

# ANALYSIS OF POTENTIAL RISK FACTORS ASSOCIATED WITH UROLITHIASIS

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## SUMMARY

**Objectives:** Eating habits, regular fluid intake, lifestyle and body composition are a primary point of research. The research focused on urolithiasis approaching potential danger, trying to interpret risk factors responsible for urolithiasis and disease recurrence.

**Methods:** Research file contains 166 patients suffering from urolithiasis, 87 (52.4%) males and 79 (47.6%) females, and 172 healthy subjects from control group. All data was accessed using fully anonymous and confidential questionnaires, then evaluated in the statistical GNU PSPP 1.4 software.

**Results:** More than ¾ patients have a BMI higher than 24.9 and almost 40% of subjects have obesity class I, II, or III. Patients have higher BMI than subjects ( $d = 1.285$ ;  $p < 0.001$ ), and females have significantly higher BMI than males ( $d = 0.385$ ;  $p = 0.007$ ). Female patients have higher BMI than Slovak healthy females ( $p < 0.001$ ; MD = 4.581; CI: 3.24–5.93). Patients have a lower daily water intake than subjects ( $\phi c = 0.157$ ;  $p = 0.04$ ) and more than ⅔ of patients have insufficient water intake. Sedentary employment prevails markedly in patients than in subjects. Patients are much less physically active than subjects ( $\phi c = 0.633$ ;  $p < 0.001$ ) and the difference is rising with increasing age of patients ( $\rho = -0.232$ ;  $p = 0.003$ ). Low physical and working activity are characteristic for patients in this study. Patients smoke more often in comparison to subjects ( $\phi c = 0.261$ ;  $p < 0.001$ ). Patients consume more meats (red and white), cocoa and lentils. A lot of patients exceed recommended daily intake of pork and beef.

**Conclusions:** Many conditions are different for the healthy population and patients' group. High BMI, low fluid intake, exceeded red meat consumption, and low physical activity are the strongest factors for developing urolithiasis. Patients should consume more fluids daily, exercise frequently and vigorously, and lower amount of red meat consumed.

**Key words:** urolithiasis, kidney stones, risk factors, physical activity, BMI, fluid intake

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## INTRODUCTION

Urolithiasis is a condition that is accompanied by the formation of kidney stones with significant morbidity. It is the third most common urinary tract disease (1), but some authors consider it the most common. Kidney stones are polycrystalline aggregations lodged in any part of the urogenital tract (UGT). Stones are mainly occurring in kidneys, less in ureter and bladder. Specific conditions result in the formation of stones. Metabolic disbalance, anatomic abnormalities or genetic predispositions participate in the process. Stones are often formed from a mixture of organic and inorganic substances and mineral components (2).

Urolithiasis prevalence depends on dietary, genetic, geographical, ethnic, and lifestyle factors and may vary among cultures and locations. Based on data estimated in 2011, from 25 to 49 million Europeans were diagnosed with urolithiasis, it means prevalence

between 3.4% and 6.6%. Similar prevalence probably occurs in Slovakia (3).

An initial stone incident mainly develops in people between 20–49 years, peaking in 35–45 years old persons. Recurrence is considerable trouble and usually fluctuates from 40% to 60% in the European population (4, 5). Urolithiasis is more frequent in men than women (rate males to females, 3 to 1). Due to an anatomical structure, infectious stones are more common in females (shorter urethra) (2).

Low daily water intake results in low urine production and leads to high concentrations of stone-forming substances. This is probably the most crucial risk factor in kidney stones formation. Metabolic disorders like hypercalciuria, hyperoxaluria, hyperuricaemia, hyperuricosuria, hypomagnesemia, hypocitraturia, and bacteria play an essential role in the evolution of stones. These disorders are often associated with high BMI. Poor eating habits may boost processes leading to the development of these disorders (6).

## Hypercalciuria

The role of excessive urinary calcium (Ca) excretion is unclear. Some authors tend to restrict or limit Ca intake to 600–800 mg/24 h (7). Other say its restriction is undesirable – lack of Ca cause hyperoxaluria and bones decalcification. Poppy seeds, yoghurt, milk, cheese, sardines, salmon, tofu, and broccoli are some of the calcium-rich foods (8).

## Hyperoxaluria

Oxalates from foods easily bind to Ca and create poorly soluble salts, and its restriction is an essential step to avoid the growth of stones and their recurrence. Plenty of oxalates are found in buckwheat, black pepper, poppy seeds, rhubarb, spinach, cocoa, and tea leaves. Oxalates may indirectly form protein metabolism (acid conversion), with origin from meat, fish, eggs, dairy products, lentils, and tofu ingestion (9, 10).

