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Role of Diet in Renal Stone Disease in Indian Population: A Case Control Study

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ABSTRACT

Background: Renal stone is a multifactorial disease with major risk factors of genetic, demographic, environmental, diet, obesity, and metabolic syndrome. This study was conducted to determine the role of diet in renal stone disease and to identify the disease risk factors.

Methods: A case control study was conducted among renal stone patients attending a tertiary hospital, East Delhi, India. Data collection was done using a questionnaire for demographic profile and food frequency questionnaire. Daily intake of calories, proteins, carbohydrates, calcium, oxalate, fiber, and salts were determined between cases and controls.

Results: The mean age was 34.4 years and the median energy intake was 1176.43 kcal/day. Daily median consumption of carbohydrate, protein, fat, and fiber among patients with renal stone was 233.96, 47.20, 10.16, and 6.37 g, respectively. Almost 90% of patients had calcium intake of <1000 mg/day with median value of 291.65 mg/day. The median daily intake of oxalate, phosphate, and magnesium, was 22.41, 1083.05, and 298.25 mg, respectively. Daily intake of sodium and potassium was 93.42 and 1048.06 mg, respectively. The median water intake was 2L/day. Significantly higher consumption of fat and calcium was found among overweight patients and the protein, potassium, and calcium consumption was higher among males.

Conclusion: The daily intake of dietary components was widely distributed in renal stone patients. No clear trends were defined. Intake of calcium and water was less among patients. Further dietary interventional studies among the population with diverse dietary patterns can provide more evidence.

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Introduction

The global prevalence of the renal stone disease is increasing and is higher in the Western world compared to the East. In Asia, the stone belt stretches across Sudan, Saudi Arabia, The United Arab Emirates, The Islamic Republic of Iran, Pakistan, India, Myanmar, Thailand, Indonesia, and the Philippine (1). Renal stone disease is a multifactorial disease with major risk factors of genetic, demographic, environmental, dietary, obesity, and metabolic syndrome ones (2, 3). Dietary components mainly, intake of calcium (4,

5), ascorbic acid, oxalate (5-7), sodium (8), fructose (9), water, beverages like fruit juice, beer (10), foods rich in animal protein, refined sugar, and salts (11) are involved in the pathogenesis of stone formation; as it influences urine pH, volume and solute concentrations and thereby leads to stone formation (12).

In India, 12% of the total population is prone to renal stone formation. The prevalence of renal stones varies between north and south India. A higher number of cases have been reported in north India when compared to south India with a prevalence of 15% and 12%, respectively. The stone belt of India includes Rajasthan, Punjab, Haryana, Delhi, West Bengal, Bihar, Maharashtra, and Gujrat (13). The geography of India extends from Kashmir to Kanyakumari and Gujarat to West Bengal. Divers food habits are seen based on geography including North Indian, South Indian, West Indian, and East Indian cuisines. The variety in the diet also differs based on the particular religion, socioeconomic status, and lifestyle in the same geographic area (13).

There are different methods to assess the food intake in a population which include food frequency questionnaires (FFQs), 24-hour recall method, and food diary. Food frequency questionnaires consist of a list of food items, amounts, and frequency of consumption over a certain duration of time. The energy and nutrient contents are calculated based upon the portion size and frequency. Food frequency questionnaire in particular has the advantage of applying to a large study population, less cost, easy to collect and less burden on the individuals participating and the persons conducting the research (14). The objective of this study was to determine the influence of diet in renal stone disease in the north Indian population using FFQs and to estimate the frequency of risk factors for stone formation in the North Indian population.

Materials and Methods

A case-control study was conducted in the Department of General Surgery in a tertiary care hospital in Delhi, the capital of India, which caters to patients from most of the North Indian states including Uttar Pradesh, Bihar, Punjab, Haryana, and Rajasthan. The study participants included patients with renal stone disease attending surgery out-patient department, who were diagnosed to have renal stone by X-ray or ultrasonography (USG). The healthy spouse of the patient or the close family member in case of unmarried patients who were staying with the patient in the same home and consuming the same diet were recruited for the study, as one control group and 15 healthy unrelated volunteers as a second control group. Both the control groups had no history suggestive of renal stone disease and screening ultrasonography to reveal any renal stone disease.

