Title

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Journal

World journal of urology, 41(1)

ISSN

0724-4983

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Publication Date

2023

DOI

10.1007/s00345-022-04221-x

Peer reviewed

Maternal family history of urolithiasis is associated with earlier age of onset of stone disease

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Abstract

Purpose: To evaluate the impact of detailed family history on the severity of disease and age of onset in patients with urolithiasis.

Methods: Prospectively collected data from a single institution between October 2015 and December 2020 was analyzed. Our primary endpoint was the number of patients experiencing at least one recurrent stone during the follow-up period.

Results: Of 1566 patients analyzed, 603 (39%) reported at least one family member with a history of stones. The percentage of patients experiencing at least one recurrent stone event was higher in patients with a family history of stones (38%) compared to those without a family history of stones (28%) over a median follow-up period of 8 months (p=0.001). On multivariate analysis, the presence of any family history of urolithiasis increased risk of recurrent stone events (odds ratio [OR] 1.62, p<0.001). The presence of both a first- and a second-degree relative with urolithiasis was associated with higher odds for a recurrent stone event (OR 2.17; p=0.003) and a younger age of onset for stones, (OR 3.32; <0.001). A maternal side relative with stones conferred a higher odds ratio for younger age of first onset of stones (OR 2.93; p<0.001).

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#Equally contributed

Conclusion: Any family history of kidney stone disease imparts an increased risk of recurrent stone event and an earlier age of onset for urolithiasis. The presence of both first- and second-degree relatives or a maternal side relative with kidney stones may be a predictor for an earlier age of onset for urolithiasis.

Keywords

family history; degree of relative; paternal side relative; maternal side relative; recurrent stone events

INTRODUCTION

The probability of stone recurrence is approximately 50% [1], and as many as half of asymptomatic stones develop symptoms within 5 years [2,3]. Tools to help prognosticate risk of stone recurrence are useful for patients and clinicians to inform the relative importance of metabolic testing and treatment as well as follow-up timing.

Family history is a known risk factor for urolithiasis [4]. Positive family history for urolithiasis is associated with a 30–50 percent higher risk of stone recurrence [5–8]. Studies have demonstrated that a family history of urolithiasis increases the relative risk of urolithiasis by 2.57-fold in men. Given the association of family history with stone recurrence, the American Urological Association guidelines recommend metabolic testing in first time stone formers with a family history of urolithiasis [9]. However, the impact of having a first- or second-degree relative with stone disease or parental sidedness of stone disease on future stone events is not well understood.

The objective of this study was to compare the impact of having a first- or second-degree relative with stone disease and parental sidedness of stone disease (paternal or maternal) on age of onset of stone disease and risk of stone recurrence.

MATERIALS AND METHODS

Study design and patient enrollment

This was an analysis of prospectively collected data at University of California, San Francisco (UCSF) between October 2015 and December 2020. After approval by the institutional review board (CHR 14–14533), consecutive new patients presenting to UCSF Urology Clinic were enrolled into the ReSKU [10]. ReSKU interfaces with the electronic medical record to automatically populate patient clinical and imaging data for research purposes. ReSKU clinical information is managed using REDCap (Research Electronic Data Capture) [11] electronic data capture tools hosted at UCSF as described previously. All subjects enrolled in ReSKU provide written consent by principal and co-investigators.

Data collection

Patient demographics, family history, and clinical data, including presence or absence of bilateral stones, total stone burden and stone number, and past stone history, were obtained at the first clinic visit. Stone burden at the initial visit and throughout the follow-up period

was determined using imaging (computerized tomography; CT, kidney, ureter, and bladder X-ray; KUB, and ultrasound; US). The age of first onset for urolithiasis and the number of previous stone episodes for patients who reported a positive past stone history were also collected. Detailed family history of kidney stones was recorded for first- and second-degree relatives, and paternal- and maternal side relatives. Total stone burden (based on imaging), self-reported symptoms, and self-reported stone passage, were collected at each follow-up visit. Detailed information about stone surgery was also captured for each patient. Metabolic stone work-up including 24-hour urine collection and serum studies and stone composition (primary component) were recorded. The initial data were included if patients underwent at least two tests at the time of data analysis.

