Urolithiasis (2017) 45:435–440
DOI 10.1007/s00240-016-0931-4

ORIGINAL PAPER

Difference in urinary stone composition between Uyghur and Han children with urolithiasis

Yang Liu[1] · Anniwaer Yasheng[2] · Kang Chen[1] · Chuangxin Lan[1] · Hamulati Tusong[2] · Lili Ou[1] · Yeping Liang[1] · Hans-Göran Tiselius[3] · Guohua Zeng[1] · Wenqi Wu[1]

Received: 9 August 2016 / Accepted: 8 October 2016 / Published online: 15 October 2016

Abstract The Objective of this study is to analyze the difference in renal stone composition between Uyghur and Han children with urolithiasis in China and possible reasons. From May 2011 to September 2013, we analyzed the stone compositions of 274 Chinese children with urolithiasis, including 151 Uyghur children from Xinjiang Province and 123 Han children from Guangdong Province. All the stone components were determined by Infrared spectroscopy and the main components were recorded. We also evaluated the data, including age, gender and geographic region of the patients. The mean age of Uyghur children was less than Han children (5.3 ± 4.2 vs 8.6 ± 5.7 years, $p < 0.001$). Calcium oxalate (CaOx) was the main stone composition in both Uyghur (35.1 %) and Han (64.2 %) children, but was more common in Han children ($p < 0.0001$). Cystine stone was also more abundant in Han children (8.9 % vs 0.7 %, $p = 0.001$). While, both uric acid (20.5 % vs 3.3 %, $p < 0.0001$) and magnesium ammonium phosphate (16.6 % vs 2.5 %, $p < 0.0001$) stones were more common in Uyghur. Interestingly, the significant differences in stone composition between the two groups were only observed in males. When the pediatric patients were further divided into three age groups which were 0–5, 6–12 and >12, the prevalence of calcium oxalate stones increased with age in both groups and was higher in Han children at each age level. The compositions of urinary stones were significantly different between Uyghur and Han children with urolithiasis, factors such as diet habit, life style, genetic diversity, environmental and medical conditions may all contribute to the variances.

Keywords Ammonium urate · Infrared spectroscopy · Pediatric · Stone composition · Urolithiasis

Introduction

Children with nephrolithiasis are often associated with high recurrence rate and the risk of detrimental long-term effects on kidney function [1–3]. Although urinary stone disease remains less frequent in children than in adults [4], worldwide increase in the prevalence of urolithiasis is also observed in the pediatric population over the past few decades [2, 5–7]. Though in China, numbers of researches on adults urolithiasis have been reported, few studies have focused exclusively on the stone compositions in pediatric population.

As literatures reported, a high percentage of children with nephrolithiasis, ranging from 33 to 93 %, was associated with metabolic abnormalities which may stem from environmental or dietary factors [7]. Identification of stone composition could benefit children by revealing the underlying metabolic risk factors and also help doctors in determining a proper strategy for stone treatment and prevention [8, 9].

The process of stone formation is complicated and could be affected by lots of factors, such as socio-economic

Y. Liu, A. Yasheng and K. Chen contributed equally to this work.

✉ Wenqi Wu
wwqwml@163.com

1 Guangdong Key Laboratory of Urology, Department of Urology, Minimally Invasive Surgery Center, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510230, China

2 Department of Urology, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, China

3 Division of Urology, Department of Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden

conditions, diet habits and environmental conditions [4, 7, 10]. Thus, stone incidence and composition vary markedly within populations between countries and ethnicities [2, 10–12]. According to a recent study reported by Wumaner et al. [11], there were significant differences in stone compositions between Uyghur and Han adult patients in China. Uyghur people, who mainly located in Xinjiang region, is one of the Chinese minorities which have a different religion, culture, diet habit, life style compared to most of the Han people [11]. As reported, pediatric urolithiasis is also an endemic problem in this area [13]. However, no previous studies have been performed to investigate regional differences in the composition of pediatric urinary stones in China.

Hence, in the present study, we analyzed the stone composition of Han and Uyghur pediatric patients in China. By evaluating the features of stones in these two different groups of children, we hope to get a better understanding of the pathogenesis of stone formation in this specific population.

Materials and methods

Ethics statement for collection of stone and urine samples

This study was approved by the Ethics Review Board of Guangzhou Medical University, Guangzhou, China. The written informed consents were obtained from all the participants. Stone samples were obtained from children patients that were collected following the first affiliated Hospital of Guangzhou medical University.

