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Original Research

Frequency and Risk Factors of Stone Formation in Kidneys of Children Experience of the Urology Department of Clinic of Tashpmi 1995-2019

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ABSTRACT:

From 1995 to 2019, 2,100 children with urolithiasis were admitted to the surgical department of the clinic of the Tashkent Pediatric Medical Institute, among them 305 children had early, bilateral, multiple, coral, nephrolithiasis with stone discharge and symptoms of polydipsia and polyuria (14.5%) who were tested for primary hyperparathyroidism. As a result of the study, primary hyperparathyroidism was diagnosed in 52 children (2.47%) (main group). For the comparison group, 54 children with urolithiasis without primary hyperparathyroidism were selected. The study was conducted at the Republican Specialized Scientific and Practical Medical Center for Endocrinology and the TashPMI clinic, in the period from 1995 to 2019. A specific norm for each of the studied indicators was established by examining 44 practically healthy peers (children who do not suffer from kidney and endocrine system diseases).

Keywords: urolithiasis, parathyroid hormone, parathyroid gland, primary hypothyroidism, urology, endocrinology

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INTRODUCTION

Urolithiasis, nephrolithiasis are synonyms that define the clinical syndrome of the formation and movement of stones in the kidneys and urinary tract. Urolithiasis is one of the most common urological diseases, the frequency of which is steadily increasing [1, 2]

Among urological diseases, urolithiasis takes one of the first places, accounting for 10-45% [3, 4, 5]. Among children, the incidence of this disease is observed as often as in adults [6]. The first place in terms of prevalence is occupied by kidney stones and their various variations (pelvic stones, calyx stones, multiple stones), the second - ureteral stones due to the discharge of a kidney stone [7, 8].

Kidney stones are unusually hard, insoluble substances that form in the rectal urinary tubules of the kidneys. Stone formation is not a simple or unambiguous mechanism, it is the result of multiple, complex and interrelated processes occurring in the kidneys [9].

The stones are more often localized in the right kidney. Bilateral stones are observed in adults in 15-30% of cases, and in children in 2.2-20.2%. Despite the change in social and demographic living conditions of the population, the persisting endemic foci of morbidity (Central Asia, the Caucasus, the Volga region, the Far North, Australia, the states of the Balkan Peninsula, Brazil, Turkey, India, the eastern regions of the United States, etc.) indicate a significant influence environmental factors and geographical conditions for the onset and development of urolithiasis [10, 11].

According to modern concepts, in a colloidal solution, which is urine, during movement along the renal tubules, there are two processes that determine the intensity of biomineralization: stimulation and

inhibition of crystallization. As a rule, these processes are in dynamic equilibrium. A shift of this equilibrium towards activation of the formation of crystals, along with other factors, ultimately leads to the occurrence of urolithiasis [12, 13].

The etiological factor of urolithiasis is primary hyperparathyroidism, hyperoxaluria, hyperuricosuria, hypocitraturia, hypomagniuria, infectious nephrolithiasis, gout and cystinuria [14].

Among the factors of stone formation, the leading place is occupied by congenital enzymopathies (tubulopathies), anatomical malformations of the urinary tract, hereditary nephroso- and nephrite-like syndromes [15, 16].

Enzymopathies (tubulopathies) are disorders of metabolic processes in the body or the functions of the renal tubules as a result of various enzymatic disorders, which can be either congenital or acquired. The most common are the following enzymopathies: oxaluria, uraturia, generalized aminoaciduria, cystinuria, galactosemia, fructosemia, de Toni-Debre-Fanconi syndrome.

Etiological factors in the development of stone formation against the background of congenital tubulopathies can be divided into exogenous and endogenous.

Exogenous factors:

Geographic, socio-economic, nutritional, gender, age, chemical composition of water, etc. Taking into account exogenous factors, increased stone formation in the warm season, especially in countries with hot climates, is explained by the theory of dehydration (in combination with high mineralization of water and an increase in urine concentration) and loss of sodium in the urine. With an increase in the hardness of drinking water and the content of calcium and magnesium in it, the frequency of stone formation increases.

