Infrared Spectroscopic Analysis of Chemical Composition of Urolithiasis Among Serving Nepalese Soldiers- An Institutional study

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Abstract

Introduction: Various pathologic and metabolic diseases might manifest as renal stones. Acquiring knowledge of the urinary stone constituents is important. Kidney stone analysis is recommended in the basic evaluation of stone disease. This study aims to identify the chemical composition of renal stones and briefly identify the predisposing factors.

Methods: This was a retrospective analytical study conducted from May 01 2018 to May 30, 2020 for a period of two years in a 750-bedded tertiary care hospital, Shree Birendra Hospital (SBH), Kathmandu, Nepal. All patients who underwent Fourier transform infrared spectroscopy (FT-IR) analysis of the retrieved calculi were included in the study. The type of surgery performed was decided by the operating surgeon based on the treatment options available at the center and the recent evidences on management of the stone. The study was conducted after an approval from institutional Review Board (IRB) of NAIHS.

Results: A total 400 patients underwent Infrared spectroscopic analysis (FT-IR) for the retrieved stone. Among them, majority of urolithiasis was seen among male population 277 (69.2%) with an age group between 31 – 45 years {204 (51%)}. Calcium - oxalate was detected in majority of cases 257 (64.25%) followed by struvite 90 (22.5%) and mixed stones 53 (13.2 %).

Conclusions: Majority of the patients in our study had kidney stone followed by ureteric stone. The predominance of calcium oxalate stones was seen in kidney stones followed by Struvite and mixed stones.

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INTRODUCTION

Urolithiasis can be defined as solid biogenous formations of the urinary system with crystalline structure and size more than one milimeter.[1] Urolithiasis is one of the oldest recorded diseases of mankind with documentation of urinary stone treatments in ancient Egyptian medical literatures dating from 1500 BC.[2] known as Randall's plaques, on renal papillary surfaces. Crystal formation and retention within the terminal collecting ducts, the ducts of Bellini, leading to the formation of Randall's plugs, is the other pathway. Both pathways require supersaturation leading to crystallization, regulated by various crystallization modulators produced in response to changing urinary conditions. High supersaturation, as a result of a variety of genetic and environmental factors, leads to crystallization in the terminal collecting ducts, eventually plugging their openings into the renal pelvis. Stasis behind the plugs may lead to the formation of attached or unattached stones in the tubular lumen. Deposition of crystals on the plug surface facing the pelvic or tubular urine may result in stone formation on the Randall's plugs. Kidneys of idiopathic stone formers may be subjected to oxidative stress as a result of increased urinary excretion of calcium / oxalate / phosphate and / or decrease in the production of functional crystallization inhibitors or in relation to co-morbidities such as hypertension, atherosclerosis, or acute kidney injury.

We have proposed that production of reactive oxygen species (ROS) The Prevalence of urolithiasis in Asia ranges from 1 to 5% with highest incidence in Saudi Arabia with 19.1%.[3,4] The recurrence rates among Asian population was 6 to 17% at one year, rises to 21-53% at three-five

years and the lifetime recurrence approximately 60 to 80%.[3]

Various pathologic and metabolic diseases might manifest as renal stone. A stone might be one of the first manifestation of systemic and metabolic disorders.[5] Stone analysis helps to identify the cause of stone formation and its growth by collecting all relevant information from the stone. Investigations of blood and urine biochemistry of each stone former can help to identify metabolic disorders or risk factors involved in lithogenesis. But these metabolic investigations might fail in actual diagnosis of the lithogenic disease if stone composition does not match.[5-8]

There are no documented research regarding spectroscopic analysis of urolithiasis among Nepalese soldiers. This study thus aims to identify the chemical composition of renal stones and briefly identify the predisposing factors among Nepalese soldiers.

METHODS

This retrospective study was conducted from May 2018 to May 2020 at Shree Birendra Hospital, Kathmandu, Nepal. This is a tertiary care teaching hospital affiliated with Nepalese Army Institute of Health Sciences with a capacity of 750 beds. All patients who underwent any form of stone removal surgery in SBH with stone fragments retrieved after the study were included in the study. Data were collected from hospital medical records section which included information on socio-demographic profile, past medical, personal and drug histories. Information of various blood parameters, urine tests, Computed Tomography (CT) findings, chemical composition of stones and stone clearance in post-operative ultrasound were gathered. Those case sheet with incomplete information were excluded from the study. Data regarding stone fragments were from a private laboratory in Kathmandu for Fourier transform infrared spectroscopy (FT-IR). Data from the completed questionnaires were entered in Excel sheet. After editing, the data were exported to SPSS 20.0 for analysis. Categorical variables were summarized using percentages, proportions, means, medians and standard deviations. Continuous data with normal distribution were presented as mean with standard deviation while data with non-normal distribution were presented as median with inter quartile range. Comparison between groups was done using Analysis of variance (ANOVA) and p value of < 0.05 was considered statistically significant. The level of significance was set at $P < 0.05$. This study was conducted after an approval from Institutional Review Board (IRB) of NAIHS Ref no. 245/ Reg. no. 470.

