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Pediatric urolithiasis in a non-endemic country: A single center experience from The Netherlands

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Abstract *Objective:* To provide insight in causative factors of pediatric urolithiasis in The Netherlands, a non-endemic country.
Patients and methods: Data from 71 children with urolithiasis and stone analyses between 1996 and 2010 in the Radboud University Nijmegen Medical Centre were studied retrospectively. Patients (48 boys, 23 girls, ratio 2.1:1) were aged 0.5—18.3 years (mean 8.8, SD 5.6). All stone analyses were performed with FTIR spectroscopy.
Results: Of the 49 patients with metabolic analysis, 78% showed one ($n = 15$) or more ($n = 23$) metabolic abnormalities. Forty-seven percent had hypercalciuria ($n = 23$), 31% had hyperoxaluria ($n = 15$), 29% hypocitraturia ($n = 14$), 10% hyperuricosuria ($n = 5$), 10% cystinuria ($n = 5$), and 6% had hypomagnesiuria ($n = 3$).

Sixty-one percent of the stones were composed of calcium phosphate, calcium oxalate, or a combination of those. Twenty-six percent consisted of pure or mixed magnesium ammonium phosphate, 8.3% pure or mixed urate, and 8.3% cystine.
Conclusion: Children with urolithiasis in The Netherlands show stone composition similar to other Western European countries. However, a high percentage of metabolic abnormalities (78%) was found, indicating the need for extensive evaluation of pediatric urolithiasis to find underlying

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causes and thereby prevent stone recurrences. A close collaboration between a pediatric nephrologist and urologist is mandatory for optimal surgical and medical treatment.

Introduction

Pediatric urolithiasis is a serious disease for the children, parents, and doctors involved because it can cause permanent kidney damage and it has a high recurrence rate. The lifetime chance of an individual having a kidney- or bladder-stone is approximately 10–15% with a nearly 60% chance of recurrence within 10 years if not treated [1]. Although usually diagnosed between the third and fourth decade of life, urolithiasis can present at all ages, including childhood.

Several studies have shown an increase in incidence and prevalence of pediatric urolithiasis over the past decades. In 2007 Vandervoort et al. described a 4.6-fold increase in admittance in New York of children with urolithiasis, comparing data from 1994 to 1996 with 2003–2005 [2]. A recent study in the United States by Routh et al. [3] described a threefold increase in pediatric urolithiasis from 18.4 per 100,000 in 1999 to 57.0 per 100,000 in 2008. Annual incidences have been reported varying from 1.8 per 100,000 children per year in Kuwait 1996–2000 [4], 6.3 per 100,000 children under 16 years of age in an Icelandic study in 1995–2000 [5], up to a prevalence of 17% in patients under 14 years of age in endemic areas like Turkey, Tunisia, and the Far East [6].

Metabolic disorders, anatomical abnormalities, urinary tract infections (UTIs), intoxications (China), and dietary and climatic factors all contribute to the risk of developing kidney stones. Koyuncu et al. [7] found that, despite conservative measures, the risk of recurrence increases threefold if at least one metabolic abnormality is present. During metabolic evaluation in children with urolithiasis, 76% of patients showed at least one abnormality in the 24-hour urine collection as an explanation for the urolithiasis [2].

This illustrates the importance of proper management protocols to optimize treatment, reduce the recurrence risk and improve outcome. Because of the large geographic variation in incidence and etiologic factors, region-specific data are needed to develop adequate management protocols. Although much research has been done on etiologic factors, there is a paucity of published data from West European countries. This study was designed to provide insight in etiologic factors of pediatric urolithiasis in The Netherlands, and compare these data with other regions.

Patients and methods

Clinical evaluation studies

This study was performed at the Radboud University Nijmegen Medical Centre, a referral center for pediatric urolithiasis for the eastern parts of The Netherlands. We included all patients aged 0–19 years with a stone analysis between 1996 and 2010 according to the laboratory database. The year 1996 was selected for the start of inclusion, as the current stone analysis spectrophotometer has been in use since then. In addition, we included all children who were diagnosed with urolithiasis in this period according to the electronic patients charts system of our Medical Centre.

