DOI: 10.7860/JCDR/2017/29465.10561

Original Article

Community Medicine Section

Risk Factors for Kidney Stones in Rural Puducherry: Case-Control Study

AMOL R DONGRE[1], M RAJALAKSHMI[2], PRADEEP R DESHMUKH[3], MR THIRUNAVUKARASU[4], RAVI KUMAR[5]

ABSTRACT

Introduction: Renal stone is a distressing chronic condition which is getting common across the world. The rigorous evidence on multiple risk factors of kidney stone from a single study is limited.

Aim: To find out the social and dietary risk factors responsible for the occurrence of kidney stone in a local community in rural Puducherry, India.

Materials and Methods: It was a hospital-based unmatched case-control study. Based on existing information, a sample of 70 cases and 140 controls was calculated and considered adequate. The exposure information on recent cases was uniformly collected by interview and review of radiologic records and exposure information for controls was collected through interviews. Associations between the occurrence of renal stone as a dependent variable and multiple independent variables such as age, sex, socioeconomic status, type of family, religion, the source of drinking water and dietary practices were studied by using multiple logistic regression analysis.

Results: We found associations 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).

Conclusion: The risk of kidney stone was found high among those who had genetic predisposition, less frequency of urination per day and those who consumed red meat once a month or more. Patients and local community should be educated to reduce the red meat consumption and increase the consumption of water and fluid, especially during the hot climates.

Keywords: Epidemiologic factors, Nephrolithiasis, Renal stone

INTRODUCTION

Renal stone (nephrolithiasis) is a distressing chronic condition which is getting common across the world. It has been known to be common in developed and industrialized countries, where its lifetime prevalence is about 10% [1]. The lifetime risk of renal stone varies from 1% to 5% in Asia, 5% to 9% in Europe and 10% to 15% in the USA [2]. Though its aetiopathogenesis is not fully understood, its occurrence has been attributed to lifestyle, diet rich in salt, animal protein, hot climate, low water intake, common systemic conditions and overweight or obesity [3]. Being a chronic and recurring health condition, it has high burden of direct and indirect cost on patients in its management [4].

Most of the studies on kidney stone were done in the West and by using limited number of variables and there is a lack of studies where the multiple risk factors are studied in a single design with adjustment of confounders. In India, the information on risk factors of kidney stone is limited. Hence, in the absence of evidence from local situations, developing context-specific treatment guidelines and preventive measures is difficult. The previously conducted study in Puducherry found the lifetime prevalence of renal stone to be 6.4% among an economically active adult population of 18-60 years [5]. It was a small-scale study and did not offer any information on the determinants of renal stone. The local community in the field practice area of our Urban Health Training Centre in Puducherry complained about high occurrence of kidney stone in the community and attributed it to the hardness of drinking water.

To find out the social and dietary risk factors responsible for the occurrence of kidney stone in our local community.

MATERIALS AND METHODS

The present study was done in tertiary care teaching hospital by the Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), Puducherry, India. It is a well-equipped, multi-speciality hospital with more than 900 beds and offers free preventive and curative services to the population of rural Puducherry and Villupuram district. Puducherry is a Union Territory located in Southern India. People speak Tamil, Telugu, Malayalam and French languages. Aboriginal people are of Tamil origin, but the region has embraced the multi-national and multi-ethnic culture. Being a coastal town, Puducherry has a humid climate and temperature varies from 20°C in winter to 38°C during summer. Most people eat mixed diet consisting of rice, vegetables, seafood, poultry, and meat.

Study design: It was a hospital-based unmatched case-control study, conducted during the period of April 2016-June 2016. The unmatched case-control study allows study on multiple risk factors. It can be analysed by using standard statistical technique called as multiple logistic regressions which offers better control over confounders and brings clarity in the results. In addition, it allows studying the effect of variables, which would have been used for matching. One cannot study the effect of variables, which are used for matching.

Sample size and sampling: The sample size for the study has been calculated, considering odds ratio=2.47 for renal stone as obtained from our previous study [5]; with power at 80%, 95% confidence interval and case-control ratio 1:2. Two controls per case were selected for better power and statistical confidence in interpretations. The percentage of exposure among control was assumed to be 50%. The number of cases required for the present study was 70 and the number of controls was 140. The sample size was calculated using EpiInfo (version 6.04d) software package.

