Original Article

Clinical profile, diagnosis and treatment of pediatric urolithiasis: a single center experience in Kazakhstan

Assel Sagymbayeva

Abstract:

Objective: The aim of our study to present the results of the clinical profile, diagnosis and treatment of children with urolithiasis in the Pediatric Urology Department of the Scientific center of Pediatria and Pediatric surgery in Almaty, Kazakhstan. ***Materials and methods:*** A retrospective data from pediatric patients with urolithiasis admitted from January 2015 to December 2021. The data was obtained from medical records and included those with diagnosis confirmed by imaging and laboratory test, as 24-hour urine exams corrected for creatinine, stone composition. ***Results:*** We reviewed 204 children with urolithiasis. The male-to-female ratio was 1.34:1. Congenital anomalies of the urinary tract were found in 40 patients (19.6%).Urolithiasis was more common in adolescent girls, whereas in boys the frequency of observation is higher between 11 and 17 years old (p = 0.006). Majority of the patients were from southern regions (51%) in our country. Renal colic, urinary tract infection and macroscopic hematuria were the most common clinical manifestations. Urinary tract infection was diagnosed in 185 patients (90.6%). The most frequent metabolic disorders were hypercalciuria, hyperoxaluria. In 35% of cases there was a metabolic disorder and appropriate therapy was prescribed. In the remaining cases, surgical treatment was used. ***Conclusion:*** In this study we presented the prevalence of urolithiasis in the pediatric population in different regions of our country. We identified a high prevalence of infective stone as an etiological factor of pediatric urolithiasis. Clinical symptoms depending on the age and location of the stones.

Keywords: Pediatric urolithiasis; clinical profile, hyperoxaluria, urinary infection, treatment.

Bangladesh Journal of Medical Science Vol. 22 No. 02 April'23 Page : 297-304
DOI: https://doi.org/10.3329/bjms.v22i2.64986

Introduction:

Urolithiasis is one of the leading urological diseases, often prone to severe course and recurrence.[1,2,3] The prevalence of urolithiasis throughout children ranges from 1% to 5% andis affected by environmental conditions, geographical, ethnic, nutritional, and genetic factors. An increased incidence of urinary stones is found in all age groups. This disease is characterized by a relapsing course with a recurrence rate of over 60% 3 years after the initial clinical diagnosis.[1,3,4,5]

The term "urolithiasis" refers to metabolic disorders caused by a variety of intrinsic and extrinsic causes. The disease is characterized by the presence of stones in the kidneys and urinary tract, which tends to recur and often has a severe and persistent course. At the same time, two types of stone formation processes are distinguished: formal genesis (crystallization and colloidal theories); causal genesis (influence of exogenous and endogenous factors).The predisposition to the onset of urolithiasis is: climate and geographic impact; social situation; occupation; genetic diseases (enzymes and tubular disorders).

According to the European Association of Urology guidelines on urolithiasis, the presence of urolithiasis in children and adolescents is a high risk of stone formation.Older children are more likely to have ureteral stones, and younger children are more likely to have kidney stones.[6]

For the last 20 years there are no works on clinical

Correspondence: Dr. Assel Sagymbayeva, Pediatric Surgeon, Asfendiyarov Kazakh National Medical University,Pediatric Urology Department, Scientific Center of Pediatrics and Pediatric Surgery, Almaty city, Republic of Kazakhstan, E-mail address: sagymbaeva.assel@gmail.com

presentation, diagnosis, treatment of pediatric urolithiasis in Kazakhstan. Therefore, *the aim* of this article is to present the results of the clinical profile, diagnosis and treatment of urolithiasis in children.

Materials and methods:

Participant selection

This is a retrospective study of children admitted to Pediatric Urology Department of the Scientific center of Pediatria and Pediatric surgery, Almaty, Kazakhstan diagnosed with urolithiasis, from January 2015 to December 2021. The study was approved by the Hospital's Research Ethics Committee (Protocol 1102/2021), and was carried out in accordance with the guidelines and the ethical standards set forth in the Declaration of Helsinki in 1964.