In total, 71 children were identified and their charts were studied retrospectively. Some of these patients were initially evaluated and/or treated elsewhere but eventually transferred to our Medical Centre for further investigation, treatment, and/or follow-up. Patients with urolithiasis were evaluated according to a standard protocol, which has been adjusted to up-to-date standards over the past 14 years. When the cause of urolithiasis was established before completing the analysis, further investigation was discontinued.

Complete evaluation included a full history, physical examination, two 24-hour urine collections, two separate urinalyses of freshly voided urine, blood chemistry studies, and, when available, stone analysis.

In the 24-hour urine collections, excretions of sodium, potassium, calcium, phosphate, magnesium, citrate, uric acid, creatinine, oxalate, amino acids, purines and pyrimidines were determined. The absolute excretion rate was considered as the most reliable marker to evaluate whether values were abnormal. If this excretion rate was not available, solute/creatinine ratios were used. In patients with hypercalciuria, the urine sodium excretion was measured as a marker of daily sodium intake [8]. Reference values used were adapted from previous publications [9–12].

All stone analyses were performed with Fourier transform infrared spectroscopy. Stones were divided in categories, based on the composition: 100% calcium oxalate, 100% calcium phosphate, mixed calcium oxalate and calcium phosphate, magnesium ammonium phosphate (pure + mixed), urate (pure + mixed), and cystine. Stones containing at least partly magnesium ammonium phosphate were accounted into that category because of the likeliness that a UTI was a causative factor in the urolithiasis. If urate was a stone compound, the stone was attributed to the urate category. Urate- and magnesium ammonium phosphate-containing stones could therefore be arranged in two categories, making the total percentage of stone analyses over a hundred percent. Stones were available for analysis in 67 of the 71 patients and 24 patients had more than 1 stone analyzed. If stones were of comparable composition (classified in the same stone category, Table 1), only the first stone analyzed was used in this study. Three patients had stones in two different categories, and one patient had stones in three different categories, resulting in a total of 72 stones. As these stones may have been caused by different underlying factors, they were all taken into account. Stone locations were divided in the following categories: kidney, ureter (combined as upper

urinary tract) and bladder or urethra (combined as lower urinary tract).

We reviewed the medical records for available clinical data including sex, race, age at diagnosis, history of UTIs, presence of anatomical abnormalities of the urinary tract, surgical treatment(s), co-morbidity, and drug use. None of the children studied were using medication affecting the mineral metabolism (such as corticosteroids, diuretics, or anticonvulsants) at time of diagnosis. Anatomical abnormalities were evaluated with imaging techniques like radiographic imaging, ultrasonography, computed tomography, micturating cystourethrography, renography (MAG3 and/or DMSA), and/or intravenous pyelography.

Literature comparison

To relate the results of our study with published data from different regions, a literature search was performed using Pubmed (1990–2012). Search terms used were pediatric/paediatric, child, urolithiasis, kidney stone, epidemiology, etiology, metabolic, risk factor, and stone analysis. Results were screened for relevance by title and/or abstract. In addition, related citations from appropriate publications were studied as well. As no attempt was made to perform a full review of the literature, but just to present a comparison with several regions, no other search engines were used. When several publications presented data from a similar region, either the largest or the most current description was included.

Statistical analysis

Comparison of two proportions of categorical data was done by the chi-square test. Pearson's correlation between urinary sodium and calcium excretion was carried out using SPSS 16.0.2 (SPSS Inc., Chicago, IL). A p-value below 0.05 was considered statistically significant.

Ethical approval

As this study was a retrospective analysis of data that was anonymized, no ethical approval was required.

Results

Clinical features

In this study, 71 children were included (48 males, male: female ratio 2.1:1) with a mean age of 8.8 years (range 0.5–18.3 years, SD 5.6). A positive family history for urolithiasis in first- or second-degree family members was reported in 28.2% of the patients. Of nine patients, one or both parents were from outside The Netherlands. Three originated from Turkey, and one each from Germany, Rumania, Somalia, Finland, Greece, and Aruba.

