

Innovative Approach to the Diagnosis of Renal Circulation in Newborn

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ABSTRACT

In recent years, there has been an increase in the pathology of the fetus, leading to a violation or impossibility of adapting the child to extrauterine life. According to the WHO Expert Committee, the incidence of children in the first year of life increased by 39.8%, mainly due to conditions that occur in the perinatal period.

Along with malformations and microbial-inflammatory diseases of the urinary system, dysmetabolic nephropathy (DMN) is the main metabolic factor in the formation of urolithiasis. The urgency of the problem is due to the high incidence of urolithiasis: 1.8-2.2% in children, 8-8.5% in adolescents and 30-40% in the adult population.

According to modern concepts, DMN is a group of diseases of various etiologies and pathogenesis, which are characterized by an interstitial process with damage to the interstitium and renal tubules due to metabolic disorders.

Numerous studies reflect that in most cases the functional state of the kidneys in metabolic pathology is largely determined by tubulointerstitial disorders, while a change in the function of the nephron tubular apparatus responsible for maintaining homeostasis is manifested by a violation of the processes of concentration, reabsorption and secretion.

Currently, the world medical community has recognized that Cystatin C is the most accurate endogenous marker of glomerular filtration rate (GFR), significantly superior to creatinine in its diagnostic characteristics. With pathology, its level in the blood rises. The more severe the renal pathology, the worse cystatin C is filtered in the kidneys and the higher its level in the blood. A single measurement of the concentration of Cystatin C in the blood allows you to assess the state of GFR.

GFR is the best marker for diagnosing impaired renal function. It is generally accepted that the determination of GFR values is necessary for the diagnosis and monitoring of impaired renal

function, for the correct dosing of potentially nephrotoxic drugs, and for assessing potential nephrotoxicity . radiopaque preparations. The degree of decrease in GFR correlates with the degree of dysfunction and, therefore, with the severity of renal failure (Velkov V.V., 2018).

In modern nephrology, it is customary to evaluate the filtration function of the kidneys by the level of endogenous creatinine or by using calculation formulas based also on the concentration of creatinine (in pediatric practice, the Schwartz formula is the most widely used for calculating the glomerular filtration rate (GFR).

However, as is known, creatinine is not a specific marker for kidney damage; therefore, in recent years, pediatricians have become more interested in cystatin C as an alternative marker for assessing the state of renal functions [2].

Cystatin 3, more often called Cystatin C (eng. Cystatin 3, CST3, Cystatin C, Gamma-trace) is a protein belonging to the second group of the cystatin genetic family . Cystatin C is contained in the blood plasma, and the function of removing the protein from the body is carried out by the kidneys [3]. This protein has the following properties: firstly, it is synthesized at a constant rate by all cells of the body that contain nuclei; secondly, it is freely filtered through the glomerular membrane; thirdly, it is completely metabolized in the kidneys; fourthly, it is not secreted by the proximal renal tubules. All these properties suggested that cystatin C could be a marker of GFR.

Studies conducted in patients on hemodialysis showed that their cystatin C level was 13 times higher than in healthy ones [3]. Comparative experiments conducted to determine the dependence of serum cystatin C levels on GFR values made it possible to use the formula for calculating GFR by cystatin C in the practice of physicians [5].

It should be noted that the concentration of cystatin C in the blood, unlike creatinine, is the same for men, women and children and almost does not depend on muscle mass, age, gender, ethnicity, diet, physical activity. In addition, cystatin C does not cross the placenta and can be measured in utero and neonatally. And a single determination of the level of cystatin C in serum makes it possible to calculate the glomerular filtration rate [1].

It has been observed that the more severe the renal pathology, the worse cystatin C is filtered in the kidneys and the higher its level in the blood. Studies have suggested that the level of cystatin C increases significantly already in the early stages of renal dysfunction. Thus, kidney function may be reduced by more than 50% by the time the creatinine level just exceeds the upper limit of normal [4].

Thus, cystatin C is probably a reliable indicator of renal function. It is a more sensitive indicator of GFR decline than creatinine and serves as an effective marker for the early detection of renal failure, even in normal creatinine levels.