Subjects

From 2011 to 2013, the compositions of stones that received from 274 Chinese children were retrospectively reviewed. Of all the 274 pediatric patients, 151 were Uyghur children from the Uyghur region in Xinjiang and the other 123 were Han children from the Han region in Guangdong. The ages of the children ranged from 0 to 18 years. Stone samples were obtained from spontaneous passage, shockwave lithotripsy, ureteroscopy, percutaneous nephrolithiasis, laparoscopy or open surgery. Any sample in this study without the information of patient's age, gender, or other significant data was excluded.

Methods

Stone composition was analyzed by the method that was described previously [14]. Briefly, the stone components in all stone samples were determined by Fourier transform infrared spectroscopy. Dried stone samples were washed and pressed into powder. Approximately 1 mg of each stone specimen was mixed with 200 mg of potassium bromide and scanned by Fourier transform infrared spectroscopy. To avoid overestimation of the percentage of a specific stone composition, only the first stone from the same patient was recorded, a method consistent with our prior work [15].

The predominant stone component of each sample was recorded and the stone compositions were then separated into seven major categories according to the classification of stone composition recommended in the European Association of Urology guidelines [16]. Magnesium ammonium phosphate (MAP), Carbonate apatite (CA), and Ammonium urate (AUU) were classified as infection stones; Calcium oxalate (CaOx), Calcium phosphate (CaP), and Uric acid (UA) were classified as non-infection stones. Xanthine, 2,8-dihydroxyadenine and stones composed of drugs were referred to as "other stone composition". To further analysis the correlation between stone composition and age, the children were sub-grouped into three age categories: 0- to 5-year olds (level 1), 6- to 12-year olds (level 2), and 13- to 18-year olds (level 3).

Statistics

The results were analyzed using SPSS 19.0. All continuous variables were expressed as mean ± SD. Chi-square test was used to compare group frequencies and gender differences. Independent-sample *t* test and Mann–Whitney *U* test were used for group comparison. *p* values of < 0.05 were considered statistically significant.

Results

The characteristics of 151 Uyghur children and 123 Han children were presented in Table 1. Of the 151 Uyghur children, 108 (71.5 %) were male and 43 (28.5 %) were female with a male/female sex ratio of 2.5:1. Of the 79 Han children, 35 (64.2 %) were male and 44 (35.8 %) were female with a male/female sex ratio of 1.80:1. The mean (±SD) age of the Uyghur children was 5.3 ± 4.2 years and was significantly younger than Han children (8.5 ± 5.7, $p < 0.001$).

The most common component in stones from Han children was CaOx (64.2 %) followed by cystine (8.9 %), CaP (8.1 %), AAU (7.3 %), CA (4.9 %), UA (3.3 %) and MAP (2.4 %). In Uyghur children, CaOx was also the most commonly encountered component (35.1 %), followed by UA (20.5 %), MAP (16. 6 %), AAU (14.6 %), CaP (7.9 %), CA (2.7 %) and cystine (0.7 %). The rates of both CaOx and cystine stones were significantly higher in Han children

Table 1 Characteristics and dominating stone component recorded in children from the Uyghur and Han

Characteristics	Uyghur ($n = 151$)	Han ($n = 123$)	p
Age, (years)	5.3 ± 4.2	8.6 ± 5.7	<0.001
Range	0.25–14	0.58–18	
Sex, n (%)			
Males	108 (71.5)	79 (64.2)	0.011
Females	43 (28.4)	44 (35.7)	
Component, n (%)			
CaOx	53 (35.1)	79 (64.2)	<0.001
CaP	12 (7.9)	10 (8.1)	0.956
CA	4 (2.7)	6 (4.9)	0.513
MAP	25 (16.6)	3 (2.5)	<0.001
UA	31 (20.6)	4 (3.3)	<0.001
AUU	22 (14.6)	9 (7.4)	0.059
Cystine	1 (0.7)	11 (8.9)	0.001
Others	3 (2.0)	1 (0.8)	0.765

CaOx calcium oxalate, *CaP* calcium phosphate, *CA* carbonate apatite, *MAP* magnesium ammonium phosphate, *UA* uric acid, *AUU* ammonium urate

Table 2 Predominant stones components of Uyghur and Han children according to gender