Endogenous factors:

General - hypercalciuria, A-avitaminosis, D-avitaminosis or vitamin D overdose, hyperparathyroidism, bacterial intoxication with general infections and pyelonephritis, the use of a large number of certain chemicals (sulfonamides, tetracyclines, antacids, acetylsalicylic acid, glucocorticoids), etc., long-term or complete immobilization, etc.

Local - leading to impaired urodynamics and strictures of the urethra and ureter, primary and secondary stenosis of the pelvic-ureteric segment, urinary tract anomalies, nephroptosis, vesicoureteral reflux, urinary tract infection, etc. Difficult outflow of urine from the kidneys and impaired excretion resorption of the constituent elements of urine, precipitation (crystallization) of salt sediment, and also creates conditions for the development of the inflammatory process [17, 18, 19].

The etiological factors of stone formation in children differ from those in adults. In children, the etiological factors of stone formation are infectious diseases, diarrheal syndrome, ulcerative colitis, resection of the small intestine, Crohn's disease. The characteristics of the factors affecting kidney stone formation in children are not well covered. The main stone-forming factors for children are urinary mucoproteins and glucosaminoglycans.

The risk of stone formation is significantly increased in the presence of several factors predisposing to the disease in the body at the same time.

Under experimental conditions, the genetic aspects of the formation of kidney stones from calcium oxalate salts have been developed and analyzed. According to the research among 36.1% of children with urolithiasis, parents suffered from this disease (probands were 15.7% fathers and 20.4% mothers).

A number of authors noted that in 5% of children renal stones formed as a result of hypercalciuria are due to primary hyperparathyroidism and in 3% of cases with renal tubular acidosis. In renal tubular acidosis, stone formation is promoted by hypercalciuria, hypocitraturia, urine alkalization, urine stasis, an increase in the ammonium content in the urine (infection), dehydration and increased acidity of urine (tubular acidosis) [20].

When analyzing the case histories of 152 children of patients (from 0.1 to 15 years of age) with nephrocalcinosis, it was found that in 34% of cases idiopathic hypercalciuria was found, in 32% of cases hereditary kidney diseases, in 9% of cases, taking large doses of vitamin D, in the rest In cases, the cause of nephrocalcinosis was a negative family environment.

Idiopathic hypercalciuria is the main causative factor in stone formation, which remains the least understood mechanism. There are reports of familial renal stones resulting from idiopathic hypercalciuria and hyperuricosuria in children. Idiopathic nephrolithiasis is observed in 10-20% of cases.

Young children, especially boys, are prone to infection stones. Cystinuria and hyperoxaluria in 5-15% of cases are causative factors of stone formation in children.

According to some authors, stone-forming factors in children are neurological problems, uniform nutrition, neurogenic dysfunctions of the lower urinary tract urodynamics, urinary tract abnormalities, etc.

Urolithiasis in newborns develops as a result of hypercalciuria, hypermagniuria, hypocalcemia, the reason for this is a violation of the intrauterine development of the Henley loop.

Recently, much attention has been paid to primary hyperparathyroidism as the cause of urolithiasis.

MATERIALS AND METHODS

From 1995 to 2019, 2,100 children with urolithiasis were admitted to the surgical department of the clinic of the Tashkent Pediatric Medical Institute, among them 305 children had early, bilateral, multiple, coral, nephrolithiasis with stone discharge and symptoms of polydipsia and polyuria (14.5%) (risk group) who were tested for primary hyperparathyroidism. As a result of the study, primary hyperparathyroidism was diagnosed in 52 children (2.47%) (main group). For the comparison group, 54 children with urolithiasis without primary hyperparathyroidism were selected. The study was conducted at the Republican Specialized Scientific and Practical Medical Center for Endocrinology and the TashPMI clinic, in the period from 1995 to 2019. A specific norm for each of the studied indicators was established by examining 44 practically healthy peers (children who do not suffer from kidney and endocrine system diseases).

The children were between 3 and 15 years old. They were monitored for 2-5 years. The surveyed children were divided into 3 age groups (Table 1).

