## **Original Research Article**

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# Spectrum of chemical analysis of 150 consecutive upper urinary tract stones with critical analysis in respect of demographic and geographical distribution

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### ABSTRACT

**Background:** The aim of the study was to evaluate the chemical composition of urinary stones and pattern of changes according to the patient's demographic and geographical distribution.

**Methods:** 150 patients of upper tract urolithiasis were prospectively selected during the study period. Chemical composition was analyzed by FTIR spectroscopy. A subgroup study based on the patient's age, sex and geographical origin was done. For subgroup analysis patients were divided into two age groups; group A (5-18 years, 14 patients) and group B (>18 years, 136 patients). The geographical origin of the patients was recorded according to the administrative division.

**Results:** Male were predominant in all age groups with ratio of 2.49:1. Most of the patients were from Rangpur (28.67%) and Mymensingh (20.67) division. Mixed composition stones were much more common than pure one (75.99% vs 24.01%). Overall, combination of calcium oxalate monohydrate with dehydrate was the most common composition (56.67%). Calcium oxalate was the predominant chemical composition in 82% of stones, followed by struvite in 9.33%, apatite in 4.67%, uric acid in 3.33% and cystine in 0.67%. The proportion of calcium oxalate stone was increasing while that of struvite, uric acid, and cystine stone was decreasing with age. But stone composition did not show any significant difference on geographical distribution.

**Conclusions:** Calcium oxalate is the most common composition of urinary stones in all age groups. Mixed stones are more common than pure ones. The incidence of calcium oxalate stone increases while that of struvite, uric acid, and cystine stone decreases with age.

**Keywords:** Chemical composition, Renal stone, Demographical variation

#### **INTRODUCTION**

Kidney stone is one of the oldest recorded disorders of human and one of the major health burdens. Urolithiasis was the second only to diseases of the prostate as the most frequent diagnosis found in a European survey.<sup>1</sup> The incidence rate varies with different geographical region of the world. The stone forming belt of the world is identified as Egypt, Sudan, Saudi Arabia, Iran, UAE, Pakistan, India, Thailand, Myanmar, Indonesia and Philippines.<sup>2</sup> A

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significant economic burden is associated with kidney stones, with annual estimates exceeding USD 5 billion in USA.<sup>3</sup> A research conducted at a rural area of Rajshahi region of Bangladesh showed that the average medical expenditure among individuals who reported kidney stone related illness in the past 30 days prior to survey was BDT 10000 to BDT 76760.<sup>4</sup> This figure is likely to be increased as renal stone disease has a tendency to recur. Recurrence rates of renal stone are approximately 10% in first year, 50% over a period of 5-10 years and 75% over 20 years' period.<sup>5</sup> Although, in the last few decades, a significant improvement has been made in the field of endourology and thus in the management of renal stone disease in our country, there still remains a lack of appropriate preventive measures to reduce the incidence of recurrence.

If successful primary treatment is to be followed by effective prevention of recurrence, the stone material must be subjected to chemical analysis as described in popular guidelines.<sup>6,7</sup> Without analysis of the stone, no specific prophylaxis can be carried out. In our regular practice this is frequently forgotten and in the long-term patient may end up receiving treatment that is no longer appropriate.

Literature review shows, approximately 80% of adults with urolithiasis have stones that consist predominantly of calcium oxalate and/or calcium phosphate. Struvite stones (magnesium ammonium phosphate) represent 10-15%, uric acid stones, 5-10%, whereas cystine stones are rare, 1-2%.<sup>5,8</sup> In children, the composition of urinary stones is somewhat different than that of adults. 9 Methods used for renal stone analysis include Fourier transform infrared (FTIR) spectroscopy, X-ray diffraction crystallography, coherent-scatter analysis, scanning electron microscopy with energy dispersion, thermogravimetry, polarizing microscopy, and wet chemical analysis. 10 Among all these methods, FTIR is a sensitive, reliable, accurate, rapid, and specific method.<sup>10</sup> This study was done to perform chemical analysis of stones to know the stone pattern in different age group patients with different geographical distribution presenting to our hospital.