The data was obtained from medical records and included those with diagnosis confirmed by imaging (ultrasound, computed tomography, intravenous urography) and laboratory test, as 24-hour urine exams corrected for creatinine.

From the patients'charts we obtained the following information: demographics (sex, age with stratification by age group in younger than 1 years, aged between 1 and 5 years, and between 6 and 10 years, and between 11 and 17 years), anthropometric (weight, height, and body mass index (BMI)/age, measured in the first appointment), 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 disorders, urolithiasis treatment. Patients who had more than one hospitalization in the period were counted only once.

The inclusion criteria were:1) Age between 1 month and 17years;2)Verification of clinical diagnosis by: abdomen X-ray, abdominal or urinary tract ultrasound (which can identify calculi ≥5 mm) and native computed tomography of the urinary tract. 3)To provide medical care in the Pediatric Urology Department of the Scientific center of Pediatria and Pediatric surgery during the above period.

Statistical analysis was performed using StatTech v. 2.6.1.Quantitative variables were assessed for normality using the Kolmogorov-Smirnov test. Quantitative variables following non normal distribution were described using median (Me) and lower and upper quartiles (Q1 – Q3).Categorical data were described with absolute and relative frequencies.

Comparisons of three or more groups on a quantitative variable whose distribution differed from normal were made using the Kruskal-Wallis test and Dunn's criterion with Holm correction as a post-hoc method.

Table 1. The clinical profile of children with urolithiasis

Presenting features	Number of patients (n)	Percentage (%)
Age		
<1	9	4.4
≥1≤5	70	34.3
>5≤10	77	37.8
>10≤17	48	23.5
Gender		
Female	87	42.6
Male	117	57.4
Family history		
positive for stone disease	81	39.7
negative	123	60.3
Clinical symptoms		
Abdominal pain	19	9.3
Renal colic	79	38.7
Macroscopic hematuria	35	17.2
Dysuria	18	8.8
Vomiting	19	9.3
Fever	9	4.4
Passage of stone	19	9.3
Asymptomatic	6	3.0
Congenital anomalies of the urinary tract		
No abnormalities	164	80.4
Vesicoureteric reflux	8	3.9
Ureterohydronephrosis	11	5.4
Primary hydronephrosis	14	6.8
Horseshoe kidney	2	1.0
Incomplete doubling of the kidney	3	1.5
Multicystic kidney disease	2	1.0
Secondary hydronephrosis		
No	101	49.5
Yes	103	50.5

