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RESEARCH ARTICLE

THE ROLE OF QUALITATIVE URINE ANALYSIS IN THE PREVENTION OF FUTURE UROLITHIASIS IN PATIENTS PRESENTING WITH ABDOMINAL PAIN OF UROLOGICAL ORIGIN

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ABSTRACT

Background and Objectives: Kidney stone disease varies in frequency and stone type between different climates and racial groups. Our aim was to identify the presence of stone forming substances, in the urine samples of patients with symptoms suggestive of urolithiasis but without radiological evidence of calculi at present, a condition often referred to as crystalluria. Data was analyzed to determine the extent of correlation between the presence of factors believed to be associated with urinary stone formation and the presence of stone precursors in urine of the study group, which would then help in prevention of actual stone formation in the future in these patients.

Methods: This 2 month prospective case series study was conducted in a tertiary level teaching hospital with a study population of 35 participants. The data was collected using a questionnaire and entered using MS-Excel. Significance of the individual risk factor and clinical presentation were established by using Chi square test in order to find out the P value and appropriate conclusions were based on the above analysis.

Result: In our study the incidence of crystalluria was found to be 17.1% with Calcium Oxalate being the only type of crystal seen in urine. Daily water intake ($P < 0.05$), Diabetes ($P < 0.05$), history of repeated Urinary Tract Infection (U.T.I.) ($P < 0.05$) were found to be significant factors resulting in crystalluria.

Conclusions: Risk factors for crystalluria were identified, i.e. decreased daily water intake, diabetes and history of repeated U.T.I., which played a significant role in its occurrence in the study population ($P < 0.05$). Symptoms such as pain, burning micturition, vomiting and hematuria, were noted but were found not to have a significant association ($P > 0.05$). A dietary chart was handed over to all the participants in order to prevent the recurrence of crystalluria and thus prevent the formation of urinary stones in the future. This study with a small subject group and of short duration was intended as a pilot study on this subject with larger and longer duration studies to follow which would make the assertions more conclusive.

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INTRODUCTION

Kidney stone disease varies in frequency and stone type across different populations and geographical conditions. Understanding the epidemiology of stones disease is important in determining its significance at the community level, the associations and risk factors for individuals, and the likelihood of stone recurrence. The overall probability of forming stones differs in various parts of the world and is estimated as 1-5% in Asia (Sandhya et al., 2010). Recurrence rates for stones are high ranging from 20% at 5 years, 35% at 10 years, to 70% at 20 years (Sandhya et al., 2010). Almost 50% of urinary calculi occur between 30 and 50 years of age (Williams et al., 2004 Arnold publishers, London ?). Several patients present with symptoms typical of urinary calculi but without confirmatory radiological evidence of their presence.

The symptoms in these patients are due to the passage of a large number of urinary salts or crystals, usually in concentrated urine, but invisible on radiology (Daudon and Jungers, 2004), the condition being referred to as 'crystalluria'. A simple, inexpensive laboratory test, in the form of a qualitative urinalysis can diagnose these stone forming substances in urine either as crystals or amorphous deposit, thus alerting the clinician to the possibility of stone disease in the near future. Corrective measures at this stage itself would prevent the actual occurrence of stones to a large extent. Our aim was to identify the presence of such stone forming substances in the urine samples and determine the extent of correlation between factors believed to be associated with stone formation and actual presence of stone precursors in urine, thus preventing future urolithiasis.

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MATERIALS AND METHODS

This prospective case series study was conducted over a period of 2 months, in a tertiary level teaching hospital in Mumbai. The total study population was 35 participants, chosen irrespective of age or sex, who visited the Hospital's surgical OPD with abdominal pain clinically suspected to be of urinary tract origin but without existing urinary calculi, and who gave consent for participation in our study. Permission of the Institutional Ethics Committee was taken before commencement of our study. An informed, written consent was taken from each participant included in our study. All patients with existing urinary calculi or other co-existent intra-abdominal pathology were excluded, a screening full abdominal ultrasonography being done for this purpose.

We hypothesized that the type of work, diet, daily water intake, alcohol consumption, diabetes, repeated U.T.I., long term medication and past history of urolithiasis as significant factors leading to crystalluria. We also hypothesized that clinical presentation, which included pain, burning micturition, vomiting and hematuria, all features associated with pain of urological origin (with or without urinary tract infection), has a strong association with crystalluria.

The study method involved routine analysis of morning mid-stream urine sample of the participant focusing on identifying the presence of stone precursors in the form of crystals or amorphous deposit. The data was entered using MS-Excel. Significance of the individual risk factor and clinical presentation were established by using Chi square test in order to find out the P value and appropriate conclusions were based on the above analysis.

