

Variation of Stone Composition According to Gender and Age: Our Experience in a Tertiary Care Centre in North East India

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ABSTRACT

Introduction and Objective: Calcium oxalate constitutes around 60%, mixed calcium oxalate and hydroxyapatite 20%; and brushite 2%. Both uric acid and struvite stones are seen in 10%. The male to female ratio is found to be 3:1. Peak incidence is seen in 4th to 6th decade. Objective of this study is to study the variation of stone composition according to gender and age in this region.

Materials and Methods: In this retrospective study a total of 150 patients, who were being operated for renal stone disease, were analysed for calcium oxalate monohydrate (COM), calcium oxalate dihydrate (COD), carbonate apatite (CA), uric acid containing stones (U) and magnesium ammonium phosphate (MAP). Gender and age were taken as the demographic variables with which stone composition are being statistically compared.

Results: Male to female ratio was 2.75:1. Mean age at presentation was 42.89 years. Composition according to gender are COM (M-58%, F-62%), COD (M-22.27%, F- 21.25%), Uric acid stones (M- 13%, F- 4.5%), CA (M- 6.55%, F- 11%) and MAP (M- 0.18%, F- 0). Relative percentage of stone composition varied in different age groups. COM decreased with age, urate increased with age and carbonate apatite remained the same. The incidences of stone composition in male patients among the various age groups showed that COM slightly decreased with age and uric acid component increased with age.

Conclusion: The variation in stone composition according to gender in this study was not statistically significant. However, the stone composition (Calcium oxalate, uric acid and carbonate apatite) varied significantly with age.

Keywords: stone composition, gender, age, northeast India.

INTRODUCTION

Stone disease has been described from antiquity although it is now one of the most common afflictions of the modern society. The prevalence of kidney stone disease over one's lifetime is approximately between 1% to 15%, which varies according

to age, gender, race, and geographic location. ^[1] There is a global rise in the prevalence of kidney stone disease.

The Afro-Asian stone-forming belt starts from Sudan, Egypt, Saudi Arabia, the United Arab Emirates, the Islamic Republic of Iran, Pakistan, India, Myanmar, Thailand,

and Indonesia up to the Philippines. The disease affects all age groups in this area, from infancy to above 70 years old. The male-to-female ratio is 2 to 1 and prevalence of calculi ranges from 4% to 20%.^[2]

Yasui et al. found rise in the age-adjusted annual incidence of first-time stone formers from 54.2/100,000 in 1965 to 114.3/100,000 in 2005.^[3]

Stamatelou et al. using NHANES data, reported a slight drop in the male-to-female ratio of stone disease, from 1.75 (between 1976 and 1980) to 1.54 (between 1988 and 1994),^[4] with the most recent data (2007-2010) showing a ratio of 1.49.^[5] However, male to female ratio as found in most studies is 3:1.^[6]

The pathogenesis of renal stone disease is multifactorial.^[7] There are several risk factors involved in renal stone formation like dietary habits, fluid intake, warm climate, familial occurrence, geographic factors and areas of high humidity and elevated temperatures.^[8,9]

Stone occurrence before 2nd decade of life is relatively uncommon but peak incidence is seen in 4th to 6th decade.^[10,11] Soucie et al. reported that, peak incidence occurred in 3rd to 4th decade of life.^[12]

Calcium is the major component of urinary stone and comprises a major constituent of about 75% of stones. Calcium oxalate constitutes around 60% of all stones; mixed calcium oxalate and hydroxyapatite about 20%; and brushite around 2%. Both uric acid and struvite (magnesium ammonium phosphate) stones are seen in 10% however cystine stones is a rarity (1%).^[13]

The metabolic derangement contributing to calcium urolithiasis alone or in combination are, hypercalciuria,^[14] hyperuricosuria, hypocitraturia and hyperoxaluria.^[15,16]

Acidic urine is necessary for uric acid stone formation.^[17] Struvite stones are infection stones that occur in alkaline urine environment due to bacteria producing

urease, while impaired renal reabsorption of cystine causes cystine stone formation.^[18]

In Western countries stone analysis is done routinely as a part of treatment, but not in this North-Eastern part of India. We have not found any large-scale data about stone composition in this region. Hence, we started a pilot study to evaluate the variation of stone composition according to gender and age of the patients in North-East India.

The objectives of this study were to determine the gender and age distribution, in relation to chemical composition of renal stones in patients of North-East India attending our tertiary care centre.