Stone composition	Male		Female	
	Uyghur (%)	Han (%)	Uyghur (%)	Han (%)
CaOx	32 (29.6)	51 (64.6)**	21 (48.9)	28 (63.6)
CaP	9 (8.3)	7 (8.9)	3 (7.0)	3 (6.8)
CA	4 (3.7)	3 (3.9)	0	3 (6.8)
MAP	20 (18.5)	0**	5 (11.6)	3 (6.8)
UA	24 (22.2)	0**	7 (16.3)	4 (9.1)
AAU	15 (13.9)	8 (10.2)	7 (16.3)	1 (2.3)
Cystine	1 (0.9)	10 (12.7)#	0	1 (2.3)
Others	3 (2.8)	0 (0)	0	1 (2.3)
Total	108 (100.0)	79 (100.0)	43 (100.0)	44 (100.0)

** $p < .001$ Han vs Uyghur by χ^2 test

# $p < .05$ Han vs Uyghur by χ^2 test

($p < 0.01$), while the rates of UA and MAP stones were significantly higher in Uyghur children ($p < 0.001$). There were no differences between the two groups in composition of CA, CaP or AAU (Table 1).

When the children were divided by gender, significant difference in stone composition was observed between males. As summarized in Table 2, the percentage of CaOx and cystine stones was much higher in males of Han children ($p < 0.01$). Conversely, a much higher percentage of UA and MAP was observed in male of Uyghur children ($p < 0.001$). Interestingly, no differences in stone composition were recorded between female children in the two ethnical groups.

Table 3 The percentage of Uyghur and Han children with stone analysis by age

Age, (years)	Uyghur (%)	Han (%)
0–5	96 (63.6)	52 (42.3)**
6–12	52 (34.5)	36 (29.3)#
>12	3 (2.0)	35 (28.5)**
Total	151	123

** $p < .001$ Han vs Uyghur by χ^2 test

# $p < .05$ Han vs Uyghur by χ^2 test

The distribution of Han and Uyghur children stone patients by age is summarized in Table 3. Overall, obviously difference was observed between two groups in terms of the distribution according to age. Although, the highest percentage of children patients in both Uyghur and Han children was recorded at age level 1, percentage of Uyghur children in age level 1 was markedly higher than in Han (63.6 vs 42.3 %, $p < 0.001$). Also, in age level 2, a higher percentage of pediatric stone patient was observed in Uyghur (34.5 vs 29.3 %, $p < 0.05$). In contrast, Han children had a higher incidence at age level 3 ($p < 0.001$). Meanwhile, the percentage of stone patients in Uyghur children decreased with age ($p < 0.01$). The similar course was not observed in Han children.

When the children were further divided by stone compositions and age (Table 4), results showed that CaOx containing stones were not only the most common type but also increased with age in both Han and Uyghur children. Although the percentage of UA containing stones decreased with age in Uyghur children, the prevalence of UA stones was higher in Uyghur children than in Han children without the respect of age. The presence of MAP stone was also more commonly seen in Uyghur than in Han children at age levels 1 (18.8 vs 3.6 %) and 2 (13.5 vs 2.8 %), but a significant difference was only recorded at age level 1 ($p < 0.05$). Another interesting finding is the higher prevalence of cystine stones in Han than in Uyghur children at each age level ($p < 0.01$).

Discussion

To date, there are limited data published in the literature on regional or racial differences in terms of composition of urinary stones, especially in pediatric patients. As high prevalence of urinary stone in children was reported in Uyghur population [13], it is worthwhile to perform a research on stone composition between Han and Uyghur children. The

Table 4 Stones compositions of Uyghur and Han children by age

Stone component	0–5 years		6–12 years		>12 years	
	Uyghur (%)	Han (%)	Uyghur (%)	Han (%)	Uyghur (%)	Han (%)
CaOx	21 (21.9)	27 (51.9)**	29 (55.8)	24 (66.7)	3 (100)	28 (80.0)
CaP	11 (11.5)	5 (9.6)	1 (2.0)	3 (8.3)	0	2 (5.7)
CA	4 (4.2)	3 (5.8)	0	1 (2.8)	0	2 (5.7)
MAP	18 (18.8)	2 (3.6)#	7 (13.5)	1 (2.8)	0	0
UA	21 (21.9)	3 (5.8)**	10 (19.2)	1 (2.8)#	0	0
AAU	19 (19.8)	9 (17.3)	3 (5.8)	0	0	0
Cystine	1 (1.0)	3 (5.8)	0	5 (13.9)#	0	3 (8.6)
Others	1 (1.0)	0	2 (3.9)	1 (2.8)	0	0
Total	96 (100.0)	52 (100.0)	52 (100.0)	36 (100.0)	3 (100.0)	35 (100.0)