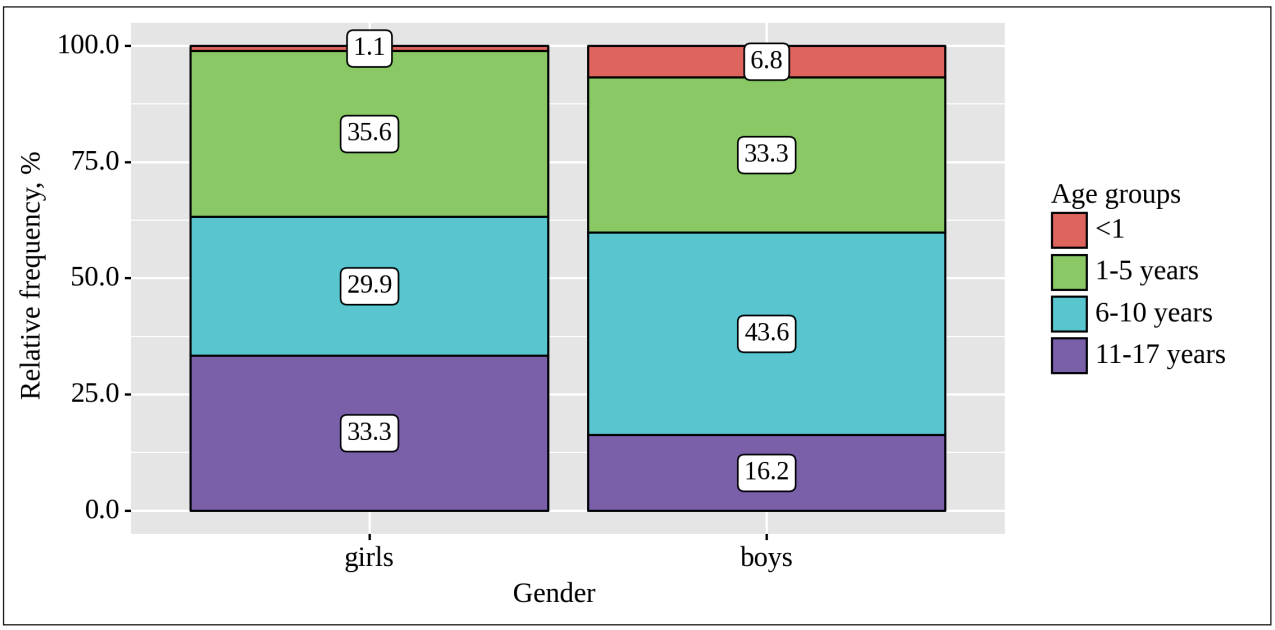

Figure 1. Analysis of age groups according to gender

Comparison of frequencies in the analysis of multifield contingency tables was performed using Pearson's chi-square test (for expected values greater than 10).

Ethical clearance: The study was approved by the Hospital's Research Ethics Committee (Protocol 1102/2021), and was carried out in accordance with the guidelines and the ethical standards set forth in the Declaration of Helsinki in 1964.

Results:

The total number of children admitted to the Pediatric Urology Department during the study period fulfilling the inclusion criteria was 204. Eleven children were excluded from the study as the urine metabolic workup was not done. Out of 204 patients, 117 (57.4%) were males, 87 (42.6%) were females and the male-to-female ratio was 1.34:1(Table1). The age group in our study was dominated by children between 5 and 10 years old. Their median ([IQR]) age was 7.00 (3.00 – 10.00) years.Congenital anomalies of the urinary tract were found in 40 patients (19.6%), and among them ureteropelvic junction stenosis was the most common (5.4%).

Statistically significant differences were revealed when comparing of age groups depending on gender ($p = 0.006$) *(applied method: Pearson's chi-square test)*. According to our data, urolithiasis was more common in adolescent girls, whereas in boys the frequency of observation is higher between 11 and 17 years old (Figure1).

Correlation analysis of the association between BMI and age was performed.

Table 2. Results of the correlation analysis of the association between BMI and age

Variables	Correlation characteristics		
	ρ	Strength of the association assesed using Chaddock scale	p
BMI – Age	0.608	Close	< 0.001*

* – differences are statistically significant ($p < 0.05$)

Observed dependence of age from BMI is described by a linear regression equation:

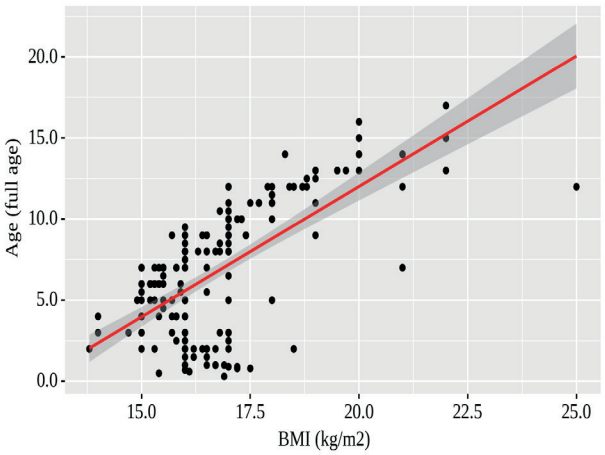

Figure 2. Regression line characterizing the dependence of age from BMI

Table 3. Analysis of BMI according to age groups

Variable	Categories	BMI (kg/m2)			p
		Me	$Q_1 - Q_3$	n	
Age groups	<1	16.90	16.00 – 17.20	9	< 0.001*
	1-5 years	16.00	15.43 – 16.50	70	$p_{11\text{-}17\ years\ –\ <1} = 0.008$
	6-10 years	16.00	15.50 – 17.00	77	$p_{11\text{-}17\ years\ –\ 1\text{-}5\ years} < 0.001$
	11-17 years	18.75	18.00 – 20.00	48	$p_{11\text{-}17\ years\ –\ 6\text{-}10\ years} < 0.001$

