

# Epidemiology of urolithiasis: an update

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## Summary

**Background & Aim.** Changing socio-economic conditions generated changes in the prevalence, incidence and distribution for age, sex and type of urolithiasis in terms of both the site and the chemical-physical composition of the calculi.

In the latter part of the 20<sup>th</sup> century the prevalence of upper urinary tract stones was increasing in Western countries whereas endemic infantile bladder stone disease was fairly widespread in huge areas of developing countries. The aim of this paper was to update previous epidemiological reports of urolithiasis by reviewing the more recent literature.

**Methods.** Citations were extracted using PubMed database from January 2003 through December 2007 on the basis of the key words epidemiology AND urinary calculi.

**Results.** An increase in the prevalence and incidence of urolithiasis was described in Germany whereas data from the United States were contradictory with stone disease rates increased only for women with a change of male-to-female ratio. Prevalence figures of stone disease observed in some developing country in tropical regions were similar to rates of Western countries with incidence of renal colic particularly high in warm months. African Americans had a reduced risk of stone disease compared to other racial groups but in renal stone patients all racial groups demonstrated a similarity in the incidence of underlying metabolic abnormalities. Upper urinary tract stones in children were associated more frequently with metabolic disturbances rather than with urinary tract anomalies and infection. Endemic childhood bladder stones are still present in some developing countries.

Dietary risk factors for stone disease were shown different by age and sex. In particular in younger women dietary calcium, phytate and fluid intake were associated with a reduced risk of stone formation whereas animal protein and sucrose increased the risk of stone incidence. In older adults there was no association between dietary calcium and stone formation whereas magnesium, potassium and fluid intakes decreased and total vitamin C intake increased the risk of symptomatic nephrolithiasis. Animal protein was associated with risk only in men with a body mass index < 25 kg/m<sup>2</sup>.

Type 2 diabetes and several other coronary heart disease risk factors, including hypertension and obesity are associated with nephrolithiasis.

**KEY WORDS:** epidemiology, urinary calculi, diet, climate.

## Introduction

The epidemiology of urolithiasis differs according to geographical area in term of prevalence and incidence, age and sex distribution, stone composition and stone location. Such differences have been explained in terms of race, diet and climate factors. Furthermore changing socio-economic conditions have generated changes in the prevalence, incidence and distribution for age, sex and type of lithiasis in terms of both the site and the chemical-physical composition of the calculi.

Epidemiological surveys have been previously reviewed showing that in economically developed countries the prevalence rate ranged between 4% and 20% (1).

In the latter part of the 20<sup>th</sup> century prevalence and incidence of upper urinary tract stones were still increasing in Western countries probably resulting from improvements in clinical-diagnostic procedures and changes in nutritional and environmental factors. Endemic infantile bladder stone disease, with characteristics similar to those previously described in Europe in the 19<sup>th</sup> century, was fairly widespread in huge areas of Turkey, Iran, India, China, Indochina and Indonesia with stones composed of ammonium urate and calcium oxalate due to malnutrition in the very early years of life and, more particularly, to precocious weaning together with the adoption of a cereal diet. In recent years the epidemiology of urinary stone disease was still changing as social conditions gradually improved particularly in the urban areas of the more affluent developing countries.

The aim of this paper was to update previous epidemiological reports of urolithiasis by reviewing the more recent literature.

## Materials and methods

The initial literature database used for the review was developed using PubMed.

The database spanned the period from January 2001 through December 2007 and was limited to study in the English language. Citations were extracted on the basis of the following key words: (epidemiology AND urinary calculi)

## Discussion

### *Prevalence and incidence*

In previous reports the prevalence of kidney stones varied greatly between geographic locations, ranging from 8% to 19% in males and from 3% to 5% in females in Western countries.

In Germany (2) a further increase in the prevalence and incidence of urolithiasis has been described. Prevalence has risen from 4% to 4.7% from 1979 to 2001. In the year 2000, the incidence of urolithiasis in Germany was found to be 1.47% (1979: 0.54%).