MATERIALS AND METHODS

This is a retrospective study that has been conducted in the Department of Urology, Gauhati Medical College Hospital from July 2016 to July 2017. A total of 150 patients, who were being operated for renal stone disease, were being analysed for stone composition.

The stones were analyzed for calcium oxalate monohydrate (COM, whewellite), calcium oxalate dihydrate (COD, weddellite), carbonate apatite (CA, dahllite), urate crystals (U), magnesium ammonium phosphate (PAM, struvite), cystine, xanthine and 2,8 dihydroxyadenine contents. Fourier Transform Infrared spectroscopy is a technique of studying the vibrational change of molecule during interaction of infrared radiation. It was used to determine the composition of a stone with respect to the nature and percentage of compounds present in the stone. Gender and age were taken as the demographic variables with which the stone compositions were statistically compared. Chemical composition of renal stones was the research variable.

STATISTICAL METHOD: We used SPSS software for statistical analysis. We used p value of ≤ 0.05 as statistically significant.

RESULTS AND OBSERVATION

Out of 150 patients with renal stones whose stones were chemically analyzed, there were 110 males (73.33%) and 40 females (26.67%). The male to female ratio was 2.75:1. The highest numbers of male patients have been found in the age group 25-39 years. As depicted in table 1, the male to female ratio is higher in the younger age groups and it is statistically significant ($p < .001$). In males, the peak incidence of stone disease was seen in 25-39 years age group

and in female it was seen in 40-54 years age group. These values are found to be statistically significant ($p = <0.001$) [table 1].

The mean age was 42.89 ± 13.6 years with a range of 14-67 years. The mean age in male was 41.22 years and in female was 47.5 years. The commonest age group involved was of 25-39 years followed by age group of 40-54 years, while the least commonly involved age group was 10-24 years.

Table 1 – Male to female ratio in incidence of stone disease in various age groups.

AGE GROUP (years)	MALE n (%)	FEMALE n (%)	TOTAL n	M:F RATIO	p value
10-24	10 (100%)	0 (0)	10		0.001
25-39	49 (89.1%)	6 (10.9%)	55	8.16	
40-54	23 (53.5%)	20 (46.5%)	43	1.15	
55-69	28 (66.7%)	14 (33.3%)	42	2	
TOTAL PATIENTS	110 (73.3%)	40 (26.7%)	150	2.75:1	

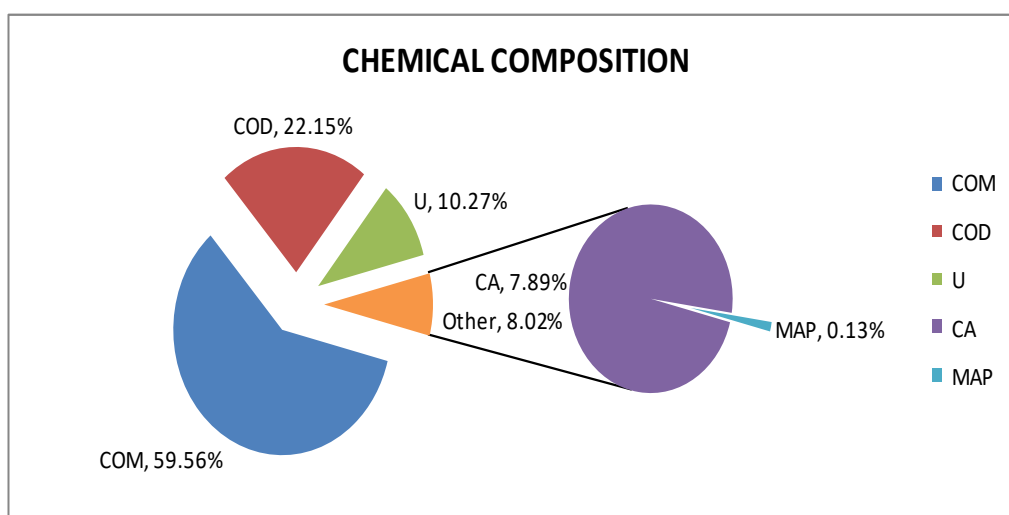


Figure 1 –Overall chemical composition of stones in the study population.

Stone analysis was done and it was found that 59.56% of patients had COM, 22.15% of patients had COD, 10.27% of patients had U, 7.88% of patients had CA and 0.13% of patients had MAP. Figure 1 depicts the stone composition. We found pure calcium oxalate stones in 41.33% of patients.