Since races/ethnicities other than White, Asian, Black, and Hispanic/Latin were too few to perform statistics, their data was omitted from the present analyses.

Classification of detailed family history

First degree relatives were defined as parents, children, or siblings and second degree relatives were defined as grandparents, uncles, aunts, nephews, or nieces [12] Paternal side relatives included father, paternal side grandparents, uncles, and aunts and maternal side relatives included mother, maternal side grandparents, uncles, and aunts. Detailed family history data was obtained by patient self-report.

Outcomes

Our primary outcome was recurrent stone events (defined as development of symptoms, stone passage, or stone intervention) during the follow-up period. Our secondary outcomes were age of initial stone presentation, bilateral stones, past stone history, and number of previous stone episodes. There is no exact definition of early onset age for kidney stones. In some previous reports, Halbritter J, et al. [13] defined it as onset age <40 years, while Daga A, et al. [14] defined it as onset age < 25 years. Given the first episode of the stone event is most likely to occur after age 30 [15], patients with first stone event at age < 30 years old were defined as young age of onset.

Statistical Analysis

Continuous, normally distributed variables were expressed with means (standard deviation), whereas non-normally distributed variables were described with medians. Categorical variables were presented with frequency (percentage). Chi-square and Fisher exact tests were used for categorical variables and unpaired Student's t-test and Mann-Whitney U test for continuous variables. Logistic regression was performed as a multivariate analysis. Each regression model was adjusted with age, gender, Metabolic syndromes (hypertension, hyperlipidemia, diabetes mellitus, obesity), and White Race. Differences were considered statistically significant at $p < 0.05$. All statistical analyses were performed using R.

RESULTS

Of 1614 patients, 1566 had detailed information about family history of stones captured and were included in analysis. Of these, 603 (39%) reported at least one family member

with a history of stones and 179 (11%) reported multiple family members with stones. Patient characteristics are summarized in Table 1. Patients with a positive family history of urolithiasis were more often female, and white race compared to those without a family history of urolithiasis. Positive family history was associated with a younger age of onset of stone disease and increasing number of prior stone episodes.

Initial management was observation in 1192 (76%) patients and surgery in 374 (24%). A total of 828 patients had at least one follow-up visit and were included in the analysis for stone related events. The percentage of patients experiencing at least one recurrent stone event was higher in patients with a family history of stones (38%) compared to those with no family history of stones (28%) over a median follow-up period of 8 months (Table 1; p=0.001).

Of patients with a positive family history of urolithiasis, 402 (67%) patients had a first-degree relative only and 75 (12%) patients had both first- and second-degree relatives with a history of urolithiasis. One-hundred eighty patients (30%) had relatives on the paternal side, and 127 (21%) patients had relatives on the maternal side with family history of stones. Compared to patients without a family history of stones, any family history (first-degree relatives only, both first- and second-degree relatives, paternal or maternal side relatives) was associated with bilateral stones, increased number of prior stone episodes, younger age of onset for the first stone event, and higher ratio of patients experiencing at least one recurrent stone event (Table 2).

Sub-analysis of detailed family history demonstrated that bilateral stones (36% vs. 24%, p=0.038) and younger age of onset (p<0.001) was more common in those with both first- and second-degree relatives with stones compared to those with only first-degree relatives with stones (Supplemental Table 1). Patients with only maternal-side relatives with stone history had a younger age of onset for the first stone event compared to those with only paternal-side relatives with stone history (p=0.046) (Supplemental Table 1).