* – differences are statistically significant ($p < 0.05$)

$$Y_{Age} = 1.609 \times X_{BMI} - 20.164$$

With a 1 kg/m2 increase of BMI 1.609 full age change of age should be expected. According to the coefficient of determination R^2 of the resulting model, 46.2% of the observed variance of age were explained.

We performed analysis of BMI according to age groups (Table 3).

According to the presented table, when comparing of BMI, statistically significant differences were revealed depending on age groups ($p < 0.001$) *(applied method: The Kruskal-Wallis test)*.

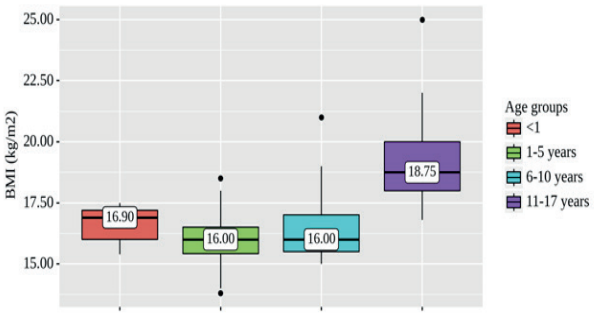

Figure 3. Analysis of BMI according to age groups

As per district wise distribution, maximum patients 53 (26%) belonged to Almaty city and Almaty region and 51 (25%) Turkistan region (Figure4). The incidence of urolithiasis in the southern regions of the country is due to the hot climate.

There was a positive family history record for urolithiasis in only 81 (39.7%) records of patients (Table1). Renal colic, urinary tract infection and macroscopic hematuria were the most common clinical manifestations prior to diagnosis (Table 1).

We performed analysis of age according to clinical manifestations (Figure5).Statistically significant differences were revealed when comparing of age depending on clinical manifestations ($p < 0.001$) *(applied method: The Kruskal-Wallis test)*.

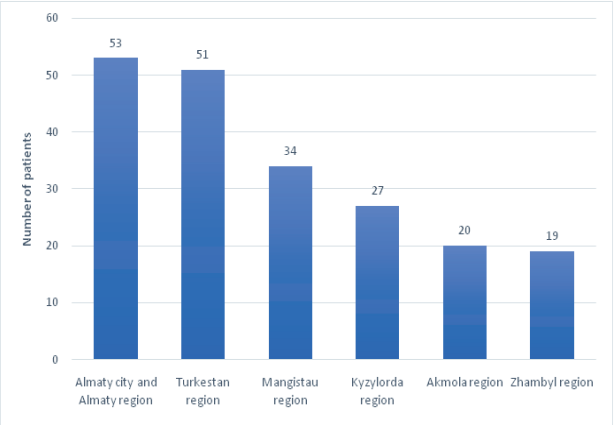

Figure 4. Frequency of hospital admissions by region

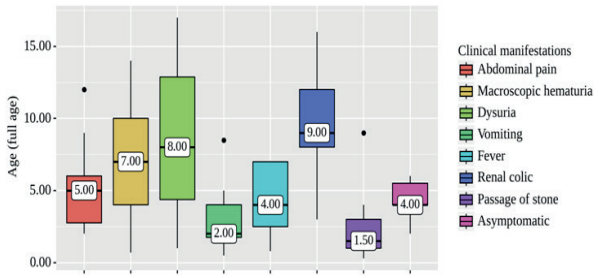

Figure 5. Analysis of age according to clinical manifestations

Urinary tract infection was diagnosed in 185 patients (90.6%) during the follow-up period. The most common pathogens were Esherichia coli (27.6%), Enterococcus faecalis (18.6%), combinations of two or more pathogen agents (16.7%).When comparing of characteristics of the pathogen spectrum of urinary tract infections depending on gender no statistically significant differences were revealed ($p = 0.230$).

