Original Article

Risk Factors of Urolithiasis: A Case Control Study

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Abstract

Introduction: Urolithiasis is one of the most common disorders of the urinary tract. In India, 12% of the population is anticipated to have urolithiasis. Out of which 50% can end up with the renal damage. This study aimed to identify the dietary and lifestyle risk factors of urolithiasis in a tertiary care Hospital of South India.
Materials and Methods: A case control study was conducted among 484 (242cases and 242 controls) patients attending the outpatient and inpatient departments of tertiary care hospital. Cases were matched on age and gender with controls. The data were collected between 28th December 2017 and 16th March 2018. The non-probability purposive sampling technique was used.
Results: The study showed statistically significant association between urolithiasis and consumption of tea (p=0.005), duration of high blood pressure (p=0.030) frequency of pickle intake in a week (p=0.007), salted nuts (p=0.001), condiments (p=0.003), frequency of meat intake in a week (p=0.001) and milk products (p=0.003). The odds of having urolithiasis among those who did not consume salted nuts is 2.139 times less than among those who consume salted nuts (OR=2.139, CI=1.112, 4.113). Other dietary factors such as intake of tea (OR=.463, CI=.259, .827), intake of pickle (OR=0.762, CI=.629, .923), and milk products (OR=0.485, CI=.310, .759) were had a reduced chance of getting urolithiasis.
Discussion and Conclusion: The study concludes that, intake of salted nuts can lead to a significant increase in the risk of urolithiasis as compared to other risk factors such as consumption of tea, milk products and intake of pickle. And also is more seen in the age group of 41-65 years and being male gender. Even though urolithiasis is caused by several factors, it will be different from one geographical area to other. Patients, family and communities should be educated about the occurrence of disease and related risk factors and has to be followed in their daily life

Key-words: kidney stone, renal calculi, risk factors, case control study, South India

Introduction

Urolithiasis is a condition in which stones are developed in the urinary tract and considered to be one of the most common urological disorders, longstanding medical illnesses and common public health problems (Singh & Sailo, 2013).

With an increasing economic status, as well as changes in people's lifestyle and diet structures,

the occurrence of urinary calculus has also shown a growing trend, and has become one of the common diseases that pose a serious threat to human health. There are many factors related to the onset of urinary calculi; however, no precise etiology has been confirmed yet (Wang, Liu, He, & Wang, 2015).

It has been reported that urolithiasis as a multifactorial recurrent disease, distributed worldwide in urban, rural, non-industrial and industrial regions with different chemical composition of analysed stones in the context to various risk factors. Besides diet, genetic factors are also reported to contribute in pathogenesis of urolithiasis (Singh & Sailo, 2013).

One of the more striking new trends appears to be the increased incidence of stone formation in women. The increase in incidence of women affected by urinary tract stone disease has outpaced that of men (Roudakova & Monga, 2014). Current gender related epidemiologic findings derived from different geographical regions are indicating a demographic shift, with an increased prevalence of stone disease in female subjects (Arampatzis, et al., 2012).

Several factors are recognized which increases the potential of a susceptible individual to develop stones. These include anatomical anomalies in the kidneys and urinary tract e.g. horseshoe kidney, ureteral stricture, family history of renal stones, hypertension, gout, hyperparathyroidism, immobilization, metabolic disorders which increase excretion of solutes, more common occurrence in hot climates, increased risk of stones in higher socio-economic groups (F, K, & L, 1996).

People living in tropical belt or “stone belt”, like India are those who suffer from renal stone ailments resulting from rising temperatures and profuse sweating. Geographical factors combined with improper hydration, genetics, gender, diet and obesity increase the risk of formation of renal stones (Vandhana & Sundaram, 2016). People in north eastern states of India are now suffering from the renal stone disease. In India, 12% of the people is estimated to have urinary stones, out of which 50% can develop loss of function of kidneys or renal failure (Sofia, Walter, & M, 2016).

Based on this literature reviews this study aimed to assess the risk factors for urolithiasis and association between risk factors and urolithiasis among patients attending OPDs and IPDs of tertiary care hospital. This study includes the factors of diet, comorbidities, family history and lifestyle factors. Patients attending the OPDs are from south Indian states i.e. Karnataka and Kerala and the number of patients attending Urology OPD with urolithiasis is on an average 10-15 per day. The following hypothesis was stated for the present study i.e. H1- there will be significant association between risk factors and urolithiasis, H0- there will be no significant association between risk factors and urolithiasis.