** $p < .001$ Han vs Uyghur by χ^2 test

# $p < .05$ Han vs Uyghur by χ^2 test

present study evaluated the stone compositions of Uyghur and Han children with urolithiasis in China, indicating that there was a significant difference between the two ethnic groups of children. Uyghur people are one of the Chinese minorities who mainly live in the Xinjiang Uyghur Autonomous Region. They have a religion, culture, diet, and lifestyle that are quite different from most of the Han people. These factors may all contribute to the differences of kidney stones compositions between the two populations. By further analysis, we suggested this variance may be caused by multiple factors.

Consistent to the findings in other reports [2, 17], male predominance was also found in our date. The male/female ratios in Uyghur and Han children were 2.51:1 and 1.80:1, respectively. Like in adults, CaOx containing stones were also reported as the most common type in stone forming children, accounting for 60 to 90 % of all stones [18–20]. Sun et al. [21] evaluated 189 pediatric stone patients in China and found the percentage of CaOx stones was 64.9 %. In our study, CaOx were the most abundant components in both Han and Uyghur children. However, the incidence of CaOx containing stones was significantly higher in Han children than in Uyghur children. A relative higher intake of vegetarian food in Han population may partially explain this difference. This kind of diet usually contains large amount of oxalate and is particularly common in Southern China, and thus it may contribute to the CaOx stone formation in Han children [15]. Accordingly, a high proportion of CaOx stones were reported in adult stone patients from the Han region in southern China [9, 15].

Another finding in our study was that the incidence of CaOx stones increased with age in both Han and Uyghur children, which was consisted with previous studies [18, 19]. Aggour et al. [19] reported in their study that CaOx stones were found in 50.8 % of children younger than 2-year olds but in 59.3 % of those older than 10-year olds. The increased intake of dietary sodium in children may attribute to the development of nephrolithiasis as well as CaOx stone formation, for a higher intake of sodium is coupled with increased excretion of urinary calcium [1, 20].

The occurrence of UA stones was significantly higher in Uyghur children than in Han children, which was consistent with the results of adults in Uyghur and Han [11]. Evidence from previous studies have shown that hyperuricosuria, low urine volumes and persistently low urine pH are the three major lithogenic factors for precipitation of uric acid [22, 23]. High-protein- and purine-rich food stuffs such as animal offal, beef, and mutton are common components of the Uyghur diet [11, 13]. In addition, Wumaner et al. [11] noticed that during pregnancy and lactation, compared to Han women, Uyghur women preferred high-protein food stuffs rather than fruits and vegetables.

Diet rich in purine is a potential risk factor for high blood levels of urate associated with hyperuricosuria and formation of uric acid stones [24]. Moreover, a transient excessive intake of protein might result in metabolic acidosis with low urinary pH [23]. Evidence also showed that the blood urate levels were higher in Uyghur adult patients than that in Han adult patients [18]. Theoretically, a higher intake of purine-rich food in Uyghur might be the reason for hyperuricosuria and UA stone formation.

In several reports, the prevalence of UA stone increased continuously with age in the adult patients [15, 25]. While in our present study, a reverse trend was observed in Han and Uyghur children. The percentage of UA containing stones was higher in age level 1 than that in age level 2 (21.9 vs 19.2 %, 5.8 vs 2.8 %). This discordance may be partially due to an extremely high excretion of urate during the neonatal period, a level that remains substantially higher throughout early childhood than in adults [26]. Evidences have shown that urinary urate excretion decreased with age in children [27, 28]. Borawski and colleagues [28] measured the risk factors of stone formation in 3- to 18-year-old healthy children and recorded a decline trend of urate excretion as the age increasing. Alaya and coworkers [29] demonstrated that UA containing stones were found in 8.6 % of children with urolithiasis younger than 2 years but not detected in children who were older than 10 years. They concluded that incomplete urate reabsorption in the immature tubules of young children, to some extent, might account for the higher occurrence of UA stone in young children.

