group, leukocytosis averaged 13.02±1.12X10 ^{9} /l, hemoglobin 111.93±2.84 g/l (Table 1), no significant pathological changes were detected in other blood components.

Table 1

Indicators of general blood test (M±m) in children on the 1st day.

No.	Groups examined-nykh / Indicators	Main group (n=30)	Group healthy children (n=20)	P
1	Leukocytes, 10^9/l	13.02±1.12	8.12 ±1.1 2	< 0.001
2	Neutrophils %	5 3.83 ±3.19	5 0.36 ±2.46	>0.5

3	Lymphocytes %	37.33±3.7	34.1±3.23	>0.5
4	Monocytes%	10.28±1.02	9.23±0.72	>0.2
5	Eosinophils %	1.15±0.24	1.61±0.25	>0.1
6	Basophils %	0.18±0.03	0.11±0.03	>0.1
7	Hemoglobin g/l	111.93±2.84	122.55±2.74	<0.01
8	T platelets, 10^9/l	221.79±9.46	271.7±18.69	<0.05
9	ESR mm/h	4.2±0.61	3.08±0.42	>0.1

Note: p - reliability of differences in indicators between children of the main and healthy groups.

When analyzing the biochemical composition of blood, despite the compatibility of blood groups, it was found that urea averaged 7.17 ± 1.14 mm o l/l , creatinine 109.67 ± 24.82 mm o l/l , nitrogen balance in the main group is increased (Table 2).

table 2

Indicators of biochemical blood analysis of young children (M±m)

No.	**Groups examined-nykh Indicators**	**Main group (n=30)**	**Group healthy children (n=20)**	**P**
1	Residual nitrogen, mm o l/l	23.15±2.44	17.85±0.53	<0.05
2	Urea in the blood mm o l/l	7.17±1.14	4.14±0.2 0	<0.05
3	Blood creatinine, m km o l/l	109.67±24.8	46.23±1.83	<0.05
4	Blood uric acid mmol/l	271.8±79.02	3.82±0.15	<0.01
5	Alkaline phosphatase, ED	302.5±0.87	263.33±7.33	<0.001

Note: p - reliability of differences in indicators between children of the main and healthy groups.

General urinalysis - urine collected in the maternity hospital, in the main group leukocytes 14.71±3.93 in the field of view , proteins, epithelium, partially red blood cells are increased compared to the healthy group, which is a sign of damage and inflammation of the bladder and kidney nephrons child. Based on urine analysis, it was established that these indicators do not exceed the norms of the physiological state in children of group II (Table 3).

Table 3

Indicators of urine analysis of newborns collected in the maternity hospital (M±m).

No.	**Groups examined-nykh Indicators**	**Main group (n=30)**	**Group healthy children (n=20)**	**P**
1	Leukocytes, V p/zr.	14.71±3.93	2.9±0.56	<0.01

2	Protein, g/l	0.12±0.03	0.01±0.01	<0.001
3	Specific gravity	1.0 18 ±0	1.0 18 ±0	>0.5
4	Epithelium, in p/z.	5.38±1.32	0.7±0.25	<0.001
5	Erythrocytes, in p/z.	2.35±0.78	0.45±0.15	<0.05
6	Cylinders, in p/z.	0.21±0.1 0	0.47±0.22	>0.2

Note: p - reliability of differences in indicators between children of the main and healthy groups.

Thus, it was found that the biomarker NGAL 236.67±23.27 ng/ml , which is a sign of acute kidney damage, was increased compared to a group of healthy children in blood plasma and urine tests taken in the maternity hospital (Table 4).

Table 4

Biomarker NGAL in blood and urine (M±m).

No.	**Groups examined-nykh Indicators**	**Main group (n=30)**	**Group healthy children (n=20)**	**P**
1	NGAL , ng/ml	298.57±28.29	220.57±23.12	<0.05
2	NGAL , ng/ml	236.67±23.27	86.86±8.46	<0.001

Note: p - reliability of differences in indicators between children of the main and healthy groups.

The glomerular filtration rate, calculated using the Schwartz formula, in newborns with kidney damage from mothers with cytomegalovirus etiology was 9.78±1.88 ml/min (26.6%) on average, in the group of children without kidney damage, from mothers with CMV this indicator was 20.23±2.3 ml/min (73.33%). This indicator in the group of healthy newborns was 29.15±29 ml/min

An ultrasound examination of the kidneys in 40% of newborns revealed pronounced changes in the main group of children examined: 7 children with white kidney syndrome, 3 children with hydronephrosis and 2 with urolithiasis. In healthy children of group II, the period of adaptation in the maternity hospital was easy, and of the above problems, a white kidney was found in only 1 child during an ultrasound examination, which disappeared during the first month of observation (Table 5).

Table 5

Indicators of ultrasound examination of the kidneys of newborn children

N	**Groups examined-nykh Indicators**	**Main group (n=30)**	**Group healthy children (n=20)**
1	White kidney syndrome	**7**	**1**
2	Hydronephrosis	**3**	**0**
3	Urolithiasis	**2**	**0**

4	Without changes	**18**	**19 _**

Follow-up observations of newborns of the main group revealed that CMV manifests itself not only in the neonatal period, but also in early childhood in the form of an inflammatory process in the kidneys - pyelonephritis and urinary tract (Table 6).

