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Original Article

Biochemical Profile of Urinary Calculi in a Tertiary Care Centre

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ABSTRACT

Background: Urolithiasis is the most common urological disease worldwide. It is multifactorial in origin and influenced by the physical and chemical conditions of the urinary system. The most common type of stone contains calcium in combination with either oxalate or phosphate. Finding the biochemical profile of urinary calculi and estimating the propensity towards its relapses will help to reduce the recurrence of stone formation.

Materials and methods: A hospital-based study was carried out in the Department of Urology of Nepal Medical College Teaching Hospital which included 114 cases of urinary calculi sent for biochemical analysis. The association between biochemical composition and relevant socio-demographic and clinical variables was analyzed using the Chi-square test.

Results: The mean age of the patients with urinary calculi was 35.91 ± 12.254 years and more commonly seen in male patients (66.7%). Pain abdomen (93%), frequency (22.8%), and hematuria (17.5%) were the main complaints. Right-sided calculi were more common (53.5%) and the proximal ureter (46.5%) was the most common site. Calcium oxalate was the major compound in urinary calculi with 47.4% pure calcium oxalate calculi and 52.6% mixed calculi. An association between the composition of calculi and median age, gender, and site area was statistically not significant.

Conclusions: Calcium oxalate is the major compound in urinary calculi in both pure and mixed form. More nutritional and metabolic studies are required to evaluate the modifiable factors so that the complications associated with urinary calculi can be limited.

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INTRODUCTION

Urolithiasis is the most common urological disease affecting both males and females worldwide.[1-3] It is also a major cause of morbidity involving the urinary tract.[3] This disorder is multifactorial in origin and is influenced by the physical and chemical conditions of the urinary system.[3] Both genetic and environmental factors contribute to stone formation. Other factors may be metabolic disturbances, infections, hormonal influences, dietary conditions, and habits or obstructions in the bladder or kidney, or increased excretion of stone-forming components.[2]

Urinary stones may contain various combinations of chemicals. The most common type of stone contains calcium in combination with either oxalate or phosphate. The prevalence is progressively rising, and in addition, recurrence rates are also in the increasing trend. It has been estimated that the recurrence rate of renal calculi is 60% in 7 years and 80% in 18.5 years. The prevalence of renal stones varies depending on race, sex, and geographical location.[2,3] Nutritional factors besides environmental and genetic factors are important lithogenic risk factors. Excessive consumption of animal proteins rich in oxalate or urates, sodium chloride, and insufficient dietary intake of fruits and potassium-rich vegetables affect urine chemistries- low urine pH, high urine calcium and uric acid excretion, and low citrate excretion.[2] Dramatic changes in dietary habits including a high protein and salt intake, and more recently a high consumption of carbonated beverages rich in fructose represent one of the major causes of an increased incidence of calcium oxalate renal stone, which now represents the most frequently diagnosed type of stone.[4]

Percutaneous nephrolithotomy (PCNL) remains the treatment of choice for several forms of stone disease including large stones, many cysteines and struvite calculi, lower pole calyceal calculi, stones associated with anomalous renal anatomy, and in morbidly obese patients.[5] Ureteroscopic lithotripsy (URSL) has also risen over the last few decades.[6] This is attributed partly to the wide availability of holmium: YAG (yttrium aluminum garnet) laser systems. URSL is the first-line treatment for ureteric calculi.[7]

Patients at high risk of recurrent stone formation are those with infection stones, uric acid, urate (i.e. mono ammonium urate, monopotassium urate, and monosodium urate monohydrate), brushite, and genetically determined stones (i.e. cystine, 2,8-dihydroxyadenine, and xanthine stones).[8] For effective management of the stone-forming patient, accurate stone analysis is an essential component of the diagnostic work-up and a prerequisite of metabolic evaluation.[9]

Urinary stones are often composed of more than one substance, which presents a difficulty in the accurate assessment of the stone composition.[10] Among analytical methods for identifying the stone components, chemical, and physical methods can be used. However, despite their low cost, chemical methods are often inadequate for accurately analyzing urinary calculi.[4] The urinary composition in the formation of stone comes from the assumption that derangements of urine biochemistries may play a pivotal role in the pathogenesis of urolithiasis. This study aims to find out the composition of stones by biochemical analysis in cases of urinary tract calculus. This knowledge of the chemical composition of urinary stones will be of great importance and it will help to give advice and suggestions for the general population and patients to carry out preventive measures in reducing the risk of prevalence, and recurrence of urolithiasis in this region.