A semi-structured questionnaire was filled for cases and controls which included the demographic profile of the patients. This included the age, sex, place of stay for the previous 10 years, and occupation of the patients. The occupation was categorized as sedentary, moderate, or heavy physical labor according to the level of activity as per the Indian Council of Medical Research (ICMR) classification. Weight in kilogram and height in meter for the patient was measured to calculate the body mass index (BMI) and to classify as underweight, normal, overweight, and obese based on World Health Organization (WHO) classification.

Dietary intake was evaluated by using food frequency questionnaires (FFQs) with the help of the consultant dietician. FFQs is a checklist of food and beverages with a frequency response section for subjects to report how often each item was consumed over a specified time period. The analytic strategy used in the food frequency questionnaire is that the frequency of consumption is multiplied by portion size and by nutrient density and these are summed up to obtain nutrient totals. The approximate daily intake of calories, proteins, carbohydrate, calcium, oxalate, fiber, and salts were then calculated from the values provided In Nutritive values of Indian foods (edition 1989), reprinted in 2004. Individual's daily fluid intake was also recorded as milliliter volume per day. The information obtained from the study subjects was kept confidential. A written consent letter was provided from each participant of the study after being confirmed in our institution ethics committee. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices.

The data were analyzed using SPSS software (version 24.0 for the Windows platform, SPSS Inc., Chicago, II, USA). Descriptive tables were generated to find the frequencies of demographic and dietary parameters among renal stone patients and also among control groups. Comparison of cases and control groups were done and the associated factors were found using Chi-Square (c2) test for categorical variables and analysis of variance (ANOVA) for continuous variables after doing log transformation of factors that were right-skewed. A p value of <0.05 was be taken as significant. All those factors found significant in ANOVA were further analyzed using Dunnett's post hoc test. Multivariate analysis was done by using binary logistic regression.

Results

Thirty-four patients diagnosed with renal stone disease were included in the study and analyzed. Thirty of the subjects were first-time stone formers and 4 subjects were recurrent stone ones. The mean age of stone formers in our study was 34.4 years (SD=14.33). Eighty-five percent of renal stone patients were less than 50 years of age. Twenty-four out of 34 patients (70.6%) were males. 76.5% of patients were employed, while the rest (23.5%) were homemakers. Almost, 60% of the patients were working in occupations requiring moderate levels of physical work; while 17.6% were working in heavy physical activities. A total of 23.5% of patients belonged to a sedentary group and developed stones. Twenty percent of patients were overweight or obese and 23.5% were underweight.

The approximate daily intake of all dietary components was very widely distributed in renal stone patients. The energy intake ranged from 400-2734 kcal/day and the protein intake had a wide range of 12.3-96.4 g/day. The mean fat intake was 10.16 g/day and the intake of carbohydrates ranged from 79.35 to 492 g/day. The mean calcium and oxalate intake of the patients was 291.65 and 22.41 mg/day, respectively. Regarding the calcium intake, there were only 8 patients (23.5%) who had less than 600 mg/day, which is the recommended daily intake. Almost, 50% of renal stone patients had a daily oxalate intake between 20 and 40 mg/day. The sodium intake among most of the renal stone patients (82.4%) was in the range of 25-200 mg/day. The mean water intake of renal stone patients was 2000 mL and in 11.8% of renal stone patients, water consumption was less than 1000 mL.

The mean daily intake of carbohydrate, fiber, oxalate, potassium, phosphate, magnesium, and water was found to be higher in recurrent stone formers, whereas the daily average intake of energy, protein, fat, calcium and sodium was found to be lower. This difference in the daily intake of dietary components among recurrent and first-time stone formers was not found to be statistically significant (p>0.05). Comparison of dietary profile according to BMI was presented in Table 1. The daily average intake of energy, protein, carbohydrate, fiber, oxalate, sodium potassium, phosphate, magnesium, and water was found to be higher in overweight stone formers. But this difference among overweight and non-overweight stone formers were not found to be statistically significant (p>0.05). The daily intake of fat and calcium was higher among overweight renal stone patients when compared to others and was statistically significant with p=0.005 and p=0.004, respectively.

