

Pediatric urolithiasis: experience at a tertiary care pediatric hospital

Urolitíase pediátrica: experiência de um hospital infantil de cuidados terciários

Authors

Luana Amancio¹

Maira Fedrizzi¹

Nilzete Liberato Bresolin¹

Maria Goretti Moreira

Guimarães Penido²

¹ Universidade Federal de Santa Catarina.

² Universidade Federal de Minas Gerais.

Submitted on: 03/02/2015.

Approved on: 09/15/2015.

Correspondence to:

Nilzete Liberato Bresolin.
Hospital Infantil Joana de Gusmão (HIJG).

Av. Rubens Arruda Ramos, nº 850/701, Florianópolis, SC, Brazil.
CEP: 9982-4148.

E-mail: nilzete.bresolin@hotmail.com

DOI: 10.5935/0101-2800.20160014

ABSTRACT

Introduction: Pediatric urolithiasis has become more prevalent in recent decades, with high recurrence rates and considerable morbidity. Most children with idiopathic urolithiasis have an underlying metabolic abnormality and proper research provides therapeutic interventions to reduce the formation of new stones and its complications. **Objective:** To identify demographic and clinical characteristics of pediatric urolithiasis, etiology, treatment management, disease recurrence and patient outcomes in a tertiary care pediatric hospital. **Methods:** A retrospective descriptive study of pediatric patients admitted to the Hospital Infantil Joana de Gusmão in Florianópolis, SC, Brazil, who were diagnosed with urolithiasis, from January 2002 to December 2012. Data were obtained from medical records. Those patients with diagnosis confirmed by imaging and 24hr urine or single sample urine were included. **Results:** We evaluated 106 pediatric patients (65% M). Average age at diagnosis was 8.0 ± 4.2 and 85% of them had positive family history of urolithiasis. Abdominal pain, renal colic and urinary tract infection were the main manifestations. 93.2% had metabolic abnormality and hypercalciuria was the most common. Pharmacological treatment was established in 78% of cases. Potassium citrate and hydrochlorothiazide were used. Surgical treatment was performed in 38% of patients. There was response to treatment in 39% of patients with recurrence of urolithiasis in 34.2% of them. Only 4.7% of patients continued follow-up, 6.6% were referred to other services, 8.5% were discharged and 73.8% lost follow-up. **Conclusion:** Pediatric urolithiasis deserves a detailed metabolic evaluation after their initial presentation for treatment, monitoring and prevention of its formation and its complications.

Keywords: abdominal pain; hematuria; hypercalciuria; urolithiasis.

RESUMO

Introdução: A urolitíase pediátrica tornou-se mais prevalente nas últimas décadas, com altas taxas de recorrência e considerável morbidade. A maioria das crianças com urolitíase idiopática tem uma anormalidade metabólica subjacente e a investigação adequada permite intervenções terapêuticas para reduzir a formação de novos cálculos e suas complicações. **Objetivos:** Identificar características demográficas e clínicas da urolitíase pediátrica, a etiologia, condutas terapêuticas, recidiva da doença e evolução dos pacientes em um hospital infantil de cuidados terciários. **Métodos:** Estudo descritivo e retrospectivo com pacientes pediátricos internados no Hospital Infantil Joana de Gusmão, Florianópolis, SC, Brasil, com diagnóstico de urolitíase, no período de janeiro 2002 a dezembro de 2012. Dados foram obtidos dos prontuários e foram incluídos aqueles com diagnóstico confirmado por exame de imagem e urina 24h ou amostra única urinária. **Resultados:** Foram avaliados 106 pacientes (65%M) pediátricos. Idade média ao diagnóstico $8,0 \pm 4,2$ e 85% tinham história familiar positiva para urolitíase. Dor abdominal, cólica nefrética clássica e infecção urinária foram as principais manifestações. 93,2% tinham alteração metabólica, sendo a hipercalciúria a mais comum. Tratamento farmacológico foi instituído em 78% dos casos. Utilizou-se citrato de potássio e hidroclorotiazida. Tratamento cirúrgico foi realizado em 38% dos pacientes. Houve resposta ao tratamento em 39% deles, com recidiva da urolitíase em 34,2%. Apenas 4,7% dos pacientes continuaram acompanhamento, 6,6% foram encaminhados para outros serviços, 8,5% receberam alta e 73,8% perderam acompanhamento. **Conclusão:** A urolitíase pediátrica merece avaliação metabólica detalhada após sua apresentação inicial para tratamento, acompanhamento e prevenção da formação lítica e de suas complicações.

Palavras-chave: dor abdominal; hematuria; hipercalciúria; urolitíase.

INTRODUCTION

Recent decades have seen an increase in the incidence and prevalence of pediatric urolithiasis,¹⁻⁶ which is related to considerable morbidity and high recurrence rates.^{5,7} The reason for this increase is not fully understood, but it has been associated with changes in the climate, diet, genetic inheritance and, possibly, other environmental factors.^{1-3,8-11}

Most children with idiopathic urolithiasis have an underlying metabolic abnormality, which underlies the importance of metabolic evaluation right after the initial diagnosis of kidney stones.¹² Identifying the metabolic abnormality enables a more specific guidance to non-pharmacological and pharmacological interventions to prevent the recurrent formation of the stones;^{12,13} and it has been shown an increase in these rates in the presence of metabolic abnormalities.^{13,14} This trend, combined with inflammatory characteristics of stone formation, can lead to a progressive decline in renal function in pediatric kidneys.