In multivariable analysis (Table 3), having a first degree relative with stone disease was associated with a 1.6 (95% confidence interval; CI 1.18–2.12, p=0.001) increased odds of recurrent stones, while having both a first and second-degree relative with stones was associated with a 2.17 (95% CI 1.29–3.63, p=0.003) increased odds of recurrent stone disease compared to those without a family history of stones. Positive family history of stone disease was associated with a higher risk of bilateral stones (OR 1.54, 95% CI 1.2–1.98, p<0.001), age of onset <30 years (OR 1.84, 95% CI 1.44–2.36, p<0.001), prior stone episodes (OR 1.55, 95% CI 1.25–1.92, p<0.001), and history of 6 or more prior stone episodes (OR 2.19, 95% CI 1.65–2.9, p<0.001). Having both a first- and a second-degree relative and a maternal side relative conferred a higher odds ratio for a younger age of onset of stones (OR 3.32, 95% CI 2.04–5.41, p<0.001, OR 2.93, 95% CI 2.09–4.11, p<0.001, respectively).

24-hour urine examinations were obtained in 433 (28%) patients. Having any family history of urolithiasis was associated with higher calcium levels and higher urinary pH than those without a family history of stone disease (Supplemental Table 2). Patients with paternal side

relatives had a larger amount of phosphate and magnesium. The amount of oxalate was smaller in patients with maternal side relatives with stone family history than those without any family members with stone history.

DISCUSSION

Although family history is a known risk factor for stone disease, detailed analysis of family history in patients with stone disease has been lacking. In this analysis of 1566 patients, having both first- and second-degree relatives with stone disease was associated with an increased risk of stone recurrence and earlier age of onset of urolithiasis compared to those with only first-degree relatives and those with no family history of stone disease. This corresponded with findings on 24-hour urine studies in which those with both first and second-degree relatives with kidney stones had higher urine calcium levels compared to those with only first-degree relatives with stone disease and those with no family history of stone disease.

Similar to our findings, Hemminki et al found an increased risk of urolithiasis in patients with two or more siblings with stone disease compared to those without stone disease using a Swedish registry containing 211718 patients with urolithiasis [16]. These findings indicate that patients with multiple family members with stone disease are at particularly high risk for future stone episodes and may warrant closer follow-up and more aggressive stone prevention techniques.

We also found that family history of stones on the maternal-side was more strongly correlated with a younger age of onset for the first stone event compared to family history of stones on the paternal-side. It is possible that both environmental and genetic factors underlie this finding. Daily dietary habits and physical activities are strongly associated with obesity and could be responsible for an increased risk of kidney stones [17]. Maternal dietary habits have been shown to transmit to children more strongly than paternal dietary habits [18,19], and mothers' physical activity is more likely associated with children's activity than fathers', attributable to mothers spending greater time with their children [20]. Johannsen et al. also showed that children's weight was related to mothers' but not fathers' BMI [21]. There data suggested children are likely to develop kidney stones if their mother has stones. There is a possible association between mitochondrial dysfunction and kidney stone disease [22–24]; while this association has not held true for several hereditary stones, mitochondrial dysfunction is x-linked and explains maternal genetic linkage for many other diseases. It may represent a plausible explanation for our result.

We found that urinary calcium levels were higher in those with a family history of urolithiasis, especially those with both first- and second-degree relatives with stone disease. Similar to our findings, Guerra et al. [7, 25] found that positive family history of urolithiasis was associated with a larger amount of calcium excretion in women, especially, maternal side of family history that influenced it. Furthermore, calcium excretion was higher in children aged 5–12 years with a urolithiasis family history compared to those without a family history of stones [26].

Since there exists the possibility that some hereditary kidney stone diseases and specific types of stones with known genetic etiology could affect the results, we performed sub-analyses excluding them. We identified 18 patients with cystinuria, 2 with Dent disease, and 1 with a drug stone in our cohort. Sub-analyses excluding those patients with genetic stones showed no affect on our primary results (Supplemental Table 3).

