Metabolic and Physico-chemical Urolithiasis Parameters in the First Morning Urine

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ABSTRACT

The 24-hour urine is golden standard for metabolic assessment of stone formers. However, due to the difficulties in collecting almost 1/3 of the samples can not be used for the analysis. Therefore, we analyzed first morning urine and calculated different risk indexes in order to asses possibility of using it in determining urolithiasis risk. Subjects were divided into 4 groups: male patients (n=31, age 18–64), female patients (n=31, age 25–63), male controls (n=16, age 25–64) and female controls (n=19, age 21–65). First morning urine pH, concentrations of calcium, magnesium, phosphate, sodium, potassium, chloride, citrate, urate, oxalate, creatinine and glycosaminoglycans were determined. Based on them, ionic concentrations and activity products of calcium oxalate and phosphate were calculated by EQUIL 2. In addition, different risk indices were calculated. The results showed that both patients and control groups had metabolic disorders, but the frequencies of occurrence were statistically independent. Significant difference in concentration of urinary constituents between corresponding patient and control groups was observed only for glycosaminoglycans in female subjects. Ca/Cit ratio and Baggio index could differentiate between both corresponding patients and control groups. The results indicate that interplay between stone formation inhibitors and promotors is responsible for urinary stone formation and that the first morning urine could be used in assessing urolithiasis risk and its prevention.

Key words: urinary stone formation, first morning urine, metabolic urine disorders, glycosaminoglycans, risk indices

Introduction

Urolithiasis, the disease of urinary stone formation, is a pathological state in which stones are formed in different parts of the kidney and urinary tract. Due to the problems associated with it, such as nephrocalcinosis, obstruction of kidneys, loss of kidney tissue and function, haematuria, infection and pain caused by passing stones, the patients often need hospital care[1].

Urolithiasis is present in the whole world, but its occurrence and frequency depends on genetical, nutritive and ecological factors. Urinary stones appear in 0.1–0.5% of world population in a given year, with relapse rate of about 80%. It was established that 12% of males and 5% of females will suffer from urolithiasis until they reach age 70. Urinary stones are equally frequent in both kidneys, with 40% of patients having them bilateraly. Most of kidney stones appear between age 20 and 40, which makes urolithiasis a serious medical and socio-economical problem[2].

In the last thirty years, our understanding of the processes leading to urinary stone formation has increased significantly. Urinary stones are formed when urine becomes supersaturated. The initial step is formation of the nucleus, followed by the growth of crystals. Conditions leading to crystal growth are not necessarily the

same as the ones leading to the formation of nucleus[3]. It is obvious that numerous components of urine can influence different phases of stone formation. Of special interest, for urolithiasis prevention and treatment, are small molecules (pyrophosphate, citrate) and macromolecules (glycosaminoglycans, Tamm-Horsfall glycoprotein, uropontine, nephrocalcine) acting as inhibitors of crystal growth and/or crystal aggregation.

Understanding urine composition process enabled us to apply specific diagnostics and specific treatments for most urolithiasis patients[4,5]. In addition, various anti-relapse drugs and easier and less invasive operative procedures become avalaible[6].

In numerous studies of urinary composition disorders, the 24-hour urine is used as golden standard. However, there are several problems connected with its collection and preservation. Collecting these samples is time demanding and unreliable. The first common error in collecting the 24-hour urine is obtaining the wrong volume, resulting in a wrong assessment of daily voiding of the urine components constituting urinary stones. In addition, during collection of 24-hour urine it is necessary to add different additives, in order to prevent precipitation of particles and bacterial growth. These additives can destroy or change the structure of urinary components, and therefore lead to incorrect results in the assessment of the crystallization characteristics of urine[7]. These problems lead to the rejection of almost one third of the samples. Therefore, reliability of urines collected in different time intervals (first morning urine, 8h urine and 16h urine) in evaluating stone formers has been and is still investigated[7–9]. It was shown that 8h and 16h urines collected during night and day, respectively, are reliable specimens for determinating metabolic abnormalities[7]. A significant correlation between calcium, oxalate (Ox), citrate (Cit) and magnesium concentrations determined in early spot urine and 24-h urine was shown[9], but the role of the glycosaminoglycans (GAG) in calcium oxalate kidney stone formation remains unclear[10]. Dispute about which urine (24 hours, first morning) should be used when assessing the risk of urinary stone formation is ongoing.

In this paper, we tried to assess possibility of using first morning urine in determining urolithiasis risk in patients with recurrent calcium oxalate urolithiasis from Eastern Croatia, with aim to facilitate targeted treatment of the patients and prevention of urinary stone formation.