Gender-wise comparison of dietary profile was demonstrated in Table 2. The daily average intake of energy, carbohydrate, oxalate, sodium, potassium, phosphate, magnesium, and water were found to be higher among male renal stone patients and fiber intake was found higher among female renal stone patients. However, this difference was not found to be statistically significant (p>0.05). The daily intake of protein and calcium was higher among male renal stone patients when compared to females and were statistically significant with p=0.038 and p=0.032, respectively. Comparison of dietary profile among cases and controls was illustrated in Table 3. The dietary factors of stone formers were compared with non-stone formers spouse/close relative and healthy volunteers using ANOVA test and Dunnett's post hoc test. The differences in the intake of dietary factors between the patients, their spouse/relative, and healthy volunteer showed no statistically significant difference (p>0.05).

Table 1: Comparison of dietary components and biochemical parameters in overweight and non-overweight renal stone patients.

Variables	Overweight (n=7)	Non-overweight (n=27)	*p* value
Dietary factors			
Energy	1534.88±442.16	1206.24±548.24	0.153
Protein	59.22±18.98	42.14±20.30	0.053
Fat	25.52±9.34	12.49 ± 9.52	0.005
Carbohydrate	264.19±13.07	240.07±111.24	0.593
Fiber	8.34±9.74	14.22±15.75	0.236
Calcium	739.26±452.23	319.06±276.39	0.004
Oxalate	26.93±10.79	24.17±17.41	0.693
Sodium	259.83±282.86	141.96±217.99	0.239
Potassium	1303.70±389.26	991.03±531.82	0.157
Phosphate	1250.94±284.64	1082.01±655.07	0.514
Magnesium	302.99±39.53	326.38±172.43	0.525
Water Intake	2285.71±809.17	2061.11±831.86	0.527

Table 2: Comparison of dietary components and biochemical parameters among males and females of renal stone patients.

Variables	Males (n=24)	Females (n=10)	*p* value
Dietary factors			
Energy	1387.64±564.19	1000.93±366.91	0.055
Protein	50.43±21.94	34.21±13.16	0.038
Fat	16.62±12.10	11.70±9.35	0.260
Carbohydrate	263.56±104.00	200.59 ± 95.16	0.109
Fiber	11.29±13.53	17.12±17.52	0.301
Calcium	489.20±389.26	204.86±124.25	0.032
Oxalate	26.69±18.19	20.03±8.80	0.280
Sodium	204.53±268.84	74.305±34.65	0.140
Potassium	1173.56±542.84	771.84±314.39	0.037
Phosphate	1192.16±663.43	935.91±367.46	0.261
Magnesium	329.19±159.25	303.26±148.12	0.662
Water Intake	2312.50±805.05	1615±654.92	0.021

Table 3: Intake of dietary factors among renal stone patients, spouse/close relatives, and healthy volunteers.