## Hyperuricosuria

High urinary excretion of uric acid leads to uricite stones, calcium stones or a mix of them. Uric acid is the final product of purine metabolism originating from excess dietary intake of purine-rich foods like entrails, seafood, red meat, wild meat, or endogenous overproduction. High sodium intake increases urinary urea concentration as well (11, 12).

## Hypocitraturia

A sufficient citrate load in urine is a crucial preventive factor for stone formation, so is calcium crystallization inhibitor. Citrate comes from citric acid dissociation during ingestion of citrus fruit, berries, tomatoes, carrots, and broccoli (13).

## Hypomagnesuria

Magnesium in adequate amount and appropriate ratio with calcium (Ca to Mg – 3 to 1) is a capable inhibitor of calcium crystallization, hypomagnesuria is a risk factor for oxalate formation. Hypomagnesuria with bacterial presence in urine forms infection stones. Magnesium is found in fish, spinach, potatoes, nuts, seeds, and dairy products (14).

Pathological conditions raise the probability of kidney stone formation. Calcium-oxalate stones represent the most frequent (67%) stone types, followed by calcium-phosphate (17%), uric acid (10%), struvite (2%), and dahllite (1%) stones. Cystine, 2,8-dihydroxyadenine and xanthine stones are rare (<1) (6, 15).

## Methodology

Research file contains patients and group of healthy persons (subjects). Patients originated from the urology department of Louis Pasteur University Hospital in Košice. Subjects are randomly selected with verification of urolithiasis in the past. All data come from questionnaires distributed among patients and subjects. The study evaluates urolithiasis risk factors based on anthropometric, demographic and social data. Daily fluid intake, selected foods intake, and physical activity are fundamental for the study.

## Statistical Analysis

Using medians and standard deviations through descriptive statistics, we illustrate demographic data. The one-sample Kolmogorov-Smirnov test is used to test whether a dataset is drawn from a particular distribution. Parametric tests are performed when data have normally distribution. If a distribution is non-normal, nonparametric tests are performed. Pearson and Spearman rank correlation are used to explain dependences between ordinal variables and between ordinal and interval variable. Comparison of our values with average ones were counted using One sample T-test. GNU PSPP 1.4 is evaluation software for all measurements. BMI is calculated from the equation: weight (kg)/height (m)<sup>2</sup>.

**Table 1. Selected demographic data (N=338)**

	Patients (n = 166) n (%)	Subjects (n = 172) n (%)
Sex		
Male	87 (52.4)	75 (43.6)
Female	79 (47.6)	97 (56.4)
Ratio (male/female)	1.1	0.8
Residence		
Rural	65 (39.2)	92 (53.5)
Urban	101 (60.8)	80 (46.5)
Education		
Basic	18 (10.8)	51 (29.7)
High school	99 (59.7)	65 (37.8)
Undergraduate	34 (20.5)	17 (9.9)
Academic or higher	15 (9.0)	39 (22.7)

**Table 2. Selected anthropometric data (N=338)**

	Patients (n = 166)			Subjects (n = 172)		Between groups
	Men	Women	p-value	Men	Women	p-value
Age, years (SD)	56.5 (13.2)	57.8 (13.2)	0.904T	23.8 (10.7)	27.5 (13)	<b>0.041T</b>
Height, cm (SD)	173.4 (8.6)	165.7 (9.6)	<b>&lt;0.001U</b>	178.5 (7.6)	165.8 (6)	<b>&lt;0.001U</b>
Weight, kg (SD)	83.3 (15.3)	82.8 (15.9)	0.305T	75.7 (12.5)	62.7 (10.9)	0.082T
BMI (SD)	27.9 (5.4)	30.3 (6.0)	<b>&lt;0.001U</b>	23.7 (3.2)	22.8 (3.8)	<b>&lt;0.001U</b>

Numbers in bold indicate statistically significant values; SD – standard deviation; T – independent sample T-test; U – Mann-Whitney U-test

**Table 3.** Distribution of patients according to BMI class and evaluation of risk (N= 166)

	Underweight n (%)	Normal weight n (%)	Pre-obesity n (%)	Obesity Class I n (%)	Obesity Class II n (%)	Obesity Class III n (%)	Total n (%)
Urban	2 (1.2)	22 (13.3)	42 (25.3)	28 (16.9)	14 (8.4)	3 (1.8)	45 (27.1)
Rural	2 (1.2)	13 (7.8)	19 (11.5)	13 (7.8)	4 (2.4)	4 (2.4)	21 (12.6)
Risk count	Low		Moderate	High			
	39 (23.5)		61 (36.7)	66 (39.8)			

Total – patients with obesity class I, II and III

## RESULTS

Patients (n= 166) were adults between 21 and 91 years of age, with a mean age of 57.1 (SD= 13.2). Subjects were adolescents and adults between 14 and 80 years of age, with a mean age of 25.9 (SD= 12.6). Other demographic data are presented in Table 1.