Limitations of this study include potential recall bias of personal and family history of stones. Because this was a single-institution study, it is possible that the patient population may not reflect the larger population. However, the ethnic breakdown in our study was similar to that seen in other stone epidemiologic studies [17]. Although data was collected prospectively, the analysis was performed retrospectively which may have introduced bias. With regard to the methods for assessing the stone presence and burdens, we utilized CT, KUB, and US. These differences in methods could affect the results, given their different accuracies. While a single method would be ideal, registry data provides a reflection of real-world practice. Our follow-up period was relatively short (median 8 months) and follow-up data was only available for approximately half of the patients. Forty-eight patients (2.9%) whose family history was unknown were excluded from analysis, and this could introduce potential confounding. Nevertheless, our sample size was relatively large with 1566 patients and 828 receiving at least one follow-up visit. Strengths of our study were use of more objective outcomes in addition to self-reported outcomes including our primary outcome of stone recurrence during the follow-up period and 24-hour urine study results.

We concluded any family history of kidney stone disease imparts an increased severity of urinary stone disease on patients. Furthermore, the presence of both first- and second-degree relatives or a maternal side relative with kidney stones may be a predictor for an earlier age of onset for urolithiasis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

REFERRENCES

1. Ferraro PM, Curhan GC, D'Addessi A, Gambaro G (2017) Risk of recurrence of idiopathic calcium kidney stones: analysis of data from the literature. J. Nephrol 30: 227–233. doi: 10.1007/s40620-016-0283-8. [PubMed: 26969574]

2. Selby MG, Vrtiska TJ, Krambeck AE, et al. (2015) Quantification of Asymptomatic Kidney Stone Burden by Computed Tomography for Predicting Future Symptomatic Stone Events. Urology 85: 45–50. doi: 10.1016/j.urology.2014.08.031. [PubMed: 25440821]

3. Kang HW, Lee SK, Kim T, et al. (2013) Natural History of Asymptomatic Renal Stones and Prediction of Stone Related Events. J Urol 189: 1740–1746. doi: 10.1016/j.juro.2012.11.113. [PubMed: 23201376]

4. Goldfarb DS, Fischer ME, Keich Y, Goldberg J (2005) A twin study of genetic and dietary influences on nephrolithiasis: A report from the Vietnam Era Twin (VET) Registry. Kidney Int 67: 1053–1061. doi: 10.1111/j.1523-1755.2005.00170.x. [PubMed: 15698445]

5. Dussol B, Verdier JM, Goff JM, Berthezene P, Berland Y (2007) Artificial neural networks for assessing the risk factors for urinary calcium stones according to gender and family history of stone. Scand J Urol Nephrol 41: 414–418. doi: 10.1080/00365590701365263. [PubMed: 17853052]

6. Basiri A, Shakhssalim N, Khoshdel AR, et al. (2010) Familial relations and recurrence pattern in nephrolithiasis: new words about old subjects. Urol J 7: 81–6. [PubMed: 20535692]

7. Guerra A, Folesani G, Nouvenne A, et al. (2016) Family history influences clinical course of idiopathic calcium nephrolithiasis: case–control study of a large cohort of Italian patients. J Nephrol 29: 645–651. doi: 10.1007/s40620-015-0225-x. [PubMed: 26296722]

8. Muslumanoglu AY, Binbay M, Yuruk E, et al. (2011) Updated epidemiologic study of urolithiasis in Turkey. I: Changing characteristics of urolithiasis. Urol Res 39: 309–314. doi: 10.1007/s00240-010-0346-6. [PubMed: 21161646]

9. Pearle MS, Goldfarb DS, Assimos DG, et al. (2014) Medical Management of Kidney Stones: AUA guideline. J Urol 192: 316–24. doi: 10.1016/j.juro.2014.05.006. [PubMed: 24857648]

10. Chang HC, Tzou DT, Usawachintachit M, et al. (2016) Rationale and Design of the Registry for Stones of the Kidney and Ureter (ReSKU): A Prospective Observational Registry to Study the Natural History of Urolithiasis Patients. J Endourol 30: 1332–1338. doi: 10.1089/end.2016.0648. [PubMed: 27758162]

11. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG (2009) Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 42: 377–81. doi: 10.1016/j.jbi.2008.08.010. [PubMed: 18929686]

12. Bennett RL, Motulsky AG, Bittles A, et al. (2002). Genetic Counseling and Screening of Consanguineous Couples and Their Offspring: Recommendations of the National Society of Genetic Counselors. J Genet Couns 11: 97–119. doi: 10.1023/A:1014593404915. [PubMed: 26141656]

