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Increased urinary uric acid excretion: a finding in Indian stone formers

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Abstract Many studies have been done to determine the risk factors associated with urolithiasis so that preventive measures can be undertaken to prevent stone formation. However the exact aetiology of urinary stones still remains elusive. A prospective control study of epidemiological factors that influence urinary stone formation was done to determine the aetiology of urinary stones. Patients with stone disease had a significantly higher body mass index. 24-h urine excretion of uric acid and phosphate was found to be significantly higher in stone patients as compared to controls. The intake of non-vegetarian food was significantly higher amongst stone formers. Stone patients had a significantly higher consumption of curd and cheese as compared to controls. There was a significant correlation noted between stone formation and a positive family and past history of stone disease. The results indicate that obese patients, especially those with a family history of stone disease, should be counselled on weight loss. Individuals with a past history of stone disease should be advised to reduce their dietary intake of foods rich in uric acid (meat, liver and beans).

Keywords Urinary stone · Indian stone formers

Introduction

Little is known about the epidemiology of urinary tract stones despite the relative frequency of this condition the world over [1]. During the past few decades, the prevalence of kidney stones in both males and females markedly increased in industrialized countries [2]. This is presumably due to changes in lifestyle and dietary habit.

Many studies have been done to determine the risk factors associated with urolithiasis so that preventive measures can be undertaken to prevent stone formation. However the exact aetiology of urinary stones still remains elusive. The incidence of recurrent stones remain as high as 50%.

This study was undertaken to determine the predisposing factors for urinary stones and to find trades and diet that are more prone to urinary calculi thus helping in taking proper measures to prevent urinary stone formation and recurrence.

Materials and methods

This study was carried out in the Urology Department, Army Hospital (R&R) during the years 2006–2008. Data on stone cases was collected from the patients with urinary stone admitted in the urology ward. Data of patients admitted to the same Urology ward with non-stone disease but other urological ailments were collected as one control group. Patients admitted to other wards with non-urological ailments formed the second control group. Data was collected for a total 300 patients as under:

All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All persons gave their informed consent prior to their inclusion in the study.

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(a) Study group with urinary stone disease: 154 patients.
(b) Control group of urology non-stone cases: 68 patients.
(c) Control group of non-stone, non-urological cases: 78 patients.

Patients and control data record included their trade, home station, places of stay, details of diet especially non-vegetarian food and milk/milk product intake, number of glasses of water or other fluids per day and any dietary peculiarities. Family and past history of stone disease was recorded along with history of any medications being taken. Personal history of smoking and alcohol intake was also taken. Examination findings were recorded. Thereafter for all stone patients Intra venous urogram findings, and where applicable, nuclear renal scan data were recorded. Haematological evaluation included estimation of haemoglobin, urea, creatinine, calcium, phosphate, uric acid, sodium, potassium and chloride. Urine examination included estimation of 24-h volume, specific gravity, 24-h calcium, 24-h phosphate and 24-h uric acid. A treatment record of stone patients was also made.

Statistical analysis of the data was carried out using SPSS version 15 software.

Results

Patients with stone disease had a significantly higher body mass index (BMI) as compared to patients without urinary stones (Tables 1, 2). No significant difference was found between age and service length between stone and non-stone cases. Fluid and milk intake between stone cases and urology non-stone cases was not found to be significantly different. Stone patients had higher serum levels of creatinine, uric acid, phosphate and potassium as compared to urology non-stone cases (Table 3). However these higher levels were within the normal range. When compared to non-urology non-stone cases, stone patients had higher serum levels of uric acid and chloride (Table 4). Once again these higher levels in stone cases were within the normal range.

Twenty-four hour urine excretion of uric acid and phosphate was found to be significantly higher in stone patients as compared to urology non-stone cases (Table 5). The 24-h urine excretion of uric acid was also significantly higher in stone patients when compared to non-urology non-stone controls. In this group the 24-h urine output was also significantly higher in the stone formers (Table 6).

The diet of both stone and non-stone control cases was predominantly a combination of wheat and rice. The intake of non-vegetarian food was significantly higher amongst stone formers (*P* value 0.031) as compared to both urology and non-urology control cases. The frequency of non-vegetarian food consumption also, was significantly higher amongst stone formers as compared to non-stone non-urology cases (*P* value 0.03). Stone patients had a significantly higher consumption of curd as compared to both non-stone control groups (*P* value 0.000). Likewise the consumption of cheese was found to be significantly higher in stone formers as compared to non-stone control cases, *P* values 0.000 and 0.05, respectively.