RESULTS AND DISCUSSION

As can be seen from the table, there is a tendency for the prevalence of the male over the female sex, boys (61.3%) get sick more than girls (38.9%).

The kidneys are one of the main targets in primary hyperparathyroidism. The frequency of their lesions ranges from 60 to 80%. Often, symptoms of kidney damage may be the only manifestation of primary hyperparathyroidism.

Data on the frequency of detection of primary hyperparathyroidism among patients with urolithiasis are very contradictory: from 1.2 - 1.8% to 5 - 15%.

According to Bilezikan J. P., among patients with urolithiasis, primary hyperparathyroidism is determined in 5-15% of cases, while according to the results of the study by Soreide J. A. and a group of authors among patients with primary hyperparathyroidism, urolithiasis is observed in 30% of cases.

Currently, the causes of kidney stone formation in primary hyperparathyroidism have not been fully elucidated. Of these, 3 factors are known; hypercalciuria, hyperphosphaturia, and an increase in urine pH. The main cause of stone formation in primary hyperparathyroidism is considered to be hypercalciuria.

Hypercalciuria in primary hyperparathyroidism is due to the following: parathyroid hormone, which enters the blood in excess, has a toxic effect on the epithelium of the convoluted renal tubules, reducing the reabsorption of inorganic phosphorus in them. Thus, hyperphosphaturia occurs. Inorganic phosphorus is replenished from the bones, its main depot. Together with phosphorus, calcium enters the bloodstream and is then excreted by the kidneys. In addition, parathyroid hormone stimulates the absorption of calcium into the blood from the intestines. This is how hypercalcemia and hypercalciuria occur.

Table 1. Distribution of children by sex, age and nosology

Examined children	Age and gender of the examined patients						Total
	3-7		8-11		12-15		
	Boys	Girls	Boys	Girls	Boys	Girls	
Urolithiasis (comparison group)	10 (18,5%)	7 (12,9%)	13 (24%)	6 (11,1%)	11 (20,3%)	7 (12,9%)	54 (50,9%)
Renal form of primary hyperparathyroidism (main group)	10 (19,2%)	7 (13,5%)	10 (19,2%)	7 (13,5%)	11 (21,2%)	7 (13,5%)	52 (49,1%)
Total	20 (18,8%)	14 (13,2%)	23 (21,6%)	13 (12,2%)	22 (20,7%)	14 (13,2%)	106

The pathogenesis of stone formation in primary hyperparathyroidism is explained by the toxic effect of parathyroid hormone on the epithelium of the proximal convoluted renal tubules, which leads to pronounced dystrophic changes. Experiments have shown that dystrophy of the renal tubular epithelium is accompanied by an increase in the level of neutral mucopolysaccharides in the blood and urine, which can form into polysaccharide cylinders, some of which absorb calcium salts.

The toxic effect of parathyroid hormone on the epithelium of the renal tubules leads to a decrease in the reabsorption of inorganic phosphorus. Normally, phosphorus reabsorption is 90-92%, if this figure is lower, then this indicates a possible primary hyperparathyroidism.

According to some authors, in primary hyperparathyroidism, changes occur mainly in the cortical layer of the kidneys. Electron microscopic examination of biopsy material taken from the kidneys of patients with primary hyperparathyroidism revealed morphological changes occurring both in the cortex and in the medulla of the kidneys.

Excessive parathyroid hormone affects the proximal and distal renal tubules, disrupts redox processes, reduces the excretion of H + ions, and urine becomes alkaline. It affects the epithelial cells of the proximal nephrons, in some nephrons these changes are necrobiotic in nature, which leads to edema of the interstitial tissue and lymphocytic infiltration of the renal tissue. In primary hyperparathyroidism, the tubular apparatus of the kidneys is affected by forming stones, which is a consequence of the negative effect of hypercalcemia and parathyroid hormone on the tubular apparatus of the kidneys.