13. Halbritter J, Seidel A, Müller L, et al. (2018). Update on Hereditary Kidney Stone Disease and Introduction of a New Clinical Patient Registry in Germany. Front Pediatr. Mar 7;6:47. doi: 10.3389/fped.2018.00047. [PubMed: 29564324]

14. Daga A, Majmundar AJ, Braun DA, et al. (2018). Whole exome sequencing frequently detects a monogenic cause in early onset nephrolithiasis and nephrocalcinosis. Kidney Int 93: 204–213. doi: 10.1016/j.kint.2017.06.025. [PubMed: 28893421]

15. Maalouf NM, Sato AH, Welch BJ, et al. (2010). Postmenopausal hormone use and the risk of nephrolithiasis: results from the Women's Health Initiative hormone therapy trials. Arch Intern Med 170: 1678–85. doi: 10.1001/archinternmed.2010.342. [PubMed: 20937929]

16. Hemminki K, Hemminki O, Försti A, Sundquist K, Sundquist J, Li X (2018) Familial risks in urolithiasis in the population of Sweden. BJU Int 121: 479–485. doi: 10.1186/s12882-018-0945-y. [PubMed: 29235239]

17. Scales CD Jr, Smith AC, Hanley JM, Saigal CS (2012) Urologic Diseases in America Project. Prevalence of kidney stones in the United States. Eur Urol 62: 160–5. doi: 10.1016/j.eururo.2012.03.052. [PubMed: 22498635]

18. Ko B, Bergsland K, Gillen DL, et al. (2015) Sex differences in proximal and distal nephron function contribute to the mechanism of idiopathic hypercalcuria in calcium stone formers. Am J Physiol Integr Comp Physiol 309: R85–R92. doi: 10.1152/ajpregu.00071.2015.

19. Young EM, Fors SW, Haye M (2004) Associations between perceived parent behaviors and middle school student fruit and vegetable consumption. Journal of Nutrition Education and Behavior 36: 2–12. doi: 10.1016/s1499-4046(06)60122-x. [PubMed: 14756976]

20. Zovko V, Djuric S, Sember V, Jurak G (2021) Are Family Physical Activity Habits Passed on to Their Children? Front Psychol. Sep 6;12:741735. doi: 10.3389/fpsyg.2021.741735. [PubMed: 34552541]

21. Johannsen DL, Johannsen NM, Specker BL (2006) Influence of parents' eating behaviors and child feeding practices on children's weight status. Obesity (Silver Spring) 14: 431–439. doi: 10.1038/oby.2006.57. [PubMed: 16648614]

22. Chaiyarit S, Thongboonkerd V (2020) Mitochondrial Dysfunction and Kidney Stone Disease. Front Physiol 11: 566506. doi: 10.3389/fphys.2020.566506. [PubMed: 33192563]

23. Unno R, Kawabata T, Taguchi K, et al. (2020) Deregulated MTOR (mechanistic target of rapamycin kinase) is responsible for autophagy defects exacerbating kidney stone development. Autophagy 16: 709–723. doi: 10.1080/15548627.2019.1635382. [PubMed: 31257986]

24. Jabalameli MR, Fitzpatrick FM, Colombo R, Howles SA, Leggatt G, Walker V, Wiberg A, Kunji ERS, Ennis S (2021) Exome sequencing identifies a disease variant of the mitochondrial ATP-Mg/Pi carrier SLC25A25 in two families with kidney stones. Mol Genet Genomic Med. 2021 Dec;9(12):e1749. doi: 10.1002/mgg3.1749. Epub 2021 Aug 4. [PubMed: 34346195]

25. Guerra A, Ticinesi A, Allegri F, et al. (2016) The influence of maternal and paternal history on stone composition and clinical course of calcium nephrolithiasis in subjects aged between 15 and 25. Urolithiasis 44: 521–528. doi: 10.1007/s00240-016-0878-5. [PubMed: 27038481]

26. Sáez-Torres C, Grases F, Rodrigo D, García-Raja AM, Gómez C, Frontera G (2013) Risk factors for urinary stones in healthy schoolchildren with and without a family history of nephrolithiasis. Pediatr Nephrol 28: 639–645. doi: 10.1007/s00467-012-2368-5. [PubMed: 23212561]

Table 1.