Materials and Methods

Subjects were divided into 4 groups: male patients (n=31, age 18–64), female patients (n=31, age 25–63), male controls (n=16, age 25–64) and female controls (n=19, age 21–65). Subjects were assigned to patient or control groups according to their medical history. Groups of patients were comprised of subjects with recurrent calcium oxalate urolithiassis, while control groups were comprised of subjects without medical history of stone formation or renal diseases. All subjects had given in-

formed consent to participate in the study. The study was approved by Ethics Committee of Medical faculty, Osijek.

The first morning urine was used for analysis. pH was measured immediately with pH-meter (Radiometer Copenhagen). Presence of the crystals was determined by optical microscopy (Olympus CX40). Urine sediment was obtained by centrifugation and treatment of urine by Urised system (Cronolab). Obtained sediment was then checked for the presence of the crystals. All urines were tested by Combur 10 test M (Roche) for possible organ damages.

The first morning urine without the added preservatives was used for biochemical analysis. Concentrations of sodium, potassium, calcium, magnesium, chloride, inorganic phosphate, urate, oxalate, citrate and creatinine were determined immediately. Part of urine was separated, centrifuged and put in the refrigerator at –20ºC for total GAG determination.

Calcium, magnesium and phosphate urinary concentrations were determined spectrophotometrically by Olympus test kits: calcium concentration was determined by o-cresolphthalein-complexon method[11], magnesium concentration was determined by Xylidyl blue method[12], phosphate concentration was determined by UV molybdate method[13].

Sodium and potassium concentration were determined by flame photometry (Flame photometer IL943). Chloride concentration were determined by coulometric titration (CTM3 chloride titrator, Radiometer Copenhagen).

Urate and creatinine concentrations were determined by Roche test kits: urate by uricase PAP method[14] and creatinine by enzymatic PAP method[15] using Olympus AU400 analyzer.

Citrate concentration was determined by Boehringer Mannheim test kit[16], oxalate concentration was determined by Sigma Diagnostic test kit[17] and total GAG concentration by carbazole method[18].

Obtained concentrations of determined urinary constituents were compared with reference values (Table 1[19,20]) to determine existence of the metabolic disorders.

Chemical compositions of the stones were determined by IR, using KBr pellets on Perkin Elmer spectrophotometer model 882.

TABLE 1
BOUNDARY VALUES OF URINARY CONSTITUENTS CONCENTRATIONS FOR DETERMINING METABOLIC DISORDERS[19,20]

Metabolic disorder	Boundary concentration [mmol/g cr]	
	Males	Females
Hypercalciuria	>4.20	>4.64
Hyperoxaluria	>0.28	>0.31
Hyperuricosuria	>3.11	>3.47
Hypocitraturia	<1.28	<1.99
Hypomagnesiuria	<1.40	<2.03

Urinary ionic concentration and activity products of calcium oxalate and brushite, defined as:

$$IAP(CaOx) = a(Ca^{2+}) \times a(Ox^{2-}) \qquad (1)$$

$$IAP(brushite) = a(Ca^{2+}) \times a(HPO_4^{2-}) \qquad (2)$$

were calculated by the computer program EQUIL 2[21] for each subject based on results of the first morning urine analysis. EQUIL 2 doesn't include GAG.

Based on calculated ionic concentrations Ca/Cit and Ca/Mg ratios were calculated, as well as three different indices: Tisselius risk index (RI), Ogawa index and Baggio index (BI).

Tisselius risk index, which uses creatinine (Cr) concentrations instead of urine volume, is defined as[22]:

$$RI = (Ca/Cr)^{0.71} \cdot (Ox/Cr) \cdot (Mg/Cr)^{-0.24} \cdot (Cit/Cr)^{-0.10} \quad (3)$$

where Ca, Ox, Mg and Cit concentrations are expressed in mmol/L and Cr in mol/L.

Ogawa index, AP(CaOx)EQ2, is defined as[23, 24]:

$$AP(CaOx)EQ2 = 6.838 \times 10^{-5} \cdot [Ca]^{0.78} \cdot [Mg]^{-0.30} \cdot [Ox]^{0.91} \cdot [Cit]^{-0.17} \qquad (4)$$

where concentrations are expressed in mmol/L.

Baggio index (BI) is defined as[25]:

$$BI = (Ox/Cit) \cdot GAG \cdot 10^4 \qquad (4)$$

where concentrations are expressed in mmol/L.