Materials and Methods

Two hundred and forty two patients with urolithiasis consulted and hospitalized in the department of Urology from 28th December 2017 to 16th March 2018 were enrolled in this study as cases. The setting for the study was a tertiary care hospital with super speciality facilities in Karnataka. According to diagnostic criteria, all cases were confirmed as urolithiasis by means of ultrasound and radiographic evaluation. The inclusion criteria were: 1) male and female patients who diagnosed as urolithiasis, 2) age between 19-65 years, 3) able to read and write Kannada or English. Patients with chronic renal failure and chronic urinary system disorder were excluded for the study. But the information on self-reported chronic comorbid conditions such as hypertension, diabetes, and gout was collected.

Controls in the study were the patients attending Medicine OPD from the same tertiary care hospital who do not have urolithiasis in the same period. Patients who had past history of urolithiasis were also excluded from the study. Cases were matched on age and gender with controls.

The sample size of this study was estimated based on the findings of previous study (Krieger, Richard, & Kronmal, 1996). Family history of urolithiasis (OR=2.03) is considered as a variable

to find the sample size of present study. It is calculated with the help of statistician.

By using the formula,

$$N= \frac{2*PQ(Z1-\frac{\infty}{2}+(Z1-\beta)2}{(P1-P2)2}$$

Where P1 & P2 are percentage of (%) of exposure of cases and controls respectively. Z1-∞/2 = 1.96 at 5% level of significance & (Z1-β) = 0.84 at 80% power and the sample size N= 242 in each group with total of 484 in both groups.

CTRI registration (CTRI/2018/01/011634) was done because as it was mandatory to register all prospective clinical studies to CTRI hosted at ICMR and as per the suggestions of Institutional Ethics Committee. Data was collected after obtaining approval from Institution Ethics Committee, administrative permission and administering informed consent to participants. A structured demographic proforma and semi structured questionnaire on risk factors of urolithiasis which includes the aspects of lifestyle, family history, dietary intake with frequency, existing comorbidities and medications were used to collect data from participants. Each participants were instructed to respond the frequency of intake of food items in a week how many times. The clinical parameters like height, weight and BMI were measured by investigator by using calibrated instruments. The purpose of the study was explained with participant information sheet and informed consent obtained from participants prior to the data collection procedure.

Statistical Analysis

The obtained data were coded and analysed by using SPSS version 16 with statistician's assistance. Demographic characteristics of participants was analysed by using descriptive statistics i.e., frequency and percentage. To find the association between risk factor and urolithiasis inferential statistics were used. The goodness of fit statistics was assessed by computing Pearson Chi square followed by binary logistic regression was done. Interpretation of data was by considering odds ratio (OR) and 95% confidence interval (95%CI). P<0.05 was considered to be significantly associated.

Results

Description of demographic characteristics:

The frequency and percentage of demographic characteristics of cases and controls are shown in Table 1.

The study results shows that, most 149 (61.6%) of the participants were in the age group of 41-65 years, 179 (74%) were males. Most 182 (75.2%) of the cases and 176 (72.7%) of the control group were belonging to Hindu religion. Regarding the area of living, majority 194 (80.2%) of cases and 192(79.4%) of controls were living in rural area. Most 141 (58.3%) of cases and 135 (55.8%) of controls were in the category of normal BMI i.e. 18.5 to 24.9 Kg/m^2

Description of risk factors: Total of 26 risk factors studied in the current research based on a dichotomous scale and frequency of few risk factors such as food items, medications, duration of comorbidities. To find the association between risk factors and urolithiasis, the null hypothesis was stated as follows: There will be no significant association between risk factors and urolithiasis. The association assessed by computing Pearson Chi square and is shown in table 2

Statistically significant association found between urolithiasis and few risk factors such as consumption of tea (x^2=7.837, p=0.005), duration of high blood pressure (x^2=10.732, p=0.030) frequency of pickle intake in a week (x^2=14.236, p=0.007), salted nuts (x^2=16.34, p=0.001), condiments (x^2=8.065, p=0.003) frequency of meat intake in a week (x^2=19.678, p=0.001) and milk products (x^2=8.996, p=0.003). There was no association found between other risk factors and urolithiasis which was assessed in this study i.e. dietary factors includes intake of coffee, 6-8 glass intake of water per day, extra salt, packed chips, pappads, processed meats, fish, Meat, green leafy vegetables, milk, soft drinks, potatoes and tomatoes. Comorbidities includes diabetes, frequent diarrhoea, family history of urolithiasis, history of UTI and holding urine for long time.