MATERIALS AND METHODS

A hospital-based study was carried out in the Department of Urology of Nepal Medical College Teaching Hospital (NMCTH). Ethical approval was taken from the Institutional Review Committee (IRC) of NMCTH. The study was conducted over nine months (June 2023 to February 2024) in which all the cases of Urinary calculi from July 2021 to December 2022 from the record book and computer of the Department of Urology was taken. All the details were entered in the Proforma. Data was evaluated by SPSS (Statistical Package for Social Science), version 16. Descriptive statistics (mean ± standard deviation) was used to analyze the quantitative outcomes. The qualitative data was presented with frequency and percentage. The association between biochemical composition and relevant socio-demographic and clinical variables was analyzed using the Chi-square test. P- value less than 0.05 was considered statistically significant.

RESULTS

A total of 114 cases of ureteric calculi were sent for biochemical analysis from July 2021 to December 2022. The youngest patient with urinary calculi was 12 years old and the oldest patient was 71 years old with a mean age of 35.91 ± 12.254 years. The commonest age group affected was 21- 30 years. (Table 1) There were more male patients (76 cases, 66.7%) than female patients (38 cases, 33.3%). Pain abdomen was the major complaint in 106 cases (93%), followed by frequency (26 cases, 22.8%) and hematuria (20 cases, 17.5%). Right-sided calculi were more common (61 cases, 53.5 %) than left-sided (48 cases, 42.1%) with 5 cases (4.4%) of bilateral presentation. Single calculus was more common (77 cases, 67.5%). (Table 2) Proximal ureteric calculi (53, 46.5%) were more common. Urinary calculi were as small as 7 mm and as large as 44 mm, with a mean size of 12.33 mm ± 8.010 mm and a median size of 9.4 mm.

Table 1: Age distribution (n=114)

Age group (years)	Frequency (n)	Percentage (%)	Mean ± S.D (years)	Median (years)
≤ 20	5	4.4	**35.91 ± 12.254**	**33**
21 – 30	45	39.5		
31 – 40	27	23.7		
41 – 50	25	21.9		
51 – 60	6	5.3		
61-70	5	4.4		
>70	1	0.9		
Total	**114**	**100.0**		

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Table 2: Location and number of stone (n=114)

Site	Frequency (n)	Percentage (%)
Proximal ureter	53	46.5
Distal Ureter	46	40.4
Kidney	15	13.2
Total	**114**	**100.0**
Number	**Frequency (n)**	**Percentage (%)**
Single	77	67.5
Multiple	37	32.5
Total	**114**	**100.0**

The most common type of calculus was mixed type (60 cases, 52.6%). Pure type of calculus was calcium oxalate where different percentage of calcium oxalate (Whewelite) and dihydrate calcium oxalate (Weddellite) was present. (Table 3)

Table 3: Composition of stones (n=114)

Stone composition		Frequency (n)	Percentage (%)
Pure			
	Calcium oxalate	54	47.4
Mixed			
	Calcium oxalate + carbonate apatite	25	21.9
	Calcium oxalate + uric acid	19	16.6
	Calcium oxalate + carbonate apatite + ammonium urate	8	7
	Calcium oxalate + ammonium urate	3	2.6
	Calcium oxalate + carbonate apatite + struvite	2	1.7
	Calcium oxalate + struvite	1	0.8
	Calcium oxalate + carbonate apatite + uric acid	1	0.8
	carbonate apatite + uric acid + struvite	1	0.8
	Total	**60**	**52.6**
Total		**114**	**100.0**

An association between the composition of calculi and median age, gender and site are shown in Table 4 and is statistically not significant.