Purpose . Development of a new method for diagnosing impaired renal function in newborns .

Materials and methods. The object of the study was 2560 birth and newborn histories, as well as 424 patients: 212 of them were newborns and their mothers (212 women in labor) hospitalized in the neonatology department of the Bukhara Regional Children's Multidisciplinary Medical Center in the period 2018-2020.

analysis of 2560 neonatal histories was performed .

Research results. Analysis of children by gender, parity and place of residence showed the predominance of boys (n = 1351, $52.7 \pm 0.4\%$) than girls (n = 1209, $47.2 \pm 0.4\%$). Analysis by place of residence showed the predominance of children living in rural areas 1345 ($52.5 \pm 0.2\%$) (Fig. 1).

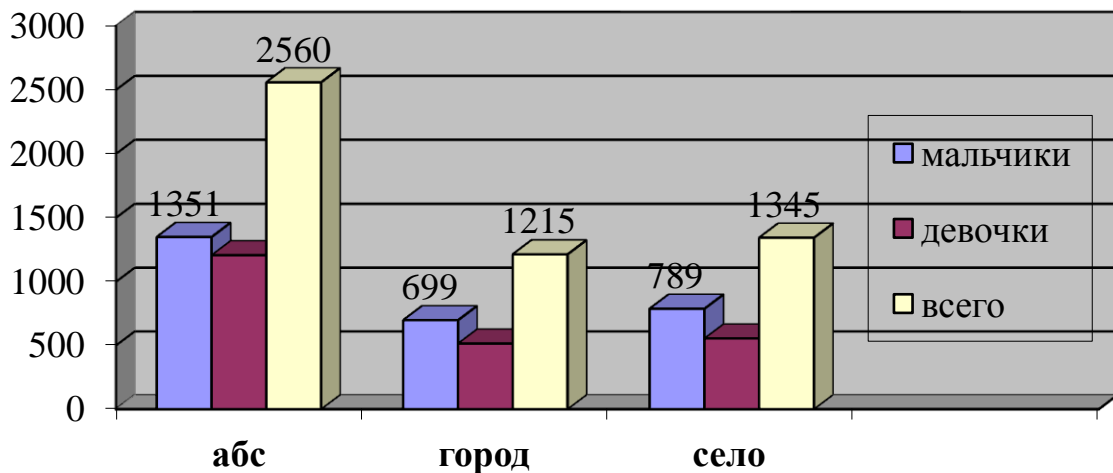


Figure 1. Distribution by place of residence and sex of newborns

By parity, it turned out that there were slightly more children with DMN ($n = 1428$) from the first pregnancy ($55.8 \pm 0.6\%$) than newborns born from the 2nd and 768 pregnancies ($30.0 \pm 1.1\%$) and from the 3rd and more pregnancies - 364 ($14.2 \pm 1.0\%$).