Dietary components	Renal stone patients (C)	Spouse/Close relatives (Sp)	Healthy volunteers (Hv)	*p* value	Dunnet's post hoc test (*p* value)
	Mean±SD	Mean±SD	Mean±SD		
Energy	3.04±0.18	3.06±0.20	3.06±0.14	0.914	C vs. Sp (0.896) C vs. Hv (0.941)
Protein	1.61±0.21	1.67±0.26	1.61±0.13	0.555	C vs. Sp (0.501) C vs. Hv (0.996)
Fat	1.04±0.36	1.08±0.42	1.13±0.38	0.793	C vs. Sp (0.935) C vs. Hv (0.729)
Carbohydrate	2.32±0.20	2.36±0.18	2.33±0.15	0.652	C vs. Sp (0.591) C vs. Hv (0.991)
Fiber	0.81±0.52	0.89±0.40	0.91±0.53	0.765	C vs. Sp (0.790) C vs. Hv (0.756)
Calcium	2.43±0.39	2.45±0.38	2.47±0.29	0.942	C vs. Sp (0.973) C vs. Hv (0.923)
Oxalate	1.30±0.31	1.31±0.53	1.43±0.44	0.575	C vs. Sp (0.998) C vs. Hv (0.526)
Sodium	2.0±0.40	1.94±0.36	2.20±0.35	0.102	C vs. Sp (0.796) C vs. Hv (0.177)
Potassium	2.98±0.33	2.96±0.24	3.01±0.16	0.827	C vs. Sp (0.936) C vs. Hv (0.914)
Phosphate	3.01±0.22	3.03±0.21	3.02±0.15	0.927	C vs. Sp (0.900) C vs. Hv (0.981)
Magnesium	2.42±0.25	2.51±0.26	2.51±0.14	0.261	C vs. Sp (0.243) C vs. Hv (0.368)
Water Intake	3.36±3.0	3.37±3.0	3.49±3.0	0.610	C vs. Sp (0.900) C vs. Hv (0.518)

All values are the log of observed values. *C: Renal stone patients; Sp: Spouse/Close relatives; Hv: Healthy volunteers

Discussion

Several dietary factors have been observed to alter the risk of kidney stone diseases. Data on dietary studies revealed that in developing countries like India; dietary deficiency of nutrients like low fluid intake, low intake of protein, lower intake of fruits and green leafy vegetables and calcium along with increased consumption of oxalate-rich foods can play a major role in the disease (15). High energy consumption is associated with renal stone formation, while the mean energy intake of patients with renal stone disease in our study was 1176.43 kcal/day. Our patients had low daily dietary energy consumption when compared to the general population of India (2360 kilocalories) (16, 17). A Western study by Leonetti *et al.* among 108 stone formers exhibited the average daily energy consumption to be 2336.2 kcal/day (18) similar to

our study, that there was no significant difference in energy consumption among cases and controls. A similar finding was also found by Ferraro *et al.* among 5,355 kidney stone patients (19).

High consumption of protein is a known dietary risk factor for renal stone formation. The mean daily intake of protein among renal stone patients in our study was 47.20 g/day. Similar to our study, another Indian case-control investigation by Rajkiran *et al*. reported the mean protein intake among stone formers in rural and urban settings to be 37.1 and 47.9 g/day, respectively (20). Conversely, higher protein intake of 87.3 g/day was observed in Western studies (16, 18). No significant differences between cases and healthy controls were seen in the daily protein intake in our study that is identical to other observational studies (16, 18, 19, 21, 22).

High fat consumption is directly related to the incidence of obesity, which is considered an independent risk factor of renal stone (23). The fat intake among overweight patients with renal stones was found to be significantly higher when compared to the rest of the renal stone patients in our study. Similar to another Indian study, there was no significant difference for the fat intake among renal stone cases and the controls (20). In contrast, a Western study has shown significantly higher daily intake with an average daily intake of 95.5 g/day and a significant difference in intake among cases and controls (16).

Zahrani *et al.* observed the dietary habits of 500 idiopathic renal stone patients and noted the average daily carbohydrate intake was 272.5 g/day and reported a significantly higher intake of carbohydrate in renal stone patients (16). In our study, the daily carbohydrate intake in patients with renal stones was 233.96 g/day and there was no significant difference in the daily intake between cases and controls. An Indian case-control study in northwest India showed the mean carbohydrate intake among stone formers to be 288, 367, and 486 g/day among tribal, rural, and urban stone forms, respectively (20). There was no significant difference between the patients with renal stones and controls in any of the settings.

Reduced intake of dietary fiber is considered a risk factor for renal stone disease (24). Two observational studies revealed that increased intake of fiber was associated with decreased risk of renal stone disease (25, 26). However, dietary intervention studies have not been able to prove the efficacy of a high fiber diet for stone prevention (27, 28). Though the intake of fiber was less among our cases, there was no statistically significant difference between groups. A contrasting result was found by Zahrani *et al.* (16) who reported a significantly higher intake of fiber among renal stone patients when compared to controls and the author ascribed the finding as dietary fiber might increase the risk of stone formation by increasing hyperoxaluria, as many foods high in fiber are also high in oxalate.

