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RESEARCH ARTICLE

EPIDEMIOLOGICAL CHARACTERISTICS OF UROLITHIASIS IN KASHMIR
DIVISION AND RELATION TO SOURCE OF WATER

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ABSTRACT

Objective: Kashmir has a high incidence of urolithiasis. This study was undertaken to understand the urinary composition, symptomology, diagnostic modality and relation of urolithiasis to water source in patients admitted in a tertiary care hospital of Kashmir division.

Methods: A total of 186 24 hr urinary samples of patients with urolithiasis from a tertiary Care hospital were analyzed by enzymatic and spectrophotometric technique to measure the concentration of calcium, magnesium, oxalate, citrate, uric acid and phosphate.

Results: Most of patients enrolled were in the age group of 15-39 yrs, 126 patients (67.7%) of study group. The youngest patient was 14 yrs old and the oldest was 67 yrs old. Most of the patients enrolled for study were males 119(64%) and females were 67(36%). Patients enrolled were from different districts of Jammu and Kashmir, but most of the patients belonged to rural areas. Most of the patients had flank pain as a predominant presenting symptom (78%), UTI with or without obstruction (11.8%) and incidental asymptomatic patients with urolithiasis (10.2%). Most common diagnostic modality used was USG (83%), Plain X-ray KUB (8.6%), IVP (8.1%) in patients with PUJ/VUJ small calculi. On metabolic evaluation of 24 hour urinary constituents in our study group of 186 patients, 113 (60.8%) patients were having hypercalciuria as predominant urinary abnormality with Mean \pm SD 9.41 \pm 2.07 which was persistently higher than normal. However there was no significant variation on the basis of gender. Hypocitraturia was the second most common abnormality found in 112 (60%) stone formers with Mean \pm SD of 1.32 \pm 0.18 which is usually not found normally, but was predominately found among males (62.2%) of our study group. Significantly increased concentration of uric acid were seen in 48(25.8%) stone formers which were again found to be statistically significant and their propensity was more in male gender. Urinary phosphate and oxalate concentration were raised in stone formers in 88 (47.3%) and 42 (25.3%) patients with Mean \pm SD of 42.32 \pm 1.87 and 41.58 \pm 5.45 respectively. Hypomagnesuria was seen in 94 (50.5%) patients more in females as compared to males.

Conclusion: The findings of the present work indicate that urolithiasis in the Kashmir division represent common urological problem and is correlated with the nutritional, environmental and genetic factors.

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INTRODUCTION

Urinary calculi have afflicted humankind since antiquity. Scientists have found evidence of kidney stones in an Egyptian mummy more than 7000 years old.

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These stones are more common in some parts of the world including India. The risk of urolithiasis shows different frequencies: 1-5% in Asia, 5-9% in Europe, 13% in North America and 20% in Saudi Arabia. Epidemiological studies show that renal stone formation is a complex multifactorial disease associated with hypercalciuria, hypocitraturia, hyperuricosuria, hyperoxaluria, hypomagnesuria.

High or low urinary pH, dietary habits, life-style, socioeconomic status, and environmental and genetic factors. Kidney stone disease varies in frequency and stone type between different climates and racial groups. Understanding the epidemiology of stones disease is important to determine the significance of the disease at a community level, the associations and risk factors for individuals and the likelihood of stone recurrence. This section attempts to describe the epidemiology of kidney stone disease including its association and risk factors.

METHODS

One eighty six urinary samples belonging to patients from different districts of Kashmir were used for chemical analysis and spectrophotometry. The samples were collected during the period January 2014 to January 2015. The sample represented patients from different districts (Srinagar, Anantnag, Kulgam, Pulwama, Shopian, Budgam, Ganderbal, Bandipora, Baramulla, Kupwara, Doda and Ramban). Urine was collected for 24 hrs from 186 patients, 10 ml sample of this urine collection was stored at 20°C before processing for urinary parameters. Metabolic diagnosis consisted of 5 categories : Hypercalciuria males: >7.5 mmol (300mg)/24hr, Female: >6.25 mmol (250mg)/24hr, hyperoxaluria 0.46 mmol (40mg)/24hr, Hyperuricosuria: >4.46 mmol (750mg)/24hr,

hypomagnesuria: <3 mmol/24 hr and hypocitraturia: <1.56 mmol (300mg)/24hr. Analyses have been carried out at the central laboratory of Tertiary Care Hospital.

Study Period: January 2014 to July 2015

RESULTS

Out of 186 patients, 119 (64%) patients were males while 67(36%) were females giving a male to female ratio of 1.77:1. The age of the patients ranged from 14 to 67 years while 126(67.7%) of the patients were in their second and third decade of life. Out of 186 patients, 17.2 % patients belong to Srinagar District, 15.6 % belong to Anantnag, 15.1% belong to Baramulla and 13.4 % patients belong to Ganderbal respectively. Most of the patient in our study had flank pain as predominant symptom(78%) of presentation to the health care provider but there were patients who were asymptomatic and were incidentally found to have renal stones(10.2%). Some of our patients presented with symptoms of urinary tract infection with or without obstruction and were found to have renal stones(11.8%). Most common diagnostic modality in our patients was Ultrasonography (83%). In some patients (8.6%) Plain X-Ray KUB was the modality of investigation to detect stones. Patients having PUJ/VUJ small calculi (8.1%) were detected by IVP.