Life style factors which includes smoking, alcoholism, working under sunlight, well as source of water. The null hypothesis was partially accepted and research hypothesis was partially rejected. Thus it was interpreted that there is association between few risk factors and urolithiasis.

A binary logistic regression was computed to find the adjusted odds ratio (OR) based on risks identified with Pearson Chi square. Table 2 is showed that intake of salted nuts (OR=2.139, CI=1.112 - 4.113, P=.023) had an association with the risk for urolithiasis. In contrast, intake of tea (OR=.463, CI=.259-.827, P=009), frequency of intake of pickle (OR=0.762, CI=.629-.923, P=006), and milk products (OR=0.485, CI=.310-.759, P=002) were associated with reduced risk for urolithiasis. It shows that the odds of having urolithiasis among those do not take salted nuts is 2.139 times less than among those who take salted nuts. Those who do not take milk products is 51.5% i.e. (1-.485*100) less than those who consume milk products. The odds of having urolithiasis among those who do not take tea is 53.7 % i.e. (1-.463*100) less than among those who consume tea. With the unit increases the frequency of the pickle intake per week the odds of urolithiasis decreases by 24 % (1-.762*100). Hence the null hypothesis is partially accepted and research hypothesis is partially rejected. As per these findings it is important to provide information to the population with risk factors to reduce the risk of developing the urolithiasis.

Table 1: Frequency (f) and percentage (%) distribution of the study participants based on demographic variables

Sample characteristics	Cases		Control	
	Frequency (f)	Percent (%)	Frequency (f)	Percent (%)
Age in years				
19-40	93	38.4	93	38.4
41-65	149	61.6	149	61.6
Gender				
Male	179	74	179	74
Female	63	26	63	26
Religion				
Christian	13	5.4	13	5.4
Hindu	182	75.2	176	72.7
Muslim Others	47 0	19.4 0	51 2	21.1 .8
Area of living				
Urban	47	19.4	47	19.4
Rural	194	80.2	192	79.4
Semi urban	1	.4	3	1.2
BMI (kg/m2)				
<= 18.4 underweight	8	3.3	7	2.9
18.5-24.9 normal	141	58.3	135	55.8
25-29.9 overweight	85	35.1	92	38
>30 Obesity	8	3.3	8	3.3

Table 2: Association between risk factors and urolithiasis

N=484 (242+242)

Risk factors	Cases	Controls	X^2	df	P
Age in years					
19-40	93	93	.001	1	1
41-65	149	149			
Gender					
Male	179	179	.001	1	1
Female	63	63			
Family history					
yes	55	41	2.547	1	.111
No	187	201			
History of UTI					
Yes	65	49	2.938	1	.087
No	177	193			
6-8 glass Intake of water per day					
yes	91	83	.574	1	.449
No	151	159			
Holding urine for long time					
Yes	30	44	3.12	1	.077
No	212	198			
Tea					
Yes	43	22	7.837	1	.005*
No	199	220			
Coffee					
Yes	30	27	.179	1	.672
No	212	215			
Extra salt					
Yes	67	56	2.719	1	.099
No	175	186			
Frequent diarrhoea					
Yes	7	14	1.509	1	.219
No	235	228			
Hypertension					
yes	41	47	.687	1	.407
No	201	195			
Duration of high BP(in years)					
No	201	195			
1-3	9	12			
4-7	3	13	10.732	4	.030*
7-10	19	9			
>10	10	13			
Smoking					
Yes	11	15	.650	1	.420
No	231	227			
Since how many years					
No	231	227			
< 5	0	4	4.035	3	.256
5-10	1	1			
>10	10	10			
Diabetes					
Yes	42	56	2.508	1	.113

No	200	186			
Duration of diabetes (in years)					
No	200	186			
1-5	5	7			
6-10	13	12	3.652	4	.455
10-15	11	17			
>15	13	20			
Working under sunlight					
Yes	10	12	.190	1	.663
No	232	230			
Exercise					
Yes	15	16	0.34	1	.853
No	227	226			
Well as source of water					
Yes	164	160	0.84	1	.772
No	78	82			
Medical illness					
Yes	15	19	.506	1	.477
No	227	223			
Medications					
Yes	22	26	.370	1	.543
No	220	216			
Alcohol intake					
Yes	29	28	.020	1	.888
No	213	214			
Packed chips					
Yes	117	125	.529	1	.467
No	125	117			
Frequency of packed chips intake in week					
No	125	117			
1	61	66			
2	39	40	1.731	4	.785
3	16	19			
>4	1	0			
Pickle					
Yes	224	211	3.837	1	.050
No	18	31			
Frequency of pickle intake in a week					
No	18	31			
One	71	68			
Two	77	98	14.236	4	.007*
Three	65	40			
>4	11	5			
Pappads					
Yes	147	153	.316	1	.574
No	95	89			
Frequency of pappad intake in a week					
No	95	89			
One	96	79			
Two	38	61	7.191	4	.126
Three	12	12			
>4	1	1			