Data from the US (United States) are contradictory. According to the data from the National Health and Nutrition Examination Survey II and III, renal stone prevalence among 20 to 74 old

US residents was greater in 1988 to 1994 than in 1976 to 1980 (5.2% vs 3.8%) and it was greater in males than females (3).

On the contrary data for the Rochester population over the years 1970-2000 demonstrated an age-adjusted incidence of new onset symptomatic stone disease for men of 155.1 and 105.0 per 100,000 per year in 1970 and 2000, respectively, and for women of 43.2 and 68.4 per 100,000 per year, respectively (4). During the 30 years, rates for women increased by about 1.9% per year, whereas rates for men declined by 1.7% per year.

Other population-based studies investigated prevalence and incidence rates of urolithiasis in different countries. A surprisingly high 15% prevalence of urolithiasis was observed in the rural population of Thebes in Greece (5).

In Iceland (6) the age-standardized prevalence for the 30-79 years age group was 4.3% for men and 3.0% for women, with no significant increase over time. The incidence was 562 per 100 000 per year among men and among women was 197 per 100 000 per year.

Data from some developing countries showed prevalence figures similar to those previously described in Western countries. In Iran (7) the prevalence was estimated as 5.7%, slightly more frequent in males (6.1%) than females (5.3%) whereas the annual incidence of urolithiasis in 2005 was 145.1.

#### *Silent stones*

In developing countries the prevalence of stones is probably underestimated considering that silent and not yet discovered kidney stones were diagnosed by renal sonography in 3% of non symptomatic subjects (8).

#### *Renal colic*

Renal colic is a common emergency department presentation. Data obtained from the 2000 National Hospital Ambulatory Medical Care Survey of the United States estimated an annual burden of more than 1,100,000 emergency department visits with a primary diagnosis of renal calculus or colic (9).

In tropical regions the incidence of renal colic was described as higher in warm months and not influenced by the fasting period of Ramadan in Iran (10, 11).

Renal colic was the most common urologic indication for air evacuation during the first 6 months of Operation Iraqi Freedom with documented spontaneous stone passage in 28% (12).

#### *Children*

Urolithiasis in children is traditionally characterised by a pattern of either endemic bladder stones in young children in developing countries or relatively rare calcium-based stones in upper tract stones in Western countries.

In children upper urinary tract were usually associated with urinary tract anomalies and infection rather than with metabolic disturbances.

A shift in the epidemiology of paediatric renal stone disease in the United Kingdom (UK) was observed over the past 30 years (13). Underlying metabolic causes are now the most common but can be masked by coexisting urinary tract infection.

In Croatia (14) stone composition, location and etiology in children were similar to those in developed Western countries, calculi being mainly located in the upper urinary tract (90%) with predominant constituent of calcium oxalate followed by struvite. The incidence of kidney stones in Icelandic children (15) is high compared with other Western populations, affecting females more than males, with an annual incidence of renal stones of

5.6 and 6.3 per 100,000 children less than 18 and 16 years of age, respectively. Underlying metabolic risk factors were identified in most patients.

In Iraqi children primary endemic bladder calculi are now less frequent than in the past. Metabolic disorders were the major causes of urinary stones, but can be masked by associated urinary tract infections (16). Staghorn calculi associated with recurrent urinary tract infection accounted for 15% of the cases.

In other countries endemic childhood bladder stones are still frequent. In Lao bladder stone incidence was associated with an history of frequent episodes of diarrhoea and early introduction of white rice into diet as early as the first week of life (17).

A peculiar form of stone disease was described in Aboriginal children living in tropical and desert regions of Australia who are at risk of developing urate stones in their upper urinary tract not associated with anatomic anomalies (18, 19).

A report from the Goldfields region of Western Australia (18) described urate renal stones as a common finding in Aboriginal children. Carbohydrate intolerance might be an aetiological factor together with chronic diarrhoea and intraluminal breakdown of sugars by enteric bacteria resulting in a condition of chronic metabolic acidosis.