#### **METHODS**

In this study the sample of 150 patients having upper tract urolithiasis were collected prospectively from ACKU (Advanced Centre of Kidney and Urology) during the period of July 2019 to March 2020. Chemical composition of urinary stones was analyzed using FTIR spectroscopy. The stones recovered from surgery were washed with distilled water to remove blood and tissue remains attached, completely dried and were sent to a third-party lab as FTIR spectroscopy technology is not available in our centre. A subgroup study based on the patient's age, sex and geographical origin was done. For subgroup analysis patients were divided into two age groups; group A (5-18 years) and group B (>18 years). The geographical origin of the study patients was also recorded according to the administrative division they belong to. Pure stones in our study were defined as stone composed of ≥90% of the

reported composition. Mixed stones were made up of more than one composition, but none of the compositions was ≥90% of the total. The stone component was considered as predominant one if it exceeded 50% of the total composition of the calculus. Ethical approval was not applicable for this study but informed written consent were taken from the patients and legal guardian. It was obtained after explaining the purpose and nature of the study. Data were entered in the computer using SPSS (Statistical package for social science) version 21.0. The statistical analysis was done using SPSS. An appropriate statistical test (Chi-square) was performed. The level of significance was considered as a p value less than 0.05 and double-checked before analysis.

#### Inclusion criteria

Inclusion criteria were patients having upper tract urolithiasis and patients who had given the written consent to participate in this study procedure.

#### Exclusion criteria

Exclusion criteria were patients below 5 years old and patients with unwillingness to give informed written consent to take part in the study.

#### **RESULTS**

In this study, there were 14 patients were in group A and 136 in group B. Mean age of the patients were 33.6 years. Male were predominant in all age groups with the ratio of 2.49:1. Most of the patients were from Rangpur division (28.67%), followed by Mymensingh (20.67%), Dhaka (14.67%), Rajshahi (10%), Khulna (8.67%), Sylhet (7.32%), Barishal (6%) and Chattogram (4%) division (Figure 1).

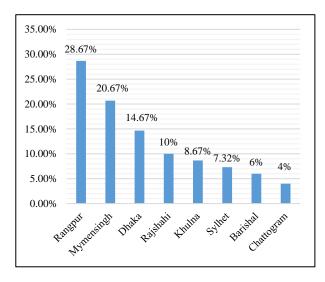


Figure 1: Geographical area of the patients.

Of the 150 stones analyzed, 93 were renal stones and 57 were ureteric stones (Figure 2).

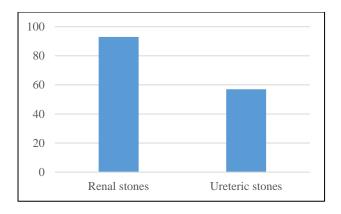


Figure 2: Types of the stones among patients.

Mixed composition stones were much more common than pure one (75.99% vs 24.01%) (Figure 3).

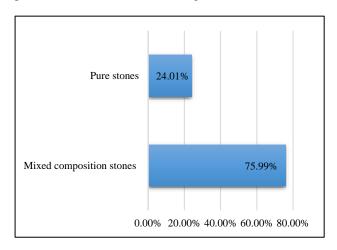


Figure 3: Composition of the stones.

Overall, combination of calcium oxalate monohydrate with dihydrate was the most common composition (56.67%). Calcium oxalate was the predominant chemical composition in 82% of stones, followed by struvite in 9.33%, apatite in 4.67%, uric acid in 3.33% and cystine in 0.67%. The proportion of calcium oxalate stone was increasing with age while that of struvite, uric acid, and cystine stone was decreasing. However, stone composition did not show any significant difference on geographical distribution.

#### DISCUSSION

Bangladesh lies near the world stone belt and hence is a high-incidence zone for stone disease. However, we have no countrywide epidemiological data regarding incidence and prevalence. In the past 100 years, researchers have produced revolutionary changes in the anatomical and clinical pathology of stone disease. Over the last several decades we have made enormous development in cost-effective and sustainable treatment options. But even today we are not in a better position than Frayer Jacques who stated, 'I have removed the stone, it is up to god to cure the patient'. It is because stone disease is notorious for its

tendency to recur. There are several reasons why research on stone composition is important: to provide an understanding of the nature of the underlying metabolic disturbances that lead to the stone formation; to be able to predict the stone fragility (i.e. the ease with which a given stone might be fragmented) and hence the suitability of a given patient for a given protocol; to predict the basic wavelength of laser light to be used for maximum effect in treatment and to permit urologists to advise patients on how to prevent further recurrence.<sup>11</sup>