Table 6

Frequency of pathology in the follow-up of examined children.

No	**Groups examined-nykh Pathology**	**Main group (n=30)**	**Group healthy children (n=20)**
1	Perinatal damage to the nervous system	13(43.3%)	1(5%)
2	Respiratory diseases	18(60%)	6(30%)
3	Diseases of the gastrointestinal tract	15(50%)	5(25%)
4	Urinary tract diseases	8(26.7%)	1(5)
5	Protracted jaundice	10(33.3%)	2(10%)
6	Death	1(3.3%)	0(0%)

Children born to mothers infected with CMV were twice as likely to have respiratory and digestive problems compared to the healthy group. Problems with the nervous system (restlessness, convulsions, delayed reaction to external influences, etc.) were much more common in sick newborns. Death occurred in only one child in the main group due to renal failure. **Conclusion.** CMV infection in pregnant women leads to damage to the fetus and all its organs and systems. An increase in the level of the NGAL biomarker in urine and blood tests of children from mothers with CMV infection is an early diagnostic marker of kidney damage in newborns. Children from mothers with CMV infection are at risk for the development of kidney pathology during follow-up and require clinical observation.

References:

1.Begaidarova R.Kh., Turlibekova S.S., Yukhnevich E.A., Beisenova G.R., Zolotareva O.A., Istleuova A.M. Congenital cytomegalovirus infection: variants of clinical course and immunological features. //Advances of modern natural science. – 2015. - No. 2. – P. 9-13.

2.Ivanova R.A., Skripchenko N.V., Grineva A.A., Rogozina N.V., Vasiliev V.V., Pochinyaeva L.M. Kaziakhmegov V.A., Zolotova M.A., Gorbunov E.F. Late manifestation of congenital cytomegalovirus infection in a child with primary immunodeficiency. Pediatrics 2019.98.No. 3 280-284 p.

3.Kirilochev O.K., Kibirova A.I., Kashirskaya E.I. Current state of the problem of cytomegalovirus infection in newborns // Astrakhan Medical Journal. - 2015. - No. 2. – P. 6-17.

4.Komarova A.A., Antonova I.V., Lyubavina A.E., Antonov O.V. To the question of the role of cytomegalovirus infection in the development of chronic secondary pyelonephritis in young children // Journal of Siberian Medical Sciences. - 2015. - No. 5. – 5 s.
5.Konkova N.E. Dlin V.V., Ignatova M.S., Turpitko O.Yu., Varshavsky V.A., Golitsina E.P., Congenital nephrotic syndrome in a child with cytomegalovirus infection. Russian Bulletin of Perinatology and Pediatrics. 3, 2010.
6.Lyndin A. A. Herpes virus infection and its role in kidney damage. Russian Bulletin of Perinatology, 6, 2010
7.Mardanly, S.G. Cytomegalovirus infection. Etiology, epidemiology, pathogenesis, clinic, laboratory diagnosis, treatment, prevention / S.G. Mardanly, G.I. Kirpichnikova, V.A. Neverov. – Elektrogorsk: JSC “Ekolab”, 2011. – 32 p.
8.Pavlov V.N., Pushkarev A.M., Rakipov I.G., Alekseev A.V., Nasibullin I.M. NGAL is an early biomarker of acute kidney injury after contact ureterolithotripsy. Medical Bulletin of Bashkortostan Vol. 8, No. 6, 2013.
9.Ryumin A.M., Sobolevskaya O.L., Sobchak D.M. Cytomegalovirus as a causative agent of intrauterine infection. Far Eastern Journal of Infectious Pathology . 2017;(33):89-94
10.Safina A. AND . Viral infections and kidney damage in children. Pediatrics 2019 volume 98 No. 2 14
11.Safina A. I, Daminova M.A. Diagnostic value of determining the level of lipocalin-2 associated with neutrophil gelatinase in the urine of newborns in critical conditions. Pediatrics/ 2011/Vol.91/No.6.
12.Smirnova N. N, Galkina O.V., Novikova V.P., Prokoyeva N.E. Modern biomarkers of kidney damage in pediatrics Nephrology 2019. Volume 23 No. 4.
13.Sotnikov I.A. Clinical and laboratory significance of the active form of cytomegalovirus infection in children with somatic pathology. Abstract 2017,
14.Kholodnova N.V., L.N. Mazankova, A.A Volter, I.E. Turin. Modern view on the problem of congenital cytomegalovirus infection. Children's infections. 2019 18 (3)
15.Tsinzerling V.A et al. 2014 Erling, V.A. Intrauterine infections: a modern view of the problem / V.A. Zinzerling // Journal of Infectology. – 2014. – T. 6. – P. 5–10.
16.Dilmuradova K.R. Pathogenetic mechanisms of development of nephropathies in children. Monograph. LAP LAMBERT Academic Publishing RU, 2022, 169 p