

### Modern Aspects of Dysmetabolic Nephropathies in Children

Mukhamedova Shakhnoza Tolibovna, Ergasheva Mukharram Uktamovna

Bukhara State Medical Institute

#### Article Information

**Received:** April 10, 2023

**Accepted:** May 11, 2023

**Published:** June 14, 2023

**Keywords:** *children, dysmetabolic nephropathy, etiology, pathogenesis.*

#### RESUME

The review article is devoted to the study of etiological factors and pathogenetic mechanisms in dysmetabolic nephropathies in children. New studies on the informative value of cystatin C and metabolic aspects of the formation of renal pathology in children are presented. The authors have generalized and systematized modern domestic and foreign data.

In pediatrics, it is practically important to identify a risk group for the formation of obesity nephropathy, metabolic syndrome and cardiorenal syndrome. The risk group should include children born with low body weight by the time of gestation, children with signs of early obesity, children from families with obesity, impaired carbohydrate metabolism and hypertension. Further research will make it possible to individualize the approach to each overweight child, diagnose and correct the leading link of impaired metabolism [4].

Dysmetabolic nephropathy (DMN) is a large group of pathologies with different etiologies and pathogenesis, developing as a result of metabolic disorders. Metabolic disorders lead to changes in the functional state of the kidneys or to structural shifts at the level of various elements of the nephron. DMN in the broad sense of the word combines pathologies associated with severe disorders of water-salt metabolism, which are the result of gastrointestinal diseases with toxic syndrome and hemodynamic disorders. These may include kidney lesions occurring against the background of defects in phosphorus-calcium metabolism in hyperparathyroidism, hypervitaminosis D and other diseases [2,6].

DMN account for about 27-64% of all diseases of the urinary system in children; every third child has signs of metabolic disorders in urine. Children with DMN are at high risk for the development of interstitial nephritis, pyelonephritis, urolithiasis [3,5].

Frequent development of DMN was noted in children born from pregnancy with late toxicosis and fetal hypoxia, as well as children with neuropathic diathesis. Primary nephropathies may be caused by metabolic disorders in the child's relatives or accumulated mutations that cause an imbalance of regulatory cellular mechanisms in the child himself [1,8].

In children with chronic dysmetabolic pyelonephritis, violations of the functioning of the

proximal nephron were mainly revealed in the form of a decrease in the reabsorption of trace elements such as zinc, calcium, sodium, and potassium. In the group of children with obstructive type of chronic pyelonephritis, more pronounced violations of the functioning of all departments of the tubular part of the nephron were found. In the proximal tubules, a decrease in the reabsorption of phosphates, amino acids, sodium, and potassium was observed. In patients with chronic secondary pyelonephritis of the obstructive type, compared with chronic secondary pyelonephritis of the dysmetabolic type, a violation of acido- and ammoniogenesis (40.7 and 17.4%) and a decrease in the concentration capacity of the kidneys (33.3 and 17.4%) were 2 times more frequent. For children with chronic secondary pyelonephritis of the obstructive-dysmetabolic type, renal dysfunction characteristic of this disease was revealed [12].

One of the urgent problems of modern pediatrics is DMN. According to statistics, to date, there is a widespread increase in metabolic disorders in the kidneys. Metabolic nephropathy ranges from 27% to 64% in the structure of urinary system morbidity in children. Every day in the practice of a general practitioner, the syndrome of metabolic disorders in urine is noted in almost every third patient. DMN is not a separate nosological unit, but is essentially a syndromic condition [7,9].

The causes of some kidney diseases that occur in childhood are the result of either congenital malformations or hereditary diseases. Most congenital diseases occur sporadically, and the pathogenesis of many of them is not clearly defined. But sometimes, some patients may have clinical signs corresponding to well-defined genetic diseases [11].

One of the etiological factors of renal abnormalities may be present during the antenatal period. At the same time, restriction of intrauterine growth develops. This is considered one of the non-immune causes of renal dysfunction [10].

In children with hypercalciuria, nephrolithiasis and nephrocalcinosis, a decrease in bone mineral density was observed in 45% of cases, with chronic obstructive dysmetabolic pyelonephritis, osteopenia was detected in half of the patients. The duration of the disease, the frequency of relapses in children with chronic pyelonephritis influenced the development of the osteopenic condition [15]

The accuracy of the determination of GFR by cystatin C was higher than that determined by creatinine. As a result, two formulas were proposed for the most accurate calculation of pediatric GFR, one of which takes into account the levels of cystatin C, the other - the levels of cystatin C and creatinine simultaneously [13].

The Schwartz formula, proposed for the determination of GFR in children back in the 70s of the last century, in fact overestimates the values of GFR (when compared with the measurement of GFR using iohexol). In the study of 349 patients aged 1 to 16 years and having GFR (iohexol) values of 41.3 ml/min/1.73 m<sup>2</sup> (median value), a more accurate (according to the authors) formula was proposed, taking into account gender, height, weight, serum creatinine levels and urea concentration in the blood [2, 14].

Cystatin C is a marker of the preclinical phase of renal pathology. As many leading scientists believe, the main contribution that the study of cystatin C has made to medical science is a new understanding of what is "normal kidney function". So, "if we assume that over the entire range of GFR, there is a continuous linear relationship between specific values of GFR and the risk of mortality in newborns (without sharp thresholds), this will lead to a new paradigm of what is meant by normal kidney function. One of the most important diagnostic values of cystatin C is that it allows quantifying the gradient of renal function in individuals who do not fall within the framework of generally accepted criteria for clinical renal pathologies" [151]. That is why the term preclinical kidney disease was proposed, characterizing individuals: a) without clinical

kidney disease, b) with creatinine GFR ( $> 60$  ml/min /1.73 m<sup>2</sup>, c) with elevated serum cystatin C ( $\geq 1.0$  mg/ml). It is believed that preclinical kidney disease – independently of other factors – predicts the development of clinical kidney diseases and the risk of CVD. Thus, cystatin C levels can predict the risk of developing CKD and signal the "preclinical" phase of renal dysfunction and the risk of CVD [3, 16].

According to various studies, modern children spend little time outdoors (up to 1 hour), move little, and spend a lot of time in front of the computer and TV (from 3 to 6 hours). Low physical activity in children is usually associated with an irrational daily routine of the child, overload with educational activities [5, 18].

With a decrease in physical activity, all organs and systems of the growing organism suffer: immunity decreases, intestinal motility slows down, causes changes in bone metabolism, posture disorders. These processes have a pathogenetic connection with metabolic processes in the kidneys and also have a negative effect in dysmetabolic nephropathies; an equally important feature of the life of a modern child is the presence of psychoemotional overstrain. Stressful situations are associated with the beginning of early learning and its intensification, the need to adapt to a new situation when entering a preschool educational institution or school, a constant increase in the flow of information, a high academic load. A priority role in the occurrence of metabolic disorders is played by irrational nutrition; a significant role in the development of dysmetabolic nephropathy, as well as its further transformation into urolithiasis is played by a violation of urodynamics [17].

### **Conclusion.**

One of the factors influencing the occurrence and progression of dysmetabolic nephropathies in children is hypokinesia (motor deficiency). The main pathogenetic moment in hypodynamia can be noted as a violation of metabolic processes in the body, which is accompanied by the formation and accumulation of lithogenic substances. 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 tubular apparatus of the nephron responsible for maintaining homeostasis is manifested by a violation of the processes of concentration, reabsorption and secretion.

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