Thirty percent of the patients ($n = 21$) had a history of recurrent UTIs before urolithiasis was diagnosed. Twenty-five patients (35%) had one or more anatomical abnormalities of the kidney or urinary tract. Prevalent were pelvi–ureteric junction obstruction ($n = 7$), neurogenic bladder ($n = 5$), extrophia vesicae ($n = 4$), vesicoureteral reflux ($n = 3$), (partial) nephrectomy ($n = 3$), horseshoe kidney ($n = 2$), and urethral valves ($n = 1$).

Stone localization and analysis

Four patients had spontaneous passage of a stone before diagnostic imaging was performed. The 67 remaining patients together had 105 stone locations: 85% of the stones were present in the upper urinary tract (52% kidney and 33% ureter) and 15% were present in the lower urinary tract. There was no significant difference in lateralization of the stones. Stone composition of the 71 stones from 67 patients is presented in Table 1.

Metabolic analysis

For 49 of the 71 patients, complete metabolic analysis was available including at least one 24-hour urine and blood chemistry study. Of these patients, 39 had one ($n = 15$) or more metabolic abnormality (Table 2). Twenty-three of the 49 patients had hypercalciuria (47%), of whom 12 with an increased sodium excretion. As expected, a positive association between urinary calcium- and sodium-excretion was found ($r = 0.504$, $p < 0.001$, Fig. 1). Fifteen patients had hyperoxaluria (31%), fourteen showed hypocitraturia (29%), five cystinuria (10%), five hyperuricosuria (10%), and three showed hypomagnesiuria (6%). Fig. 2 illustrates the potential extensive stone burden in a 6-year-old patient with cystinuria.

Metabolic abnormalities and stone composition

A total of 44 patients (66%) had 44 stones consisting of calcium phosphate, calcium oxalate or a combination of those. For 31 of these patients a metabolic evaluation was available; 27 patients had one or more metabolic abnormalities (87%). Hypercalciuria was most prevalent (17/31 patients, 55%). More than half ($n = 9$) of those patients also had a high sodium intake. Other abnormalities found were hyperoxaluria in 12/31 patients (39%), hypocitraturia in 10/31 patients (32%), hyperuricosuria in four out of 31 patients (12.9%), and hypomagnesiuria two out of 31 patients (6.5%).

Eighteen patients had stones composed of pure or mixed magnesium ammonium phosphate. Again, hypercalciuria

Table 1 Composition of urinary tract stones in children.

Urinary tract stones	n (%)
Calcium oxalate	15 (20%)
Calcium phosphate	12 (16%)
Calcium oxalate + calcium phosphate	17 (23%)
Magnesium ammonium phosphate (pure + mixed)	19 (25%)
Urate (pure + mixed)	6 (8%)
Cystine	6 (8%)
Total	75[a]

[a] The total number of stones is more than 71 as some stones are arranged in more than one category.

Table 2 Metabolic abnormalities found in children with urolithiasis.

Country	Authors	Period	*n*=	Age (yrs)	No. of metabolic analyses	Met.# (%)	↑Ca (%)	↓Ci (%)	↓Mg (%)	↑P (%)	↑Ur (%)	↑Ox (%)	↑Cys (%)	NOS (%)	Total (%)
Pakistan	Rizvi et al. [14]	1987–2000	1440	0–14	154/1440	93	11	63	51		27	40			192
Argentina	Spivacow et al. [6]	1994–2000	90	0–16	90/90	84	40	38	16		12	9	3		118
Iceland	Edvardsson et al. [5]	1995–2000	26	0–15	23/26	96	78	13			4	13			108
UK	Coward et al. [15]	1997–2001	121	0–15	121/121	44	57				2	17	23	2	100
Turkey	Alpay et al. [13]	1998–2008	162	0–16	162/162	87	34	33		21	25	27	6		145
Nether–lands	Current study	1996–2010	71	0–19	49/71	84	45	25	6		8	29	8		121

Met.#, Metabolic abnormalities found; ↑Ca, Hypercalciuria; ↓Ci, Hypocitraturia; ↓Mg, Hypomagnesiuria; ↑P, Hyperphosphaturia; ↑Ur, Hyperuricosuria; ↑Ox, Hyperoxaluria; ↑Cys, Cystinuria. NOS, Not otherwise specified.

was the most prevalent metabolic abnormality present in four out of 18 patients (22.2%), with a high sodium intake in one patient (5.6%). In addition, hypocitraturia was found in two patients (11.1%), hyperoxaluria in two patients (11.1%), and hypomagnesiuria in one patient (5.6%).