In the present study, the incidence of MAP containing stones was observed in 2.5 % of Han children, which was consistent with the previous study reported by Sun et al. [21]. However, a significantly higher incidence of MAP stones was found in Uyghur children. The MAP stone formation was closely associated with urinary tract infections (UTIs). A relative worse medical condition in Xinjiang may be related to the more popular UTIs in Uyghur people. The incidence of UTIs was as high as 43.3 % in Uyghur children with urinary stones [13]. We speculated that the common UTIs in Uyghur children may be responsible for the higher prevalence of MAP stone.

Cystine stone accounts for 1–5 % of pediatric patients and is the only phenotypic manifestation of cystinuria [21]. In our study, cystine stones were observed in 8.9 % of Han children which was similar to the result of the another study in China (9 %) [21]. While the rate of cystine stone in Uyghur children was much lower than that in Han children which was only 0.7 %. The genetic diversity between populations in the Uyghur and Han might be the most likely explanation for the different rates of pediatric cystine stones. Further epidemical studies should be done on this issue.

Our results support the assumption that the formation of stones in children has multifactorial etiologies [1, 27]. We assume that certain differences, if not all, demonstrated between the two groups of children can be explained by genetic variation. Other than genetic influence, many other regional factors such as dietary and climate differences might contribute to the stone formation [7]. The occurrence of nephrolithiasis tends to be more common in areas with hot climates [30]. In Xinjiang, the typical ecological characteristics is dry and hot, with the average temperature remains above 35 °C more than 100 days per year [31]. The risk factors of dehydration, decreased urine volumes and low pH resulted from the extremely climate consequently contribute to transiently high levels of supersaturation with UA and UA stone formation [13].

We are aware of certain limitations of our study. Firstly, due to the limited sample size of this study, these percentages of stone composition might not totally represent the true situation. In the future, we will try our best to enlarge the sample size and to improve the quality of our studies. Secondly, the analysis was retrospective and we only had access to the major stone component. We thus did not know anything about the patients' history, stone location or composition of urine. The mechanisms underlying the stone formation were, thus, concealed and it was accordingly not possible to draw definite conclusions on the stone etiology. The deep reasons still remain unknown and required further investigation. Nevertheless, we succeeded to get the analytical data from a reasonable number of children from the two regions.

Conclusions

In this study, we present the significant difference of stone composition between Uyghur and Han children with kidney stones in China. We speculated that factors such as diet, life style, genetic diversity, environment as well as medical conditions may contribute to the difference of stone composition between Han and Uyghur children. Further understanding of the relationship between these etiological factors and stone composition in different ethnic groups might be an important prerequisite for improved primary and secondary stone prevention.

Acknowledgments This work was supported by a Grant from General Guide Project of Guangzhou City Bureau of Education (No. 20123C055); Science and Technology Planning Project of Guangdong Province, China (No. 2014A020209085); and Guangzhou science and technology project (No. 201604020001).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The written informed consents were obtained from all the participants.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Mandeville JA, Nelson CP (2009) Pediatric urolithiasis. Curr Opin Urol 19:419–423
2. Novak TE, Lakshmanan Y, Trock BJ, Gearhart JP, Matlaga BR (2009) Sex prevalence of pediatric kidney stone disease in the United States: an epidemiologic investigation. Urology 74:104–107
3. Hulton SA (2001) Evaluation of urinary tract calculi in children. Arch Dis Child 84:320–323