Selection of cases and controls: The primary study base for the selection of cases and control was Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. Patients of both genders

in the age group of 20-70 years, who were recently diagnosed (last three months) with renal stone and who reported with acute onset of symptoms were included as cases. Patients previously operated for renal stone were excluded from the study. Cases were recruited from the Urology Outpatient Department (OPD) of SMVMCH. The cases were selected during the morning OPD hours. The department maintained a register for this purpose during the study period. Initial 70 consecutive cases coming to Urology OPD during the period of April 2016-June 2016 were selected. All cases were uniformly selected by following the above mentioned criteria.

Controls were selected from the same study base that gave rise to the cases. For each case, two hospital-based controls were selected. The controls were defined as the patients who had never been diagnosed with renal calculus at any time in the past. Patients with currently associated symptoms of renal calculus such as abdomen pain, vomiting, and burning micturition were not included as controls. First two patients waiting in waiting room of OPDs of Medicine, who met our definition for control, were invited to participate in the study. The controls were selected during the afternoon OPD hours. The controls were selected till the desired number of 140 was achieved. The information on self-reported chronic comorbid conditions such as hypertension, diabetes, and gout was collected for both cases and controls. The confounders were adjusted using multiple logistic regression analysis. All the controls who gave consent to join the study were interviewed.

Data collection: The exposure information on cases and controls was collected by interview and review of records. After obtaining informed consent, trained postgraduate from the Department of Community Medicine collected the data by using a predefined and structured questionnaire. Investigator was instructed to ensure to the same degree of accuracy in measurement of exposure in cases and controls.

The structured questionnaire covered information on socio-demographic aspect, family history of renal stone, symptoms, frequency of urination and food frequency questionnaire with one week reference period. Colour of ration card, which is distributed under public distribution system in India, was taken as an indicator of socio-economic status (Pink colour card-Below Poverty Line, (BPL) and Green colour card- Above Poverty Line, (APL)). Food frequency questionnaire is a well-accepted method for quantitative retrospective assessment of usual dietary intake of the individual. From the epidemiological and statistical perspective, food frequency questionnaire is the only dietary intake measure that minimizes the high intra-individual, day-to-day variability in nutrient intake [6]. Considering our experience from previous studies, local culture and input from the Nephrologist, we worked out the list of food item under various food groups such as vegetables, milk, and milk products, meat products, poultry products, fruits and beverages routinely consumed by the local people. Each respondent was asked the frequency of consumption of each of these items under the enlisted food groups on the scale of once a day, more than once a day, once a week, more than once a week, once a month and never. In addition, information on tobacco and alcohol consumption and family history of renal stone was obtained. Respondents were asked about the source of drinking water and frequency of urination in a typical day.

Ethical Consideration: Clearance from the Research Committee and Institutional Ethical Committee of Sri Manakula Vinayagar Medical College and Hospital, Puducherry was obtained prior to initiation of the study. Informed consent was obtained from all participants prior to the interview and privacy was ensured during the interview. All information was coded and stored electronically.

STATISTICAL ANALYSIS

The descriptive statistics on background characteristics of cases and controls were presented as percentages. Associations between the renal stone as a 'dependent' variable and each of the 'independent' variables such as age, sex, occupation, socioeconomic status, type of family, religion, family history of renal stone, addictions, the source of drinking water and dietary practices were carried out by using bivariate analysis. The information collected under various items of food groups was merged to form the categories as milk products, poultry products (eggs, chicken), red meat (mutton, beef, pork) and fruits and vegetables. The frequency of consumptions of various items on a scale under various food groups in food frequency questionnaire was merged to form the frequency of its consumption as > once a day, > once a week, once a month and never. The cases and controls who had at least one chronic morbidity such as hypertension, diabetes and gout were grouped as a single variable. The association between a dependent variable and each independent variable was measured as Odds Ratio (OR) with 95% Confidence Intervals (CI). Finally, multiple logistic regressions using enter method was carried out to get the final model of risk factors for renal stones by adjusting the confounders. All the variables used for bivariate analysis were pulled for multivariate analysis. The magnitude of the standard error was checked to rule out