Six patients had pure or mixed urate stones. Three of them had metabolic analyses. Abnormalities found were hypercalciuria combined with hypernatriuria in one patient, and hypocitraturia combined with hyperuricosuria in the other.

Pure cystine stones were present in six patients: five of them had a metabolic analysis. As expected, all five had cystinuria. One patient showed multiple metabolic abnormalities besides cystinuria: hypercalciuria, hypernatriuria, hypocitraturia, and hyperoxaluria. The data on metabolic disturbances associated with urolithiasis are summarized in Table 2.

Urological treatment

Seventy-nine percent ($n = 56$) of the patients underwent urological treatment in order to remove the stones, of which 28 had multiple types of treatment. Fifty-seven percent ($n = 32$) underwent extracorporal shock wave lithotripsy, with a mean of 2.4 (SD 1.5) sessions per patient. Thirty-eight percent ($n = 21$) had ureterorenoscopy and/or urethrocystoscopy. Surgical treatment was indicated due to stone size or type and performed in 61% ($n = 34$) of the patients.

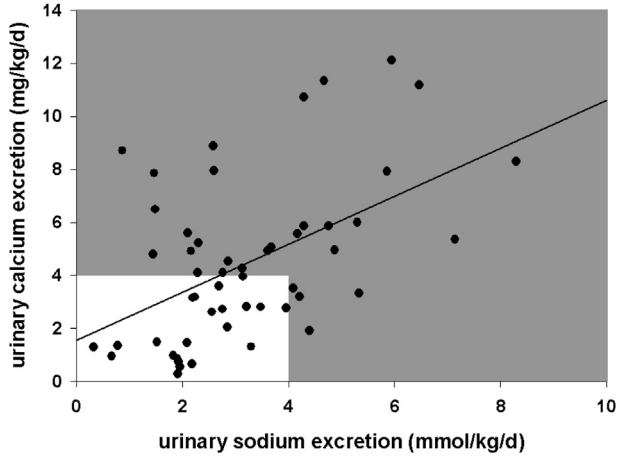

Figure 1 Correlation between the urinary sodium excretion and calcium excretion.

Medical treatment

To prevent recurrence of urolithiasis, some patients were treated with drugs such as potassium citrate (15/71), hydrochlorothiazide (11/71), prophylactic antibiotics (7/71), tiopronin (3/71), sodium bicarbonate (2/71), and pyridoxine (1/71).

Follow-up

The mean duration of follow-up was 117 (SD 108) months. At the end of the study period 6% of the patients were still suffering from urolithiasis, despite extensive treatment. During the follow up period 30% ($n = 21$) of the patients had stone recurrence(s).

Literature comparison

We compared our data with results from previously published cohorts from other regions (Table 2) [5,6,13–15]. Table 3 shows the stone composition of high endemic areas compared with those from low endemic areas, such as the UK and The Netherlands [15–17]. Table 4 shows regional differences in stone localization [15–17].

Discussion

In our European single-center study in The Netherlands, data on 71 children with urolithiasis were available to provide insight into the (metabolic) causes of pediatric urolithiasis in our region.

