Obesity and Calcium Oxalate Renal Stones

Nicola Th[1], Dobreanu Minodora[2], Buda Brînduşa[3], Oşan V[4], Gliga Florina[3], Satan Edit[1]

[1] Department of Laboratory Medicine, County Emergency Clinical Hospital, Tîrgu Mureş, Romania
[2] Department of Laboratory Medicine, University of Medicine and Pharmacy, Tîrgu Mureş, Romania
[3] Department of Pathophysiology, University of Medicine and Pharmacy, Tîrgu Mureş, Romania
[4] Department of Urology, University of Medicine and Pharmacy, Tîrgu Mureş, Romania

Introduction: Kidney stones are a major cause of morbidity. The lifetime prevalence of symptomatic renal stones is approximately 10% in men and 5% in women. The rate of backsliding for calcium oxalate stones is 10% in one year, 30% in 5 years and 50% in 10 years. Urine pH is one of the important factors for urinary stone formation.
Material and methods: We studied 283 renal stone formers (131 men, 152 female), divided according to their BMI (body mass index) in normal body weight (BMI <25 kg/m^2), overweight (BMI 25–30 kg/m^2) and obese (BMI >30 kg/m^2).
Results: Urine pH is inversely related to BMI among patients with urolithiasis (higher BMI will have lower urine pH). The mean urine pH of the normal body weight, overweight, and obese groups was 6.1, 5.5 and respectively 5.7 (p <0.0001).
Conclusions: Obesity is associated with both hypercalciuria and with proteinuria, demonstrated factors in the etiology of urolithiasis, and urinary pH is inversely related to BMI in patients with urinary stones.

Keywords: renal stones, prevention, obesity, risk factors

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Introduction

Recorded in medical writings from ancient times, urinary stones (urolithiasis) remain a public health problem with increasing incidence, predominantly affecting the younger, socially active age segment [1].

Any calculus is aggressive to the urinary system and can produce physio- and pathological consequences that depend on:

– lithiasis characteristics: volume, number, location of stones;
– association of urinary obstruction: level, type of installation, time;
– pre-existing condition of the urinary tract [2,3].

Urinary stones are a major cause of morbidity. The lifetime prevalence of symptomatic renal stones is 10% in men and 5% in women. The majority of urinary calculi, more than 80%, contain calcium, and most of them contain calcium oxalate. Recurrence rate for calcium oxalate stones is 10% in a year, 30% in 5 years, 50% in 10 years and 75% in 20 years [4,5,6].

Obesity is one of the biggest public health problems facing the contemporary world, affecting most of the developed societies [7]. Around the world, more than one billion people are now overweight or obese. In the last decade, the prevalence of obesity in European countries has doubled [8,9].

Increased normal body weight may raise urinary excretion of calcium, oxalate, uric acid, increasing the risk of calcium kidney stones. Also, recent studies have shown the influence of body weight on urinary pH [10,11,12,13].

Nephrolithiasis was found to be influenced by genetic and environmental factors, among which the most important is diet [14,15]. There are numerous epidemiological evidence to support that diet influences the formation of kidney stones. Food and nutrition problems are always present and to the attention of researchers, ensuring a healthy diet being a priority objective [6,8,16,17].

The expression of this concern is that, although we are still far from ideal therapeutic formula (chemolitic drugs), urological therapeutic approach was the favorite field of innovation in medical technology. The means and treatment techniques of kidney stones have been developed rapidly, following a direction determined by the principle of "minimal invasion", the most used methods being extracorporeal shock wave lithotripsy and endoscopic surgery [18,19].

Minimally invasive interventional therapy, en vogue today, started in urology in the 1970s (endoscopic lithotripsy of urolithiasis and ureter), and extracorporeal shock wave lithotripsy (ESWL) for kidney stones in 1982 has completed the entire palette of modern therapy, able to solve over 90% of upper urinary stones [20].

Although the progress in the treatment of urinary lithiasis is spectacular, the rate of recurrence of the renal stones requires further research in preventing formation of new calculi and growth inhibition of residual stones [21,22].

Evaluation of patients should be directed towards identifying risk factors and recurrent urinary calculi formation in order to provide appropriate and individualized treatment. Identifying risk factors that can be influenced may suggest new methods of prevention and treatment of urolithiasis.