The 24-hour urine metabolic evaluation in children with urolithiasis is shown in Table 4. Only 71(35%) children underwent 24-hour urine metabolic evaluation and all of them had at least one metabolic

abnormality. In the present study, 25 (12.3%) patients had hyperoxaluria (Table4).

Table 4. Metabolic disorders in the 24-hour urine urinary analysis of patients with urolithiasis*

Metabolic disorder	n	%
Hypercalciuria	18	8.8
Hyperoxaluria	25	12.3
Hypocitraturia	9	4.4
Hyperuricosuria	14	6.9
Hypercalciuria+ Hypocitraturia + Hyperuricosuria	5	2.5

*Total of the sample: n=71.

We analyzed metabolic disorders according to age groups (Figure6). According to the data obtained when comparing of metabolic disorders statistically significant differences were revealed depending on age groups (p = 0.015) *(applied method: Pearson's chi-square test)*.

As for the location of the stones, 151 patients (74%) had kidney and 32 (15.7%) ureteral stones (Table 5). The median stone size in kidney was 15,7 (10.00 – 20.20) mm, secondary hydronephrosis was found in 103 patients (50.5%). The most type of renal pelvis was intrarenal 135 (67.8%).

Table 5. Location, type of renal pelvis in children with urolithiasis*

Characteristics	n	%
Location		
Kidney	*151*	*74*
Right	110	53.9
Left	79	38.7
Bilateral	15	7.4
Ureter	*32*	*15.7*
Bladder	*7*	*3.4*
Kidney + Ureter	*14*	*6.9*
Type of renal pelvis		
Intrarenal	135	66.2
Extrarenal	30	14.7
Combined	39	19.1

*Total of the sample: n=204.

Stone analysis was performed in 138 patients (67.6%): 41.7% was calcium oxalate, 8.3%struvite stones, and only 9.8%were combined stones (Table6).

Table 6. Stone composition*

Characteristics	n	%
CaOx	85	41.7
CaP	10	4.9
Urates	6	2.9
Struvite stones	17	8.3
Combined stones	20	9.8

*Total of the sample: n=138.

Treatment management used in the children with urolithiasisare presented in Table 7.

Table 7. Treatment management in children with urolithiasis (n:204)

Treatment	n	%
Conservative	46	22.5
Stenting	25	12.2
Ureteroscopic removal of the stone	11	5.4
Laparoscopic ureterolithotomy	3	1.5
Laparoscopic nephrectomy	4	2.0
Pyelolithotomy	51	25.0
Nephrolithotomy	7	3.4
Ureterocalycoplasty	2	1.0
Pyeloureterolithotomy	13	6.4
Cystolithotomy	7	3.4
Others	35	17.2

In 46 patients, the stones were evacuated with conservative treatment. The smallest size of stone surgically removed in children with urolithiasis was 8 mm, and it was a ureteric calculus removed by an ureteroscopic method. The largest size of stone surgically removed was 55 mm, and it was removed by cystolithotomy from the bladder (Table7).

Discussion:

This study presented the clinical and diagnostic profile, treatment of pediatric urolithiasis in our country. The problem of urolithiasis is widespread not only in adults but also in children, with an increasing prevalence in both age groups.[7]In our study, it is the ratio of men to women was 1.34:1, which is equal according to the world literature.[16] However, according to last studies no gender and age differences in recent decades.[8] Some studies in the pediatric population that have shown an increasing incidence of female nephrolithiasis over the last two decades.[9,10]It is important to note that the majority of recurrent stone formers were female.[11]

In the present study, a positive family history of urolithiasis was found in 81 (39.7%) patients. This result equal with study of Issler N.and her group.[12]According to Amancio et al. a family history of urolithiasis was found in 85% of children.[13]