According to the stone composition, The Netherlands seems to be comparable to the UK (Table 3). In the United

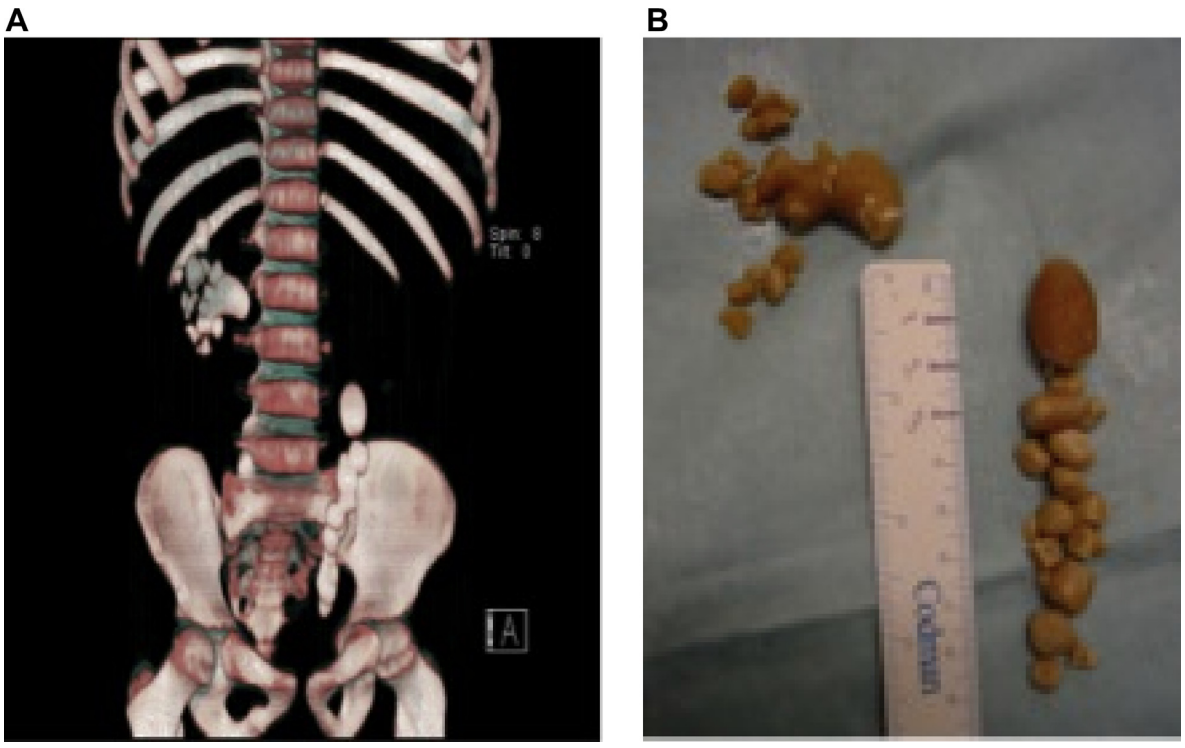

Figure 2 Example of a 6-year-old girl with a high cystine stone load. Patient with bilateral cystine stones (A). First treatment session with ureterorenoscopy, double JJ catheter placement for drainage on the left side and stone material collection for analysis. Second urological procedure with open lumbotomy, pyelotomy, pyeloscopy with stone removal, open ureterotomy with ureteroscopy and stone removal (B).

States, childhood stone composition has been described to consist mainly of calcium oxalate and/or calcium phosphate (45–65% and 14–30%). uric acid, struvite, and cystine stones account for 5–10% [18,19].

We found that 59% of the urinary tract stones consisted of calcium oxalate and/or calcium phosphate stones, comparable with the UK (50%), as is the quantity of magnesium ammonium phosphate stones (25% in our study vs. 29% in the UK) [15]. In high endemic areas like Tunisia and Turkey it is noticeable that calcium oxalate and phosphate stones account for 77–86% of all stones, and magnesium ammonium phosphate stones only for 8–12% [16,17]. As may be expected, causes of urolithiasis in The Netherlands are of comparable distribution with those found in the UK, and have a different distribution from those in the Middle East.

Although stone composition is often a good indicator of the underlying cause of the urolithiasis, we found a different prevalence and distribution of metabolic abnormalities in our study than Coward et al. [15] did in the UK. As can be seen in Table 3, metabolic abnormalities were found in 84% of our patients that were analyzed. In the UK 44% [15] were found to have an abnormality, in Iceland 96% [5] and in endemic areas around 90% [16,17]. Although differences appear to be large, comparing results is difficult because not all children from the listed studies underwent a metabolic evaluation. In our study for example, some children did not undergo an extensive metabolic evaluation if the cause was considered to be clear by stone composition and clinic. Therefore, there might have been a negative selection in our patient group.