Baseline characteristics of those with and without family history of stone disease

		FMH (−)	FMH (+)	p-value
Initial clinical visit		**N=963**	**N=603**	
Age	(y.o)	58.0 (16.6)	52.3 (16.6)	<0.001
Male gender (%)		532 (55.2)	297 (49.3)	0.026
Body mass index	(kg/m^2)	28.2 (7.0)	28.0 (7.1)	0.555
Metabolic syndrome (%)		251 (26.1)	182 (30.2)	0.086
Race/Ethnicity (%)	White	665 (69.1)	468 (77.6)	<0.001
	Hispanic/Latino	129 (13.4)	55 (9.1)	
	Asian	112 (11.6)	65 (10.8)	
	Black	57 (5.9)	15 (2.5)	
Bilateral stones (%)		177 (18.4)	164 (27.2)	<0.001
Total stone burden	(mm)	7.00 [0.00, 100.00]	7.00 [0.00, 157.00]	0.784
Total stone number	0	262 (27.2)	159 (26.4)	0.672
	1	321 (33.3)	187 (31.0)	
	2	133 (13.8)	83 (13.8)	
	3	63 (6.5)	41 (6.8)	
	≧4	184 (19.1)	133 (22.1)	
Age of first onset for stone (%)	≦10 (y.o)	16 (1.7)	10 (1.7)	<0.001
	11 and 20	52 (5.4)	72 (11.9)	
	21 and 30	117 (12.1)	111 (18.4)	
	31 and 40	130 (13.5)	116 (19.2)	
	41 and 50	157 (16.3)	115 (19.1)	
	51 and 60	193 (20.0)	87 (14.4)	
	≧61	298 (30.9)	92 (15.3)	
Past stone history (%)		477 (49.5)	364 (60.4)	<0.001
Number of previous stone episode (%)	1	192 (40.9)	104 (29.0)	<0.001
	2	80 (17.1)	52 (14.5)	
	3	42 (9.0)	34 (9.5)	
	4	26 (5.5)	14 (3.9)	
	5	20 (4.3)	16 (4.5)	
	≧6	109 (23.2)	139 (38.7)	
Follow up clinical visit		**N=493**	**N=335**	
Duration of follow up	(month)	7.00 [0.00, 56.00]	9.00 [0.00, 54.00]	0.068
Increase of stone burden (%)		73 (19.1)	62 (23.1)	0.448
Recurrent stone event ≧1 (%)		136 (27.6)	128 (38.2)	0.001
		N=242	**N=166**	
Primary stone component	Calcium Oxalate	158 (65.3)	102 (61.4)	0.072

	FMH (−)	FMH (+)	p-value
Initial clinical visit	**N=963**	**N=603**	
Calcium Phosphate	37 (15.3)	27 (16.3)	
Urate	15 (6.2)	15 (9.0)	
Cystine	4 (1.7)	10 (6.0)	
Other	28 (11.6)	12 (7.2)	

FMH = family history; y.o = years old.

Table 2.

Stone outcomes of patients with family history of stone disease compared to those without a family history of stone disease