Variables	Cases (n=70) (%)	Control (n=140) (%)
Age in years		
20-40	35 (50)	69 (49.3)
41-60	19 (27.1)	41 (29.3)
61-70	16 (22.9)	30 (21.4)
Sex		
Male	50 (71.4)	85 (60.7)
Female	20 (28.6)	55 (39.3)
Occupation		
Housework	3 (4.3)	3 (2.1)
Agricultural work	18 (25.7)	29 (20.7)
Labourer	29 (41.4)	33 (23.6)
Job	9 (12.9)	28 (20)
Not working	11 (15.7)	47 (33.6)
Years of education		
Illiterate	13 (18.6)	18 (12.9)
Primary	30 (42.9)	44 (31.4)
Higher secondary	17 (24.3)	42 (30)
Degree	10 (14.3)	36 (25.7)
Religion		
Hindu	68 (97.1)	133 (95)
Muslim	2 (2.9)	5 (3.6)
Christian	-	2 (1.4)
Colour of ration card		
Below Poverty Line	17 (24.3)	35 (25)
Above Poverty Line	52 (74.3)	104 (74.3)
Do not have it	1 (1.4)	1 (0.7)
Marital status		
Married	62 (88.6)	110 (78.6)
Never married	8 (11.4)	30 (21.4)
Type of family		
Joint	41(58.6)	38(27.1)
Nuclear	27(38.6)	97(69.3)
Living alone	2(2.9)	5(3.6)
Health insurance		
Yes	49 (70)	104 (74.3)
No	21 (30)	36 (25.7)

[Table/Fig-1]: Distribution of cases and controls across background characteristics.
Figures in parenthesis are percentages

Variables	Cases (n=70)	Controls (n=140)	OR, 95%CI
Age			
20-40 yrs	35 (50)	69 (49.3)	1.03 (0.56-1.90)
41-60 yrs	19 (27.1)	41 (29.3)	0.90 (0.45-1.79)
61-70 yrs	16 (22.9)	30 (21.4)	1
Sex			
Male	50 (71.4)	85 (60.7)	1.62 (0.83-3.15)
Female	20 (28.6)	55 (39.3)	1
Occupation			
Housework	3 (4.3)	3 (2.1)	1
Agricultural work	18 (25.7)	29 (20.7)	1.39 (0.64-2.74)
Labourer	29 (41.4)	33 (23.6)	2.29 (1.18-4.44)
Job	9 (12.9)	28 (20)	0.59 (0.24-1.41)
Not working	11 (15.7)	47 (33.6)	0.37 (0.17-0.81)
Colour of ration card			
Below Poverty Line	17 (24.3)	35 (25)	0.96 (0.47-1.97)
Above Poverty Line	52 (74.3)	104 (74.3)	1.00 (0.49-2.03)
Do not have it	1 (1.4)	1 (0.7)	1
Marital status			
Married	62 (88.6)	110 (78.6)	2.11 (0.86-5.36)
Never married	8 (11.4)	30 (21.4)	1
Types of family			
Joint	41 (58.6)	38 (27.1)	3.79 (1.99-7.28)
Nuclear	27 (38.6)	97 (69.3)	0.28 (0.15-0.53)
Living alone	2 (2.9)	5 (3.6)	1
Family history of renal stone			
Yes	18 (25.7)	4 (2.9)	11.77 (3.52-43.35)
No	52 (74.3)	136 (97.1)	1
Current smoker			
Yes	26 (37.1)	20 (14.4)	3.55(1.71-7.39)
No	44 (62.9)	120 (85.6)	1
Current alcoholic			
Yes	29 (41.4)	23 (16.5)	3.60(1.78-7.29)
No	41 (58.6)	117 (83.5)	1
Source of drinking water			
Ground water	24 (34.3)	44 (31.4)	1.13(0.61-2.09)
River water	46 (65.7)	96 (68.6)	1
Frequency of passing urine in a day			
< 5 times	38 (54.3)	27 (19.3)	4.97 (2.53-9.83)
More than 5 times	32 (45.7)	113 (80.7)	1
At least one chronic co-morbidities			
Yes	20(28.6)	52(37.1)	0.67(0.36-1.26)
No	50(71.4)	88(62.9)	1
Milk products			
≥ Once a day	39 (55.7)	77 (55)	1.02 (0.57-1.83)
≥ Once a week	19 (27.2)	40 (28.6)	0.93 (0.49-1.77)
Once a month	5 (7.1)	13 (9.3)	0.75 (0.25-2.19)
Never	7 (10)	10 (7.1)	1
Red meat (mutton, beef, pork)			
≥ Once a week	41 (58.6)	10 (7.1)	18.3 (8.2-40.9)
Once a month	20 (28.6)	36 (25.8)	1.15 (0.60-2.19)
Never	9 (12.8)	94 (67.1)	1
Fruits and vegetables			
≥ Once a day	27 (38.5)	104 (74.2)	0.22 (0.12-0.40)
≥ Once a week	43 (61.4)	36 (25.7)	1

[Table/Fig-2]: Bivariate analysis for the risk factors of renal stone.
Figures in parenthesis are percentages

multi-co-linearity between the variables. The multiple coefficient of determination (R^2) was used as the goodness-of-fit for the model. The $p<0.05$ will be considered significant. There are three methods to adjust for confounding (matching, stratification and multivariate analysis). Out of these three methods we used multiple logistic regressions to adjust the confounders. Data was analysed using SPSS 24.0 software (SPSS Inc., Chicago, Illinois, USA) package.

