Incidence of Hyperuricemia in Patients of Renal Calculi and Their Comparison with Chemical Analysis of Renal Stones

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Introduction: The targeted medical prophylaxis required reliable information on stone type which when combined with relevant blood and urine analysis allows identification of treatable risk factors.

Objective: The exact determination of the compositional structure of the renal stone enables the classification of the disease and its subsequent treatment.

Methods: A total of 50 consecutive patients both male and females with upper urinary tract calculi will be included in this study. This is a comparative study between the patients and age matched controls. These patients and controls will have preoperative assessment of serum uric acid. After surgery the chemical examination of stones will be done by Merck kit.

Results: The mean serum uric acid in S.F (3.91 ± .87 mg/dl) was greater than N.S.F (3.79 ± .78 mg/dl) and the difference was statistically not significant. Eight stones (16%), were pure calcium oxalate, while the rest of stones were of mixed variety. Calcium was found in all the 50 (100%) stones,oxalate in 45 (90%). Urates were present in 30 (60%) cases and no pure uric acid stone was found. Phosphate were also present in 5 (10%) cases. Ammonium was present in 7 (15%) stones in mixed form. Magnesium was present in only 2 (5%) stones.

Conclusion: The mean serum uric acid level in Stone Formers was greater than Non Stone Formers but the difference was statistically not significant. Therefore serum uric acid in our study is not a predisposing cause in renal stone formation. It is concluded that most of the stones (84%) were of the mixed variety and calcium oxalate urates and phosphates were the predominant constituents.

Key Words: Hyperuricemia, calcium oxalate, urates.

Introduction

The high incidence of stone disease in southern Punjab was laid bare by McCarrison in 1931. Similar findings were demonstrated by Anderson in 1968 who showed high incidence of stone disease in the Indian Punjab. Keeping in view these surveys, Khan and Khan in 1986-87 carried out a comprehensive stone survey of the Punjab hospitals. For the purpose of analysis, the hospitals were divide into southern and northern regions. The line of demarcation passed through Sahiwal, Jhang, Sargodha and Mianwali. According to 1981 census, the population of southern and northern Punjab constituted 38.73% (13,966,000) and 61.27% (22,097,000) of the total population of Punjab. Operation registers of the hospitals were consulted to demonstrate the incidence of the stone disease. The results were astonishing and opposite to the magnitude of population of the two regions. A total of 3194 operations were performed, and southern and northern Punjab constituted 70.78% (2261) and 29.22% (933) of the total operations respectively. For upper urinary tract stone disease, southern and northern Punjab constituted 54.70% (751) and 45.30% (622) of the total operations. If we further analyse this data, southern and northern Punjab constituted 5.36 and 2.82 upper urinary tract operations per 100,000 population and 16.15 and 4.22 total urinary tract stone operation per 100,000 population, respectively. Therefore the incidence was almost double in southern Punjab for upper tract stone surgery and four times for the total urinary tract stone surgery. Upper tract urolithiasis is the commonest urological ailment and most of the patients in Pakistan are ultimately managed by surgical therapy.[4] Raised serum and/or urinary uric acid is a well established risk factor for calcugenesis,[5] but uric acid stones may form even in the absence of above factors. In these cases, chronic dehydration or persistent low urinary pH may by the causative factors.[6] In some cases, uric acid crystals act as nucleus and calcium oxalate crystals get deposited around the uric acid nucleus due to epitaxy and lead to uric acid induced, calcium oxalate stones.[7]

The targeted medical prophylaxis required reliable information on stone type which when combined with relevant blood and urine analysis allows identification of treatable risk factors; Drach $(1986)_5$ has maintained the importance of stone analysis. The composition of each urinary stone must be identified Beukes et al $(1987)_8$. Many studies have been carried out from DG Safdar et al $(1995)_9$ Karachi, Khanum $(1981)_{10}$ Rizvi $(1975)_{11}$ Rizvi & Naqvi $(1982)_{12}$ No study on incidence of hyperuricemia is available from Lahore. Therefore it would be interesting to compare our results with other studies from this region and those from developed countries.

Material and Methods

A total of 50 consecutive patients both male and females with upper urinary tract calculi will be included in this

study. This is a comparative study between the patients and age matched controls. These patients and controls will have preoperative assessment of serum uric acid. After surgery the chemical examination of stones will be done by Merck kit. Stones were powered with a pestle and mortar. Qualitative chemical analysis was carried out using Merckognost urinary calculi analysis kit. A little powdered stone material was acidified with hydrochloric acid. Aliquote of this acidified solutions were submitted to the tests as described by sutor.[13]

Aims and Objectives

1. The exact determination of the compositional structure of the renal stone enables the classification of the disease and its subsequent treatment.
2. Its relationship with dietary factors.

Results

The age range of the patients was between 13-75 years. The mean age was 31.2 years. Family history of stone disease was found in 52% of the patients.