4. Valentini RP, Lakshmanan Y (2011) Nephrolithiasis in children. Adv Chronic Kidney Dis 18:370–375
5. Clayton DB, Pope JC (2011) The increasing pediatric stone disease problem. Ther Adv Urol 3:3–12
6. Bush NC, Xu L, Brown BJ, Holzer MS, Gingrich A, Schuler B, Tong L, Baker LA (2010) Hospitalizations for pediatric stone disease in United States, 2002–2007. J Urol 183:1151–1156
7. Sas DJ (2011) An update on the changing epidemiology and metabolic risk factors in pediatric kidney stone disease. Clin J Am Soc Nephrol 6:2062–2068
8. Kamoun A, Daudon M, Abdelmoula J, Hamzaoui M, Chaouachi B, Houissa T, Zghal A, Ben Ammar S, Belkahia C, Lakhoua R (1999) Urolithiasis in Tunisian children: a study of 120 cases based on stone composition. Pediatr Nephrol 13:920–925 **(discussion 926)**
9. Sun X, Shen L, Cong X, Zhu H, He L, Lu J (2011) Infrared spectroscopic analysis of 5248 urinary stones from Chinese patients presenting with the first stone episode. Urol Res 39:339–343
10. Lopez M, Hoppe B (2010) History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol 25:49–59
11. Wumaner A, Keremu A, Wumaier D, Wang Q (2014) Variation in urinary stone composition between adult Uyghur and Han patients with urolithiasis in Xinjiang, China. Urology 84:772–778
12. Coward RJ, Peters CJ, Duffy PG, Corry D, Kellett MJ, Choong S, van't Hoff WG (2003) Epidemiology of paediatric renal stone disease in the UK. Arch Dis Child 88:962–965
13. Wumaner A, Keremu A, Wumaier D, Wang Q (2014) High incidence of urinary stones in Uyghur children may be related to local environmental factors. J Pediatr Urol 10:289–293
14. Wu W, Yang D, Tiselius HG, Ou L, Liang Y, Zhu H, Li S, Zeng G (2014) The characteristics of the stone and urine composition in Chinese stone formers: primary report of a single-center results. Urology 83:732–737
15. Wu W, Yang B, Ou L, Liang Y, Wan S, Li S, Zeng G (2014) Urinary stone analysis on 12,846 patients: a report from a single center in China. Urolithiasis 42:39–43
16. Skolarikos A, Straub M, Knoll T, Sarica K, Seitz C, Petrik A, Turk C (2015) Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines. Eur Urol 67:750–763
17. Dursun I, Poyrazoglu HM, Dusunsel R, Gunduz Z, Gurgoze MK, Demirci D, Kucukaydin M (2008) Pediatric urolithiasis: an 8-year experience of single centre. Int Urol Nephrol 40:3–9
18. Gabrielsen JS, Laciak RJ, Frank EL, McFadden M, Bates CS, Oottamasathien S, Hamilton BD, Wallis MC (2012) Pediatric urinary stone composition in the United States. J Urol 187:2182–2187
19. Aggour A, Ziada AM, AbdelHamid AZ, AbdelRahman S, Morsi A (2009) Metabolic stone composition in Egyptian children. J Pediatr Urol 5:132–135
20. Dwyer ME, Krambeck AE, Bergstralh EJ, Milliner DS, Lieske JC, Rule AD (2012) Temporal trends in incidence of kidney stones among children: a 25-year population based study. J Urol 188:247–252
21. Sun X, Shen L, Cong X, Zhu H, Lv J, He L (2011) Infrared spectroscopic analysis of urinary stones (including stones induced by melamine-contaminated milk powder) in 189 Chinese children. J Pediatr Surg 46:723–728
22. Ngo TC, Assimos DG (2007) Uric Acid nephrolithiasis: recent progress and future directions. Rev Urol 9:17–27
23. Shekarriz B, Stoller ML (2002) Uric acid nephrolithiasis: current concepts and controversies. J Urol 168:1307–1314
24. Tracy CR, Best S, Bagrodia A, Poindexter JR, Adams-Huet B, Sakhaee K, Maalouf N, Pak CY, Pearle MS (2014) Animal protein and the risk of kidney stones: a comparative metabolic study of animal protein sources. J Urol 192:137–141
25. Daudon M, Dore JC, Jungers P, Lacour B (2004) Changes in stone composition according to age and gender of patients: a multivariate epidemiological approach. Urol Res 32:241–247
26. Koyuncu H, Yencilek F, Erturhan S, Eryildirim B, Sarica K (2011) Clinical course of pediatric urolithiasis: follow-up data in a long-term basis. Int Urol Nephrol 43:7–13
27. Sarica K (2006) Pediatric urolithiasis: etiology, specific pathogenesis and medical treatment. Urol Res 34:96–101
28. Borawski KM, Sur RL, Miller OF, Pak CY, Preminger GM, Kolon TF (2008) Urinary reference values for stone risk factors in children. J Urol 179:290–294 **(discussion 294)**
29. Alaya A, Nouri A, Najjar MF (2011) Urinary stone composition in pediatric patients: a retrospective study of 205 cases. Clin Chem Lab Med 49:243–248
30. Alon US (2009) Medical treatment of pediatric urolithiasis. Pediatr Nephrol 24:2129–2135
31. Wumaner A, Wang Q, Keremu A, Wumaier D (2014) Response to letter to editor re: 'high incidence of urinary stones in Uyghur children may be related to local environmental factors'. J Pediatr Urol 10:573–574