Material and methods

Our study included 440 patients hospitalized in the Urology Clinic of Tîrgu Mureş in the period November 1, 2010 – October 1, 2011 diagnosed with urinary stones. Demo-

Correspondence to: Theodor Nicola
E-mail: theodoralexandru@yahoo.com

graphic data and BMI were recorded. Patients with hyperparathyroidism, intestinal diseases, renal tubular acidosis, specific diet or other systemic diseases were excluded. Finally, the study group (64.3%) consisted of 283 patients (131 men, 152 women) who met this criteria and had calcium oxalate urinary stones.

Patients were grouped according to body weight (body mass index – BMI) in normal (BMI <25 kg/m^2), overweight (BMI 25 to 29.9 kg/m^2) and obese (BMI >30 kg/m^2). Underweight persons were excluded.

Laboratory evaluation

We applied a protocol that included the physicochemical analysis of 24-hour urine and stone analysis.

Stone analysis

Some preliminary data like the origin of the calculi, the size and possibly weight, color, if the surface is smooth or rough, brittle, etc., were registered.

Chemical structure shows a combination of chemicals, substances which are optically transparent (but radiographically detectable) and insoluble in water. From the results, conclusions can be drawn about the mechanism of formation, growth and dissolving effects of treatments.

We considered Berenyi's method [23] as the most accessible to our laboratory, because it requires a small amount of sample (<5 mg) and can analyze the chemical structure of stones with more than one component.

The technique involves as a first step the cleaning of contaminants from the exterior of the calculi, deposited during handling (traces of blood, urine, etc.).

The components of the calculi are analyzed, requiring a minimum amount of material; under microscopic observation, the fragment is introduced into the reagents mixture. The reaction given by the calculus fragment is observed, then other pieces are extracted from all parts of the calculus.

Calciuria determination

In a neutral environment, in the presence of the Arsenazo III reagent, calcium ion forms a colored compound. The color intensity is directly proportional to the concentration of Ca in the sample. A urine sample of approximately 100 ml from the 24-hour urine is placed in a disposable container, and analyzed on the same day. If this is not possible, urine can be stored at 2–8°C for maximum 4 days.

Proteinuria determination

We used the quantitative determination of total protein concentration in urine, Pyrogallol Red, direct colorimetric method. Protein molecules in urine bind to the molybdate Pyrogallol Red complex. The formation of the protein-dye complex causes a shift in the absorbance maximum from 467 nm to 598 nm.

The following data were obtained using the Olympus 600 analyzer (37°C) with Pyrogallol-Red color reagent.

pH determination

We determined pH using the LABUreader analyzer with LabStrip U11Plus strips.

Primary urine sample is obtained by early collecting by the patient, preferably from the first morning urine, collected in a disposable cap container.The amount collected must be 10–100 ml; sample processing is done in the first 2 hours after collecting, otherwise, is kept at 2–8°C and later processed on the same day.

The strip is inserted into the urine, making sure that each parameter is moistened, removed and then is inserted horizontally into the analyzer. The results are automatically recorded in the laboratory database.

Statistical analysis

The Chi-square and Fisher's exact tests were used where appropriate to analyze categorical data, with $p < 0.05$ chosen to indicate statistically significant differences. To estimate the meaning and magnitude of association the relative risk was calculated.

Results

In our study of 283 patients, 131 were men and 152 women, with an average age of 45±13 years. Recurrence of urolithiasis occurred in 61.8% of cases (175 patients).

It is generally accepted that the presence of excess calcium in the urine is one of the most important risk factor for calcium kidney stones. In our study, urinary calcium concentration was analyzed in the 24-hour urine of 162 patients (CaU); hypercalciuria (urinary calcium >220 mg/24 h) was registered in 6 patients with BMI 25–30 kg/m^2 (RR 1.803, 95% CI 1.089–2.986 mg/24 h, $p < 0.0001$), and 6 patients with BMI >30 kg/m^2 (RR 2.136, 95% CI 1.117–4.085 mg/24 h, $p < 0.0001$). The mean age of the patients according to sex and presence or absence of calciuria is shown in Table I, the associations were not statisticallly significant.

Recent studies have shown that obesity is a risk factor for the occurrence of proteinuria, leading to the occurrence and the recurrece of kidney stones. In our study we determined proteinuria (ProtU) above normal in 28 patients with normal weight (14.81%), 21 overweight patients (40.38%) and 23 obese patients (54.76%).