We followed 'the Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) guidelines for reporting the present study [7].

RESULTS

The cases and controls were similar with respect to age distribution, gender, years of education, religion, socio-economic status, marital status and health insurance. Significantly more cases were on daily wages (41.4%) and belonged to joint family (58.6%) as compared to controls. Significantly more controls reported as not working (33.6%) and belonged to nuclear family (69.3%). There was no significant difference between cases and control with respect to other variables [Table/Fig-1].

The odds for kidney stone occurrence was 1.03 times (CI; 0.56-1.90) greater among 20-40 years and 0.90 (0.45-1.79) times among 41-60 years as compared to odds in 61-70 years. Among male respondents, the odds of kidney stone were 1.62 times higher as compared to odds among female respondents. The odds was 2 fold (OR = 2.11) higher among married persons compared to odds among never married. Though the risk of developing kidney stone was 1.13 times (CI; 0.61-2.09) higher among those who consumed ground water compared to odds among those who consumed river water, it was not statistically significant. The odds of developing renal calculus was 2.29 times (CI; 1.18-4.44) significantly greater among respondents working as daily wage labourers compared to odds among who were currently not working. Respondents living in the joint family were 3.79 times (CI; 1.99-7.28) at risk of developing kidney stone as compared to those who were living alone. The odds of kidney stone among respondents with a family history of the similar event was 11.77 times (CI; 3.52-43.35) higher at as compared to those without the family history of renal calculus. The odds of kidney stone occurrence among current smokers and alcoholics were 3.55 and 3.60 times higher as compared to odds among non-smokers and non-alcoholics respectively. The odds of renal stone among respondents who passed urine less than five times in a day was 4.97 times (CI; 2.53-9.83) higher as compared to odds among those who passed urine more than or equal to five times in a day. The odds of developing renal stone among red meat consumer for ≥once a week and once a month had 18.3 times (CI; 8.2-40.9) and 1.15 times (CI; 0.60-2.19) higher risk respectively as compared to those who never consumed red meat. The odds was protective (OR-0.22, CI; 0.12-0.40) for those who daily consumed

Variables	Cases (n=70)	Control (n=140)	Adjusted OR, 95%CI
Family history of renal calculus			
Yes	18 (25.7)	4 (2.9)	16.98(3.02-95.25)
No	52 (74.3)	136 (97.1)	1
Frequency of passing urine in a day			
< 5 times	38 (54.3)	27 (19.3)	5.95 (1.03-34.19)
More than 5 times	32 (45.7)	113 (80.7)	1
Red meat (meat, beef, pork)			
≥ Once a week	41 (58.6)	10 (7.1)	32.28 (9.7-143.2)
Once a month	20 (28.6)	36 (25.7)	5.20 (1.44-18.77)
Never	9 (12.8)	94 (67.2)	1

[Table/Fig-3]: Multiple logistic regression analysis: Final model of risk factors for renal stone.
Figures in parenthesis are percentages

vegetables and fruits as compared to those who consumed it on a weekly basis or less [Table/Fig-2].

Final multivariate regression model after adjustment of confounders had three variables i.e., family history of renal stone, the frequency of urination and consumption of red meat. The respondents with the family history of renal calculus were 16.98 times (CI; 3.02-95.25) at high risk of developing renal calculus as that of those without the family history of renal calculus. The odds for those had a history of passing urine less than five times in a day was 5.95 times (CI; 1.03-34.19) higher as compared to odds among those who passed urine more than or equal to five times in a day (we considered frequency of urination as a surrogate indicator for water consumption). The risk of developing renal calculus in respondents consuming red meat (≥once a week) was 32.28 times (CI; 9.7-143.2) higher as that of those who never consumed red meat. The odds of developing renal calculus were 5.2 times (CI; 1.44-18.77) more among those who consumed red meat once a month as compared to odds among who never consumed the red meat [Table/Fig-3]. The Nagelkerke R^2 value for the model was 67.5 percent. The magnitude of the standard errors for variables ranged from 0.63 to 2.3 which indicated the statistical stability of the model.

DISCUSSION

In the present study, we found that factors such as genetic predisposition, less frequency of urination (< 5) per day and dietary habit of red meat consumptions were the risk factors for the development of renal stone among residents of rural Puducherry. There were no age and gender differentials for the occurrence of kidney stone. Thus, the present study explored the two modifiable risk factors in the prevention of kidney stone among the patients and in study population.