The majority of stone patients were non-smokers. There was no correlation noted with alcohol intake and stone formation. There was a significant correlation noted between stone formation and a positive family and past history of stone disease (*P* values 0.03 and 0.001, respectively).

The trades thought to be at higher risk of forming stones i.e. drivers/cooks were not found to have a significantly higher incidence in this study. Although the majority of stone patients were hailing from the Northern India, when compared to the control cases no significant difference was noted.

Table 1 Comparison of height, weight, BMI and age between stone cases and non-stone urology patients

	Stone cases	Urology non-stone controls	*t* test and *P* value
Height (cm)	169.74 ± 4.62	171.16 ± 5.17	−1.949, 0.054
Weight (kg)	68.13 ± 8.06	67.31 ± 6.78	0.776, 0.439
BMI	23.66 ± 2.77	22.97 ± 2.12	2.024, 0.045*
Age (years)	32.81 ± 8.59	34.28 ± 8.48	−1.184, 0.238

* Statistically significant

Table 2 Comparison of height, weight, BMI and age between stone cases and non-stone non-urology patients

	Stone cases	Non-urology non-stone controls	*t* test and *P* value
Height (cm)	169.74 ± 4.62	170.63 ± 4.88	−1.358, 0.185
Weight (kg)	68.13 ± 8.06	66.56 ± 8.36	1.380, 0.175
BMI	23.66 ± 2.77	22.85 ± 2.57	2.221, 0.028*
Age (years)	32.81 ± 8.59	34.45 ± 7.97	−1.439, 0.152

* Statistically significant

Discussion

This study found that. Stone formers had a significantly increased body mass index (BMI), as compared to non-stone control cases. Taylor et al. [3] have similarly reported that an increasing body weight, BMI and waist line are associated with an increasing risk of stone formation. The magnitude of the increased risk has been found higher in women. A BMI of 21 to 23 was associated with a 30% increased risk of stone formation in men and a 50% increased risk in women.

Table 3 Comparison of serum biochemistry between stone cases and non-stone urology patients

	Stone cases	Urology non-stone controls	*t* test and *P* value
Blood urea nitrogen (mg/dL)	13.26 ± 5.05	12.56 ± 3.32	1.224, 0.222
Serum creatinine (mg/dL)	1.266 ± 1.14	1.056 ± 0.36	2.074, 0.039*
Serum calcium (mg/dL)	9.80 ± 0.81	9.97 ± 0.64	−1.717, 0.888
Serum phosphate (mg/dL)	3.42 ± 0.75	3.16 ± 1.02	2.13, 0.034*
Serum uric acid (mg/dL)	5.872 ± 1.41	4.991 ± 1.02	5.250, 0.000*
Serum sodium (meq/L)	139.55 ± 4.58	139.74 ± 4.82	−0.275, 0.784
Serum potassium (meq/L)	4.134 ± 0.451	4.268 ± 0.45	−2.052, 0.042*
Serum chloride (meq/L)	103.86 ± 7.91	102.93 ± 3.60	1.205, 0.229

* Statistically significant

Table 4 Comparison of serum biochemistry between stone cases and non-stone non-urology patients

	Stone cases	Non-urology non-stone controls	*t* test and *P* value
Blood urea nitrogen (mg/dL)	13.26 ± 5.05	15.18 ± 10.29	−1.494, 0.139
Serum creatinine (mg/dL)	1.266 ± 1.14	1.33 ± 1.21	−0.373, 0.710
Serum calcium (mg/dL)	9.80 ± 0.81	9.77 ± 0.63	0.251, 0.802
Serum phosphate (mg/dL)	3.42 ± 0.75	3.291 ± 0.90	1.049, 0.297
Serum uric acid (mg/dL)	5.87 ± 1.41	5.41 ± 1.08	2.631, 0.009*
Serum sodium (meq/L)	139.55 ± 4.58	138.31 ± 4.52	1.881, 0.062
Serum potassium (meq/L)	4.13 ± 0.451	4.09 ± 0.43	0.675, 0.488
Serum chloride (meq/L)	103.86 ± 7.91	102.44 ± 2.67	1.982, 0.049*

* Statistically significant

Table 5 Comparison of 24-h urine values between stone cases and non-stone urology patients