As an end point of our study, and to emphasize the ultimate benefit to the community that our study was aimed at, a dietary chart was handed over to all participants in order to prevent crystalluria and thus avoid urinary stones in the future.

RESULTS

The study group of 35 consisted of 21 males and 14 females with a mean age of 39.9 ± 11.4 years

Table 1. Age group and sex ratio of population

AGE GROUP	MALE	FEMALE	TOTAL
20-30 YEARS	6 (60.0%)	4 (40.0%)	10
30-40 YEARS	6 (66.6%)	3 (33.3%)	9
40-50 YEARS	6 (54.5%)	5 (45.4%)	11
50-60 YEARS	3 (75.0%)	1 (25%)	4
60-70 YEARS	1 (100.0%)	0 (0.0%)	1
TOTAL	22 (62.8%)	13 (37.1%)	35

6 of these participants (17.1%) were found to be suffering from crystalluria; 4 males and 2 females.

Table 2. Patients having crystalluria

AGE GROUP	NUMBER	CRYSTALLURIA
20-30 Yrs.	10 (28.6%)	1 (2.9%)
30-40 Yrs.	9 (25.7%)	0 (0.0%)
40-50 Yrs.	11 (31.4%)	3 (8.5%)
50-60 Yrs.	4 (11.4%)	1 (2.9%)
60-70 Yrs.	1 (2.9%)	1 (2.9%)
TOTAL	35 (100.0%)	6 (17.1%)

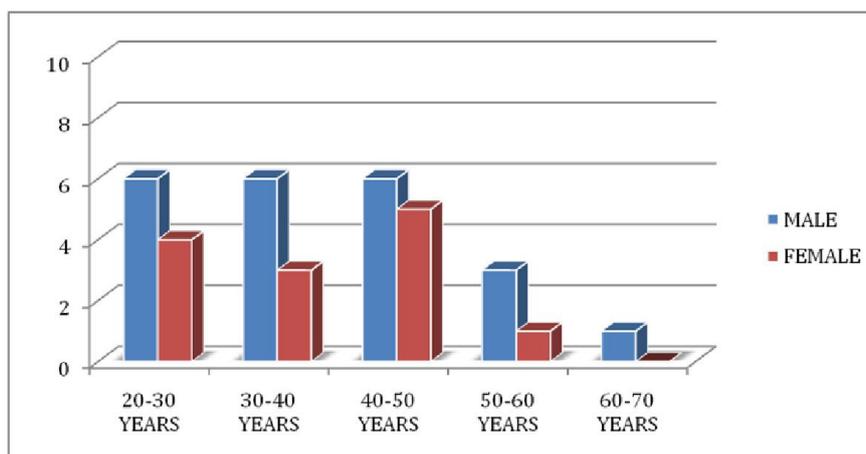


Fig. 1. Demographic data

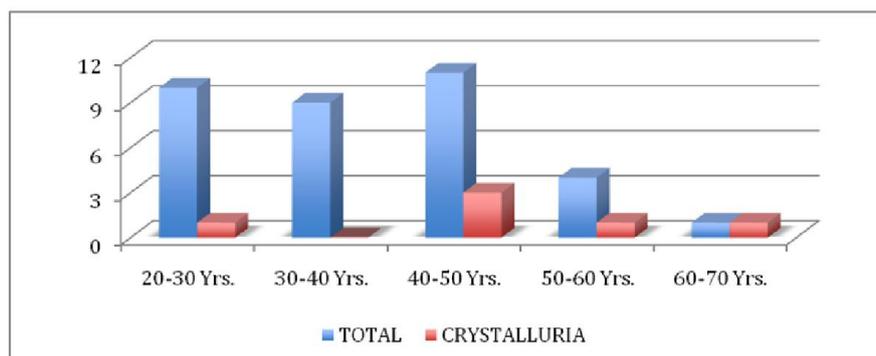


Fig. 2. Crystalluria

Urinary crystals

In our study, 6 (17.1%) participants had calcium oxalate urinary crystals. No other types of urinary crystals were found.

Table 3. Types of crystals

URINARY CRYSTALS	TOTAL	PERCENTAGE
Calcium Oxalate	6	17.1%
Triple Phosphate	0	0%
Uric Acid	0	0%
Cystine	0	0%
Xanthine	0	0%

Address (hailing from)

In our study of 35 patients, 22 (63%) were living in urban areas and 13 (37%) were living in rural areas. Out of the 6 participants who had crystalluria, 3 (8.5%) were from urban areas and 3 (8.5%) were from rural areas.