Urolithiasis occurs in children of all ages.[14]In our

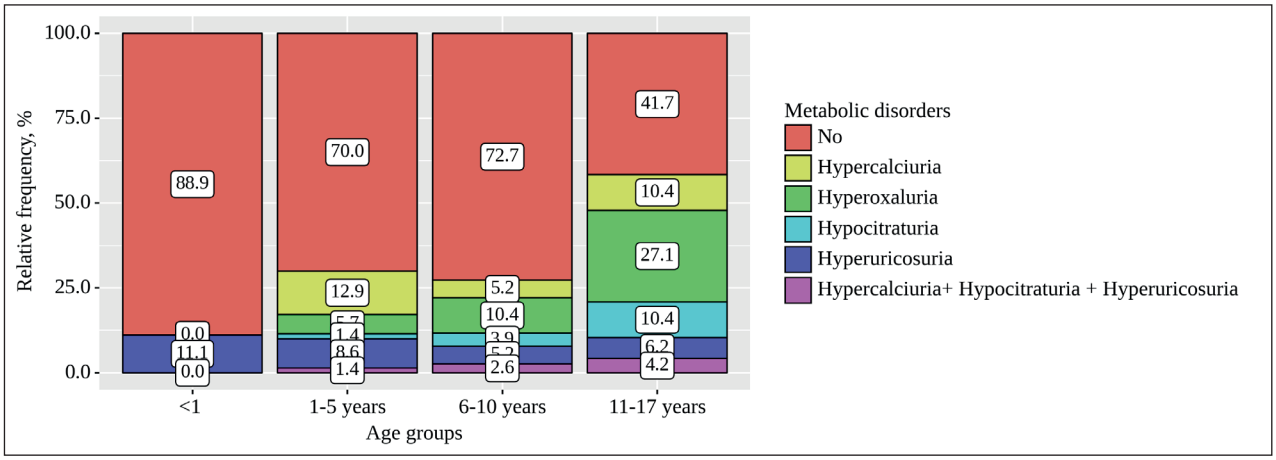

Figure 6. Analysis of metabolic disorders according to age groups

study, the median (IQR) age of symptoms onset of the 204 patients was 7 (3.00 – 10.00) years. This is similar compared to other studies.[15,16]According to our study, when comparing of BMI, statistically significant differences were revealed depending on age groups ($p < 0.001$).

According to our data, congenital anomalies of the urinary tract were found in 40 patients (19.6%), of which ureteral pelvic junction stenosis was the most common (5.4%).

It is remarkable that this is the first study which illustrates the distribution of urolithiasis by regions. Due to the environmental and climatic factors, the majority of the patients (51%) came from the south. (Figure 4).

Clinical symptoms depending on the age and location of the stones, according to our data in children withurolithiasis up to one year old (<1) the common presenting symptoms were passage of stone (44.4%), vomiting (33.3%), fever (11.1%) and macroscopic haematuria (11.1%). In children with age category 1-5 years,urolithiasis had the most clinical signs as passage of stone (20%), vomiting (21.4%),abdominal pain (17.1%), asymptomatic (5.7%). In older children, the predominant symptoms were such as classic renal colic and dysuria (Figure5). These results are similar to those of the world literature.[17]

Urinary tract infections deserve special attention, in the current study we showed that 90.6% of patients had urinary tract infections and it can be etiological factor of urolithiasis.According to available literature, urinary tract infections in children ranged 8-70%.[13,18,19]

Congenital anomalies of the urinary tractwere found in 40 patients (19.6%). We noted that among of anatomical abnormalities the ureteropelvic junction stenosis was the most common (6.8%). A similar result was presented byother authors.[13,20]

In our study, only 35% of children with urolithiasis had metabolic abnormalities. According to other studies metabolic disordersranged in 33-93% of children with urinary calculi.[21,22]Hyperoxaluria and hypercalciuria were the the most common metabolic disorders found in our study.These results are identical to other authors' studies.[20,23]In this study, the following metabolic disorders prevailed by age group: hyperuricosuria in 11.1% of infants, hypercalciuria in 12.9% of children 1-5 years old and hyperoxaluria in 27.1% of school-age children with urolithiasis (Figure6).