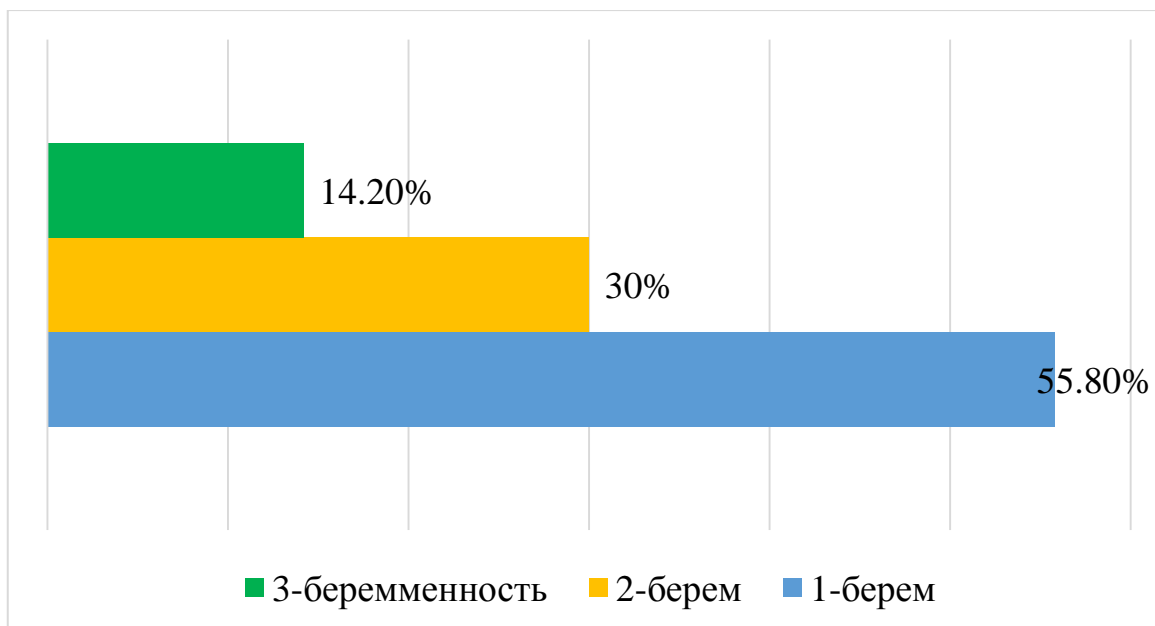


Figure 2. Distribution of patients by parity

The postnatal age of children ranged from 2 days to 28 days of life. All newborns were full-term, with a gestational age at birth of 38 to 42 weeks. Cases of consanguineous marriage were found in 120 newborns, which is $4.68 \pm 1.1\%$.

When studying the health status of mothers of newborns (parturient mothers), a high incidence of anemia I - II degree ($n = 1114$, 43.5%), gestational hypertension ($n = 439$, 17.2%), preeclampsia ($n = 347$, 13.5%), diffuse goiter ($n = 361$, 14.1%), pyelonephritis ($n = 75$, 2.9%) (Figure 3, Table 1).