	FMH (−)	first-degree relative	p-value	FMH (+) first-&second-degree relative	p-value	Paternal side relative	p-value	Maternal side relative	p-value
Initial clinical visit	N=963	N=402		N=75		N=231		N=174	
Bilateral stones (%)	177 (18.4)	104 (25.9)	0.002	27 (36.0)	<0.001	64 (27.7)	0.002	44 (25.3)	0.044
Age of first onset for stone (%) ≦10 (y.o)	16 (1.7)	5 (1.2)	<0.001	2 (2.7)	<0.001	2 (0.9)	<0.001	6 (3.4)	<0.001
11 and 20	52 (5.4)	42 (10.4)		17 (22.7)		27 (11.7)		29 (16.7)	
21 and 30	117 (12.1)	71 (17.7)		20 (26.7)		45 (19.5)		45 (25.9)	
31 and 40	130 (13.5)	74 (18.4)		15 (20.0)		54 (23.4)		35 (20.1)	
41 and 50	157 (16.3)	83 (20.6)		15 (20.0)		49 (21.2)		28 (16.1)	
51 and 60	193 (20.0)	64 (15.9)		3 (4.0)		26 (11.3)		17 (9.8)	
≧61	298 (30.9)	63 (15.7)		3 (4.0)		28 (12.1)		14 (8.0)	
Past stone history (%)	477 (49.5)	246 (61.2)	<0.001	52 (69.3)	0.001	147 (63.6)	<0.001	107 (61.5)	0.005
Number of previous stone episode (%) 1	192 (40.9)	69 (28.7)	0.002	13 (25.0)	0.003	46 (31.5)	0.005	28 (26.4)	0.011
2	80 (17.1)	37 (15.4)		5 (9.6)		19 (13.0)		18 (17.0)	
3	42 (9.0)	21 (8.8)		3 (5.8)		12 (8.2)		10 (9.4)	
4	26 (5.5)	10 (4.2)		3 (5.8)		4 (2.7)		6 (5.7)	
5	20 (4.3)	13 (5.4)		2 (3.8)		7 (4.8)		2 (1.9)	
≧6	109 (23.2)	90 (37.5)		26 (50.0)		58 (39.7)		42 (39.6)	
Follow up clinical visit	N=493	N=229		N=51		N=140		N=100	
Recurrent stone event ≧1 (%)	136 (27.6)	89 (38.9)	0.003	23 (45.1)	0.014	60 (42.9)	0.001	44 (44.0)	0.002

FMH = family history; y.o = years old.

Table 3.

Multivariate analysis of clinical outcomes for stones regarding detailed stone family history.

Logistic regression model		odds ratio	p-value	95% CI
Bilateral stones	any FMH	1.54	<0.001	(1.20–1.98)
	first-degree relative	1.30	0.06	(0.99–1.70)
	first-&second-degree relative	1.92	0.009	(1.17–3.16)
	Paternal side relative	1.37	0.056	(0.99–1.89)
	Maternal side relative	1.19	0.37	(0.82–1.72)
Age of first onset for stone 30 y.o	any FMH	1.84	<0.001	(1.44–2.36)
	first-degree relative	1.42	0.01	(1.09–1.85)
	first-&second-degree relative	3.32	<0.001	(2.04–5.41)
	Paternal side relative	1.53	0.008	(1.11–2.10)
	Maternal side relative	2.93	<0.001	(2.09–4.11)
Past stone history	any FMH	1.55	<0.001	(1.25–1.92)
	first-degree relative	1.47	0.001	(1.16–1.86)
	first-&second-degree relative	2.01	0.007	(1.21–3.33)
	Paternal side relative	1.57	0.002	(1.17–2.11)
	Maternal side relative	1.44	0.028	(1.04–2.01)
Number of previous stone episodes 6	any FMH	2.19	<0.001	(1.65–2.90)
	first-degree relative	1.71	<0.001	(1.27–2.29)
	first-&second-degree relative	2.66	<0.001	(1.60–4.42)
	Paternal side relative	1.84	<0.001	(1.31–2.59)
	Maternal side relative	1.70	0.007	(1.15–2.51)
Recurrent stone event ≧1	any FMH	1.62	<0.001	(1.23–2.13)
	first-degree relative	1.58	0.001	(1.18–2.12)
	first-&second-degree relative	2.17	0.003	(1.29–3.63)
	Paternal side relative	1.93	<0.001	(1.38–2.71)
	Maternal side relative	1.72	0.004	(1.18–2.51)

Each regression model was adjusted with age, gender, Metabolic syndromes (hypertension, hyperlipidemia, diabetes mellitus, obesity), and White Race.

FMH = family history; CI = confidence interval; y.o = years old.