RESULTS

A total of 400 patients meeting the inclusion criteria were included in the study. Among them, majority 277 (69.2%) were males and 123 (30.8%) were females. The age distribution ranged from 22 years to 44 years with a mean of 32.02 ± 4.64 years. Among them majority of patients belonged to age group between 31- 45 years 204 (51%) Table 1. Most of the patients, 343 (85.7%) were from the hilly region and 57 (14.3%) were from Terai - Madesh region. Majority of patient with urolithiasis belonged to Janjatis followed by Brahmins with 30.75% and 24.25% respectively.

A total of 304 (76.75%) of patient belonged to lower rank soldiers including Non-commissioned Officers (NCO) and Junior Commissioned Officers (JCO) as shown in Table 1.

Table 1. Demographic profile of the patient with urolithiasis

Variables	Frequency(n)	Percentage (n%)
Age in years		
18 - 30	91	22.75
31 - 45	204	51.0
46 - 60	58	14.5
> 60	47	11.75
Sex		
Male	277	69.2
Female	123	30.8
Geographical location		
Hill	343	85.7
Terai / Madhesh	57	14.3
Ethnicity		
Brahmin	97	24.25
Chhetri	70	17.5
Janjati	123	30.75
Dalit	65	16.25
Medeshi	45	11.25
Army personnel ranks		
NCO	184	46.0
JCO	123	30.75
Officers	93	23.25

Majority of the patients in our study had kidney stone 224 (56 %) followed by ureteric stone 176 (44%) as shown in Table 2. All patients with kidney stones underwent percutaneous nephrolithotomy (PCNL) and patients with ureteric stones were managed with ureteroscopic lithotripsy (URSL). Kidney stones were most commonly present on lower pole calyx, followed by pelvi-ureteric junction, upper pole and mid pole, while five patients had stones in multiple calyces. Among the patients with ureteric stones, three were in upper ureter and two each in mid ureter and vesicoureteral junction as depicted in Table 2.

Table 2. Stone localization among patient presented with urolithiasis

Variables	Frequency (n)	Percentage (n%)
Stone localization		
Kidney stone	224	56.0
• Lower pole calyx	97	43.30
• Pelvi-ureteric junction	67	29.90
• Upper pole calyx	43	19.19
• Midpole	17	7.5
Ureteric stone		
• Upper ureteric stone	176	44.0
• Mid ureteric stone	81	46.02
• Lower ureteric stone	57	32.38
	38	21.59

The size of stones ranged from 8 mm to 47 mm in largest diameter with the median of 15 mm (IQR= 7). Mean Hounsfield unit (HU) of calcium oxalate stones was 1142.86 ± 202.8, that of struvite stones was 1259.89 ± 216.86 and that of mixed stones was 1384.6 ± 77.01. The HU differ significantly between calcium oxalate stone type (p = 0.04) and struvite stone (p = 0.23) but there were no statistically significant differences in HU value struvite stones mixed stones (p = 0.51).

Table 3. mean size and CT Hounsfield Unit (HU) of urolithiasis

Variables	Mean	P value
Mean stone size	15 ± 7 .0	
Mean HU of stone		
• Calcium oxalate stones	1142.86 ± 202.8	0.04
• Struvite stones	1259.89 ± 216.86	0.49
• Mixed type	1384.6 ± 77.01	0.51

The most common type of was calcium oxalate 257 (64.25%) containing mainly 80% Calcium Monohydrate + 20% Calcium Dihydrate 112 (28%) of all the urolithiasis followed by Struvite stones 90 (22.5%) composed of 80 - 100% of Magnesium phosphate trihydrate and 20% cholesterol and mixed stones 53 (13.25%) as shown in Table 4. Calcium oxalate stones were mixture of variable proportions of calcium monohydrate and calcium dihydrate. Majority of the stones contained at least two identifiable components.

Table 4. Stone composition among the patient presented with urolithiasis

Particulars	Variables		Frequency (%) N
Stone composition	Calcium Oxalate	Calcium Mono- 90% hydrate + 10% Calcium Dihydrate	64 (16%)
		Calcium Mono- 80% hydrate + 20% Calcium Dihydrate	112 (28%)
		Calcium Mono- 70% hydrate + 30% Calcium Dihydrate	37 (9.25%)
		Calcium Mono- 60% hydrate + 40% Calcium Dihydrate	44 (11%)
	Struvite Stones		90 (22.5%)
	Mixed Stones		53 (13.2%)
	Total		400 (100%)

Post-operative ultrasound showed majority of the patients had stone clearance. The stone clearance rate following PCNL was 97.12% while URSL achieved 100% clearance. One patient with residual stone had Struvite stone while two had Calcium oxalate stones.