Contrary to extensive publications on urolithiasis in adults concerning the incidence, metabolic abnormalities, recurrence rates and spontaneous clearance of stones, there are only a few studies directed exclusively to the pediatric population. As a result, children are often assessed and treated similarly to adults with the same condition.¹³ However, it is noteworthy that the limited data available on pediatric urolithiasis suggests that there are indeed differences between the formation of stones in children and in adults,¹³ which justifies the need to obtain a better understanding of the metabolic basis, as well as environmental factors, so that we can improve prevention strategies.

Urinary tract anatomical malformations, urinary infections and nutritional changes are conditions often found in children and adolescents, and are factors that can predispose to urinary infections.^{7,10} Infectious stones are composed of struvite and/or carbonate apatite. They can fill the collector system (staghorn calculi), they grow fast and compromise the renal parenchyma. Similarly, tubular diseases (especially complete or incomplete distal renal tubular acidosis) are more common in children, they may have clinical manifestation of urolithiasis and culminate with nephrocalcinosis - which also compromises the renal parenchyma.^{7,10} In order to reduce morbidity and the long term effects of

pediatric urolithiasis, it is essential to devise a proper clinical management.¹⁵

Within this scope, this retrospective study aimed to identify demographic and clinical characteristics, stone formation etiology, clinical strategies adopted, presence of relapses and evolution of pediatric patients with urolithiasis admitted to a tertiary care hospital.

METHODS

This is a descriptive and retrospective study of children and adolescents admitted to a tertiary care children's hospital in Florianópolis, SC, Brazil, diagnosed with urolithiasis, from January 2002 to December 2012. The data was obtained from medical records and included those with diagnosis confirmed by imaging (ultrasound, computed tomography, simple abdominal radiography) with or without outpatient follow-up, and tests carried out in 24-hour urine exams corrected for creatinine,¹⁶ or single urine sample - also corrected for creatinine.¹⁶⁻¹⁹

From the patients' charts we obtained the following information: demographics, family history of urolithiasis, previous signs and symptoms and/or those present upon diagnosis, findings on physical examination, systemic disease and/or associated anatomical abnormalities, laboratory tests and imaging, location, size and composition of the stones, metabolic disorder diagnosis, urolithiasis treatment and recurrent episodes. Patients who had more than one hospitalization in the period were counted only once. Four patients were excluded because there was no confirmation of urolithiasis, as well as those with other systemic illnesses as well as those with previous diagnosis of chronic kidney disease.

The study was approved by the Hospital's Research Ethics Committee, under registration number 009/2013, and was carried out in accordance with the guidelines and regulatory standards for research involving human beings (Resolution 466/12 of the National Health Council) and the ethical standards set forth in the Declaration of Helsinki in 1964.

Fifty-nine patients (56%) underwent metabolic study at least one month after diagnosis of urolithiasis while they were asymptomatic and at a regular diet and physical activity. Patients included in the study were evaluated according to a protocol. We obtained two 24-hour urine samples followed by a blood sample. In the 24-hour urine and/or single urine

sample we analyzed: creatinine, calcium, citrate, uric acid, cystine, magnesium, oxalate, and phosphate. The blood sample was analyzed for: creatinine, uric acid, calcium, phosphorus, magnesium, sodium, chlorine, potassium, pH, bicarbonate and PTH. Standard laboratory tests we ordered from the hospital laboratory to analyze the elements in the 24h urine, single urine and blood samples. The criteria for defining abnormal urinary excretion of the studied elements are shown on Table 1. Where applicable, results were expressed as mean \pm standard deviation.

To define arterial hypertension (AH) we used blood pressure values greater than or equal to the 95th percentile of the Task Force in 2004 according to gender. The response to pharmacological treatment was considered in cases on which we had the normalization of urinary solute values and no stones recurrence during the study period.

RESULTS

We evaluated 106 patients, for a total of 166 hospital admissions (some patients were hospitalized more than once), representing about one for every 100 hospital admissions in the surgical care unit. Most were males, with mean age of symptom onset of 8.00 ± 4.25 years, from other cities in the state of Santa Catarina, different from the capital - Florianópolis. There was a positive family history record for urolithiasis in only 40 records of patients and, of these, 85% were positive (Table 2).

Nonspecific abdominal pain, classic renal colic and urinary tract infection were the most common clinical manifestations prior to diagnosis (Table 3). Hematuria and leukocyturia were the most frequently found changes in the urinary sediment exam (Table 4).