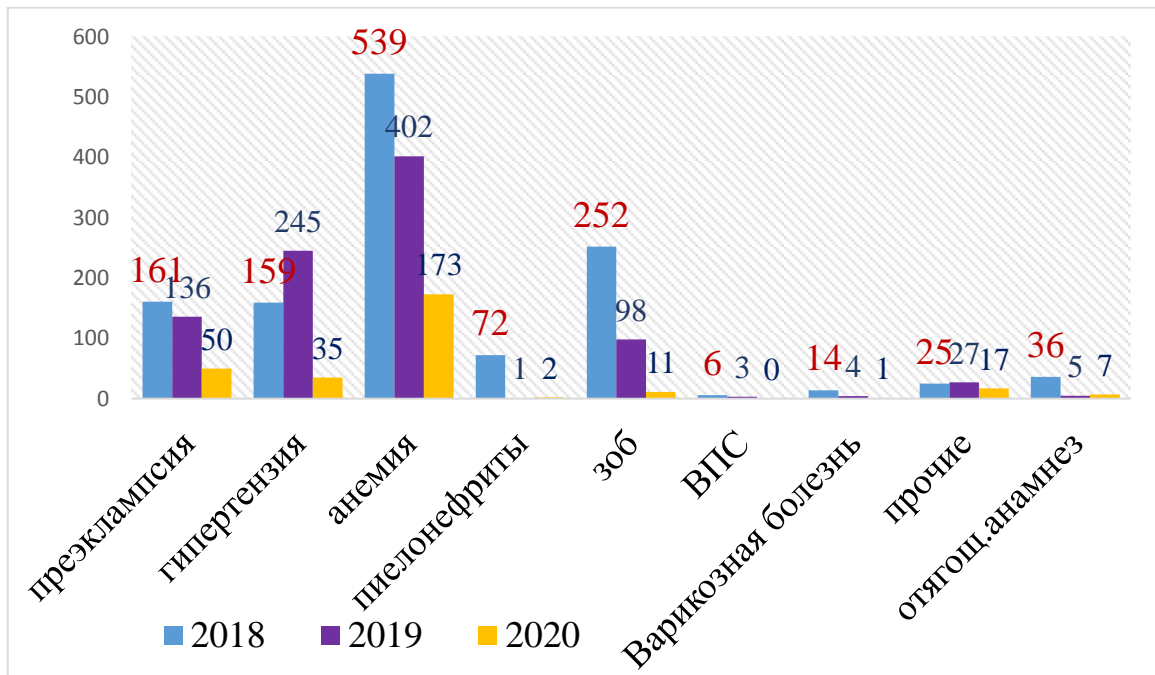


Figure 3. Structure of morbidity in pregnant women

Table 1. Maternal illnesses during pregnancy

nosology	2018	2019	2020	Total
	abs	abs	abs	Abs(%)
Preeclampsia	161	136	50	347 (29.3)
hypertension	159	245	35	439 (37.2)
Anemia	539	402	173	1114 (43.5)
Pyelonephritis	72	1	2	75 (2.9)
Goiter	252	98	eleven	361 (30.6)
UPU	6	3	-	9 (0.76)
Varicose disease	14	4	1	19 (1.61)
Other diseases	25	27	17	69 (5.85)
Burdened obstetric history	36	5	7	48 (4.1)

All established conditions and comorbidities occur against the background of a burdened obstetric anamnesis-48 (1.87%).

We compiled a structure of diseases and conditions of the mother for a detailed study and identification of the leading causal factors in the development of hypoxia and hypoxemia in newborns. As a result, risk factors for the development of perinatal hypoxia in newborns were identified (Table 2).

Table 2. Risk factors for the development of perinatal hypoxia in newborns

Risk factors	Quantity	%
Moderate and/or severe anemia	298	82.8
Cardiovascular pathology of pregnant women (gestational hypertension)	106	29.4
Toxicosis of pregnant women	308	85.5
Multiple pregnancy	12	3.3
Chorioamnionitis / STI	98	27.2
Polyhydramnios	38	10.6

Anomaly in the location of the fetus (pelvic / transverse)	24	6.7
Overbearing of the fetus	16	4.4
Umbilical cord pathology / fetoplacental insufficiency	14	3.9
Anomalies of labor activity	14	3.9

Of the risk factors, toxicosis of pregnancy predominates - 308 (85.50%), moderate and / or severe anemia - 298 (82.8%) and cardiovascular pathology (gestational hypertension) of pregnant women 106 (29.4%) . And also chorionamnionitis/ STI was established in 98 (27.2%) women, polyhydramnios 38 (10.6%) and anomaly in the location of the fetus (pelvic / transverse) in 47 (3.9%) women.

For a prospective study, 212 newborns were selected. Among them, the main group consisted of 182 newborns with dysmetabolic nephropathies (DMN), of which 60 had oxaluria, 62 had uraturia, and 60 had a mixed form of DMN. The control group consisted of 30 healthy newborns with a favorable course of the neonatal period.

Each group of newborns were distributed depending on the type of DMN:

group 1 - control - 30 healthy newborns;

group 2 - 60 newborns with oxaluria;

group 3 - 62 newborns with uraturia;

group 4 - 60 newborns with a mixed form of DMN.

Predisposing risk factors for the birth of a child with renal pathologies, indicators of calcium metabolism (parathyroid hormone, serum calcium, vitamin D 3 (25OH)), cystatin C, urea and creatinine in the blood were studied.

Taking into account the risk factors and comorbid condition in the mother, as well as their impact on the health status of the newborn, a comparative analysis of the biochemical parameters of the mother's blood during pregnancy, 7 days after birth was performed (Table 3)

As a result, a tendency to a decrease in the level of calcium in the mother's blood was established, as well as a significant decrease in parathyroid hormone after childbirth by 2.5 times - up to 24.2 ± 1.5 pg/ml ($P < 0.05$). At the same time, the level of vitamin D increases 1.6 times - up to 60.7 ± 4.7 ng / ml , urea - 1.5 times - up to 4.045 ± 0.11 μ mol / l against the indicators of pregnant women ($P < 0.05$).