Table 2 describes basic anthropometric data and shows the difference between sexes and between patients' and subjects' groups. Females from patients' group have a significantly higher BMI than males – Cohen's D (d) = 0.385 (p= 0.007). Patients are older than subjects (d> 1; p= 0.041) and have significantly higher BMI (d= 1.285; p< 0.001). There is no significant relationship between BMI and age.

Up to 127 (76.5%) of patients have higher than normal BMI. Their distribution through BMI groups within the rural or urban region with the intended risk is presented in Table 3.

Patients have a lower daily water intake than subjects – Cramér's phi ( $\phi$ ) = 0.157 (p= 0.04). In subjects daily water intake escalates with increasing BMI – Spearman's rank correlation coefficient (rs) = 0.337 (p< 0.001). Details are displayed in Table 4.

In 148 (89.2%) patients and 115 (66.9%) subjects there is a balanced diet, the best representation of their lifestyle. Meat prevails over other food elements in 13 (7.8%) patients and 52 (30.2%) subjects. Only 5 (3%) patients and 5 (2.9%) subjects are vegetarians. Differences in nutrition habits are significant ( $\phi$  = 0.291; p< 0.001).

In 69 (41.6%) patients and 60 (34.9%) subjects prevail sedentary employment, and 32 (19.3%) patients and 47 (27.3%) subjects daily perform active work. Other patients (n= 65; 39.2%) and subjects (n= 65; 37.8%) do not work. The majority work environment for patients (n= 66; 39.8%) and subjects (n= 80; 46.5%) is indoor, 24 (14.5%) patients and 16 (9.3%) subjects work outdoor, and 11 (6.6%) patients and 11 (6.4%) subjects work in a hot environment. Ratio of sedentary/active work is 2/2 for patients and 1/3 for subjects.

Up to 112 (67.5%) patients do not perform physical activity, but only 16 (9.3%) subjects are physically inactive. From physically active patients, 44 (26.5%) perform activity irregularly, 9 (5.4%) are active 2–3 times per week and only 1 (0.6%) patient exercise more often. Subjects keen on activity form a majority, 79 (45.9%) are active irregularly, 42 (24.4%) perform activity 2–3 times per week and 35 (20.3%) do a physical activity more often. Differences between patients and subjects are considerable ( $\phi$  = 0.633; p< 0.001). In patients, the amount of physical activity decreases with rising age – Pearson correlation coefficient ( $\rho$ ) = -0.232 (p= 0.003).