Table 3 Stone composition.

Country	Authors	Period	$n=$	Age (yrs)	No. of stone analyses	CaOx/Ca PO_4 (%)	$MgNH_4$ PO_4 (%)	Urate (%)	Cystine (%)	Other (%)	Total (%)
UK	Coward et al. [15]	1997–2001	121	0–15	67	50	29		3	18	100
Tunisia	Jallouli et al. [16]	1990–2004	525	0–17	120	77	12	5	3	4	100
Turkey	Bak et al. [17]	1999–2005	72	0–14	65	86	8	1.5	3	1.5	100
The Netherlands	Current study	1996–2010	71	0–19	75	59	25	8	8		100

Table 4 Stone localization.

Country	Authors	Period	*n*	Age (yrs)	Upper urinary tract (%)	Lower urinary tract (%)	Upper + lower urinary tract (%)
UK	Coward et al. [15]	1997–2001	121	0–15	90	4	6
Tunisia	Jallouli et al. [16]	1990–2004	525	0–17	80	20	
Turkey	Bak et al. [17]	1999–2005	72	0–14	78	18	4
The Netherlands	Current study	1996–2010	71	0–19	76	12	12

Worldwide, hypercalciuria is seen as the most prevalent risk factor in the formation of calcium oxalate stones. In contrast, Tekin et al. [20] stated that in their study group only hypocitraturia distinguished idiopathic calcium stone formers from normal children. Hypercalciuria was most prevalent in all studies listed in Table 3, except in the study results from Spivacow et al. [6] from Argentina, where hypocitraturia was the most prevalent [5,13–15].

Almost a third of the patients in our cohort (31%) had a history of recurrent UTIs before urolithiasis was diagnosed. Typical infection stones are composed of struvite (magnesium ammonium phosphate), which was found in a quarter of all patients. The combination of UTI and struvite stones was present in 10 patients (14%). However, most of the time it remains unclear whether the urolithiasis is preceded and thereby caused by a UTI or vice versa.

We found a male–female ratio of approximately 2:1, which corresponds with data from Kuwait and the UK [4,15]. Even though there is a large variation in male–female ratios (ranging from 0.6:1 in the United States to 2.95:1 in Pakistan), most studies show that boys are more likely to develop urolithiasis [2,4,6,7,14–17,21–23]. The male predominance may be partly explained by boys having more anatomical abnormalities of the urinary tract, such as urethral valves. Indeed, out of the 25 patients in our study with anatomical abnormalities, 17 were boys. Nine of them had metabolic analyses, and all were found to have one or more metabolic abnormalities as well.

Of the 67 patients with known stone locations, 16 (24%) had bladder stones. Half ($n = 8$) of them also had stones located in the upper urinary tract. Coward et al. [15] found a location in the upper and lower urinary tract of 90% and 4%, respectively, with 6% of the patients having both upper and lower urinary tract stones. Apparently, in comparison to the available information from Europe, our cohort showed a relatively high percentage of lower urinary tract lithiasis. In Turkey and Tunisia similar numbers have been found of about 80% upper and 20% lower urinary tract lithiasis [16,17].

Our study has some limitations. First, even though our data were collected using a standard protocol for testing, our cohort was evaluated retrospectively, which inevitably implicates missing data. In order to minimize the effect of missing data on our results, we considered all missing data to be in the normal range. Second, the standard protocol used to evaluate pediatric urolithiasis was adapted to up-to-date standards twice in the period when the study was performed, becoming more extended. Therefore, not all evaluations were performed according to the same protocol in all patients. Thirdly, with this small number of included patients, statements can be made concerning the more prevalent causes of urolithiasis, but rare and often serious underlying pathology remains under or becomes overexposed.