In the present study, among red meat eaters, the risk of renal stone was found to be high and it was low among those who consumed vegetables and fruits on daily basis. Turney BW et al., examined the association between diet and kidney stone in a hospital-based cohort data in England. They found that meat eaters have a higher risk of development of renal stone as compared to vegetarians [8]. Thus, dietary modifications such as less consumption of red meat can play important role in dietary management and in the prevention of kidney stone.

Puducherry being the coastal region has hardness present in ground water. Notably, in the present study, the hardness of water did not come out as a predictor for renal stone. Similarly, Ramello A et al., in Italy did not find any association between kidney stone and dietary calcium intake and tap water hardness [9]. Hence, an effort to educate patient and community to eliminate this misconception would be required.

We have also noted in a bivariate analysis that labourers were at more risk of development of renal stone. In multivariate analysis, less frequency of urination emerged as a predisposing factor for renal stone. Thus, it seems, hot and humid climate in Puducherry stimulates excess perspiration, leading to decrease in urine volume and subsequent concentration of relatively insoluble salts, which might lead to formation of stone [10]. Tasian GE et al., did a time series analysis to study the association of daily mean temperature with kidney stone and found that the presentation of kidney stone increased with higher daily mean temperature [11]. Borghi L et al., in Italy found that workers exposed to heat stress were at risk of developing renal stone [12]. Soucie JM et al., found that temperature and sunlight levels are associated with renal stones which also explain the geographical variability in the occurrence of renal stone [13]. This finding has an implication for context-specific health advice for labourers on adequate consumption of water and fluid intake to cope with the loss of water due to perspiration in hot climate.

In the present study, chronic diseases were treated as potential risk factor and/or confounder. We elicited self reported history of presence or absence of chronic condition and analysed. The cases and controls who had at least one chronic morbidity such as hypertension, diabetes and gout were grouped as a single variable. It was adjusted as confounder during the multiple logistic regression analysis.

In recent times, it is understood that kidney stone is related not only to diet and hydration but also to common chronic conditions including metabolic syndrome, cardiovascular diseases, chronic kidney diseases and obesity [3,14]. Taylor EN et al., in a 44 year follow-up study in the USA, found an association between diabetes and renal stone [15]. Cappuccio FP et al., found an association between kidney stone and hypertension [16]. However, we did not find any association between chronic conditions such as hypertension and diabetes with renal stone. Considering high prevalence of hypertension (25.3%) and diabetes (8.3%) in rural Puducherry [17,18], additional studies are required in the future to examine the relationship between diabetes, hypertension, metabolic syndrome, obesity and kidney stone.

To the best of our knowledge, we did not find much research on risk factors of renal stone in India. The evidences from the previous studies were based on limited variables with poor control over confounders and these studies were mostly done in the West. The present study measured the multiple risk factors for kidney stone in a single study design and adjusted the confounders to detect the risk factors. The findings of the present study confirm the collective findings from the various studies done in different populations. According to Bradford Hill's criteria such a consistency of association across different population brings more confidence in causal relationship between the exposure and outcome [19]. The findings have implications for patient management in hospital setting and prevention program in a community setting to change the epidemiology in the given context.

LIMITATION

The limitations of the present study should be kept in mind. Being a hospital-based case-control study, there could be variation in recall in exposure status among cases and controls. The wider confidence intervals in odds ratio indicate smaller sample size in the present study. Hence, more confirmatory research on a large sample size in community setting would be required in the future. The findings of the present study would be useful in calculation of sample size and planning the future research work.

CONCLUSION

In conclusion, we found an association between genetic predisposition, less frequency of urination per day and dietary habit of eating red meat with the occurrence of renal stone in the local community. The hardness of water was not found associated with the occurrence of kidney stone. Patients and local community should be educated to reduce the red meat consumption and increase the consumption of water and fluid, especially during the hot climates.

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PARTICULARS OF CONTRIBUTORS:
1. Professor and Head, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.
2. Postgraduate Student, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.
3. Professor, Department of Community Medicine, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Maharashtra, India.
4. Assistant Professor, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.
5. Professor and Head, Department of Nephrology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Amol R Dongre,
Professor and Head, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital,
Puducherry-605107, India.
E-mail: amolrdongre@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Apr 24, 2017**
Date of Peer Review: **Jun 12, 2017**
Date of Acceptance: **Jul 13, 2017**
Date of Publishing: **Sep 01, 2017**