Fig.3. Types of crystalluria

ADDRESS (HAILING FROM)	NUMBER	CRYSTALLURIA
Urban	22 (62.9%)	3 (8.5%)
Rural	13 (37.1%)	3 (8.5%)
Total	35 (100.0%)	6 (17.1%)

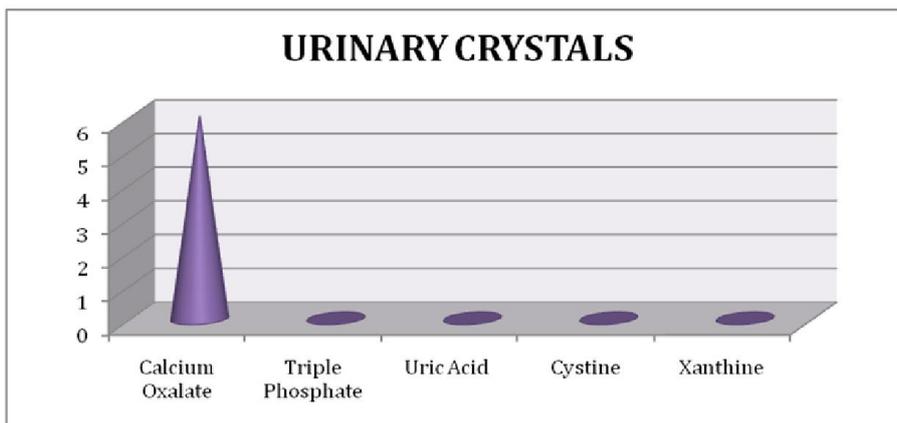


Fig.3. Types of crystalluria

All patients included in the study presented with flank pain and a variety of associated features, the commonest being nausea.

Table 4. Complaints

COMPLAINTS	TOTAL	PERCENTAGE
Flank Pain	35	100%
Burning Micturition	17	48.6%
Urinary Retention	4	11.4%
Nausea	27	77.1%
Vomiting	12	34.3%
Hematuria	10	28.6%

Type of work

A major population of our study was into sedentary type of work 26 (74%) and the remaining were into non-sedentary type of work 9 (26%). Out of the 6 participants who had crystalluria, 2 (5.7%) were non-sedentary type of workers and 4 (11.4%) were sedentary workers.

Table 6. Type of labor

TYPE OF WORK	NUMBER	CRYSTALLURIA
Non-sedentary type of work	9 (25.7%)	2 (5.7%)
Sedentary work	26 (74.3%)	4 (11.4%)
Total	35 (100.0%)	6 (17.1%)