#### *Male to female ratio*

Renal stones were usually described as more frequent in men. A change in the prevalence by gender has been reported in the United States during the last decade.

Scales et al (20) observed a dramatic increase from 1997 to 2002 of the adjusted rate of discharges for stone disease in females in a representative sample of United States population with a change in the prevalence by gender of treated stone disease from a 1.7:1 to 1.3:1 male-to-female ratio.

The increasing incidence of nephrolithiasis in women might be due to lifestyle associated risk factors, such as obesity.

Accordingly, Lieske et al. (4) reported a decrease from 3.1 to 1.3 male-to-female ratio during the last 30 years. In particular the male-to-female ratio of the incidence of symptomatic ureteral stones was different between the Hispanic (1:1) and the Caucasian (2.5:1) population whereas no significant sex differences were noted in the symptomatic presentation of kidney stones (21).

In developing countries the male-to-female ratio range from 1.15:1 in Iran (22) and 1.6:1 in Thailand (23) to 2.5:1 in Iraq (24) and 5:1 in Saudi Arabia (11).

#### *Type of stones*

Some Authors reported about stone composition and location of urinary stones in their countries.

In Iraq (24) urinary stones were predominantly composed of calcium oxalate and in renal or ureteral location whereas bladder stones accounted about 15% of the total. Infection stones associated to urea splitting bacteria were still common in females.

Ammonium acid urate (AAU) calculi are a rare urolithiasis in developed countries but are endemic in developing countries. Ammonium acid urate calculi were observed in 0.38% of Japanese patients with urinary stones (25). Pure AAU stone formers predominantly consisted of young, thin women whereas the mixed group consisted of middle-aged men. Laboratory findings showed trends of low levels of serum protein, potassium, and urine pH in the pure AAU group.

In Okinawa (Japan) (26) uric acid stones, predominantly the anhydrous and/or dihydrate forms, showed a relatively high frequency.

In Japan (27) magnesium ammonium phosphate (MAP) stones in the upper urinary tract, accounting for the majority of staghorn stones, had dramatically decreased during the last decade.

Calcium oxalate renal stones are predominant in Nepal (28-30) with hyperoxaluria as an important risk factor in more than one fourth of the stone formers, but urinary bladder stones are still frequent.

Upper urinary tract stones are relatively uncommon in Nigeria (31) probably being related to chronic dehydration exacerbated by religious fasting.

Recent improvements in socio-economic conditions of some areas have changed the clinical picture of urinary stones, including bladder calculi.

In Dubai (32) calcium oxalate was found in 78% of patients with bladder calculi and acute urinary retention as the most common presenting symptom of bladder stones.

In Saudi Arabia (33) calcium oxalate stones were the commonest followed by uric acid and phosphate stones. Saudis are more prone to development of stones with the stone frequency being 2.5 times more in Saudis as compared to non-Saudis.

In Thailand oxalate was found in most upper urinary tract stones and uric acid was found in most lower urinary tract stones (34).

#### *Race*

In the United States nephrolithiasis disproportionately affects white patients although an increase in the incidence of stone disease in other populations has been observed.

African Americans had a reduced risk of stone disease (1.7%) compared to Caucasians (5.9%), and Mexican Americans (2.6%) (35).

However in renal stone patients all racial groups demonstrated a similarity in the incidence of underlying metabolic abnormalities suggesting that dietary and environmental factors may be as important as ethnicity in the etiology of stone disease. In particular hypocitraturia, hyperuricosuria, hyperoxaluria, gouty diathesis and high sulphate levels were equally represented among all ethnic groups (36).

An high prevalence of nephrolithiasis was described in Native American (25%) (37) and in the Hmong refugee population (46%) from the highlands of Laos now living in the Metropolitan Minneapolis-St. Paul area (Minnesota) (38). In fact uric acid stones (50%) and staghorn calculi (25%) are a common finding in the Hmong population.