Salted nuts					
Yes	26	60	16.34	1	.001*
No	216	182			
Condiments					
Yes	32	57	8.605	1	.003*
No	210	185			
Processed meats					
Yes	44	50	.475	1	.491
No	198	192			
Fish					
Yes	199	198	0.14	1	.906
No	43	44			
Frequency of fish intake in a week					
No	43	44			
One	101	88			
Two	34	46	2.899	4	.575
Three	50	52			
>4	14	12			
Meat					
Yes	172	187	2.427	1	.119
No	70	55			
Frequency of Meat intake in a week					
No	70	55			
One	111	120			
Two	28	54	19.678	4	.001*
Three	24	11			
>4	9	2			
Green leafy vegetables					
Yes	155	147	.564	1	.453
No	87	95			
Frequency of green leafy vegetables in a week					
No	87	95			
One	114	96			
Two	26	39	5.209	4	.267
Three	11	10			
>4	4	2			
Milk					
Yes	112	133	.531	1	.466
No	130	109			
Soft drinks					
Yes	98	97	.009	1	.926
No	144	145			
Milk products					
Yes	199	171	8.996	1	.003*
No	43	71			
Potatoes					
Yes	208	210	.070	1	.791
No	34	32			
Tomatoes					
Yes	236	229	2.684	1	.101
No	6	13			
Frequency of tomato intake in week					

No	6	13			
One	12	17			
Two	88	80	5.383	4	.250
Three	64	72			
>4 times	72	60			

*= level of significance <0.05

Table 3: Logistic regression analysis of risk factors of urolithiasis.

N=484 (242+242)

Risk factor	**df**	**OR**	**95% confidence interval**		**Sig. (p)**
			Upper limit	**Lower limit**	
Intake of Tea	1	.463	.259	.827	.009*
Frequency of pickle intake in a week	1	.762	.629	.923	.006*
Intake of Salted nuts	1	2.139	1.112	4.113	.023*
Consumption of Milk products	1	.485	.310	.759	.002*
Duration high Blood pressure	1	1.029	.871	1.216	.733
Intake of Condiments	1	1.332	.703	2.524	.378
Frequency of meat intake in a week	1	.972	.779	1.183	.778

*= level of significance <0.05

Discussion

The present study findings showed that most 149 (61.6%) of the participants were in the age group of 41-65 years and 179 (74%) were males. Most 182 (75.2%) of cases and 176 (72.7%) of control group belongs to Hindu religion. The majority 194 (80.2%) of cases and 192 (79.4%) of controls were living in rural area. Most 141 (51.3%) of cases and 135 (55.8%) of control group were in the category of normal BMI i.e. 18.5 to 24.9 kg/m^2.

The similar study findings were revealed in a cross sectional study conducted by Shamsuddeen SB et al. in his study. It was conducted in 2013 among 50 patients visiting King Khalid hospital of Hail city of Saudi. Participants were in the age group of 16-90 years. Data collected by interview method and the similar findings showed that both men and women in adult age ranging from 25 to 45 years are very much prone to renal calculi the total mean age ± SD was 42.20 ± 19.41 years (range 16-90) and the mean BMI ± SD was 24.65 ± 4.93 (Shamsuddeen, Bano, Shammari, & Al Enezi, 2013). A study conducted by Sofia et.al. (2016) in National Institute of Siddha, Chennai on prevalence and risk factors of kidney stone also found the similar findings that nephrolithiasis is more common in men (64.56%) than in women (35.44%) and it is more prevalent between the ages of 20 to 40 in both sexes (57.50%) (Sofia, Walter, & M, 2016).

A cross sectional study was conducted by Arpan Chandubhai Patel et.al in 2014 at Gujarat, India with the objective to identify the barriers in their dietary modification and to understand the epidemiological characteristics. Study carried out among 50 patients with urolithiasis. Current study supports the findings of this study is that most of them were belonged to Hindu caste (82%) among the patients who had urolithiasis (Patel & Mehta, 2014).

The current study revealed that most 141 (51.3%) of cases and 135 (55.8%) of control group were in the category of normal BMI i.e. 18.5 to 24.9 kg/$m^{2.}$ Different findings were found in a study conducted at Taiwan in the year 2009, i.e. increase of body size increases the risk of renal stone formation and higher BMI is associated

with an increased risk of urolithiasis 35 (39.5%) (Li, et al., 2009).