Transplantation of the parathyroid gland to animals in a state of hypocalcemia, influenced as an immunosuppressant, the excess parathyroid hormone produced by the transplanted gland, in the tubular apparatus of the corticomedullary zone of the kidneys, it formed calculus plates, consisting of calcium oxalate and calcium phosphate. The number of plates, the size and rate of increase in the calculus volume were directly proportional to the size of the transplanted gland. These changes in primary hyperparathyroidism can be called one of the pathogenetic mechanisms of kidney stone formation.

The data available in the literature indicate a possible role of parathyroid hormone in the development of sclerotic changes in renal tissue. It causes a specific disorganization of the plasma membranes of cells, plays a leading role in the genesis of the inflammatory process, stimulates the synthesis of collagen, and the active metabolite of vitamin D3 - (1.25 (OH) 2D3) in the renal tubules, which in turn activates collagenogenesis.

The distribution of children in groups is practically the same, and amounts to 33.9% in the third age group, in the second - 33.8% and in the first age group - 32%. Renal failure (RI) was recorded in 45 (42.4%) children out of 106 children with urolithiasis (Table 2).

Table 2. Distribution of children according to the functional state of the kidneys

Examined children	Age and functional state of the kidneys						Total
	3-7		8-11		12-15		
	with renal failure	without renal failure	with renal failure	without renal failure	with renal failure	without renal failure	
Urolithiasis (comparison group)	6 (11,1%)	11 (20,2%)	9 (16,6%)	8 14,8%)	6 (11,1%)	14 (25,9%)	54 (50,9%)
Renal form of primary hyperparathyroidism (main group)	10 (19,2%)	12 (23,1%)	7 (13,5%)	9 (17,3%)	7 (13,5%)	7 (13,5%)	52 (49,1%)
Total	16 (14,4%)	23 (21,3%)	16 (15,1%)	17 (16,5%)	13 (13,1%)	21 (19,3%)	106 (100%)

The incidence of children with renal failure by age did not differ significantly.

With the help of instrumental examination methods (overview and excretory urogram, ultrasound of the kidneys and urinary tract), the characteristics and location of calculi in the kidneys were revealed in the examined children (Table 3).

Table 3. The nature of kidney damage by calculus in the analyzed groups

Type of urolithiasis	Analyzed groups				Total	
	Urolithiasis (n = 54)		Renal form of primary hyperparathyroidism (n = 52)			
	Abs	%	Abs	%	Abs	%
one sided single stone	23	42,5	12	23,0	27	25,4
one sided multiple stone	12	22,2	4	7,6	24	22,6
double sided single stone	10	18,5	17	32,6	25	23,5
double sided multiple stone	9	16,6	19	36,5	30	28,3
Total	54	50,9	52	49,1	106	100

Unilateral kidney damage by calculus was observed in 48.1% (51) children, bilateral in 51.8% (55) cases. Among unilateral renal lesions by calculus, the proportion of patients with renal form of primary hyperparathyroidism accounted for 30.7% (16) children, of which 11 (68.7%) children had multiple unilateral stones.

CONCLUSION

Damage to both kidneys with calculus was observed in 55 (51.8%) children, of which 25 (45.4%) children had single kidney stones, and 30 (54.5%) children had bilateral multiple stones.

In children of patients, the renal form of primary hyperparathyroidism, bilateral kidney damage by calculus was observed in 36 (69.2%) children, of whom bilateral single stones in 14 (38.8%), multiple bilateral - in 22 (61.1%).

Recurrence of stones was observed in 36 children (33.9%) of them in the comparison group in 13.9%, in the group of children with renal form of primary hyperparathyroidism, recurrent renal stones were observed in 86.1% of the child. According to the analysis of anamnestic data, recurrence of renal stones in children with renal form of primary hyperparathyroidism occurred within a period from 1.5 to 2 months to 2 years after surgery. 59.6% of children The renal form of primary hyperparathyroidism had previously undergone operations on the kidneys and urinary tract from 1 to 3 operations. The number of operations performed on the kidneys and MEP in children of patients with the Renal form of primary hyperparathyroidism was 3.5 times more than in children of the control group.

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