Table 4: Association between median age, gender, site and composition (n=114)

		Composition			Chi	P
		Pure	Mixed	Total	square	value
Median age	≤ 33	25	34	**59**	1.224	0.269
	>33	29	26	**55**		
Total		**54**	**60**	**114**		
Gender	**Male**	36	40	**76**	0.000	1.000
	Female	18	20	**38**		
Total		**54**	**60**	**114**		
Site	**Proximal ureter**	26	27	**53**	1.374	0.503
	Distal Ureter	23	23	**46**		
	Kidney	5	10	**15**		
Total		**54**	**60**	**114**		

DISCUSSION

The annual incidence of stone formation is constantly increasing in industrialized as well as developing countries.[2] The prevalence of renal stones varies depending on race, sex, diet, genetic factor, and geographical location and it may vary from 1% to 20%.[2,7,11] In countries with a high standard of life such as Sweden, Canada, or the USA, renal stone prevalence is notably high (> 10%). The recurrence risk of urinary calculus is determined by the disease or disorder causing the stone formation.[7]

Kidney stone occurrence is relatively infrequent before the age of 20, but its incidence peaks during the fourth to sixth decades of life.[12] In our study, the mean age of the patients with urinary calculi was 35.91± 12.254 years and the median age was 33 years. A study done in the Eastern rim of Kathmandu Valley showed a slightly higher mean age (38.94 ± 14.01) of the patients compared to our study.[13] Similarly, another study done in the Nepalese population showed a mean age of 41.45 years.[14] In a study by Cheng et al., the average age of patients was much higher (52.9 ± 15.2 years).[15] Khalil et al.[16] conducted a study where the mean age of participants was 49.94 years. Our study showed the maximum number of urinary calculi in the age group 21- 30 years. However, Siener et al. found that the peak incidence of kidney stones occurs between the ages of 40 and 59 years.[9]

There was male predominance (66/7%) in our study similar to other studies done in Nepal and other parts of the world.[7,11-14, 17-19] This gender distribution sheds light on the prevalence of kidney stones among different sexes. It may be linked to different dietary habits. Excessive alcohol and coffee intake by men may lead to stone development and it could be the risk factor for renal stone formation. Testosterone can promote stone formation, while estrogen inhibits it by regulating 1,25-dihydroxy-vitamin D synthesis. Dietary habits, hormone levels, and health outcomes are interconnected. Making informed choices can prevent stone formation and promote well-being. [20, 21]

Initially, stone formation does not cause any symptoms. Later, signs and symptoms of the stone disease consist of renal colic, flank pain, hematuria, obstructive uropathy, urinary tract infections, blockage of urine flow, and hydronephrosis. These conditions may result in nausea and vomiting with associated suffering from the stone event.[22] In our study 93% of the patients had pain abdomen followed by frequency and hematuria. Right-sided urinary calculi were more common in our study. Alshoabi et al[23] also found that calculi were more common on the right side (51.5%). In their study, 85.9% of calculi were in the kidneys and only 14.1% in the ureters. However, renal calculi were less common in our study and proximal ureteric calculi were more common (46.5%). Sigdel *et al*[14] also showed that ureteric calculi were more common than renal calculi, accounting for 49% and 31% respectively.[14]

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There are various methods to analyze the chemical compositions of the urinary stones. Physical methods such as infrared spectroscopy, X-ray diffractometry, and solid-state nuclear magnetic resonance spectroscopy have the advantage of determining the structures of the stones. Infrared spectroscopy is used for stone analysis which is one of the recently introduced technologies. This technology is superior to previously used techniques like chemical analysis.[14] The chemical composition of kidney stones depends on the abnormalities in the urine composition of various chemicals.[24] Based on variations in mineral composition and pathogenesis, kidney stones are commonly classified into different types.[22]

Calcium stones are predominant renal stones comprising about 80% of all urinary calculi. The proportion of calcium stones may account for pure calcium oxalate (50%), calcium phosphate (apatite) (5%), and a mixture of both (45%). Calcium oxalate is found in the majority of kidney stones and exists in the form of Calcium oxalate monohydrate (whewellite), and Calcium oxalate dihydrate (weddellite), or as a combination of both which accounts for greater than 60%.[25]