Relative percentage of stone composition varied in different age group as shown in table 2. The presence of COM in stone decreased with age ($p = 0.0001$), while that of uric acid increased with age (p

$= 0.001$) and carbonate apatite remained same ($p = 0.046$)

Table 2 : Relative stone composition in various age groups

Age group	COM (%)	COD	U	CA	MAP
10-24Y	69%	10%	11%	10%	0
25-39Y	59.56%	22.15%	10.27%	7.89%	0.13%
40-54Y	66.16%	16.28%	7.44%	10.12%	0
55-69Y	42.62%	27.62%	20.48%	9.29%	0
p value	0.0001	0.114	0.001	0.046	0.326

The stone composition in both the genders is given below in figure 2. Out of them, CA stones are seen more commonly in females and uric acid stones are more commonly seen in male than in females ($p = 0.014$)

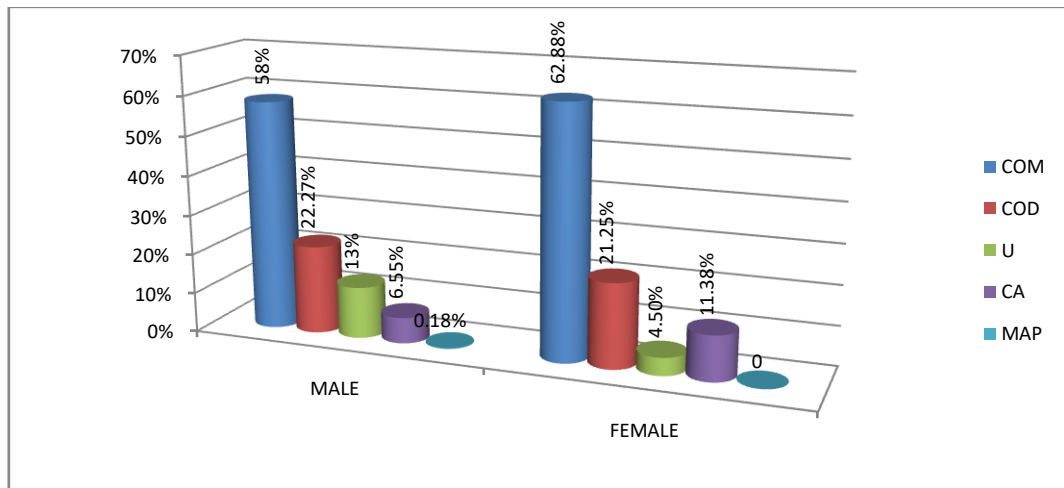


Figure 2 – Stone composition according to gender

On analysis of the combined association of age and sex with stone incidence, the incidence of stone composition in male patients among the various age groups are shown in figure 3. The COM slightly decreased with age ($p = 0.0001$) and uric acid component increased with age ($p = 0.0001$). However in females, the changes as depicted in figure 4 were not statistically significant.