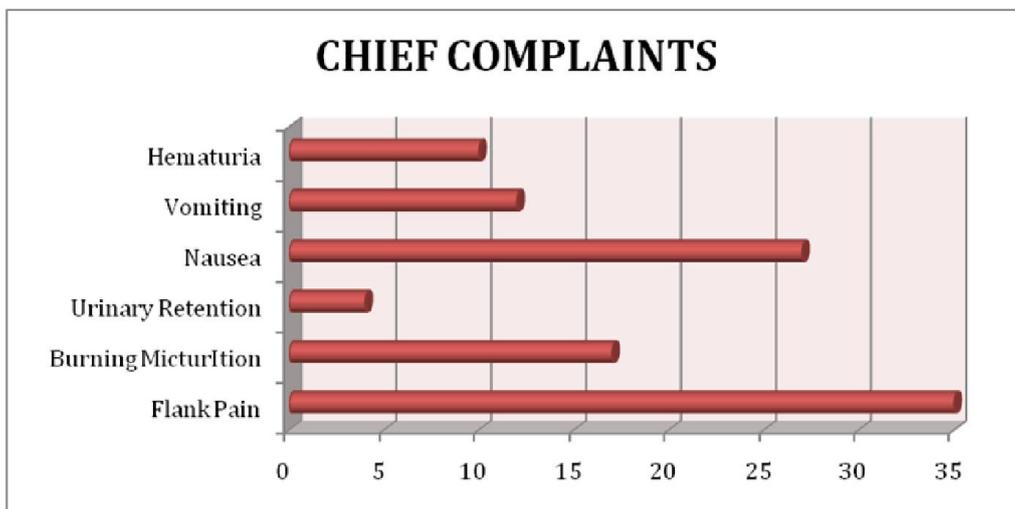


Fig.4. Depiction of complaints

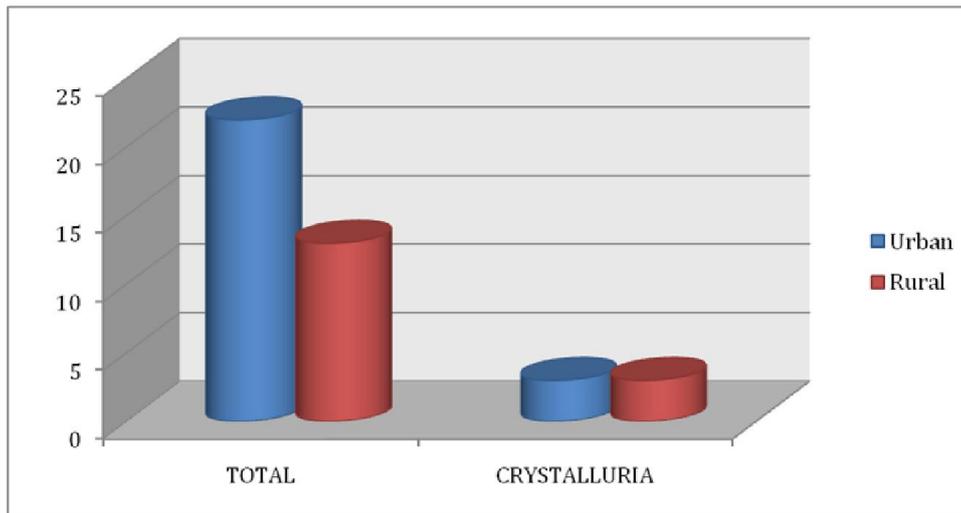


Fig.5. Urban v/s rural distribution of crystalluria

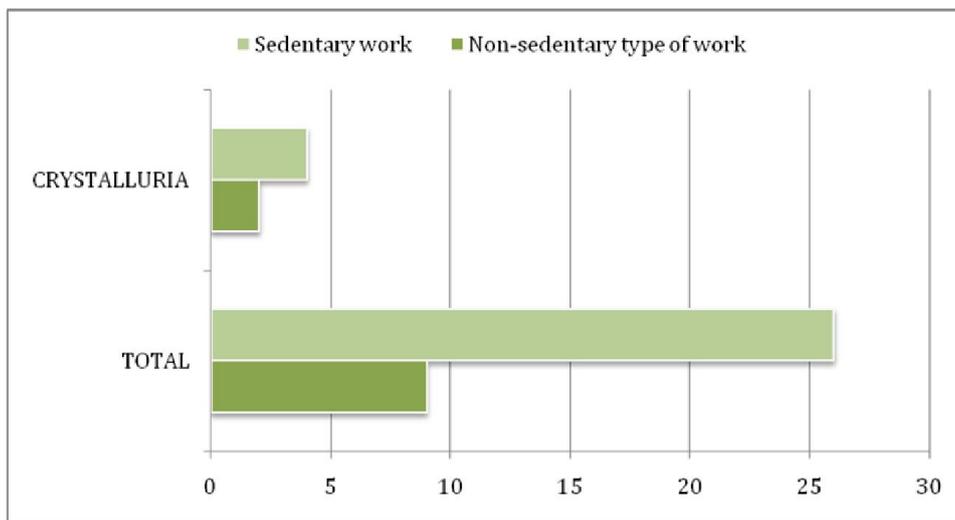


Fig.6. Type of work associated with crystalluria

Dietary habits

28 (80%) participants had a mixed type of diet and 7 (20%) were strictly vegetarians. A large proportion of population in our study had a mixed type of diet (veg.+ non-veg.). Out of the 6 participants who had crystalluria, 3 (8.5%) were having a vegetarian diet and 3 (8.5%) were having a mixed type of diet.

Table 7. Diet association with crystalluria

DIET	NUMBER	CRYSTALLURIA
Vegetarian	7 (20.0%)	3 (8.5%)
Mixed	28 (80.0%)	3 (8.5%)
Total	35 (100.0%)	6 (17.1%)