Urinary tract infection (UTI) was diagnosed in 26 patients (37.1%) during the follow-up period, equally distributed between the genders. The main causative

TABLE 1 ABNORMAL VALUES FOR URINE SOLUTE VOLUME AND EXCRETION IN A SINGLE 24H URINE SAMPLE IN CHILDREN AND ADOLESCENTS

	24h Urine	Single creatinine-corrected sample	Single GFR-corrected sample
Creatinine	2 to 3 years: 6 to 22 mg/kg > 3 years: 12 to 30 mg/kg		
Calcium	> 4.0 mg/kg or > 0.10 mmol/kg		> 0.10
		Age	mg/mg
		0-6 months	> 0.80
		6-12 months	> 0.60
		1-2 years	> 0.40
		2-18 years	> 0.21
			mmol/mmol
Citrate	> 400 mg/g creatinine	> 0.28 (mmol/L/mmol/L)	> 0.18 (mg/L/mg/L)
Calcium/Citrate	> 0.33	> 0.33	
Uric acid	< 815 mg/1.73m ² SC	< 0.65	< 0.56 mg < 0.03 mmol
Cystine	< 60 mg/1.73 m ² SC	< 0.02 (mg/mg) < 0.01 (mmol/mmol)	
Magnesium	> 88 mg/1.73 m ² SC		
Oxalate	< 50 mg/1.73m ² SC < 0.49 mmol/1.73m ² SC	Age	(mg/mg)
		0-6 m	< 0.30
		7 m - 4a	< 0.15
		> 4a	< 0.10
Phosphate		TP/GFR < 4.4 mg/dL*	

GFR: Glomerular filtration rate; TP: Tubular phosphate reabsorption. Hellerstein et al. Creatinine excretion rates for renal clearance studies. *Pediatr Nephrol* 2001;16:637-43;¹⁶ Penido et al. Excreção urinária de cálcio, ácido úrico e citrato em crianças e adolescentes. *J Pediatr (Rio J)* 2002;78:153-60;¹⁷ Srivastava et al. Essentials of laboratory medicine for the nephrology clinician. *Pediatr Nephrol* 2007;22:170-82.19

TABLE 2 CHARACTERISTICS OF HOSPITALIZED PATIENTS WITH UROLITHIASIS BETWEEN 2002 AND 2012

Characteristics		N (%)
Gender	Female	37 (34.9%)
	Male	69 (65.1%)
Age (years) of symptom onset	Mean ± SD*	8.00±4.25
Interval (months) between symptoms and diagnosis	Mean ± SD*	5.32±15.79
Family History **	Yes	34 (85%)
	No	6 (15%)
City of Origin	Florianópolis	15 (14.2%)
	Another SC ^c city	91 (85.8%)

* SD: Standard deviation. ** Forty patients evaluated. SC^c: State of Santa Catarina, Brazil.

TABLE 3 CLINICAL MANIFESTATIONS OF HOSPITALIZED PATIENTS WITH UROLITHIASIS BETWEEN 2002 TO 2012

Clinical Manifestations	N (%)
Abdominal pain	59 (56.7%)
Classic renal colic	46 (44.2%)
Urinary infection	39 (37.5%)
Macroscopic hematuria	33 (31.9%)
Vomits	29 (27.9%)
Urinary symptoms	25 (24.0%)
Stones elimination	25 (24.0%)
Fever	15 (14.4%)
Nausea	13 (12.5%)
Microscopic hematuria	6 (5.8%)
Other	2 (2.0%)

TABLE 4 CHANGES IN THE SIMPLE URINE EXAM OF PATIENTS WITH UROLITHIASIS HOSPITALIZED FROM 2002 TO 2012

Alterations in the urine test	N (%)
Hematuria	56 (58.3%)
Leukocyturia	55 (57.3%)
Alkaline pH	26 (27.1%)
Crystals	3 (3.1%)
Phosphates	3 (3.1%)
Urates	3 (3.1%)
Oxalates	2 (2.1%)
Cystine	1 (1.0%)
Acid pH	0 (0.0%)
Other	6 (6.3%)

agents were *Escherichia coli* (46.0%) and *Proteus vulgaris* (38.4%).

No abnormality was found in the patients' biochemical blood test. However, 19 patients (23.5%) had acute changes in renal function during hospitalization, which returned to normal after treatment.

Only 59 patients (56%) were submitted to a urine metabolic study and 55 of them (93.2%) had at least one metabolic change. The most common metabolic alterations were: hypercalciuria (74.6%), hypocitraturia (44.0%) and hyperuricosuria (30.5%) (Table 5). Twenty-five patients (42.4%) had only one metabolic change and 19 of them (76%) had hypercalciuria. Family history of urolithiasis was evaluated in 30 patients (54.5%) with metabolic disorders, and was present in 25 (83.3%). Of the 44 patients with hypercalciuria, 26 were investigated for a family history of urolithiasis, being positive in 21 patients (80.6%).