Table 1: *Age and Sex n = 50.*

Age Range	13 – 75 Year
Mean Age	31.25 years
Male patients	30
Female Patients	20
Male/Female ratio	1.5 :1

Table 2: *Stone Side and Site n=50.*

Kidney Stones	35
Upper ureteric stones	10
Lower ureteric stone	5
Right side	22.40%
Left side	28.60%

Table 3: *Size of Stones n=50.*

< 2 cm.	15
2 – 3 cm.	12.5
> 3 cm.	22.5

The mean serum uric acid level in Stone Former (S.F.) was 3.91 ± .87 and in Non Stone Former (N.S.F.) 3.79 ± .78

The chemical analysis of stones showed that calcium was present in all the 50 (100%) stones examined (Table 5).

In 5 stones (10%), it was found as pure calcium oxalate, while in rest of 45 (90%) cases, the stones were of mixed variety (Table 6).

Table 4: *Mean ± S.D. of Serum uric acid level in stone former (n=50) and non stone former (n=50).*

Stone Formers	Non Stone Former
3.91 ± .87`	3.79 ± .78

Oxalate was found in all the 40 (90%) stones. In 5 (10%) cases, it was present as pure radical while in remaining 45 (90%) stones, it was present alongwith other radicals.

Table5: *Composition of Upper Tract Stones.*

Radical	No. of Stones	% age
Calcium	50	100%
Oxalate	45	90%
Uric Acid	40	80%
Phosphate	5	10%
Ammonium	7	15%
Magnesium	2	15%

Urates were presents in 40 (80%) stones and no pure uric acid stone was seen. Phosphates were also found in 5 (10%) of stones. It was present in a mixed form. Ammonium was found in 7 (15%) stones in mixed form. Magnesium was also present in only 2 (5%) stones in mixed form.

Table 6: *Composition of chemicals found in Upper Tract Stones.*

Radical	No. of Stones	% Age
Ca + OX	8	16%
Ca + OX + UA	30	60%
Ca + OX + UA+PO_4	2	4%
Ca + OX + PO_4	2	4%
Ca + OX + UA Am + Mg	2	4%
Ca +OX + $PO+_4$ + Am	6	12%

Discussion

Urinary uric acid crystals also tend to impair the action of urinary inhibitors and thus help calcugenesis. Various studies done in Pakistan[2,14-16] have shown higher mean serum uric acid levels in Stone former (S.F) than Non stone former (N.S.F) but none in hyperuricaemic range. But in each study, the difference was statistically significant except

Khan et al at Bahawalpur[16] who have demonstrated statistically non significant difference. Khan at D.G. Khan[17] in 100 S.F. and 100 N.S.F. has demonstrated hyperuricaemia in 31% and 19% of cases respectively. Though hyperuricaemia has not been demonstrated in our study at Lahore but mean serum uric acid levels were greater in S.F. (3.91 ± .87 mg/dl) than N.S.F. (3.79 ± .78 mg/dl) and the difference was statistically not significant. Therefore, raised serum uric acid is not potential risk factor in Lahore. Common methods used for stone analysis are chemical, optical and radiographic crystallography. Each method has its proponents as well as opponents. Chemical methods being simple and has only 2% error in detection of composition of stones. These methods are best for practical use in the hospitals.[5]

Most of the studies have been carried out by crushing the whole stone followed by chemical analysis of the pulverized material. Shahjehan and Rehman[18] are probably pioneers in analyzing stones in layers in Pakistan. They have demonstrated that about 50% of the renal calculi were of mixed composition and 35.4% were pure calcium oxalate. Layer by layer analysis showed that most of the calculi were of mixed variety and calcium oxalate constituted 90% of the stone burden and pure calcium oxalate made up 20% of the sample. The surprising finding was that urates formed 80% of the sample. Other interesting finding was that the nucleus of the bladder as we as the renal calculi were of the same composition, but the surrounding layers were of different composition. This difference has been attributed to the difference in environments in the urinary tract at different levels of urine formation and storage.

Rana M. N and khan (19) at Lahore in 1976 analyzed 128 urinary calculi, which included 63 renal, 6 ureteric, 55 bladder calculi and 4 were collected after thety were passed in the urine. Out of 128 calculi, 16 were analyzed in layers which included 7 renal and 9 vesical calculi. The rest were analyzed as a whole. They showed that the renal calculi contained 52.3% calcium oxalate and 26.9% urates, while bladder stones were 58.1% urates and 29% calcium oxalate. The outermost layer of renal and bladder calculi did not show any remarkable difference.

Khanum[10] in 1981 at Karachi chemically examined 198 stones and demonstrated that majority (70%) of the stones were of mixed variety with calcium, oxalate and urate present in 91%, 43%, and 68% of the stones respectively. Pure uric acid and oxalate constituted 9% and 7% of the calculi.