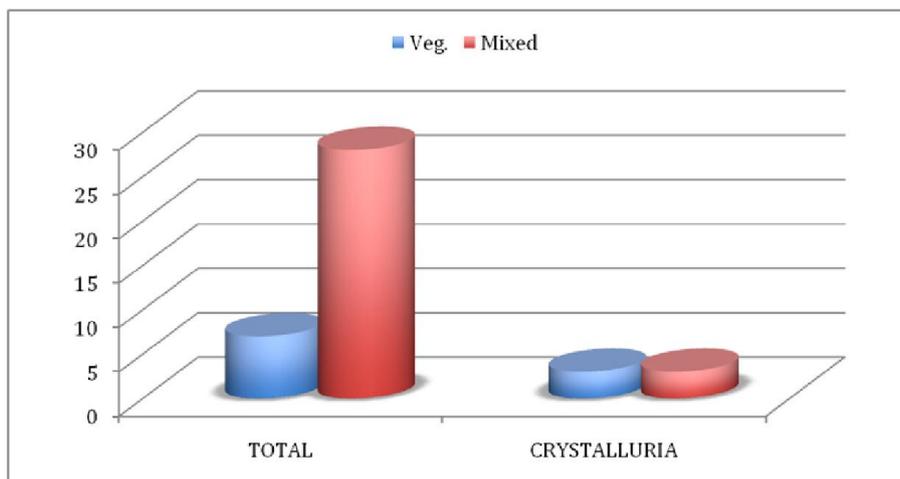


Fig.7. Diet association with crystalluria

Fig.7. Diet association with crystalluria

DAILY WATER INTAKE	NUMBER	CRYSTALLURIA
< 2 lit.	20 (57.1%)	6 (17.1%)
2 lit. & above	15 (42.9%)	0 (0.0%)
Total	35 (100.0%)	6 (17.1%)

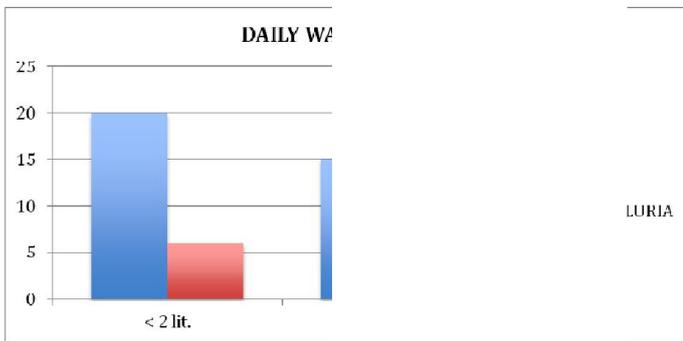


Fig. 8. Water intake and crystalluria

Table 10. Association of UTI with crystalluria

H/o repeated U.T.I.	Number	Crystalluria
Yes	10 (28.6%)	4 (11.4%)
No	25 (71.4%)	2 (5.7%)
Total	35 (100.0%)	6 (17.1%)

History of long term medication

Majority of our subjects were not take any long term medications, 32 (91%). 3 (9%) of our participants took long-term medications. No participants, who had crystalluria, were on long-term medications.

Table 11. Medication and crystalluria

H/O OF LONG TERM MEDICATION	NUMBER	CRYSTALLURIA
Yes	3 (8.6%)	0 (0.0%)
No	32 (91.4%)	6 (17.1%)
Total	35 (100.0%)	6 (17.1%)

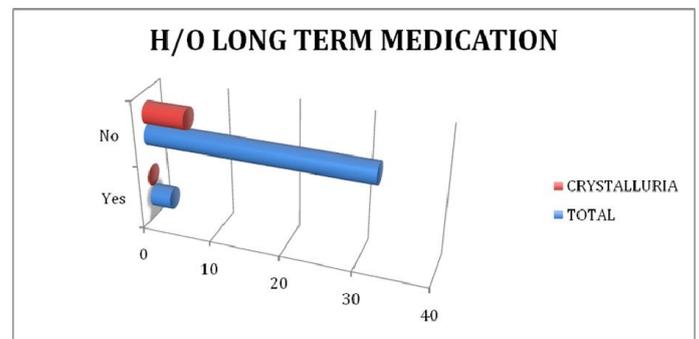


Fig.10. Medication and crystalluria

Pre existing medical disorders

In our study, majority of the participants (24) did not have any Pre-existing medical disorders (60.6%). A large number of participants did have diabetes mellitus 11 (31.4%), followed by hypertension 3 (8.6%). There were 2 participants who were suffering from other disease like asthma and tuberculosis respectively. There were 3 participants who had 2 diseases together. 1st participant had diabetes and hypertension together, the 2nd participant had hypertension and tuberculosis and the 3rd participant had diabetes and asthma together.

Table 9. association of medical disorders and crystalluria

Pre existing medical disorders	Number	Percentage
Hypertension	3	8.6%
Diabetes Mellitus	11	31.4%
Other	2	5.7%
None	24	60.6%

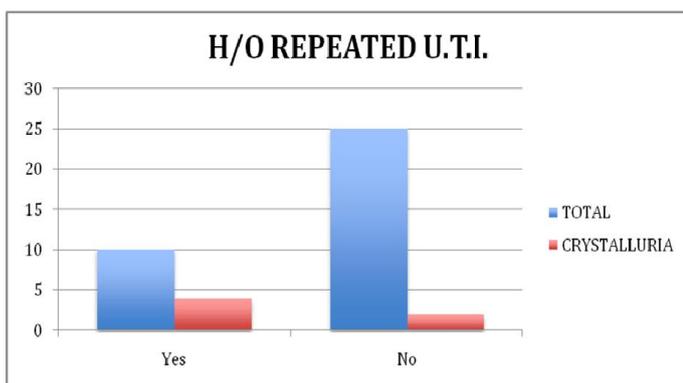


Fig. 9. Repeated UTI and crystalluria

History of repeated urinary tract infection

Significant number of participants had repeated history of U.T.I. 10 (22.9%). Whereas 25 (77.1%) had no such history, 4 (11.4%) out of 6 participants, who had crystalluria, had suffered from repeated U.T.I.