Dietary calcium is an important factor in renal stone formation. Randomized and prospective trials have noted that the incidence of kidney stones increases two-fold in the dietary calcium restricted group in comparison to the normal calcium intake group, while the higher intake of dietary calcium reduced the risk of kidney stones by preventing the absorption of oxalate by the formation of calcium oxalate complexes; thereby decreasing the urinary excretion of oxalate (26, 29-31). Some Indian studies have noted calcium intake of 460 mg/day in an urban setting and 431 mg/day in a rural setting in renal stone patients and few have noted less in stone formers (30, 31). The average calcium intake was less in our study with an average intake of 291.65 mg/day with no significant difference between the groups. Most of our patients with renal stones had less than 1000 mg of calcium per day which is a significant finding noted.

Increased absorption of dietary oxalate may be observed more in renal stone patients than controls (32). However, oxalate quantity of the diets is not the only reason for renal stone formation, but other factors also are included like genetic differences or colonization of an enteric oxalate degrading organism such as *Oxalobacter formigemenes* (33). The mean intake of oxalate among stone formers was 22.41 mg/day and no significant difference among cases and controls was noticed in our study. In a prospective study by Taylor and Curhan in Health Professionals follow up study of Nurses Health Study (NHS) I and II, while the median daily oxalate intake was 194, 166, and 151 mg, respectively, except for NHS II that it did not show any significant difference for oxalate consumption among stone formers and non-stone formers. This study does not implicate dietary oxalate as a risk factor for renal stone formation (33).

The exact role of magnesium in stone formation is not known. However, Taylor *et al.* in a cohort study of 27,001 Finnish male smokers found that magnesium intake was inversely associated with the risk of kidney stones (4). In contrast, some of the epidemiological evidences did not indicate any significant association between magnesium intake and prevalence of renal stone (34). Our study had similar daily consumption of magnesium among patients with renal stone disease which is similar to that of another Indian study (20).

Increased sodium intake causes urinary loss of calcium as they share the same transport in the

kidney. Therefore a high sodium diet can lead to hypercalciuria, which is a known cause of renal stone formation. However, in a 14-year follow-up of HPFS, Taylor *et al.* did not find excessive intake of sodium as an independent risk factor for renal stone formation (4). In contrast, prospective studies demonstrated higher dietary potassium intake to be associated with a decreased risk of stone formation (4, 35). Curhan *et al.* reported that the potassium intake was found to be inversely related to the risk of kidney stone formation which means with a lower intake of potassium (<74 mmol/day), there was a higher risk of stone formation (26). This effect of potassium is described because of the increase in urinary calcium and decrease in urinary citrate induced by low potassium intake. The average intake of sodium and potassium was not significantly different among cases and controls in our study.

An epidemiology study found a 30-40% risk reduction associated with fluid intake of 2.5 liters/day or more (26). It also reduced the risk of renal stone recurrence (36, 37). A dietary intervention study by Kirac *et al.* on the effect of 24-hour urine parameters found that 34.3% of the patients had a fluid intake of less than 1 L/day (38). More than 65% of our renal stone patients had a daily water intake of less than 2 liters. Similar results were noted by another Indian study by Apurba *et al.* (39).

Conclusion

The approximate daily intake of all dietary components was very widely distributed in renal stone patients. No clear trends were visible as such intake of calcium and water was less in a majority of our patients. The approximate dietary intake of nutrients among cases and controls was almost similar. The literature review has shown that low intake of water, fiber, calcium, potassium and high consumption of energy, protein, fat, oxalate, and sodium can play a major role in renal stone formation. Further dietary interventional studies among a population with diverse dietary patterns can provide more evidences regarding the relationship between diet and renal stone formation.

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Conflict of Interest

None declared.

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