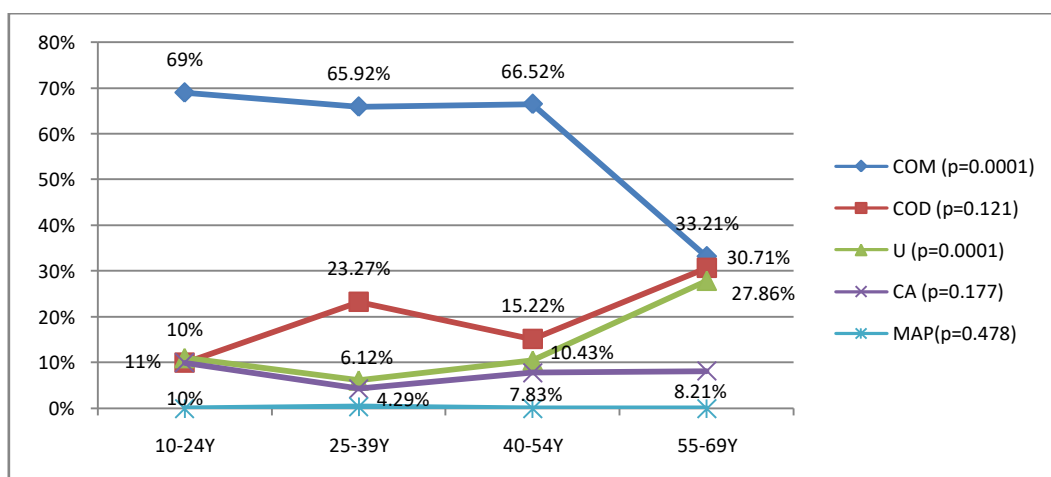


Figure 3 - Incidence of stone composition according to age in male group

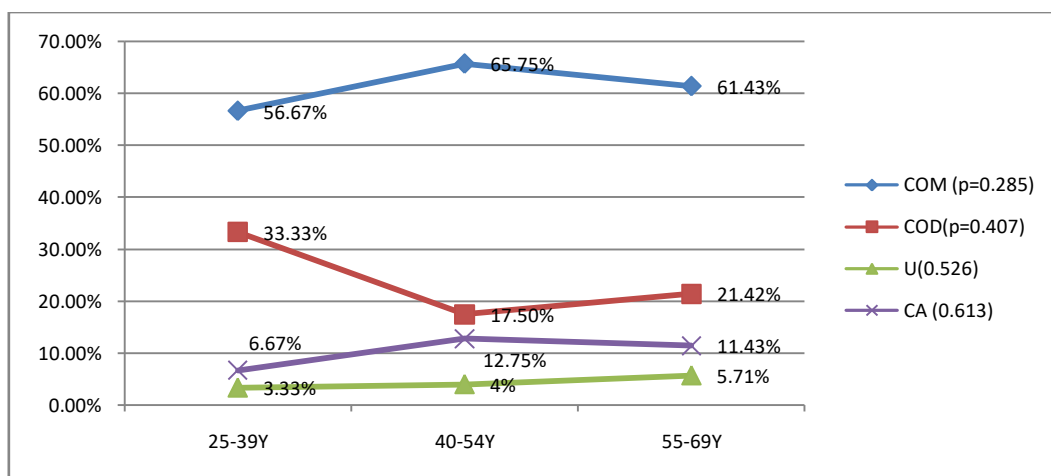


Figure 4 - Incidence of stone composition in female population among the various age groups.

DISCUSSION

In our study, the mean age was 42.89 years (range: 14-67 years) (Table 3). The commonest age group present was 25-39 years followed by 40-54 years. Stone disease was least common in age group 10-24 years. Ansari M S et al. in their study have found the average age to be 30 years. [19] Khan G et al. have found that the commonest age group involved was of 21-40 years while the least commonly involved age group was of more than 60 years. [20] Ahmad S et al. have found the mean age of 41.45 for men and 39.20 for women. [21] In our study, the mean age in male was 41.22 years and in female was 47.5 years. M. Bouatia et al. have found the average age of 49 (range 20–87) years for men and 48 (range 18–86) years for women. [22]

Table 3 – Average age of presentation of stone disease

Study	Average age (years)
Ansari M S et al. (2005) [19]	30
Khan G et al. (2014) [20]	33
M. Boutia et al. (2015) [22]	49
Our series	42.89

We found male to female ratio of 2.75:1 which similar to other studies (Table 4). Incidence in male is more in younger than the older age group in our study. Ahmad S et al. have found that incidence in male increased with age and highest ratio of 4.9:1 in age above 60 years. [21] Lieske JC et al. found that male to female ratio increased mildly with age, with male to female ratio of 2.09:1 in age group 70-79 years. [23] Men have higher protein intake in comparison to females, [24] and also their urine is oversaturated with CaOx, [25] suggesting higher risk of kidney stone formation. [26]

Table 5 – Comparison of stone composition among various studies.

	Our series (% of patients)	M. Bouatia et al. (2015) [22] (% of patients)	Ansari MS et al. (2005) [19] (% of patients)	Djellou et al. (2006) [34] (% of patients)	Lieske et al. (2014) [23] (% of patients)
COM	59.56	56.4	74.43	50.3	67.3
COD	22.15	10.2	18.6	16.7	
U	10.27	8.10	0.95	10.6	8.3
CA	7.89	4.40	1.8	16.7	16.1

In our study, we found uric acid more common in males and CA to be more common in females. Lieske et al. found

Table 4 - Male to female ratio in stone disease.

Study	Male to Female ratio
Hossain et al. (2003) [27]	2.7 : 1
Ansari M S et al. (2005) [19]	2 : 1
M. Bouatia et al. (2015) [22]	2.03 : 1
Our series	2.75 : 1

In our study, we found CaOx to be highest in 81.71% of the patients. Similarly in other studies, CaOx was the most common component (Table 5). We found uric acid component in 10.27% of patients while other studies found it between 0.95% to 10.6% (Table 5).