PAST HISTORY OF UROLITHIASIS

13 (37%) participants in our study had past history urinary stones. 22 (63%) participants have never had urinary stones. 1 (2.8%) participant out the 6 participants, who had crystalluria, had a past history of urolithiasis.

Table 12. Past history of urolithiasis and crystalluria

Past history of urolithiasis	Number	Crystalluria
Yes	13 (37.1%)	1 (2.8%)
No	22 (62.9%)	5 (14.3%)
Total	35 (100.0%)	6 (17.1%)

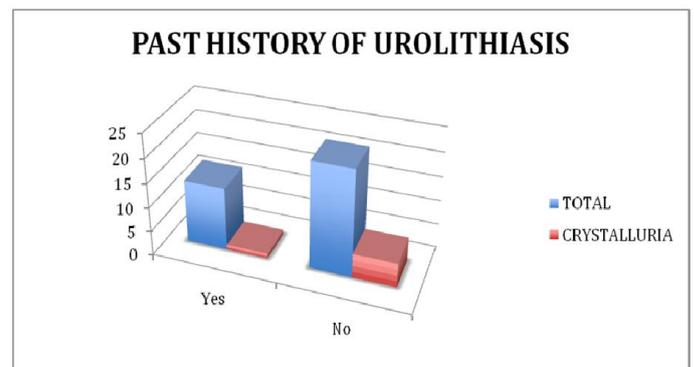


Fig. 11. Past history of urolithiasis and crystalluria

Summary of relationship of crystalluria with studied factors

- 6 (30.0%) out of 20 subjects who were drinking less than 2 lit. of water daily had crystalluria and none out of the 15 participants who were drinking 2 lit. or more of water daily had crystalluria. The difference between the two values was significant ($P < 0.05$).
- 4 (36.6%) out of 11 participants, who had diabetes, had crystalluria and 2 (8.3%) out of 24, who did not have diabetes, had crystalluria. The difference between the two values was significant ($P < 0.05$).
- 4 (40.0%) out of 10 participants, who suffered from repeated U.T.I., had crystalluria and 2 (8.0%) out of 25 participants, who did not suffer from U.T.I., had crystalluria. The difference between the two values was significant ($P < 0.05$).
- 4 (11.1%) out of 26 participants who had a sedentary type of work, had crystalluria and 2 (22.2%) out of 9 participants who had a non-sedentary type of working pattern, had crystalluria. The difference between the two values was not significant ($P > 0.05$).

- not consume alcohol, had crystalluria. The difference between the two values was not significant ($P > 0.05$).
- None of the 3 subjects, who were on long-term medications, had crystalluria and 6 (18.8%) out of 32 participants, who did not take long-term medications, had crystalluria. The difference between the two values was not significant ($P > 0.05$).
- 1 (7.7%) out of 13 participants, who had history of urolithiasis, had crystalluria and 5 (22.7%) out of the other 22 participants, who had no history of urolithiasis, had crystalluria. The difference between the two values was not significant ($P > 0.05$).

DISCUSSION

Urological pain is a frequent emergency in medical practice ranging from anything between a dull ache in the back, to an excruciating, spasmodic pain in the flank with a typical 'loin-to-groin' radiation, known as ureteric colic. Though many of these patients already have urinary stones, an equally good number, if not more, may only have stone precursors passing in urine giving rise to these symptoms.