Jehangir[20] in 1981 from Lahore demonstrated by chemical examination of the calculi that 80% were of the mixed variety, with calcium, oxalate, phosphate, ammonium, urates and magnesium constituting, 100%, 97%, 47%, 57%, 37%, and 13% of the stones respectively. 20% of the total stones were of pure variety. Pure calcium oxalate stones were found in 17% of the total cases.

Khaliq et al[21] in 1984 analyzed 125 calculi by infrared spectroscopy and demonstrated that 53 (42.73%) were pure stones and 71 (57.27%) mixed. Of the pure stones (53), calcium oxalate monohydrate, dehydrate, uric acid and magnesium ammonium phosphate constituted 33.1% (41) 1.6% (2), 0.8% (1) respectively. If the mixed stone group (n = 71) calcium oxalate was the sole constituent in 14.1% (10) of cases. It was present in the nucleus mixed with others constituents. Tricalcium phosphate in 45.07% (32) of cases, uric acid 4n 8.4% (6) of cases, with ammonium hydrogen urate and carbonate appatite in 8.45% (6) and 1.4% (1) of cases respectively. Ammonium hydrogen urate was present in the nuclei alone in the pure form (50%) or mixed with calcium oxalate monohydrate.

Rizvi et al[12] in 1985 analyzed ten years collection of 100 renal stones (July 1973-June 1983) in layers either by X-ray crystallography or infrared spectroscopy and demonstrated that most stones (78%) were of mixed variety. Calcium oxalate was the most common constituent, forming 90% of the nucleus and 85% of the outer surface layer. Phosphate constituted 30% of the nucleus and 50% of the outer layer. On the other hand, uric acid formed 40% of the nucleus and only 5% of the outer layer.

Various studies from India as well as from other parts of Asia show high urate content in renal calculi. Singh et al[22] in 1969 from Delhi analyzed 243 renal stones, and showed urates in 38.25% stones. Rao et al[23] in 1964 from Gawalior (India) found even higher proportion of urates, while calcium oxalate was seen only in 3.5% of stones. Simi-larly Anderson (24) in 1962 from Ahmad Nagar (India) demonstrated urates in 23% of renal calculi. Urates constituted 31.6% and 76 and of renal calculi in Taiwan and Thailand respectively cited by Shahjehan and Rehman, 1971. Cifeuntes and Pourmand[25] in 1980 from Iran demonstrated that majority of the stones were of mixed variety, pure calcium oxalate and uric acid stones formed 6.66% and 5.8% respectively of the total stones examined. Overall calcium oxalate and uric acid content was 85% and 24.2% respectively.

In the west, the chemical composition of the stones is different. Lonsdale[26] in 1968 demonstrated that majority of renal stones from United States of America and Czechoslovakia have high calcium oxalate and calcium magnesium phosphate content. Similar findings were reported by Prien and Prien[27] in 1968 from U.S.A They analyzed one thousand stones and demonstrated that the majority of the stones were composed of calcium oxalate and urates were found in traces. Results reported by Sutor et al[28] in 1974 from Europe also show high calcium oxalate and low urate contents.

Beukes et al[19] in 1987 from South Africa analyzed 1002 stones and compared their results with eleven studies from South Africa, USA Sudan, Czechoslovakia, Europe and Thailand. All the studies from South Africa, Europe and USA had high calcium oxalate content (more than 62%) except from Leeds by Sutor and Wooley[20] where the calcium oxalate was only 31% but the sample size was also small (33 stones). From Thailand and Sudan, the reported concentration of calcium oxalate stones was only 34% and 45% respectively. The incidence of struvite stones from South Africa, Europe and USA was less than 10% while

from Thailand and Sudan it was 24% and 29% respectively. Furthermore, the total urates reported from South Africa, USA, and UK, was 16% 2.5 – 7.7% and 0.5-5.5% respectively. From Thailand and Sudan, the total urate concentration reported was 19% and 16% respectively.

In our study at Lahore, 90% of the stones were of mixed variety and we have reported only 10% pure stones which were pure calcium oxalate stones while no pure uric acid stone was found. Among the mixed stones, calcium and oxalate was present in all the 50 stones (100%). Urate, phosphate, ammonium and magnesium were present in 30 (60%), 30 (60%), 10 (20%) and 10 (20%) stones respectively.

These are very interesting results. Studies from Europe and USA show majority of the stones as pure calcium oxalate with less struvite and urate content, while reports from south east Asia are altogether different. Majority of the stones from Indo-Pakistan, Thailand and Iran are of mixed variety with more urate content. This is very difficult to explain but the reason may be that in the underdeveloped countries, patients usually do not seek medical advice even for years. This delay may lead to comparatively more struvite stones in the underdeveloped countries as well as high urate contents in mixed stone.

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