Urinary calculus disease usually occurs in working age group and leads to an economic burden on the society. Jindal et al in their study showed a mean age of 38 years for urolithiasis.<sup>12</sup>

In our study, the mean age was 33.6 years. Bangash et al reported the mean age of 43.9 years, with insignificant sex difference. <sup>13</sup> Males were found to have more stone disease in our study than females with the ratio of 2.49:1. This was consistent with most of the other studies. <sup>12,14</sup>

The available literature on chemical analysis of urolithiasis shows a different stone pattern across the world. In an extensive analysis of 10617 calculi by FTIR spectroscopy, Daudon et al found that 65.98% were oxalate calculi. <sup>15</sup> Alaya et al and Daudon et al also found decreasing frequency of struvite and calcium phosphate stones with age. <sup>14,15</sup> We found no cystine stone in group B. It may be due to the fact that the formation of cystine stone is genetically determined and most patients present in childhood.

Herring presented observations from 10000 urinary calculi and showed that 31.4% of stones were COM and 40.9% were COD.<sup>16</sup> Mandel et al showed in their study, after analysis of 10163 calculi, that 55.4% were COM and 34.6% were COD.<sup>17</sup> As compared to the Western studies, the data from the subcontinent are different. In 1976, Rao et al analyzed 51 calculi from patients in the region of Delhi and found that 96% of the stones contained COM.<sup>18</sup> In a study by Ahlawat et al analysis of 435 upper urinary tract calculi showed that oxalate stones comprised 97% of the total. 90% of these stones were predominantly COM, 4.6% being predominantly COD. 19 These studies are showing a significantly higher incidence of calcium oxalate stones, especially COM than that in Western countries. In the present study the incidence of calcium oxalate stone was in consistent with subcontinent series and was as high as 84%. The other common compositions were uric acid in 4.28%, struvite in 2.29%, calcium phosphate in 1.49%, and cystine in 0.4%. This pattern of calcium oxalate as predominant composition was seen in all age groups. Some of the reasons for the high incidence of COM in northern India might be as follows: (i) high carbohydrate intake (especially rice), which provides an acidic milieu to urine favoring calcium oxalate stones formation (ii) vegetarian diet (with high oxalate content) and (iii) high mineral contents of water. 20,21

On subgroup analysis based on the patient's age, we observed that the proportion of calcium oxalate stone was increasing whereas that of uric acid, struvite and cystine was decreasing with age (Figure 1). Gabrielsen et al reported similar trends while evaluating the stone composition in pediatric patients in a large retrospective study.<sup>22</sup> Other studies also showed peak incidence of calcium oxalate stones between the age of 30 and 50 years.<sup>23,24</sup>

Pure uric acid stone was present in 21.42% of patients in group A in contrast to only in 0.74% of patients in group B. Urinary uric acid excretion rates decrease with age in pediatric patients and might impact on stone formation. Struvite stones are the best marker of urinary tract infection. The incidence of struvite and apatite stones is decreasing because of early detection and vigorous treatment of urinary tract infection with antibiotics nowadays.

We found that most of our patients were from Rangpur division. It does not mean that Rangpur division is the highest incidence zone for stone disease in Bangladesh. Our centre is a tertiary level service providing hospital and most of the stone related patients are referred from different peripheral centers. The lowest number of our study patients is from Chattagram division. This may be due to availability of modern endourological interventions like PCNL, RIRS etc. are available in Chattagram division and hence patients from that area are less likely to be referred to. Our study showed no significant difference of stone composition on variation of geographical distribution.

A study from George Washington University Hospital showed that, there were very few differences in stone composition between regions of the United States. <sup>26</sup> They concluded that the climate, diet and lifestyle played a stronger influence on the composition of stones between countries. Our country is a smaller one and climate, diet or lifestyle is almost the same in all over the country. However, our series is too small to make comment that can be generalized on the whole population.

#### Limitations

The limitation we found in our study was the sample size. For better outcomes, larger study population can be more helpful in future. Moreover, single center study was also a limitation.

#### **CONCLUSION**

To prevent stone recurrence, one must be able to detect underlying metabolic abnormality and know the stone composition. The present study concludes that, calcium oxalate is the most frequent composition of urinary stones in all age groups. The incidence of calcium oxalate stone increases while that of apatite, struvite, uric acid, and cystine stone decreases with age. Stone composition does

not differ in geographical variation. A large-scale multicentre study is needed to explore the scenario in detail.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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