Table 13. Summary of various factors associated with crystalluria

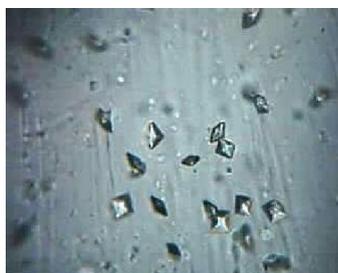
		Crystalluria (N=6)		P' VALUE
		Crystalluria (n=6)	No crystalluria (n=29)	
Type of work	Sedenatary	4 (11.1%)	22 (84.6%)	$P > 0.05^*$ (NS)
	Hard labour	2 (22.2%)	7 (77.8%)	
Diet	Veg.	3 (42.9%)	4 (57.1%)	$P > 0.05^*$ (NS)
	Mixed	3 (10.7%)	25 (89.3%)	
Daily water intake	<2 lit.	6 (30.0%)	14 (70.0%)	$P < 0.05^*$ (S)
	2 lit. & above	0 (0.0%)	15 (100%)	
Alcohol c0nsumption	Yes	1 (11.1%)	8 (88.9%)	$P > 0.05^*$ (NS)
	No	5 (19.2%)	21 (80.8%)	
Diabetes	Yes	4 (36.3%)	7 (63.6%)	$P < 0.05^*$ (S)
	No	2 (8.3%)	22 (91.6%)	
H/o repeated u.t.i.	Yes	4 (40.0%)	6 (60.0%)	$P < 0.05^*$ (S)
	No	2 (8.0%)	23 (92.0%)	
H/o long term medication	Yes	0 (0.0%)	3 (100%)	$P > 0.05^*$ (NS)
	No	6 (18.8%)	26 (81.3%)	
H/o urolithiasis	Yes	1 (7.7%)	12 (92.3%)	$P > 0.05^*$ (NS)
	No	5 (22.7%)	17 (77.3%)	

*(CHI SQUARE TEST) with YATE'S correction.

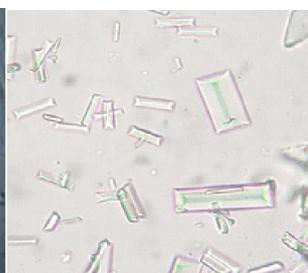
(NS) – Not Significant

(S) – Significant

Calcium-oxalate



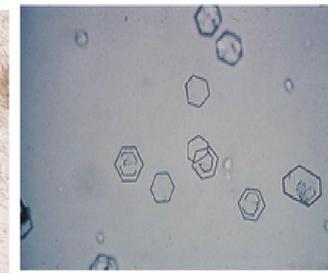
Triple phosphate



Uric acid



Cystine



- 3 (42.9%) out of 7 participants who were having vegetarian type of diet had crystalluria and 3 (10.7%) out of 28 participants who were having a mixed type of diet, were having crystalluria. The difference between the two values was not significant ($P > 0.05$).
- 1 (11.1%) out of 9 participants who consumed alcohol had crystalluria and 5 (19.2%) out of 26 participants, who did

A simple, inexpensive laboratory test, in the form of a qualitative urinalysis, if carefully interpreted, could diagnose these stone forming crystals in urine, a condition referred to as 'crystalluria'. Corrective measures at this stage itself could prevent future urolithiasis.

Four types of stone precursors may be seen in the urine of patients who are likely to suffer from urinary stones in future. These are Calcium-oxalate, Calcium Ammonium Magnesium (Triple) phosphate, Uric-acid and Cystine crystals;

Of these, Calcium-oxalate crystals are by far the commonest type. This is corroborated by Schubert *et al.* (1990), who conducted a study across 3 cities with 10,729 subjects and found that calcium-oxalate crystals were the commonest to be found in urine. Our study however was only a short term one with few participants. Out of the 35 participants studied, 6 (17.1%) had crystalluria and all of them showed calcium-oxalate crystals in urine. There are several factors which contribute to this increased propensity towards crystalluria in certain people and we studied a few of these. One such factor is the passage of highly concentrated urine, which would contain thousands of these crystals akin to passing a shower of 'microscopic stones' in urine. A major contributory factor towards this would be an inadequate intake of oral fluids. While accepting that requirements of fluids would vary across geographic and climatic conditions, a fluid intake of around 2 liters/day is considered adequate under most conditions in an average adult. All our subjects, who had crystalluria, consumed less than 2 lit. Of water daily ($P < 0.05$), suggesting significance of low fluid consumption as an important factor related to occurrence of crystalluria. Miladipour *et al.* (2012) and Mirzazadeh *et al.* (2012) showed a similar co-relation between decreased water consumption and crystalluria. In fact Mirzazadeh *et al.* (2012) went a step ahead to attribute crystalluria to increased hardness of the consumed water. Hardness of the water consumed by our subjects couldn't be assessed as facilities were not available.

Our hypothesis of a particular type of a diet playing a significant role in the occurrence of crystalluria was not proved ($P > 0.05$) in the study with 28 of our subjects having a non-specific, mixed dietary habit, which included 3 out of the 6, who suffered from crystalluria, the other 3 being strict vegetarians. However Pendse and Singh (1986) observed that vegetarian diet lacking in animal proteins, consumption of oxalate rich vegetables and over consumption of tea, gives rise to significant crystalluria, concluding that diet does play a significant role in the occurrence of the condition.