In the present study, 74% of urinary calculi were located in the kidney and 53.9 % the calculus was on right side. Stone location in the upper urinary tractis similar to the findings of other studies.[23]However, the location of the stones in kidney varies according to the side, for instance, in other literature the left side was more frequently located than the right side.[12]

According to our study type of stone 41.7% was calcium oxalate and this composition of stone most frequently reported in the world literature between 40-65% .[13,17,23]

In our data, it is known that approximately 90% of the cases had an infectious etiology, so conservative therapy consisted of elimination of the bacteria. In 35% of cases there was a metabolic disorder and appropriate therapy was prescribed. In the remaining cases, surgical treatment was used (Table7).

Study limitations

The primary restriction of this studyis retrospective

design. Urinary citrate is not measured on a daily basis. Therefore, our study cannot reflect the actual number of patients with hypocitrateuria. No genetic studies have been conducted. Cases of stone recurrence are not listed. This is probably due to the difficulty of moving to a hospital in the host city, as most of the patients come from remote areas of our country. Despite the limitations of our study, the data obtained will help primary care physicians tackle pediatric urolithiasis.

Conclusion:

In conclusion, this study presented the prevalence of urolithiasis in the pediatric population in different regions of our country. In the current study, we identified a high prevalence of infective stone as an etiological factor of pediatric urolithiasis. In the metabolic disorders, hyperoxaluria remains the most frequently found.Clinical symptoms depending on the age and location of the stones.Furthermore, all pediatric patients presenting abdominal pain, therefore they should always be investigated for the possibility of urinary stone disease. As is known, urolithiasis is a multifactorial, polyetiologic disease. It is necessary, in the management of this disease, the approach should be multidisciplinary, patient management should be individual.

Funding. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest. The authors declare no conflicts of interest.

Authors'contribution:

Data gathering and idea owner of this study: AS;
Study design: AS;
Data gathering: AS;
Writing and submitting manuscript: AS;
Editing and approval of final draft: AS.

References:

1. Skolarikos A, Straub M, Knoll T, et al. Metabolic evaluation and recurrence prevention for urinary stone patients: *EAU guidelines* 2015;**67**:750-763.
2. Xu LHR, Adams-Huet B, Poindexter JR, et al. Temporal Changes in Kidney Stone Composition and in Risk Factors Predisposing to Stone Formation. *J. Urol.* 2017;197:1465-1471. https://doi.org/10.1016/j.juro.2017.01.057
1. Noori N, Honarkar E, Goldfarb DS, et. al. Urinary lithogenic risk profile in recurrent stone formers with hyperoxaluria: a randomized controlled trial comparing DASH (Dietary Approaches to Stop Hypertension)-style and low-oxalate diets. *Am. J. Kidney Dis.* 2014;63:456-463. https://doi.org/10.1053/j.ajkd.2013.11.022
2. Simon I, Roumeguère T, Devuyst F,et al.Recurrent episodes of brushite nephrolithiasis revealing primary hyperparathyroidism. *Rev. Med. Brux.* 2015;**36**:172-176.