In KwaZulu Natal province (South Africa) (39) only a few variations in the metabolic risk factors between Indians and Whites renal stone formers were observed that could be attributed to genetic or dietary habits. The high incidence of renal tubular acidosis in Indian patients could explain the higher prevalence of urinary stone disease in this group than in other racial groups.

#### *Climate*

Robertson (40) stressed the problem of the increasing incidence of renal stone disease in the tropics where the risk of stone formation is compounded by low urine volume. As living standard increase, particularly in the urban areas of the more affluent developing countries, so the incidence of upper urinary tract stones is increasing being characterised by calcium oxalate stones often mixed with calcium phosphate and uric acid.

In particular the South Western Asia represents a high risk environment for stone disease.

In Kuwait in a cohort of healthy personnel of Department of US Defense, during a well-defined period of increased risk of stone formation, the time to formation of symptomatic urinary calculi was computed in 93 days (41).

#### *Diet*

It is well accepted that greater intakes of dietary calcium, potassium, and total fluid reduce the risk of kidney stone formation, while supplemental calcium, sodium, animal protein, and sucrose may increase the risk. However some dietary risk factors may differ by age and sex.

In younger women an higher intake of dietary calcium decreased the risk of kidney stone formation, but supplemental calcium was not associated with risk. Phytate intake and fluid were associated with a reduced risk of stone formation whereas other dietary factors, such as animal protein and sucrose, increase the risk of stone incidence. On the contrary in this group the intakes of sodium, potassium, and magnesium were not independently associated with risk after adjusting for other dietary factors (42).

Also in older adults the relation between diet and kidney stones may be different because the metabolism of many dietary factors, such as calcium, may change with age.

For men aged < 60 years, the risk for stone formation is decreased by an higher dietary calcium but in contrast, there is no association between dietary calcium and stone formation in men aged 60 years or older. Magnesium, potassium and fluid intakes decrease and total vitamin C intake (1000 mg or greater versus 90 mg/day) seems to increase the risk of symptomatic nephrolithiasis.

Animal protein was associated with risk only in men with a body mass index < 25 kg/m<sup>2</sup>. Sodium, phosphorus, sucrose, phytate, vitamin B6, vitamin D, and supplemental calcium were not independently associated with risk (43).

The chewing of betel quid is a common practice in many countries of the world, particularly in Southeast Asia. The use of calcium hydroxide in the betel quid is a cause of urinary stones in its users (44). In fact the quid consists of a preparation of areca nut, betel leaf and calcium hydroxide "lime" paste ("chuna").

#### *Drugs*

Nephrolithiasis is a possible adverse event of treatment with atazanavir in HIV-infected patients (45).

#### *Chronic renal failure*

Nephrolithiasis promoted progression to end stage renal disease requiring renal replacement therapy in some populations. In an Afro-American population undergoing haemodialysis in the United States the prevalence of pre dialysing renal stone disease was significantly higher than in the age, race and sex adjusted general population (8.3% vs 2.8%) (46).

In the North African countries primary urolithiasis is a frequent cause of obstructive nephropathy (hyperoxaluria and cystinuria) and can be a cause of end-stage chronic renal disease (ESRD) owing to the inadequacy of medical care facilities (47).

#### *Bone disease*

In the population-based Canadian Multicentre Osteoporosis Study men reporting versus not reporting past nephrolithiasis appeared to have clinically relevant lower bone mineral density values, although results were statistically inconclusive (48).



Among healthy postmenopausal women, calcium with vitamin D supplementation increased the risk of kidney stones (49). Vitamin D receptor (VDR) genotypes may be associated with increased calcium excretion in hypercalciuric stone formers (50).

#### Diabetes

Type 2 diabetes, obesity, and hypertension are associated with nephrolithiasis, in particular diabetes may be a factor in the development of uric acid stones (51).

Insulin resistance, characteristic of the metabolic syndrome and type 2 diabetes, results in lower urine pH through impaired kidney ammoniogenesis so promoting uric acid stone formation (52).