TABLE 5 METABOLIC DISORDERS IN THE URINARY ANALYSIS OF PATIENTS WITH UROLITHIASIS HOSPITALIZED IN HIJG DURING THE PERIOD OF 2002 TO 2012*

Metabolic Disorders	N (%)
Hypercalciuria	44 (74.6%)
Hypocitraturia	26 (44.1%)
Hyperuricosuria	18 (30.5%)
Hyperoxaluria	5 (8.5%)
Cystinuria	3 (5.1%)
Hyperphosphaturia	1 (1.7%)
Hypomagnesuria	1 (1.7%)
Hypercalciuria + Hypocitraturia	8 (14.5%)
Hypercalciuria + Hyperuricosuria	7 (12.72%)
Hypercalciuria + Hypocitraturia + Hyperuricosuria	7 (12.72%)

* In a 24h urine or a single urine sample

Imaging tests were performed to assess and identify the stones: abdominal ultrasonography in 103 patients (97.2%), abdomen X-ray in 36 (34%), non-contrast abdominal CT scan in 33 (31.1%), excretory urography (26.4%), voiding cystourethrogram in 28 (14.2%), static renal scintigraphy in 14 (13.2%) and dynamic renal scintigraphy in 3 (2.8%).

There was spontaneous stone elimination in 48 patients (46.2%), including the elimination of stones prior to diagnosis and during follow-up. The mean size of the stones eliminated was 5.34 ± 2.86 mm.

As for the location of the stones, 36 patients (34%) had pyelocaliceal and ureteral stones, 31 (29.2%)

renal, 19 (17.9%) ureteral, 10 (9.4%) bladder and 2 (1.9%) urethral. The mean stone size was 9.4 ± 6.3 mm, hydronephrosis was found in 50 patients (49%) and vesicoureteral reflux in 5 (4.8%).

Stone analysis was performed in 8 patients (7.5%): 50% was oxalate and calcium phosphate, 25% calcium phosphate and ammonium magnesium phosphate, 12.5% phosphate and calcium oxalate and magnesium ammonium phosphate and only 12.5% were composed of calcium oxalate.

Anatomic abnormalities were found in 15 patients (14.2%), and among them ureteropelvic junction stenosis was the most common (6.3%). Three patients (2.8%) had nephrocalcinosis.

Pharmacological treatment for the metabolic changes was given to 46 patients, 78% of those who had them. We used potassium citrate (89.1%) and hydrochlorothiazide (47.8%), and response was obtained only in 18 (39%) of them. Surgical treatment was performed in 40 patients (38%) with 21% undergoing open surgery, 15% extracorporeal lithotripsy (ESWL), 7.5% had endoscopic extraction, percutaneous nephrolithotomy to 6.6% and 2.8% to other procedures.

Eighteen (20.2%) patients had urinary stone formation recurrence, of the 89 patients evaluated. Among the patients who had recurrence of urinary stone formation, thirteen of them had metabolic disorders and were being treated for it, two had metabolic diseases and were not treated, and 3 patients had no metabolic changes. There was no statistically significant difference in relapse among patients who received or did not receive drug treatment for metabolic disorders ($p = 0.57$).

Of the 106 patients evaluated, five (4.7%) continued on follow-up, seven (6.6%) were referred for follow-up at another service. Nine (8.5%) patients were discharged from hospital monitoring under good performance and imaging tests within normal limits. No patient developed chronic kidney disease due to urolithiasis as of the evaluation period of this study.

DISCUSSION

While changes in the epidemiology of urolithiasis in adults have been described, there still are only a handful of studies involving the pediatric population.^{1,20,21}

However, pediatric urolithiasis is associated with significant morbidity, primarily because the stones tend to recur and thus it should not be underestimated.

In the last decade, a marked increase in the incidence of pediatric urolithiasis has been reported.¹⁻⁶ Among the reasons involved in this increase is the introduction of computed tomography (CT) in emergency services and their frequent use in the evaluation of patients with abdominal pain and flank pain, obesity, global warming, changes in lifestyle and changes in feeding habits^{1-3,9,10}. Based on these reports in the literature, this study evaluated pediatric patients with urolithiasis admitted to a tertiary care hospital to help in the understanding of pediatric urolithiasis.

Bush *et al.*²² evaluated all pediatric patients admitted between 2002 and 2007 in the Pediatric Health Information System database, and found that girls accounted for only 46% of all hospitalizations, but accounted for 56% of admissions for urolithiasis. The authors showed that one in 685 pediatric hospitalizations in this country were due to urolithiasis. They also concluded that females had a relative risk of 1.5 for admission for urolithiasis. Similarly, Novak *et al.*²¹ also found that girls experienced more hospitalizations for urolithiasis than boys. In this study it was shown that one for every 100 hospital admissions in the pediatric surgical care unit was motivated by urolithiasis. Probably the higher proportion of hospitalization may have its explanation in the fact that most of the patients were from other cities in the state of Santa Catarina, referred to this tertiary care hospital in Florianópolis.

The prevalence of urolithiasis among males in the population followed up (male/female ratio 1.8:1.0) is consistent with data from other studies of countries considered to be developing countries, which recorded rates ranging from 1.2:1 up to 4:1, as it happens in adults.^{6,23-26} In contrast, North American series were not significantly different between the genders.^{4,15}

Urinary stones affect children of all ages.²⁷ In the present study, the average age of symptoms onset of the 106 patients was 8 ± 4.25 years (0.5 to 16.8). This finding goes hand-in-hand with what is described in the literature for developing countries such as Turkey, Pakistan, Armenia and Tunisia (average of 7.3).²⁸⁻³¹

However, in the North American series the average age of diagnosis was a bit higher, ranging from 11.3 to 13.2 years.^{3,4,15} Sas *et al.*^{2,13} demonstrated lower risk for urolithiasis development in patients aged 0 to 3 years and a consistent increase in the risk throughout adolescence.