In conclusion, our study of children with urolithiasis in The Netherlands shows that stone composition is comparable to other Western European countries, as may be expected. However, we found a very high percentage of metabolic abnormalities (78%), which is more similar to high endemic areas. In addition, the prevalence of bladder stones is remarkably high. The differences found indicate the importance of collecting region-specific data. In addition, extensive evaluation of pediatric urolithiasis is essential to find underlying abnormalities and thereby prevent stone recurrences.

Conflict of interest

None.

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References

[1] Resnick MI, Persky L. Summary of the National Institutes of Arthritis, Diabetes, Digestive and Kidney Diseases conference on urolithiasis: state of the art and future research needs. J Urol 1995;153:4–9.

[2] 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.

[3] Routh JC, Graham DA, Nelson CP. Epidemiological trends in pediatric urolithiasis at United States freestanding pediatric hospitals. J Urol 2010;184:1100–4.

[4] Al-Eisa AA, Al-Hunayyan A, Gupta R. Pediatric urolithiasis in Kuwait. Int Urol Nephrol 2002;33:3–6.

[5] Edvardsson V, Elidottir H, Indridason OS, Palsson R. High incidence of kidney stones in Icelandic children. Pediatr Nephrol 2005;20:940–4.

[6] Spivacow FR, Negri AL, del Valle EE, Calvino I, Fradinger E, Zanchetta JR. Metabolic risk factors in children with kidney stone disease. Pediatr Nephrol 2008;23:1129—33.
[7] 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.
[8] Schreuder MF, Navis GJ, Nauta J. Minder zout op de kinderleeftijd: jong geleerd is oud gedaan. Ned Tijdschr Geneeskd 2009;153:B140.
[9] Avner ED. Pediatric nephrology. 6th ed. Berlin: Springer; 2009.
[10] Matos V, van Melle G, Boulat O, Markert M, Bachmann C, Guignard JP. Urinary phosphate/creatinine, calcium/creatinine, and magnesium/creatinine ratios in a healthy pediatric population. J Pediatr 1997;131:252—7.
[11] Matos V, Van Melle G, Werner D, Bardy D, Guignard JP. Urinary oxalate and urate to creatinine ratios in a healthy pediatric population. Am J Kidney Dis 1999;34:e1.
[12] Hoppe B, Kemper MJ. Diagnostic examination of the child with urolithiasis or nephrocalcinosis. Pediatr Nephrol 2010;25: 403—13.
[13] Alpay H, Ozen A, Gokce I, Biyikli N. Clinical and metabolic features of urolithiasis and microlithiasis in children. Pediatr Nephrol 2009;24:2203—9.
[14] 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.
[15] Coward RJ, Peters CJ, Duffy PG, Corry D, Kellett MJ, Choong S, et al. Epidemiology of paediatric renal stone disease in the UK. Arch Dis Child 2003;88:962—5.
[16] 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.
[17] Bak M, Ural R, Agin H, Serdaroglu E, Calkavur S. The metabolic etiology of urolithiasis in Turkish children. Int Urol Nephrol 2009;41:453—60.
[18] Stapleton FB. Childhood stones. Endocrinol Metab Clin North Am 2002;31:1001—15.
[19] Milliner DS, Murphy ME. Urolithiasis in pediatric patients. Mayo Clin Proc 1993;68:241—8.
[20] Tekin A, Tekgul S, Atsu N, Sahin A, Ozen H, Bakkaloglu M. A study of the etiology of idiopathic calcium urolithiasis in children: hypocitruria is the most important risk factor. J Urol 2000;164:162—5.
[21] Alaya A, Najjar MF, Nouri A. Changes in stone composition according to age in Tunisian pediatric patients. Int Urol Nephrol 2010;42:621—8.
[22] Aggour A, Ziada AM, AbdelHamid AZ, AbdelRahman S, Morsi A. Metabolic stone composition in Egyptian children. J Pediatr Urol 2009;5:132—5.
[23] Ertan P, Tekin G, Oger N, Alkan S, Horasan GD. Metabolic and demographic characteristics of children with urolithiasis in Western Turkey. Urol Res 2011;39:105—10.