Urinary pH is an important factor in pathogenesis of urolithiasis. Metabolic syndrome, frequently associated with obesity, can change the renal acid-base balance decreasing the urinary pH and increased the risk of urinary

Table I. The mean age of the patients according to age and gender

	Age (years)	
	Women	Men
CaU <220 mg/24 h	44.89±12.635	45.92±12.784
CaU >220 mg/24 h	50.73±8.284	46.6±12.779
p value	p = 0.1424 RR = -2.001–13.672	p = 0.9083 RR = -11.094–12.461

Table II. Association of BMI and proteinuria

	ProtU–	ProtU+	Total	
BMI 20–25kg/m^2	161	28	189	
BMI 25–30 kg/m^2	31	21	52	p <0.0001 RR = 1.429 95%CI = 1.134–1.801 mg/24 h
BMI >30 kg/m^2	19	23	42	p<0.0001 RR = 1.883 95%CI = 1.343–2.641 mg/24h

Table III. Average urinary pH of patients according to BMI

	Average urinary pH	No. of patients	
BMI 20–25kg/m^2	6.1±0.66	189	
BMI 25–30 kg/m^2	5.557±0.75	52	p <0.0001 RR = 2.044 95%CI = 1.459–2.862
BMI >30 kg/m^2	5.714±0.80	42	p<0.0001 RR = 1.651 95%CI = 1.211–2.250

lithiasis. In our study, the arithmetic mean of urinary pH for those with normal weight, overweight and obesity was 6.10, 5.6 and 5.7, respectively (p <0.0001). Urinary pH is inversely related to BMI in patients with urinary stones (the greater BMI the lower urinary pH).

Discussions

Hypercalciuria (urinary calcium >220 mg/24 h), the most common metabolic abnormality associated with urolithiasis, is present in about half of patients with urinary lithiasis recurrence [19]. The most common cause appears to be increasing intestinal calcium absorption.

We found that there is a positive statistically semnificative association between calciuria and BMI (p <0.0001, r^2 = 0.2466).

There are recent studies that suggested a link between proteinuria and lithogenesis [24]. In our study the association between proteinuria and BMI was positive and statistically significant (p <0.0001, r^2 = 0.09921).

Recent studies showed that increased body weight is associated with decreased urinary pH. Although lower urinary pH is usually associated with urinary uric acid stones, it can lead to hypocitraturia, an important risk factor in calcium oxalate urinary stones [25,26]. In our study, we found that in patients with urinary stones, a greater BMI was associated with a lower urinary pH. The negative association between BMI and urinary pH is statistically significant (p <0.0001).

Obesity is frequently associated with insulin resistance and compensatory hyperinsulinemia, metabolic changes that may promote oxalate stones.

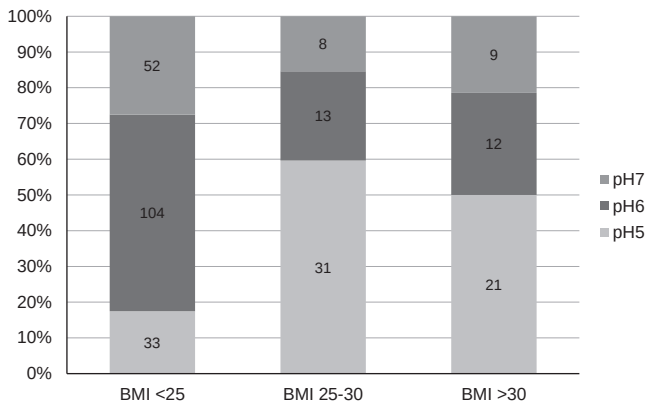

Fig. 1. Distribution of urinary pH according BMI

Increased body weight causes increased renal circulatory flow and increased glomerular filtration rate, appearing as an increase in urinary calcium excretion and thus increasing the risk of kidney stones containing calcium [4,7,16].

In recent decades, the role of diet in urinary lithiasis etiopathogenesis has been widely discussed, given the transition from traditional diet with a balanced intake of protein, calcium, salt, vegetable and fruits, to urbanized lifestyle, characterized by speed and competitive spirit accompanied by fast-food diets and adaptive stress disorder.

Weight loss should be explored as a potential way to prevent the formation of kidney stones. Prevention of urolithiasis offers clinicians a new reason to encourage weight loss through diet.

Conclusions

Urinary lithiasis has not just one etiological factor, and the role of obesity in the developing kidney stones is supported by the following results:

- Obesity is associated with both hypercalciuria and with proteinuria, demonstrated factors in the etiology of urolithiasis;
- Urinary pH is inversely related to BMI in patients with urinary stones.

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