Table 1. Demography and clinical characteristics of patients

| Demographic and clinical characteristics | Frequency (n=186) | % Frequency |
|--|-------------------|-------------|
| Patients age (in yrs) | | |
| <15 | 8 | 4.3% |
| 15-39 | 126 | 67.7% |
| ≥40 | 52 | 28.0% |
| Gender of patients | | |
| Male | 119 | 64.0% |
| Female | 67 | 36.0% |
| Patients as per District | | |
| Srinagar | 32 | 17% |
| Anantnag | 30 | 16% |
| Baramullah | 28 | 15% |
| Ganderbal | 24 | 13% |
| Pulwama | 17 | 10% |
| Budgam | 11 | 6% |
| Kupwara | 11 | 6% |
| Kulgam | 9 | 5% |
| Bandipora | 8 | 4% |
| Other | 16 | 8% |
| Most common presenting symptoms | | |
| Flank pain | 145 | 78% |
| Burning micturation | 22 | 11.8% |
| Asymptomatic | 19 | 10.2% |
| Common diagnostic modality | | |
| USG | 154 | 83% |
| Plain X-Ray KUB | 17 | 9% |
| IVP | 15 | 8% |
| Source of water in patients | | |
| Tap water | 109 | 58.6% |
| Ground water | 77 | 41.1% |

Table 2. Chemical composition of water (www.indiawater.com)

| District | Nitrate (mg/l) | Fluoride (mg/l) | Chloride (mg/l) | pH | Alkalinity (mg/l) | Calcium (mg/l) | Hardness (mg/l) | Sulphates (mg/l) | Magnesium (mg/l) |
|-----------|----------------|-----------------|-----------------|------|-------------------|----------------|-----------------|------------------|------------------|
| Srinagar | 5 | 0.24 | 50 | 7.28 | 70 | 35.84 (high) | 300 (very high) | 30 | 1.8 |
| Anantnag | 10 | 0.5 | 60 | 7.9 | 100 (high) | 16 | 300 (very high) | 0 | 0 |
| Shopian | 10 | 0.5 | 20 | 7.3 | 80 | 36 | 50 | 20 | 0 |
| Baramulla | 5 | 0.4 | 30 | 7.2 | 20 | 24 | 110 | 0 | 0 |
| Ganderbal | 0 | 0 | 30 | 7.12 | 0 | 0 | 0 | 0 | 0 |
| Pulwama | 30 | 0 | 40 | 7.68 | 0 | 0 | 0 | 0 | 0 |

On metabolic evaluation of 24 hour urinary constituents in our study group of 186 patients, 113 (60.8%) patients were having hypercalciuria as predominant urinary abnormality with Mean \pm SD 9.41 ± 2.07 which was persistently higher than normal. However there was no significant variation on the basis of gender. Hypocitraturia was the second most common abnormality found in 112 (60%) stone formers with Mean \pm SD of 1.32 ± 0.18 which is usually not found normally, but was predominately found among males (62.2%) of our study group.

Significantly increased concentration of uric acid were seen in 48(25.8%) stone formers which were again found to be statistically significant and their propensity was more in male gender. Urinary phosphate and oxalate concentration were raised in stone formers in 88 (47.3%) and 42 (25.3%) patients with Mean \pm SD of 42.32 ± 1.87 and 41.58 ± 5.45 respectively. Hypomagnesuria was seen in 94 (50.5%) patients more in females as compared to males.

end of 1 week of the same amount of bottled hard or soft water. As compared with both tap and soft water, hard water was associated with significant 50 % increases in the urinary calcium concentration in the absence of changes of oxalate excretion.

The calcium citrate index revealed a threefold increase during ingestion of hard water as compared with soft water. The study suggested that, in the preventive approach to calcium nephrolithiasis, the extra meal intake of soft water is preferable to hard water, since it is associated with a lower risk for recurrence of calcium stones. The data obtained from the Government of India website www.indiawater.com shows On chemical analysis the level of hardness in water in Srinagar and Anantnag district is much greater than other districts of Kashmir, so is the number of patients in our study, which may hint towards the possible effect of water hardness on nephrolithiasis.