Positive family history for urolithiasis was found in 85% of the children assessed in these regards in this study. This same story was found in 83.3% of patients with metabolic changes, in which we evaluated the presence or absence of family members with kidney stones. Likewise, it was observed in 80.6% of patients with hypercalciuria. It is known that about 40% of children with urolithiasis have positive family history.^{1,32,33} According to their study, Naseri *et al.*³⁴ found positive family history in 62.7% of 142 pediatric patients with kidney stones who were prospectively evaluated. Vandervoort *et al.*¹ also demonstrated in a retrospective study, a positive family history in half of the cases evaluated, confirming the important role of family history in the occurrence of urolithiasis in children.

Nonspecific abdominal pain, renal colic and urinary tract infection (Table 3) were the most common clinical manifestations prior to the diagnosis of urolithiasis in children evaluated in this study. According to the literature, despite teenagers showing symptoms similar to adults, as classic renal colic, hematuria and spontaneous stone elimination, younger children have varied presentations, including vomiting, restlessness and nonspecific localized abdominal, flank and pelvic pain, as well as urinary symptoms, recurrent or isolated urinary tract infections.^{25,35} These reports are consistent with that observed in this study. However, urinary symptoms (dysuria, suprapubic or urethral pain, urge/incontinence, enuresis) were found in 24% of the patients, a higher percentage than what is found in the literature, which is 10% of pediatric cases with urolithiasis.^{33,35} Attributed to this finding is the fact that the hospital involved in the study is a reference in the region, where the most symptomatic patients are referred to.

Urinary tract infection (UTI) was diagnosed in 37.1% of patients, *Escherichia coli* (46.0%) and *Proteus vulgaris* (38.4%) were the main agents. There are reports of UTI incidence in 8% to 70% of pediatric patients with urolithiasis;^{29,36} however, the exact role UTI plays in stone formation is uncertain and may be the cause or consequence of urolithiasis.

Metabolic alterations were described in 33% to 93% of pediatric patients with urinary stones.^{1,4,5,10,20,32,34} In our study we found at least one metabolic disorder in 93.2% of the evaluated patients (59 patients). Hypercalciuria was the most common, followed by hypocitraturia and

hyperuricosuria (Table 4). Several authors have shown that hypercalciuria is present in 72% to 88% of pediatric urolithiasis patients.^{2,4,1,12,15,22,25,32,35,37} This information is consistent with what our study demonstrated. Idiopathic hypocitraturia ranks second among the most common metabolic disorders in pediatric urolithiasis⁴ and the same was also found in this study (Table 4). However, for hyperuricosuria, we found higher values (30.5%), unlike those already described⁴. It may be that, at least in some patients, hyperuricosuria is a causal factor and does not represent the main etiology of urolithiasis. It is quite possible that the differences in the incidence depends on the characteristics of the population, as well as their eating habits. The high rates of metabolic abnormalities observed in this and other studies enable us to state that a complete metabolic study should always be part of the workup in pediatric urolithiasis.

The vast majority of urinary stones identified in patients evaluated with the use of imaging tests, particularly for abdominal ultrasound, was located in the upper urinary tract (81.1%). This result corroborates the findings of other recent studies.^{1,7,10,37} Similar to the results found in this series, authors have reported much lower rates of lower urinary tract lithiasis. In recent decades, the pattern of pediatric urolithiasis changed in developing countries, and the incidence of lower urinary tract stones has decreased significantly.

Forty-six percent of children and adolescents studied had spontaneous elimination of the stones, with an average size of the stone eliminated being of 5.3 ± 2.9 mm. Van Savage *et al.*³⁸ showed a reduction in spontaneous elimination of stones in children and adolescents whose stones were larger than 3 mm. However, Pietrow *et al.*²⁰ and Kit *et al.*¹⁵ showed reduced spontaneous elimination of stones when they were larger than 4 mm. The average size of all stones evaluated in the study was 9.4 ± 6.3 mm, a much higher figure than that found by Kit *et al.*¹⁵

Calcium stones were the ones most found in the study, although only 8 patients (7.5%) had their stones analyzed. Similar to what was retrospectively analyzed by Rellum *et al.*⁵ in 71 pediatric patients, the composition of the analyzed stones showed predominantly calcium phosphate, calcium oxalate and magnesium ammonia phosphate. Other authors have also shown that the majority of urinary stones

are made of calcium; with calcium oxalate and phosphate accounting for about 80%.^{35,37}

Anatomical and/or urodynamic changes predispose the formation of stones for modifying urinary dynamics, causing urinary stasis (promoting crystal precipitation in the urine) and facilitating the incidence of UTI.¹⁸ Anatomical abnormalities were found in 15 patients (14.2%), and among them the ureteropelvic junction stenosis was the most common (6.3%). A similar result was observed by Safaei Asl & Maleknejad,¹² who reported 14.3% of anatomical changes in their patients, most of whom had ureteropelvic junction stenosis.