Insulin resistance (and predisposition to uric acid stone formation) can precede the diagnosis of diabetes by decades, in fact the risk of incident diabetes in participants with a history of kidney stones was increased (53).

#### Cardiovascular disease

Calcium oxalate stone formation was significantly associated with several coronary heart disease risk factors, including smoking habit, hypertension, hypercholesterolemia, and obesity (37, 54).

#### Gout

In primary gout 39% of patients had urinary stones of which about 30% were silent and diagnosed only by ultrasonography, meaning the prevalence of urolithiasis in gout is likely higher than commonly reported. A higher urinary H<sup>+</sup> ion concentration was associated with urolithiasis (55).

The age of onset, clinical manifestations, risk factors and disorders associated with gout have recently changed in Taiwan (56, 57). The age at onset of gout was lower and the percentages of female gout (8%) and familial gout were increased. The percentages of obesity, hypertriglyceridaemia and nephrolithiasis were higher, while the percentages of hypertension and hypercholesterolaemia were lower.

#### Obesity

The obesity epidemic can be a cause of the increasing numbers of patients with stone disease. Patients with central adiposity or high waist-to-hip ratios appear to have the highest risk (58).

The greater incidence of kidney stones in the obese may be due to an increase in uric acid nephrolithiasis.

Obesity and weight gain increase the risk of kidney stone formation. The magnitude of the increased risk may be greater in women than in men. In particular a body mass index (BMI) of 30 or greater was associated with a greater risk of kidney stone formation. Waist circumference was also positively associated with risk (59).

Subjects with greater BMIs excreted more urinary oxalate, uric acid, sodium, and phosphate than those with lower BMIs and there was an inverse relation between BMI and urine pH.

Urinary supersaturation of uric acid increased with BMI whereas no relation between BMI and urinary supersaturation of calcium oxalate was found (60).

#### Hypertension

The links between kidney stones and blood pressure (BP) was heterogeneous due to the differential effects of nephrolithiasis among subgroups of individuals.

In fact overweight female renal stone formers may be at signifi-

cantly increased risk for hypertension with a 69% increase in odds of self-reported hypertension whereas no significant difference was found in men. The estimated difference in mean systolic and diastolic BP comparing stone formers with non-stone formers increased with body mass index in both sexes, but was more pronounced in women (61).

#### Menopause

No association was found between menopause and postmenopausal hormone use and incident kidney stones (62). Surgical menopause, however, may be associated with an increased risk.

#### Pregnancy

The incidence of nephrolithiasis requiring hospital admission during pregnancy is relatively low, but these women have an increased risk of pre term delivery. A cumulative incidence of 1.7 admissions per 1,000 deliveries was described. Women admitted for nephrolithiasis during pregnancy had nearly double the risk of pre term delivery compared with women without stones (63). About 25% of women had one or more procedures for kidney stones during prenatal hospitalisation although undergoing a procedure and the trimester of admission did not affect the risk of preterm delivery.

Urinary lithiasis during pregnancy (1 in 244 pregnancies) occurred more commonly in Caucasian than African American women and it was associated with a higher rate of preterm premature rupture of membranes (7% vs 2.9%) (64).

#### Economics

The burden of urological diseases on the American public was analysed in the year 2000.

Urolithiasis was the primary diagnosis for almost 2 million office visits, more than 600,000 emergency room visits, and more than 177,000 hospitalisations, totalling more than 2 billion dollars in annual expenditures (65).

The cost of appeared to be increasing with time despite a shift in inpatient to outpatient treatment and the emergence of minimally invasive treatment modalities, perhaps because the prevalence of stone disease is increasing. The rate of inpatient hospitalisations for a diagnosis of urolithiasis decreased by 15% and hospital length of stay decreased from 2.6 to 2.2 days between 1994 and 2000. Hospital outpatient visits increased by 40% between 1994 and 2000 and physician office visits increased by 43% between 1992 and 2000 (66).

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