Table 3. Risk factors for stone formation

| | |
|---|--|
| Anatomic abnormalities | Medullary sponge kidney, ureteropelvic junction stenosis, pyelo-ureteral duplication, polycystic renal disease etc, |
| Epidemiological factors and genetic predisposition | Dietary risk factors, climate, occupation, family history of stones |
| Excessive excretion of promoters of urinary crystallization | Idiopathic hypercalciuria, enteric hyperoxaluria, uric acid hyperexcretion |
| Abnormalities of urinary pH | Renal tubular acidosis, gouty diathesis, struvite stones |
| Reduced excretion of inhibitors of urinary crystallization | Hypocitraturia |
| Metabolic syndromes and obesity | Pure uric acid stones |
| Low urine volume | Reduced intake or loss of water |
| Hypercalcemic disorders | Primary hyperparathyroidism, other disturbances of calcium metabolism |
| Lithogenic Drugs | Triamterene, indanavir, sulfadiazine, uricosuric agents |
| Genetic monogenic disease | Primary hyperoxaluria, cystinuria, autosomal dominant hypocalcemic hypercalciuria, hypophosphatemia associated with hypercalciuria |

Water Hardness

The key role of water in urinary stone formation is generally accepted by public, nevertheless, only the quantitative facet of this idea is justified-insufficient intake of water and other liquids surely increases the urolithiasis of all types. On the other hand qualitative assessment shows that the content of water minerals, more precisely of magnesium and calcium, plays a less important role. Urinary stone formation is a process involving multiple factors,i-e.not only intake of liquids, but also genetic predisposition, eating habits, climatic, gender and social conditions etc. Several studies documented that higher water hardness is associated with higher incidence of urolithiasis among the population supplied with such water. In contrast more studies found softer water to be associated with higher risk of urolithiasis.

Any correlation between water hardness, or the drinking water calcium or magnesium level, and the incidence of urolithiasis was not found in the last vast USA epidemiological study with 3270 patients. The quoted Japanese studies did not find that the water calcium and magnesium levels alone has an effect on the incidence of urolithiasis but did find that the magnesium to calcium ratio had. One study reported the lower Mg to Ca ratio to be associated with higher risk of urolithiasis. (Kohri et al., 1989). Another study found a correlation between the higher Mg to Calcium ratio and higher incidence of phosphate urolithiasis. (Kohri et al., 1993). Another study done on 18 patients with idiopathic urolithiasis, maintained at fixed dietary intake of calcium (800mg/day) ,after drinking for 1 week 2 litres of water per day, between meals, of tap water and at the

Even the calcium level and alkalinity in water in Srinagar district and anantnag district is greater than others, which may point towards their role in the aetiology of Urolithiasis.

Table 4. Inhibitors and promoters of kidney stones

| Inhibitors | Promoters |
|--------------------------------|-----------------------|
| Citrate | Calcium |
| Magnesium | Sodium |
| Pyro phosphate | Oxalate |
| Tamm-horsfall protein | Urate |
| Urinary Prothrombin fragment 1 | Low Urine pH |
| Renal lithostathine | Tamm-horsfall protein |
| Glycosaminoglycans | |
| Osteopontin | |
| Nephrocalcin | |
| High urine volume | Low urine volume |

DISCUSSION

Renal stones represent major urological problem in all parts of the world including India. About 12% of the population of the European Union suffers at least one process related to urolithiasis with variable frequency as shown with the epidemiological studies such as Italy (13%), Sweden (8.9%) and Spain (12.3%). Urinary stones incidence is higher in countries with warm or hot climates. Exposure to sunlight and seasonal variation may enhance calcium absorption and urinary excretion, which leads to stone formation. An increase of stone formation was noticed among American army personnel deployed in Kuwait from March through August 2003.Reports from different parts of the world indicate that geographical

variations in the incidence of urinary calculi are correlated with socio-economic conditions. Obesity, calculi family history together with high protein, fat, energy and vitamins intake is also risk factors. No evidence of stone formation risk was found in relation to drinking tap water but due evidence is reported from taking hard water. The population of Kashmir division is about 6,907,623 as per 2011 census. The present study shows that males of this province are more affected with urolithiasis than females with a ratio of 1.77:1. The male predominance may be related to the climate conditions and life-style in Kashmir where women, in contrary to men, spend most time indoors with their families.

Chronic exposure to environment and sweating with subsequent dehydration and urine concentration increase the prevalence of urolithiasis. Some studies ascribed the high prevalence of nephrolithiasis in males to the effect of sex hormones on some lithogenic risk factors where androgens appear to increase and estrogen to decrease urinary oxalate excretion and kidney calcium oxalate deposition. The present work shows urolithiasis in Kashmir Province develops more frequently in the age group of the second and third decade of life. In the present study, 17.2 % patients belong to Srinagar District, 15.6 % belong to Anantnag, 15.1% belong to Baramulla and 13.4 % patients belong to Ganderbal respectively showing the higher prevalence of stone formers from Srinagar district and anantnag district.

Most of the patient in our study had flank pain as predominant symptom (78%) of presentation but there were patients who were asymptomatic and were incidentally found to have renal stones (10.2%). Some of our patients presented with symptoms of urinary tract infection with or without obstruction and were found to have renal stones. Most common diagnostic modality in our patients was Ultrasonography (83%). In some patients (8.6%) Plain X-Ray KUB was the modality of investigation to detect stones. Patients having PUJ/VUJ small calculi (8.1%) were detected by IVP. On metabolic evaluation of 24 hour urinary constituents in our study group of 186 patients, 113 (60.8%) patients were having hypercalciuria as predominant urinary abnormality which was persistently higher than normal. However there was no significant variation on the basis of gender. Hypocitraturia was the second most common abnormality found in 112 (60%) stone formers with which is usually not found normally, but was predominately found among males (62.2%) of our study group.

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