The clinical treatment of urolithiasis aims to reduce or prevent the emergence of new stones, or prevent existing ones to increase in size, thus reducing morbidity and the need for surgical intervention. This clinical approach includes non-pharmacological and pharmacological treatment. The universal approach, and perhaps the most important, includes the increase in urine output resulting from increased fluid intake and dietary adequacy. However, children and adolescents are rarely adept to such approach and often pharmacological intervention is required. In this study, the pharmacological treatment was instituted in 78% of the patients who had hypercalciuria or hypocitraturia. Most used potassium citrate, and thiazide diuretic was used in fewer patients.

Citrate therapy caused a reduction in the recurrence of new stones in children and adolescents, reducing the growth of residual stones resulting from extracorporeal shock wave lithotripsy (ESWL) and reduction of stone formation in children with hypocitraturia.³⁶ This is also indicated in the treatment of patients with hyperuricosuria; it is rarely necessary to use allopurinol in patients with this metabolic disorder.¹⁸ According to the experience of experts, thiazide diuretic remains the therapy of choice for patients with calcium stones, reducing their formation.³⁹

Surgical treatment was performed in 40 patients (38%), and 21% underwent open surgery, 15% to ESWL, 7.5% to endoscopic extraction, percutaneous nephrolithotomy in 6.6% and 2.8% to other procedures. Bush *et al.*²² reported similar results to those of our study regarding endoscopic extraction (7.6%) and percutaneous nephrolithotomy (3.8%). Regarding ESWL, they found only 2.8% of this procedure and believe that there has been

underreporting because many of them were carried out by mobile units and were not included in the total procedures.

Urolithiasis recurrences in our series was found in 18 patients (20.2%). Close values (24%) were observed by Kit *et al.*¹⁵ in a series of pediatric patients seen at a tertiary hospital such as ours. The results obtained by Pietrow *et al.*²⁰ are also very similar to ours. These authors found recurrence in 19% of all their patients and a third of those who had metabolic disorders. However, Vandervoort *et al.*¹ found relapses in 39% of their patients and Koyuncu *et al.*²⁴ in 50% of their pediatric patients with an identified metabolic cause. These differences in stone formation relapse rates may be related to the type of sample studied, the follow-up duration, and also the presence of functional and morphological urinary tract abnormalities.

We pointed out an important limitation of our study in relation to the comparison of the number of stone formation relapses in patients receiving pharmacological treatment for metabolic disorders and those who did not receive this treatment ($p = 0.57$). It is likely that we did not find statistical significance due to the small number of subjects in our sample and absence of metabolic studies in almost half of all 106 patients.

Regarding follow-up, we lost most of the patients (78.3%) hospitalized for urolithiasis from 2002 to 2012. This may be due to several factors such as age higher than what the hospital would take; symptom improvement, with no further recurrences; difficulty in scheduling return visits, or another factor that has made it difficult to travel to the hospital in the host city, considering that most of the patients came from other cities.

There are limitations to this study that should be mentioned, especially with regards to its design. Retrospective series like this one are restricted by the level of details in the medical record. Although it was possible to identify 106 pediatric patients with urolithiasis, only 7.5% of them had the stones analyzed for their composition and only 56% of the patients were submitted to a metabolic study. In addition, epidemiological trends in the incidence of urolithiasis observed in the hospital of the study cannot be applied to all pediatric populations, considering geographic, economic and ethnic differences. Being a tertiary care hospital reflects that pediatric urolithiasis

patients who sought medical care were consequently more symptomatic and with worse complications. Thus, the data obtained in the study provide only part of the clinical and epidemiological information regarding pediatric urolithiasis. However, despite these limitations, we believe that the results found may contribute to better understanding this issue and help devise better prevention strategies.

CONCLUSIONS

This study identified a high prevalence of metabolic disorders as an etiological factor of pediatric urolithiasis. Hypercalciuria remains the most frequently found, followed by hypocitraturia. This finding supports the need for metabolic evaluation in all children and adolescents diagnosed with urolithiasis. In this way, one can institute early and adequate treatment for the prevention and reduction of recurrence, which is a hallmark of urinary stones. All pediatric patients presenting flank pain or chronic recurrent abdominal pain should always be investigated for the possibility of urinary calculi; because the clinical manifestation of pediatric urolithiasis, in most cases, it is not like the classic renal colic.

Long-term monitoring is effective for patient and family education about the importance of eating habits, water intake and treatment compliance.

Finally, we stress that in the hospital of the study, there started a collaborative work between nephrologists and urologists, which certainly brings about improvements in the etiological assessment of pediatric urolithiasis, its approach and follow-up.