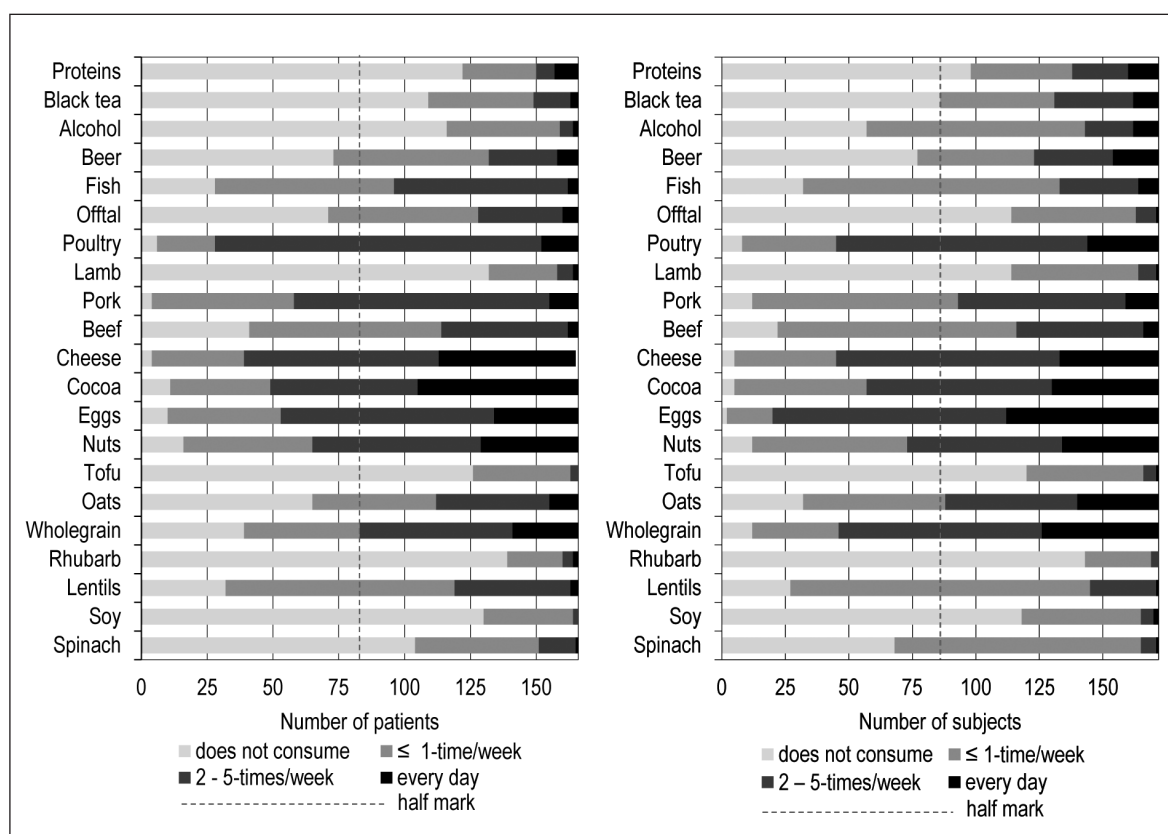
Majority of patients (n= 87; 52.4%) and subjects (n= 120; 69.8%) do not smoke. Other patients smoke occasionally (n= 29; 17.5%), 5–15 cigarettes daily (n= 27; 16.3%), 1 whole cigarette pack daily (n= 11; 6.6%), or smoke more (n= 11; 7.2%). Subjects with positive relationship to cigarettes smoke occasionally (n= 32; 18.6%), 5–15 cigarettes daily (n= 15; 8.7%) or smoke 1 cigarette pack per day (n= 5; 2.9%). The differences between groups are significant ( $\phi$  = 0.261; p< 0.001). Subjects who smoke more often have higher alcohol intake ( $\rho$  = 0.25; p= 0.001).

Patients eat more fish ( $\phi$  = 0.247; p< 0.001), offal ( $\phi$  = 0.290; p< 0.001), poultry ( $\phi$  = 0.184; p= 0.009), pork ( $\phi$  = 0.213; p= 0.002), cocoa ( $\phi$  = 0.173; p= 0.018), and lentils ( $\phi$  = 0.177; p= 0.014) compared with subjects. Patients consume less proteins ( $\phi$  = 0.269; p< 0.001), black tea ( $\phi$  = 0.197; p= 0.004), alcohol ( $\phi$  = 0.376; p< 0.001), beef ( $\phi$  = 0.161; p= 0.033), eggs ( $\phi$  = 0.270; p< 0.001), oats ( $\phi$  = 0.261; p< 0.001), wholegrains ( $\phi$  = 0.273; p< 0.001), and spinach ( $\phi$  = 0.288; p< 0.001) than subjects. More than ½ of patients eat poultry, pork, cheese, cocoa, eggs, nuts and more than ½ of subjects eat poultry, cheese, cocoa, eggs, nuts, and wholegrains at least 2–5 times per week. Milk is not a component of the diet in 43 (25.9%) patients. Vitamin C in dose  $\leq$  250 mg/24 h is received by 66 (39.8%) patients. Food consumption frequency is shown in Figure 1.

**Table 4.** Estimated patients' and subjects' daily water intake (N= 338)

Daily water intake	Risk probability	Patients (n= 166)		Subjects (n= 172)	
		Men n (%)	Women n (%)	Men n (%)	Women n (%)
<0.5 L	R	10 (6)	14 (8.4)	2 (1.2)	7 (4.1)
0.5–1 L	R	19 (11.5)	20 (12.1)	10 (5.8)	32 (18.6)
1–1.5 L	R	25 (15.1)	26 (15.7)	25 (14.5)	36 (20.9)
> 1.5 L	–	33 (19.9)	19 (11.5)	38 (22.1)	22 (12.8)

L – litre; R – higher probability of recurrence risk



**Fig. 1.** Food consumption frequency in patients ( $n = 166$ ) and subjects ( $n = 172$ ).

## DISCUSSION

Gender ratio 1/1 is much lower in comparison to ratio 1/6 (16), but similar to ratio 1/01 (17). Difference between BMI of female patients ( $M = 30.3$ ;  $SD = 6$ ) and Slovak females ( $M = 25.7$ ;  $SD = 1$ ) is significant ( $p < 0.001$ ;  $MD = 4.581$ ;  $CI: 3.24-5.93$ ) (18). We observe a higher number of male patients belonging to the obese group in comparison with Slovak males. The same relationship is detected between female patients and Slovak females (19). Average BMI is higher in women, so they are at greater risk to get recurrence. High BMI also increases the risk of developing metabolic syndrome as a risk factor of urolithiasis (20, 21). Details and comparison with other authors are shown in Table 5.