Statistics

Results of the urine analysis are given per g of creatinine and expressed as mean±standard deviation (SD). All data were tested for the normality of distribution. When data were not normally distributed, square root or log transformations were applied for ensuring normality. One way ANOVA was used to determine differences between groups (in all cases variances were homogeneous). Mean differences were separated by Tukey test. For nominal data (stone composition, crystalluria, metabolic disorders) contingency analysis was used (please note that null hypothesis for this analysis is that the data are coming from independent populations, therefore $p > 0.05$ means that the data are significantly different). The level of significance was set at $p < 0.05$. All analyses were performed using statistical for software SAS 9.1 or JMP 6.0.

Results and Discussion

Stones composition

Urolithiasis is a special form of biomineralization[26]. Its frequency increased during 20th century, especially in industrially developed countries. This led to increased interest in elucidating processes and mechanisms involved in urinary stone formation, especially calcium urolithiasis, compromising about 80% of stones mainly calcium oxalates, and rarely calcium phosphates[6].

Composition of the stones of both male and female patients in this study is given in Table 2. All patients had

TABLE 2
COMPOSITION AND FREQUENCY OF OCCURANCE OF URINARY STONES IN MALE AND FEMALE PATIENTS

Stone type	Number of stone formers / total number of patients	
	Male	Female
COM	14/31	20/31
COD	1/31	1/31
COM, COD	5/31	3/31
COM, HAP	8/31	7/31
COD, HAP	2/31	–
COM, COD, HAP	1/31	–

COM – calcium oxalate monohydrate, COD – calcium oxalate dihydrate, HAP – hydroxyapatite

calcium-oxalate stones, pure or mixed with hydroxyapatite. Contingency analysis showed that there is a statistically significant difference in stone composition between male and female patients ($p > 0.327$).

Many previous studies have shown that, pure or mixed, calcium oxalates are the most frequent constituents of urinary calculi (50–86%, e.g.[27,28]). When comparing urtolithiasis data for Croatia with those for some developed European countries (France, Germany) no significant difference can be observed[27].

Crystalluria

The formation of the stones, especially calcium ones, is a complex process depending on many factors. Basic condition for calcium stone formation is urine supersaturation with calcium oxalate or calcium phosphate, or both, which can lead to precipitation of one or more solid phases. However, urine of majority of persons is usually found in upper concentration part of metastable region where nucleation usually happens and where presence of promotors induces precipitation at even lower activity product than usual[8]. Therefore, crystalluria can be often found in persons who do not form stones, making its prognosis value controversial[29]. In addition, crystalluria is often not correlated with metabolic disorders, which can be explained by retention of the crystals at tubular level or strong inhibitory effect of the macromolecules on stone formation[30].

TABLE 3
FREQUENCY OF THE CRYSTALLURIA (NUMBER OF SUBJECTS WITH DIFFERENT TYPES OF CRYSTALLURIA / TOTAL NUMBER OF PATIENTS OR CONTROLS) IN PATIENTS AND CONTROLS

Crystals type	patients	controls
CaOx	8/62	3/35
CaP	5/62	2/35
H_2U	2/62	1/35
no crystals	48/62	29/35

CaOx – calcium oxalate, CaP – calcium phosphate, H_2U – uric acid

Occurrence of crystalluria in investigated groups is given in Table 3. Three types of crystals have been detected, calcium oxalate, calcium phosphate and uric acid. Higher frequency of crystalluria in patients in comparison with controls has been observed. Contingency analysis showed that this difference is statistically significant (p>0.258). Earlier studies have shown that in addition to higher crystalluria occurrence rate in patients, formed crystals are also larger[8]. Robertson[31] has shown that in the urine of the stone formers bigger aggregated calcium oxalate dihydrate (COD) crystals can be found, while in the urine of the non-stone formers smaller calcium oxalate monohydrate (COM) crystals can be found.

Urine composition

The precise identification of abnormal excretion of metabolic risk factors is at the basis of any method for preventing urinary stone formation[7]. Therefore, the first step in investigating urolithiasis is determination of urine composition. Average values of first morning urine metabolic parameters for the investigated groups are given in Table 4.

In investigated groups 64% of male and 65% of female subjects had urine pH lower than 6, which is in accord with data from earlier study where there was 70% of such subjects[7].

Comparison of the concentrations of other parameters showed that statistically significant difference in concentration of calcium (p>0.017), urate (p>0.027), citrate (p>0.001) and GAG (p>0.002) exist between different groups. However, only significant difference between corresponding patients and control groups were found for GAG concentration in female subjects.