DISCUSSION

Serving soldiers are a distinct group of people with higher level of physical activities, relatively healthy with no underlying co-morbidities and sharing a similar working environment and diet with each other. As urolithiasis is a disease with high recurrence rate, knowledge about the composition of the stone could guide in further metabolic workup and individualized as well as group directed preventive measures. This is the first study regarding the composition of urinary stones done using FT-IR in Nepal. Previous studies done had used wet chemical analysis of stone composition. Wet chemical analysis can only identify the individual ions and cannot determine the compound and also needs 10 - 15 mg of material which may not be always available. FT-IR on the other hand has high accuracy in determination of the relative percentages of different components and some rare stone types can only be detected by FT-IR.

The mean age of the patients in our study was 32.02 ± 4.64 years which is similar to the mean age of 32.6 years among the soldiers deployed in Iraq.[9] The mean age however is low compared to general population as shown in study done by Chou et al in Taiwan which showed mean age of the patients with urolithiasis was 52.5 ± 13.5 years.[10] This difference is largely due to the structure of our study population which only included young serving soldiers. This could also be due to the fact that the peak

age of stone formation in men is 30 years and in women is 35 and 55 years. The male to female ratio was 9:1 in our study. Studies by Hesse et al[6] in Germany showed males were more prone to nephrolithiasis. But very high male to female ratio in our study is probably the reflection of male predominance in the army.

In our study, the most common location of stone was kidney. The study done by Tang R et al[11] showed that most common anatomical location of stone was kidney (45.29%) followed by bladder and ureter.[12] The most common type of calculi in our study was calcium oxalate stones. The risk factors for calcium stones includes hypercalciuria, hyperparathyroidism, hypocitraturia and renal tubular acidosis but in our study population there were no reported comorbidities however detailed workup for the presence of co-morbidities were not carried out.[13] The consumption of animal protein which leads to increased excretion of oxalate in urine could be one of the risk factors for calcium oxalate stones in our population. The second most common stone in our study was struvite stone. These stones are mainly result of urinary tract infection by urease forming organisms like Proteus and Escherichia coli. In our population, only three patients with struvite stone gave history of urinary tract infection. This could be because of recall bias or lack of diagnosis due to unavailability of proper health facilities in rural parts of the country. Durgawale et al[13] reported the stone analysis reports of 125 patients from Maharastra, India showed magnesium ammonium phosphate (struvite) stone was most predominant constituent of followed by calcium oxalate and calcium carbonate.[13] Liu et al reported findings of 10,000 urinary stone analyses showed that 73% of stones were calcium oxalate containing stones, 9.22% stones were struvite stones, 7.48 % were uric acid stones, 6. 6 % were calcium apatitie stones and remaining were rare stones.[14]

Mandel et al[15] showed that 41% of stones were comprised of single component, 42% had two components and 17% had three identifiable components when they reported 88,768 kidney stones.[15] However in our study, majority of the stones contained at least two identifiable components (73.8%), 16.67% had single component and all were struvite stones and 9.5% of stones had three identifiable components. Kadlec et al showed that among patients with bilateral stones 74.6% had the same primary stone in both kidneys, while 25.4% of the patients had discordant stones. Most of the discordant stone formers were younger, with better renal function and larger stones.[16] As all the patients in our study had undergone intervention on only one side, we do not have data on discordance of stone composition but as our patients are mostly young soldiers with normal renal function stone discordance should be considered.

CT scan is the modality of choice in evaluation of suspected urinary stones. Patel et al[17] demonstrated that HU measurement on NCCT may be useful in distinguishing calcium oxalate monohydrate and calcium oxalate dihydrate stones.[17] In our study, there was statistically significant differences in HU measurement of calcium oxalate and mixed stones ($p = 0.04$) but there was no difference in HU values of struvite stones compared with calcium oxalate or mixed stones. As most of the stones were composed of calcium oxalate monohydrate, the difference between calcium oxalate monohydrate and calcium oxalate dihydrate could not be studied. Torricelli et al[18] showed that single energy NCCT may be inadequate in definitive differentiation of stones due to overlap in radiographic profiles of cystine and uric acid stones.[18]

Our study also showed high stone clearance rate of 91.42% with PCNL and 100% with URSL. As there was no difference in stone clearance rate among different stone types in our study, and also due to high rate of stone clearance in endourological procedures, stone composition might not play any significant role in predicting stone clearance in endourological procedures.

Our study did not include description of imaging findings, histopathology and intraoperative / postoperative complications. Also, the findings of this single institution study done among the serving personnel of Nepalese Army may not be generalizable to the entire population of the country.

CONCLUSIONS

Calcium oxalate stone was the most the most common type of stone in the serving soldiers followed by struvite and mixed stones. Stone clearance rates following endourological procedures are independent of stone composition.

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