In our study we have found COM to be decreasing with age in both sexes, U to be increasing with age in male in comparison to female and CA remained same. As in our study, M. Boutia et al. found that COM showed a decreasing trend from 60% in 18-30 years to 31.2% in those 60 years, and uric acid showed an increasing trend from 6% in 18-20 years to 49.5% in more than 60 years. [22] However, CA showed an increasing trend with age. Knoll T et al., Krambeck AE et al., and Daudon M et al. found increasing trend of uric acid stones with age. [28-30] Lieske et al. found an increasing proportion of apatite and decreasing proportion of CaOx stones with age. [23]

Obesity, insulin resistance, and type 2 diabetes mellitus increases with age and are associated with lower urinary pH and uric acid stones. [31] Increased uric acid stone may be due to acidic urine caused by type 4 renal tubular acidosis associated with CKD in aging individuals. [32] As GFR declines with age, urinary calcium excretion is decreased which may lead to decreased incidence of calcium stones with age. [33]

more women than men were likely to have CA (25.0% versus 9.6%). [23] Similarly, Parks et al. found higher incidence of CA in

female. [35] Lieske et al. and M.Boutia et al. found U stone composition increases markedly in both sexes after the age of 50 years. [23, 22]

Women stone formers are at increased risk of urinary tract infection. If infection is caused by urease forming organism there is an increase in pH of urine thus favouring hydroxyapatite supersaturations. [35] During the postmenopausal age, stone compositions in women are quite similar to that of men of the same age. The incidence of kidney stones also increases after menopause. [36,37] In postmenopausal females who are on estrogen replacement therapy, their urinary pH and citrate tend to be higher compared to those without estrogen supplementation. It suggests that postmenopausal changes of estrogen decline make women almost similar to men of respective age in the risk of kidney stone formation. [38, 39]

We found that MAP was the least common component, unlike western studies where struvite is the least common. Ahmad S et al. found that magnesium ammonium phosphate (MAP) constitutes 2% of all stones. [21] M. Bouatia et al. and Daudon et al. found that MAP constituted 4.4% and 1.7% of their stones respectively. [22, 30]

The incidence of renal stone in the North Eastern region of India has not been reported earlier. In comparing earlier studies from Northern India, we found that CaOx stones were higher than in our study. Rao et al. found COM in 96% of their patients. [40] Ahmad S et al. found that 93% were calcium oxalate stones, out of which 80% were COM and 20% were COD. [19] Sharma et al. found the incidence of calcium oxalate stones to be 86.1%. [41]

The high percentage of CaOx stones in North-Eastern India (81.71%) may be due to high oxalate content in the diet; high carbohydrate intake (rice), which is associated with acidic urine favouring CaOx stone formation. [42] Drinking water quality whether hard or soft and its mineral contents especially high fluoride levels can cause increased urolithiasis. [43] Fluoride content

of water is found to be higher in stone belt areas of North East India. Fluoride increases oxalate excretion in urine and excretion of insoluble calcium fluoride. [43] Betel nut chewing is very much common in north-eastern India. Betel nut is a factor for chronic kidney disease. [44] There is an increased risk of kidney stone formation in patients with CKD. [45]

CONCLUSION

Incidence of urolithiasis is on the rise globally and North-Eastern India is no exception. Although there are a several studies on kidney stone composition from other parts of India, this is the first study from north-eastern India. Chemical analysis of urinary stones provides important information on stone composition, distribution, and risk factors. Stone disease is commonest in third and fourth decade with increased male predilection. Calcium oxalate is the most common composition out of which Calcium oxalate monohydrate surpasses Calcium oxalate dihydrate. Uric acid stone is the next most common type and it increases with age in males more than in females. Carbonate apatite is found more commonly in females than males. Struvite stones are rare in this region like other parts of India but unlike Western countries. There are various other demographic factors like dietary habits containing high purine rich foods, excessive betel nut intake, high intake of oxalate containing tuberous food and fluoride composition in ground water which had influenced the incidence and composition of kidney stones in this part of India. Further studies evaluating these factors in a larger population will throw more light on the factors causing increasing trend in urinary tract stones and may help to arrive at taking certain steps in prevention of stone disease in the near future.

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