3. Parvin M, Shakhssalim N, Basiri A, et al. The most important metabolic risk factors in recurrent urinary stone formers. *Urol. J.* 2011;**8**:99-106.
4. Pietrow PK, Pope JC 4th., Adams MC, et al. Clinical outcome of pediatric stone disease. J Urol 2002;167:670–673.https://doi.org/10.1097/00005392-200202000-00060
5. Penido MGMG, Srivastava T, Alon US. Pediatric primary urolithiasis: 12-year experience at aMidwestern Children's Hospital. *J Urol* 2013;**189**:1493-1497https://doi.org/10.1016/j.juro.2012.11.107
6. PearleMS,GoldfarbDS,AssimosDG, et al. Medical management of kidney stones: AUA guideline.*Journal of Urology* 2014;**192**(2):316-324. https://doi.org/10.1016/j.juro.2014.05.006
7. Sas DJ, Hulsey TC, Shatat IF, et al. Increasing Incidence of Kidney Stones in Children Evaluated in the Emergency Department. *J Pediatr* 2010;**157**:132-7. https://doi.org/10.1016/j.jpeds.2010.02.004
8. 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.https://doi.org/10.1016/j.juro.2012.03.021
9. Li Y, Bayne D, Wiener S, et al. Stone formation in patients less than 20 years of age is associated with higher rates of stone recurrence: Results from the Registry for Stones of the Kidney and Ureter (ReSKU). *J Pediatr Urol.* 2020 Jun;**16**(3):373.e1-373.e6. https://doi.org/10.1016/j.jpurol.2020.03.014
10. Issler N, Dufek S, Kleta R, et al. Epidemiology of paediatric renal stone disease: a 22-year single centre experience in the UK. *BMC Nephrol.* 2017 Apr 18;**18**(1):136.https://doi.org/10.1186/s12882-017-0505-x
11. Amancio L, Fedrizzi M, Bresolin NL, et al. Pediatric urolithiasis: experience at a tertiary care pediatric hospital. *J Bras Nefrol.* 2016Mar;**38**(1):90-8.https://doi.org/10.5935/0101-2800.20160014
12. Penido MG, Tavares Mde S. Pediatric primary urolithiasis: Symptoms, medical management and prevention strategies. *World J Nephrol.* 2015; **4**(4):444-454.https://doi.org/10.5527/wjn.v4.i4.444
13. Robinson C, Shenoy M, Hennayake S. No stone unturned: The epidemiology and outcomes of paediatricurolithiasis in Manchester, United Kingdom. *J Pediatr Urol.* 2020 Jun;**16**(3):372.e1-372.e7. https://doi.org/10.1016/j.jpurol.2020.03.009
14. Rauturier C, Machon C, Demède D, et al. Composition of urinary stones in children: clinical and metabolic determinants in a French tertiary care center. *Eur J Pediatr.* 2021;**180**(12):3555-3563.https://doi.org/10.1007/s00431-021-04151-7
15. Copelovitch L. Urolithiasis in children: medical approach. *PediatrClin North Am.* 2012 Aug;**59**(4):881-96. https://doi.org/10.1016/j.pcl.2012.05.009
16. Erbagci A, Erbagci AB, Yilmaz M, et al. Pediatric urolithiasis--evaluation of risk factors in 95 children. Scand J UrolNephrol 2003;**37**:129-33.https://doi.org/10.1080/00365590310008866
17. Sarica K, Erturhan S, Yurtseven C, et al. Effect of potassium citrate therapy on stone recurrence and regrowth after extracorporeal shockwave lithotripsy in children. *J Endourol* 2006;**20**:875-9. https://doi.org/10.1089/end.2006.20.875
3. SafaeiAsl A, Maleknejad S. Pediatric urolithiasis: an experience of a single center. *Iran J Kidney Dis* 2011;5:309-13.
18. Rellum DM, Feitz WF, van Herwaarden AE, et al. Pediatric urolithiasis in a non-endemic country: a single center experience from The Netherlands. *Journal of Pediatric Urology* 2014;**10**(1):155-61. https://doi.org/10.1016/j.jpurol.2013.07.019
19. Alemzadeh-Ansari MH, Valavi E, Ahmadzadeh A. Predisposing factors for infantile urinary calculus in south-west of Iran. *Iranian Journal of Kidney Diseases* 2014; **8**(1):53-7. PMID: 24413722.
20. Milosevic D, Batinic D, Turudic D, Batinic D, Topalovic-Grkovic M, Gradiski IP. Demographic characteristics and metabolic risk factors in Croatian children with urolithiasis. *European Journal of Pediatrics* 2014;**173**(3):353-9. https://doi.org/10.1007/s00431-013-2165-6