Study conducted during September 2008 to August 2010 to conclude the prevalence of urolithiasis and to assess the association between urolithiasis and selected variables of interest in Manipur. A pre-designed and pre-tested interview was used for data collection. This study reported that urolithiasis is commonly present in the age group of 25-44 years. Urolithiasis was observed to be significantly more common among those individuals who had history of urinary tract infection (UTI) (37.3%), and those who consumed only 2-4 glasses of water per day and with family history of stones (67%) (Marak, K, Singh, Singh, & Singh, 2013).

Present study findings shows that, intake of salted nuts (OR=2.139, CI=1.112, 4.113) is associated with the increased risk for urolithiasis. In contrast, intake of tea (OR=.463, CI=.259, .827), intake of pickle (OR=0.762, CI=.629, .923), and milk products (OR=0.485, CI=.310, .759) were associated with reduced risk for urolithiasis.

The findings observed in a study which is carried out in Himachal Pradesh. Eating habits of 130 renal stone patients from various hospitals of Palampur of Kangra District in Himachal Pradesh, North India were studied. Many (40%) of them were taking more salted food items. The amount of water intake revealed, majority (59.23%) of the patients were consuming 1000 ml of water per day (Awasthi, Malhotra, & Modgil, 2011).

Mishra et.al (2018) conducted a study among 253 patients with renal calculi at Rewa Madhya Pradesh. Different study findings revealed in study that high salt (43%), coffee and tea intake (73%) and non-vegetarian diet (86%), and less intake of water (47%) is also common risk factors for urolithiasis. Also found that diabetes and hypertension were other risk factors for renal calculi present in 17% and 23% patients respectively (Mishra & Singh, 2018).

The binary logistic regression of present study supported by the findings of a study which is conducted at Iran i.e. negative association was found between urinary stone and intake of coffee (OR 0.8; 95% CI 0.6–1.2; *P* = 0.03), intake of dairy products (OR 0.6; CI 0.4–1.3; *P* = 0.03), consumption of cereals (OR0.08; 95% CI 0.06–1.71; *P* = 0.02), and educational status (OR 0.8; 95% CI 0.6–1.2; *P* = 0.02). A positive association was not found with consumption of fish (OR 1.17; 95% CI 0.66–1.91; *P* = 0.072), intake of vegetables (OR 1.22; 95% CI 0.90–1.81; *P* = 0.062) or intake of fruits (OR 1.34; 95% CI 0.91–1.67; *P* = 0.08) (Safarinejad, 2007).

Contradictory findings were observed in a population-based study conducted at Iran. Findings revealed, positive association between urinary stones and drinking of tea (OR 1.64; 95% CI 1.32–2.62; *P* = 0.03) and meat intake (OR 1.38; 95% CI 1.29–2.21; *P* = 0.02), obesity (OR 1.74; 95% CI 1.21 2.31; *P* = 0.04), high blood pressure (OR 1.88; 95% CI 1.26–2.18; *P* = 0.04), unemployment (OR 2.10; 95% CI 1.43–2.14; *P* = 0.04), intake of cola (OR 1.49; 95% CI 1.23–2.19; *P* = 0.02) (Safarinejad, 2007).

A case control hospital based study which is conducted in Puducherry also showed a contradictory findings that includes the factors of occurrence of kidney stone with genetic predisposition (OR:16.98, CI;3.02-95.25), less frequency of urine per day (OR:5.95, CI;1.03-34.19) and dietary habit of eating red meat once a week (OR:32.28, CI; 9.7-143.2) and even once a month (OR:5.20, CI;1.44-18.77) (Dongre, Rajalakshmi, Deshmukh , Thirunavukarasu , & Kumar, 2017).

Present study shows that family history of urolithiasis is not associated with the urolithiasis. An updated epidemiological study of urinary stones in Turkey shows that urolithiasis was significantly associated with a positive family history of urinary stones. The OR was highly significant (3.1, 95% CI 1.8–5.1) for a family history of urolithiasis in siblings (Muslumanoglu, et al., 2011). These findings are contradicting the present study findings.

According to the findings of the present study, the factors which are at more risk to get urolithiasis is intake of salted nuts. Other factors

such as intake, consumption of tea, intake of pickle in a week and consumption of milk products are less risk to get urolithiasis. As per these findings it is important to provide information to the population with risk factors to reduce the risk of developing the urolithiasis.

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