Our study showed pure calcium oxalate (47.4%) calculi and mixed calculi (52.6%). Among the mixed forms of calculi, calcium oxalate with carbonate apatite (21.9%) was the commonest one followed by calcium oxalate mixed with uric acid, ammonium urate, and struvite in different proportions. Zhang *et al*[17] also found out that the most common stone component was calcium oxalate (77.5%), followed by calcium phosphate (8.7%), infection stone (7.6%), uric acid stone (5.3%), and cysteine (0.9%). Mixed stones consisting of calcium oxalate and calcium phosphate were the predominant constituent in 74.2% of stones, followed by uric acid, struvite, and cystine stones.[12] Studies done in Nepal also showed that the majority of the stones contain calcium, phosphate, oxalate, and uric acid. Other constituents were amino acids, carbonate, magnesium, and cystine.[14] Stones were of mixed composition with dominance of calcium phosphate and calcium oxalates.[13,14]

In a study done in India, calcium oxalate was the predominant chemical composition in 91.5%of stones, followed by uric acid in 4.3%, struvite in 2.3%, calcium phosphate in 1.5%, and cystine in 0.4%. Mixed-composition stones were much more common than pure ones (74.8% vs. 25.2%) which is similar to our findings. Overall, the combination of calcium oxalate monohydrate with dihydrate was the most common composition (58.0%). Calcium oxalate was the predominant chemical composition in 91.5% of stones, followed by uric acid in 4.3%, struvite in 2.3%, calcium phosphate in 1.5%, and cystine in 0.4%.[26] In a study conducted by Siener, R. *et al*,[18] it was revealed that struvite (2.1%), brushite (1.3%), protein (0.5%), and cystine (0.4%) stones were only rarely diagnosed, highlighting the prevalence of calcium oxalate in comparison. In our study also, struvite mixed with calcium oxalate was less common.

Siener *et al*[9] showed that the most common main stone component was calcium oxalate (71.4%), followed by carbonate apatite (75%) and uric acid stones (81%). Calculi were more frequently obtained from men than women ($P < 0.001$) and it was statistically significant. However, in a study done by Kumar *et al*,[27] distribution patterns were seen in male and female groups where the P value was 0.621 and was statistically not significant. In a study done by Habbani *et al*[28], the age of the patients was compared with calcium oxalate stones and uric acid stones and patients with uric acid stones were older but were significant with calcium oxalate stones (P=0.004). When the association between the composition of calculi and median age, gender, and site were evaluated in our study, it showed statistically no significance. Similar to our study, Alshoabi et al[23] also showed no significant relationship between gender and the side of the calculi ($P = 0.238$). The overall male-to-female sex ratio was high in most of the studies. Hong *et al*[29] in their study showed that stones in the upper urinary tract were significantly more frequent in men than in women between the ages of 31 and 60. However, such stones were significantly more frequent in women than men over 80 years ($P < 0.05$). Cystine, sodium urate, carbonated apatite, and uric acid indicated significant differences between different age categories (all $P < .001$). The components of renal and ureteral calculi vary significantly based on age and sex, with calcium oxalate calculi being more frequent in men while magnesium ammonium phosphate stones are more frequent in female patients.[29]

CONCLUSIONS

Calcium, as the most common inorganic constituent of urinary stone disease, plays a significant role in the formation of these stones. Studies have shown that the presence of calcium in urinary stones varies among different populations. In our study, calcium was found in all stones, while in other studies, the percentage of calcium ranged from 76.9% to 100%. This variability highlights the importance of understanding the composition of urinary stones in specific populations. Moreover, the incidence of urinary stone disease is notably high in the age group of 21- 30 years. Understanding the different constituents of renal/ urinary stones is crucial for developing targeted interventions and improving patient outcomes. Ultimately, a comprehensive understanding of urolithiasis will guide for more personalized and effective management.

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