REFERENCES

1. VanDervoort K, Wiesen J, Frank R, Vento S, Crosby V, Chandra M, et al. Urolithiasis in pediatric patients: a single center study of incidence, clinical presentation and outcome. *J Urol* 2007;177:2300-5. DOI: <http://dx.doi.org/10.1016/j.juro.2007.02.002>
2. Sas DJ, Hulsey TC, Shatat IF, Orak JK. Increasing incidence of kidney stones in children evaluated in the emergency department. *J Pediatr* 2010;157:132-7. PMID: 20362300 DOI: <http://dx.doi.org/10.1016/j.jpeds.2010.02.004>
3. Dwyer ME, Krambeck AE, Bergstralh EJ, Milliner DS, Lieske JC, Rule AD. Temporal trends in incidence of kidney stones among children: a 25-year population based study. *J Urol* 2012;188:247-52. DOI: <http://dx.doi.org/10.1016/j.juro.2012.03.021>
4. Penido MG, Srivastava T, Alon US. Pediatric primary urolithiasis: 12-year experience at a Midwestern Children's Hospital. *J Urol* 2013;189:1493-7. DOI: <http://dx.doi.org/10.1016/j.juro.2012.11.107>
5. Rellum DM, Feitz WF, van Herwaarden AE, Schreuder MF. Pediatric urolithiasis in a non-endemic country: a single center experience from The Netherlands. *J Pediatr Urol* 2014;10:155-61. DOI: <http://dx.doi.org/10.1016/j.jpuro.2013.07.019>
6. Sáez-Torres C, Grases F, Rodrigo D, García-Raja AM, Gómez C, Frontera G. Risk factors for urinary stones in healthy schoolchildren with and without a family history of nephrolithiasis. *Pediatr Nephrol* 2013;28:639-45. DOI: <http://dx.doi.org/10.1007/s00467-012-2368-5>
7. Spivacow FR, Negri AL, del Valle EE, Calviño I, Fradinger E, Zanchetta JR. Metabolic risk factors in children with kidney stone disease. *Pediatr Nephrol* 2008;23:1129-33. DOI: <http://dx.doi.org/10.1007/s00467-008-0769-2>
8. Thomas BG. Management of stones in childhood. *Curr Opin Urol* 2010;20:159-62. DOI: <http://dx.doi.org/10.1097/MOU.0b013e3283353b80>
9. López M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. *Pediatr Nephrol* 2010;25:49-59. DOI: <http://dx.doi.org/10.1007/s00467-008-0960-5>
10. Alpay H, Ozen A, Gokce I, Biyikli N. Clinical and metabolic features of urolithiasis and microlithiasis in children. *Pediatr Nephrol* 2009;24:2203-9. DOI: <http://dx.doi.org/10.1007/s00467-009-1231-9>
11. Güven AG, Koyun M, Baysal YE, Akman S, Alimoglu E, Akbas H, et al. Urolithiasis in the first year of life. *Pediatr Nephrol* 2010;25:129-34. DOI: <http://dx.doi.org/10.1007/s00467-009-1296-5>
12. Safaei Asl A, Maleknejad S. Pediatric urolithiasis: an experience of a single center. *Iran J Kidney Dis* 2011;5:309-13.
13. Sas DJ. An update on the changing epidemiology and metabolic risk factors in pediatric kidney stone disease. *Clin J Am Soc Nephrol* 2011;6:2062-8. DOI: <http://dx.doi.org/10.2215/CJN.11191210>
14. Schwarz RD, Dwyer NT. Pediatric kidney stones: long-term outcomes. *Urology* 2006;67:812-6. DOI: <http://dx.doi.org/10.1016/j.urology.2005.10.020>
15. Kit LC, Filler G, Pike J, Leonard MP. Pediatric urolithiasis: experience at a tertiary care pediatric hospital. *Can Urol Assoc J* 2008;2:381-6.
16. Hellerstein S, Simon SD, Berenbom M, Erwin P, Nickell E. Creatinine excretion rates for renal clearance studies. *Pediatr Nephrol* 2001;16:637-43. DOI: <http://dx.doi.org/10.1007/s004670100622>
17. Penido M, Diniz JS, Guimarães MM, Cardoso RB, Souto MFO, Penido MG. Excreção urinária de cálcio, ácido úrico e citrato em crianças e adolescentes. *J Pediatr (Rio J)* 2002;78:153-60.
18. Bresolin NL, Penido M, Diniz JS, Guimarães MM, Cardoso RB, Souto MFO, Penido MG. Programa Nacional de Educação Continuada em Pediatria – PRONAP - Ciclo XVI. São Paulo; 2013. p.39-67.
19. Srivastava T, Garg U, Chan YR, Alon US. Essentials of laboratory medicine for the nephrology clinician. *Pediatr Nephrol* 2007;22:170-82. DOI: <http://dx.doi.org/10.1007/s00467-006-0233-0>
20. Pietrow PK, Pope JC 4th, Adams MC, Shyr Y, Brock JW 3rd. Clinical outcome of pediatric stone disease. *J Urol* 2002;167:670-3. DOI: [http://dx.doi.org/10.1016/S0022-5347\(01\)69121-3](http://dx.doi.org/10.1016/S0022-5347(01)69121-3)
21. Novak TE, Lakshmanan Y, Trock BJ, Gearhart JP, Matlaga BR. Sex prevalence of pediatric kidney stone disease in the United States: an epidemiologic investigation. *Urology* 2009;74:104-7. DOI: <http://dx.doi.org/10.1016/j.urology.2008.12.079>
22. Bush NC, Xu L, Brown BJ, Holzer MS, Gingrich A, Schuler B, et al. Hospitalizations for pediatric stone disease in United States, 2002-2007. *J Urol* 2010;183:1151-6. PMID: 20096871 DOI: <http://dx.doi.org/10.1016/j.juro.2009.11.057>
23. Wumaner A, Keremu A, Wumaier D, Wang Q. High incidence of urinary stones in Uyghur children may be related to local environmental factors. *J Pediatr Urol* 2014;10:289-93. DOI: <http://dx.doi.org/10.1016/j.jpuro.2013.09.002>
24. Koyuncu H, Yencilek F, Erturhan S, Eryildirim B, Sarica K. Clinical course of pediatric urolithiasis: follow-up data in a long-term basis. *Int Urol Nephrol* 2011;43:7-13. DOI: <http://dx.doi.org/10.1007/s11255-010-9791-y>