Table 3. Comparative analysis of biochemical parameters of blood

indicators	mothers	
	1-gr (pregnant)	2-gr (parturient women)
Calcium (mmol/l)	3.13 ± 0.8	1.8 ± 0.1
Parathormone (pg/ml)	61.29 ± 8.5	24.2 ± 1.5 *
Vitamin D 3 (25 OH) (ng/ml)	36.5 ± 3.1	60.7 ± 4.7 *
With cystatin	1.64 ± 0.07	1.78 ± 0.06
Urea (μ mol/L)	2.64 ± 0.12	4.045 ± 0.11 *
Creatinine (μ mol/l)	54.1 ± 1.97	55.1 ± 2.17

Note: * - differences in relative data of the 1-group

(* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$)

The C values of cystatin and creatinine were at the level of the 1st group, within 1.78 ± 0.06 and 55.1 ± 2.17 $\mu\text{mol/l}$, respectively, in relation to the data of the 1st group: 1.64 ± 0.07 and 54.1 ± 1.97 $\mu\text{mol/l}$, respectively.

Therefore, the results of the analyzes show a clear shift in the studied biochemical parameters of the blood of pregnant women after childbirth, which is manifested by calcium deficiency, a decrease in the level of parathyroid hormone against the background of hypervitaminosis D, and a violation of protein metabolism with a shift towards acidosis.

In newborns examined, a biochemical blood test was also performed on days 3-7 of life. As a result, a statistically significant decrease in parathyroid hormone in the blood of patients of the 3rd group was found - up to 45.42 ± 3.86 pg/ml versus control - 57.0 ± 2.45 pg/ml ($P < 0.05$), (Table 4).

Table 4. Indicators of calcium metabolism in the blood of newborns depending on the type of dysmetabolic nephropathies

Indicators/ groups _	Calcium (mmol/l)	Parathormone (pg/ml)	Vitamin D3 (25OH) (ng/ml)
1-gr control	2.7 ± 0.45	57.0 ± 2.45	58.8 ± 3.67
2-group	1.9 ± 0.04	53.9 ± 6.84	33.3 ± 2.10 *
3-group	1.92 ± 0.04	45.42 ± 3.86 *	33.07 ± 2.03 *
4-group	2.0 ± 0.02	54.0 ± 6.84	$6, 5 \pm 0.07$ ***

Note: * - differences in relative data of the 1-group

(* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$)

Parathyroid hormone (PTH) is known to be a peptide hormone produced in the parathyroid glands. It regulates the exchange of calcium and phosphorus, while providing the optimal amount of calcium ions in the blood.

PTH also regulates the processes of calcium release from bones, absorption of calcium from the intestines and removal of calcium from the body with urine. If the amount of calcium in the blood decreases, then parathyroid hormone is additionally produced, which restores balance. PTH induces the synthesis of vitamin D.

The study of the concentration of vitamin 25 (OH) D showed a significant decrease to 33.3 ± 2.10 ng/ml and 33.3 ± 2.03 ng/ml in newborns of the 2nd and 3rd examination groups, respectively, against the control 58.8 ± 3.67 ng/ml . The result obtained indicates an adequate level of vitamin 25 (OH) D both in newborns of the control group and in newborns with oxaluria and uremia. But at the same time, a sharp decrease in the concentration of vitamin 25 (OH) D by 9.1 times was also revealed in newborns with a mixed form of nephropathy ($p < 0.001$).

Thus, a biochemical analysis of the blood of the mother and child shows the importance of taking into account the state of calcium and uric acid metabolism in the management of pregnant women in the period before and after childbirth. And also, in the period after childbirth, women have a calcium deficiency, a decrease in the level of parathyroid hormone against the background of hypervitaminosis D, and a violation of protein metabolism with a shift towards acidosis. With a mixed form of DMN in newborns, a decrease in the concentration of vitamin 25 (OH) D by 9.1 times is observed.

of cystatin in the blood of newborns, established by us, is independent of the type of metabolic disorders of calcium and uric acid salts.

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