Quantity of patients with normal weight in urban (13.3%) and rural (7.8%) areas is notably lower in comparison to Slovak population from urban (23.1%) and rural (19.6%) areas. Number of patients with overweight in urban (25.3%) and rural (11.5%) areas is higher than in Slovak urban (18.3%) and rural (20.2%) people. Also a number of obese patients from urban (27.1%) and

rural (12.6%) areas is remarkably higher than in Slovak population from urban (7.5%) and rural (9.4%) areas (19).

Independent of individual risk of stone formers, all should drink at least 2.5–3 L/24 h (6). Daily fluid intake of 114 (68.7%) patients is insufficient ( $\leq 1.5$  L/24 h) when compared to recommended values. Low fluid intake is probably the strongest risk factor for all types of stones. The right modification of drinking regime is the leading point of prophylaxis and metaphylaxis of urolithiasis (24–26).

Not working patients and patients with sedentary employment ( $n = 134$ ; 80.8%) may be in danger for weight gain. Ratio (2/2) of sedentary/active job is the same as an overall ratio for countries involved in the S.E.G.U.R. study (27).

Physical inactivity of 112 (67.5%) patients is a risk factor of urolithiasis and may develop their overweight and obesity. The risk is higher in older patients (28).

Higher rates of smoking in patients agree with results of other authors (29). Growing smoking rates in patients with alcohol consumption increases the risk of uric acid stones and obesity several times.

**Table 5.** Distribution of patients and Slovak healthy population within BMI categories

	Underweight (%)			Normal weight (%)				Overweight (%)				Obesity class I–III (%)			
	P	SP	Study 1	P	SP	Study 1	Study 2	P	SP	Study 1	Study 2	P	SP	Study 1	Study 2
Men	3.4	0.3	1.1	24.1	32.4	–	50.2	44.8	46.5	–	40.7	27.5	20.8	–	8
Women	1.3	3.6	11.2	17.7	45.9	–	60.2	27.8	31.8	–	19.9	53.1	18.7	–	8.7
Total	2.4	2	5.3	21.1	39.3	32	54.4	36.7	38.9	42	31.9	39.8	19.7	26	8.3

P – patients; SP – Slovak healthy population; Study 1 – Wrobel et al. (23); Study 2 – Trinchieri et al. (22)



Insufficient milk intake in 43 (25.9%) patients can lead to calcium and magnesium deficiency. The risk of calcium-oxalate urolithiasis is increasing. These results are similar in comparison to other European countries (27, 30, 31).

Regular vitamin C intake in 66 (39.8%) patients can accelerate a formation of calcium-oxalate stones, due to urinary vitamin C conversion to urinary oxalate. In comparison with other author's results, our patients have higher vitamin C intake (32, 33).

Cocoa (average content of oxalates in food –  $\sigma\text{OX}$  = 623 mg/100 g) and nuts ( $\sigma\text{OX}$  = 422 mg/100 g) are rich in oxalates. Their frequent consumption promotes oxalate stones formation. Cocoa contains theobromine which reduce a risk of uric acid stone formation (34). Nuts (average content of fats in food –  $\sigma\text{F}$  = 52 g/100 g), cheese ( $\sigma\text{F}$  = 28 g/100 g) and poultry ( $\sigma\text{F}$  = 25 g/100 g) are rich in fats and may increase weight and BMI. Poultry, pork, and cheese contain higher protein amounts (average content of proteins in food –  $\sigma\text{p}$  = 19–29 g/100 g), and their higher intake may cause calcium-oxalate and uricite stones (11).

Consumption of poultry and nuts in patients is probably not over Slovak recommendations (0–2 portions of poultry and a handful of nuts per day). A lot of patients exceed recommended daily intake of pork and beef (once per week) (35).

## CONCLUSION

Our outcome reflects current social conditions in some features. It is evident from the results that high BMI, low fluid intake, exceeded red meat consumption, and low physical activity are the strongest factors for developing urolithiasis. These factors have the most significant impact on kidney stone formation and must be adjusted to avoid recurrence.

Patients should consume more fluids daily. We urged patients to reduce an intake of red meat to once per week. It is very important to perform at least 30 minutes of physical activity (walking, jogging, exercises) daily. Properly performed physical activity can lower a risk of recurrence and decrease a BMI.

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## Conflicts of Interests

None declared

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