	Stone cases	Urology non-stone controls	*t* test and *P* value
Urine volume	3486.60 ± 1168.67	3543.94 ± 743.82	−0.436, 0.663
Specific gravity	1012.49 ± 9.11	1011.02 ± 3.48	1.731, 0.085
24-h calcium (mg)	183.42 ± 119.52	211.06 ± 156.32	−1.284, 0.202
24-h phosphate (mg)	484.35 ± 263.92	361.93 ± 241.95	3.342, 0.001*
24-h uric acid (mg)	563.79 ± 269.47	381.00 ± 177.64	5.922, 0.000*

* Statistically significant

Table 6 Comparison of 24-h urine values between stone cases and non-stone non-urology patients

	Stone cases	Non-urology non-stone controls	*t* test and *P* value
Urine volume	3486.60 ± 1168.67	2945.08 ± 784.41	3.927, 0.000*
Specific gravity	1012.49 ± 9.11	1014.33 ± 6.58	−1.642, 0.103
24-h calcium (mg)	183.42 ± 119.52	161.19 ± 113.80	1.272, 0.206
24-h phosphate (mg)	484.35 ± 263.92	550.79 ± 269.47	−1.578, 0.118
24-h uric acid (mg)	563.79 ± 269.47	419.23 ± 164.88	4.765, 0.000*

* Statistically significant

Several population based studies have found that the incidence rates of stone disease begins to rise after age 20, peaks between 40 and 60 years and then begins to decline [4–6]. The bulk of our patients were in the 20–40 years age range. In this study, incidence of stone disease was not found to be significantly different with age.

Fluid intake by stone patients in the study ranged from 3 to 5 L/day and was not significantly different from other non-stone-urological control cases. This was explained by the fact that most urological patients are as a dictum advised to increase their fluid intake. A randomized control trial has demonstrated the importance of fluid intake in

reducing the likelihood of stone formation [7], while other studies have shown that when the urine output is less than 1 L/day the risk of stone formation is markedly high [5, 8, 9]. No significant difference in urine output of stone patients vis-a-vis non-stone urology controls was observed in this study.

This study found a significantly higher level of serum uric acid in stone patients as compared with non-stone cases (both urology and non-urology controls), even though the values were within the normal range. Stone patients also had significantly higher levels of serum creatinine, serum potassium and phosphate as compared to non-stone urology controls but these values were not significantly higher in the non-urology non-stone controls. Notably, serum calcium was not found to be significantly higher in stone patients. Uric acid has been identified as a component of kidney stones.

A significantly higher urinary uric acid excretion amongst stone formers was found in this study. Uric acid production results from the degradation of purines, derived exogenously from diet and endogenously from purine biosynthesis that includes nucleic acid turnover. Hyperuricosuria (defined as excretion greater than 600 mg/day) is seen more frequently in patients who form calcium stones than in normal subjects [10].

Stone patients had a significantly higher intake of curd and cheese as compared to non-stone cases. The constitution of urine is influenced by our diet. Both calcium and animal protein have been implicated in renal stone formation. Although dietary calcium had been strongly suspected in raising the risk of stone formation and confirmed in our study, men with a higher intake of dietary calcium were found to have a lower risk of nephrolithiasis, in some other larger studies [5, 8, 9]. Dietary calcium restriction is at present not advised based on these large studies which found low calcium intake to increase oxalate reabsorption and urinary excretion. Low calcium intake was also found to accelerate bone loss. However, in spite of similar bio availability supplemental calcium appears different from dietary calcium. High animal protein intake leads to increased calcium and uric acid excretion as well as decreased urinary citrate [11], all of which increase the risk of stone formation.

No association was found in this study between smoking and stone formation. Even though stone patients had a higher frequency of alcohol consumption than non-stone urology controls, this was not corroborated with non-stone non-urology controls. Some observational studies have found a reduced risk of stone formation with coffee, tea, beer and wine consumption [12, 13].

A strong correlation was found in the present study between a positive family and past history of stone disease. Stone patients had a significantly higher incidence of a positive family and past history of stone disease as compared to non-stone cases. The risk of becoming a stone former is more than 2.5 times greater in individuals with a history of stone disease [11] A positive past history of stone disease increases by 30–40% the likelihood of forming another stone at 5 years [6].

It has been indicated that urinary calculi are much more likely to be found in individuals who have sedentary occupations. However no significant correlation was found between occupation and stone formation in the present study. Blacklock reported that the incidence of urinary calculi was higher in administrative and sedentary personnel of the Royal Navy than in manual workers [14]. The highest incidences were found in cooks and engineering room personnel in their study.

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