25. Ali SH, Rifat UN. Etiological and clinical patterns of childhood urolithiasis in Iraq. *Pediatr Nephrol* 2005;20:1453-7. DOI: <http://dx.doi.org/10.1007/s00467-005-1971-0>
26. Elmaci AM, Ece A, Akın F. Clinical characteristics and metabolic abnormalities in preschool-age children with urolithiasis in southeast Anatolia. *J Pediatr Urol* 2014; 10:495-9. DOI: <http://dx.doi.org/10.1016/j.jpuro.2013.11.004>
27. Cameron MA, Sakhaee K, Moe OW. Nephrolithiasis in children. *Pediatr Nephrol* 2005;20:1587-92. DOI: <http://dx.doi.org/10.1007/s00467-005-1883-z>
28. Rizvi SA, Naqvi SA, Hussain Z, Hashmi A, Hussain M, Zafar MN, et al. Pediatric urolithiasis: developing nation perspectives. *J Urol* 2002;168:1522-5. PMID: 12352448 DOI: [http://dx.doi.org/10.1016/S0022-5347\(05\)64509-0](http://dx.doi.org/10.1016/S0022-5347(05)64509-0)
29. Erbagci A, Erbagci AB, Yilmaz M, Yagci F, Tarakcioglu M, Yurtseven C, et al. Pediatric urolithiasis--evaluation of risk factors in 95 children. *Scand J Urol Nephrol* 2003;37:129-33. DOI: <http://dx.doi.org/10.1080/00365590310008866>
30. Sarkissian A, Babloyan A, Arikants N, Hesse A, Blau N, et al. Pediatric urolithiasis in Armenia: a study of 198 patients observed from 1991 to 1999. *Pediatr Nephrol* 2001;16:728-32. DOI: <http://dx.doi.org/10.1007/s004670100647>
31. Jallouli M, Jouini R, Sayed S, Chaouachi B, Houissa T, Ayed M, et al. Pediatric urolithiasis in Tunisia: a multi-centric study of 525 patients. *J Pediatr Urol* 2006;2:551-4. DOI: <http://dx.doi.org/10.1016/j.jpuro.2005.12.002>
32. Alemzadeh-Ansari MH, Valavi E, Ahmadzadeh A. Predisposing factors for infantile urinary calculus in south-west of Iran. *Iran J Kidney Dis* 2014;8:53-7.
33. Hoppe B, Kemper MJ. Diagnostic examination of the child with urolithiasis or nephrocalcinosis. *Pediatr Nephrol* 2010;25:403-13. DOI: <http://dx.doi.org/10.1007/s00467-008-1073-x>
34. Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. *Iran J Kidney Dis* 2010;4:32-8.
35. Copelovitch L. Urolithiasis in children: medical approach. *Pediatr Clin North Am* 2012;59:881-96. DOI: <http://dx.doi.org/10.1016/j.pcl.2012.05.009>
36. Sarica K, Erturhan S, Yurtseven C, Yagci F. Effect of potassium citrate therapy on stone recurrence and regrowth after extracorporeal shockwave lithotripsy in children. *J Endourol* 2006;20:875-9. DOI: <http://dx.doi.org/10.1089/end.2006.20.875>
37. Milošević D, Batinić D, Turudić D, Batinić D, Topalović-Grković M, Gradiški IP. Demographic characteristics and metabolic risk factors in Croatian children with urolithiasis. *Eur J Pediatr* 2014;173:353-9. DOI: <http://dx.doi.org/10.1007/s00431-013-2165-6>
38. Van Savage JG, Palanca LG, Andersen RD, Rao GS, Slaughenhaupt BL. Treatment of distal ureteral stones in children: similarities to the american urological association guidelines in adults. *J Urol* 2000;164:1089-93. DOI: [http://dx.doi.org/10.1016/S0022-5347\(05\)67259-X](http://dx.doi.org/10.1016/S0022-5347(05)67259-X)
39. Xu H, Zisman AL, Coe FL, Worcester EM. Kidney stones: an update on current pharmacological management and future directions. *Expert Opin Pharmacother* 2013;14:435-47. DOI: <http://dx.doi.org/10.1517/14656566.2013.775250>