Diabetes is known to increase the chances of urinary stone formation. This occurs due to the acidification of urine, which promotes crystallization in urine. 4 out of 6 of our study subjects with crystalluria were diabetics ($P < 0.05$) suggesting a significant correlation. Mbarki *et al.* (2005) studied the occurrence of urinary crystals in morning urine samples of 208 diabetic patients and concluded that diabetic patients had an increased incidence of urinary stone formation. Our diabetic patients with crystalluria were therefore all potential future stone formers. The occurrence of crystalluria is influenced by repeated urinary tract infections. This is due to alkalization of urine leading to an increased bacterial count. This in turn results in increased urinary excretion of salts, which manifests as crystalluria. In our study, we observed this to be significant ($P < 0.05$), as 4 out of 6 participants with crystalluria had a history of repeated U.T.I. Anderson (2002) in

his study done in 2002, to identify risk factors for stone formation, observed a similar result.

Ureteric colic is generally associated with pain, burning micturition, vomiting and hematuria with individual variations in severity. Though present in varying degrees in our study subjects, these were not found to be significant factors ($P > 0.05$) in their association with crystalluria in the context of our study. Though our results largely matched with most published data on crystalluria, we were constrained by the short duration of our study and (therefore) a small study population. As a part of this initiative each of our patients was given a diet chart to be followed which would go a long way in preventing future urolithiasis.

Dietary Chart For Patients With Urinary Stones & Their Prevention

Drink at least 12 GLASSES OF WATER (2-3 lit.) per day, preferably soft water; in case of hard water, boil adequately before drinking.

Foods recommended	Foods restricted
Coconut water – It is high in potassium and magnesium, hence prevents stone formation.	Vegetables – Tomato, palak, amaranth greens (They have high oxalate content which can lead to urinary stones). Cauliflower, brinjal, mushroom (It has high uric acid/purine content which causes stone formation).
Vegetables – Carrots, bitter gourd (They are rich in minerals which acts as stone inhibitors).	Fruits & Juices – Chikoo & grapes (They have high oxalate content which can lead to urinary stones). Pumpkin (It has high uric acid/purine content which causes stone formation).
Fruits & Juices – Bananas (They are rich in Vit. B ₆ , which break down oxalic acid in the body and thereby prevent stone formation). Lemon (It is rich in citrates, thereby preventing calcium oxalate stone formation). Pineapple juice (It contains enzymes which breakdown fibrin, thereby preventing renal stone formation).	Non – Vegetarian food – Mutton, chicken, fish, egg (They have high uric acid/purine content which causes stone formation).
Fibers – Barley, oats (They are rich in stone inhibitors) Almonds (They are rich in potassium and magnesium which act as stone inhibitors).	Other – Cashew nuts (It has high oxalate content which can lead to urinary stones). Chocolate/cocoa, other chocolate drink mixes, tea & coffee (They have high oxalate content which can lead to urinary stones).

Diets for specific types of Urinary Crystals

Calcium oxalate crystals	Struvite crystals	Uric acid crystals	Cystine crystals
Drink 10-12 glasses of water daily.	Drink 10-12 glasses of water daily.	Drink 10-12 glasses of water daily.	Drink 10-12 glasses of water daily.
Limit high calcium like dairy products & high-oxalate foods like colas, peanuts. Don't overuse antacids.	Caused by infections, you must follow your antibiotic regimen and drink lots of water.	Limit high purine foods like meat, vegetables, beer, and wine.	Limit intake of fish (It is high in methionine).

Conclusion

As mentioned earlier, we aimed to look into the co-relation of crystalluria with some of the factors thought to be essential in its causation, and thereby, occurrence of future urinary calculi. We observed that a majority of our participants with crystalluria (4 out of 6) had a sedentary occupation and were diabetic. A history of low daily water intake was a significant factor as seen in all our patients with crystalluria. Repeated attacks of urinary tract infection is a known factor in the formation of urinary crystals, and was corroborated in our study though, none of the subjects with crystalluria had a history of long-term medication and only 1 had a past history of urolithiasis. Symptoms such as pain, burning micturition, vomiting and hematuria, were noted as a part of clinical history from the patient, but were not found to have a significant association ($P > 0.05$) with the occurrence of crystalluria.

The present study with a small sample size and limited period could be considered as a pilot study on the subject. A large volume study is required for us to be more definitive in our assertions and extrapolate our results to the general population. A larger study is essential, specially since we are dealing with a fairly common problem in the population in the drier, western parts of India (sometimes referred to as the 'stone belt' of the country), with long term implications in preventive community health care.

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Conflicts of interest – None.

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