Both male and female patients had higher, although not statistically different, urinary calcium concentration than respective control groups. This agrees with earlier findings that stone formers have higher average first morning urinary calcium concentrations than non-stone formers[32], indicating the significant promoter role of calcium in stone formation.

In contrast, both male and female patients had lower, although not statistically different, urinary citrate concentration than respective controls. Both female patients and control had higher citrate concentrations than corresponding groups of male subjects. This agrees with literature data[32] and points to the significant inhibitory role of citrate, more expressed with female subjects.

The highest urate content has been detected in urine of female patients. Urate content in urine of male patients was significantly lower than the one in urine of female patients, while urate content in urine of both control groups was not significantly different from values obtained in patients groups.

The highest GAG content was detected in female controls. This value was significantly higher than the ones obtained for male and female patients. The value obtained for male controls was not significantly different from the ones obtained in all other groups. This finding points to a possible inhibitory role of GAG, which is in accordance with some of earlier results. GAGs are present at apical surface of tubular kidney cells[33], in that way inhibiting and preventing crystal adhesion to kidney cells, which is an important step in urolithiasis[34,35]. Damage of GAGs layer may result in increased retention of CaOx crystals[36]. However, there are contradictory data. This is a consequence of significantly different role that different GAGs have in different stages of stone formation[10,37].

Comparison of the other parameters, revealed no significant differences. In general, all concentrations were higher in female subjects, which could be explained by the lower creatinine amount that females excrete in urine due to smaller muscular mass. Other literature

TABLE 4

AVERAGE CONCENTRATION OF THE FIRST MORNING URINE CONSTITUENTS (MEAN ± SD) FOR MALE AND FEMALE PATIENTS AND CONTROLS. VALUES IN THE SAME ROW WITH DIFFERENT SUPERSCRIPTS ARE STATISTICALLY DIFFERENT.

Constituent	Patients		Controls		p>F
	Male	Female	Male	Female	
pH	5.85±0.72	5.82±0.61	6.11±0.81	5.95±0.73	0.554[NS]
Sodium (mmol/g cr)	115.7±52.6	148.1±61.8	117.6±74.2	135.6±65.1	0.173[NS]
Potassium (mmol/g cr)	37.9±17.1	45.8±16.3	40.7±20.6	49.6±32.9	0.367[NS]
Chloride (mmol/g cr)	132.0±55.8	162.5±76.4	128.5±77.6	150.0±82.3	0.387[NS]
Calcium (mmol/g cr)	3.92±2.41[A,B]	4.45±2.74[A]	2.66±1.53[B]	2.98±1.66[A,B]	0.0178
Magnesium (mmol/g cr)	2.77±0.91	2.95±1.08	2.47±1.07	3.37±1.34	0.112[NS]
Phosphate (mmol/g cr)	14.07±5.25	15.04±5.47	16.20±9.77	16.81±6.28	0.474[NS]
Urate (mmol/g cr)	2.31±0.76[B]	2.82±0.76[A]	2.36±0.74[A,B]	2.74±0.72[A,B]	0.028
Oxalate (mmol/g cr)	0.22±0.08	0.24±0.12	0.18±0.09	0.19±0.11	0.103[NS]
Citrate (mmol/g cr)	1.59±0.90[B]	2.44±0.99[A]	2.20±0.91[A,B]	3.16±1.17[A]	<0.001
Glycosaminoglycans (mg/g cr)	4.16±2.02[B]	4.85±2.05[B]	5.70±1.69[A,B]	6.59±2.85[A]	0.002

NS – Not statistically different

data confirm that these parameters have a smaller influence on urinary stone formation[32].

Metabolic disorders

Urine analysis showed that both patients and control groups (both male and female) have metabolic disorders (Table 5, boundary values after ref.[19,20]). Contingency analysis showed that the values obtained for control groups and patients, for both male (p>0.269) and female (p>0.504), are significantly different. Significant differences were also observed between male and female controls (p>0.264) and patients (p>0.188). These findings agree with earlier studies[38,39].

Hypercalciuria is the most frequent disorder observed in both male and female patients. Hyperoxaluria and hyperuricosuria were also detected in high frequencies. These three stone promoting factors have been determined in 27 of 47 males and 30 of 50 females, similar to other studies. Hypocitraturia has been found in higher frequency than in other studies[38].

These results indicate that the risk of urinary stone formations cannot be evaluated based on a single metabolic parameter.

Risk indices

In order to assess the risk of urinary stone formation as precisely as possible, different risk indices have been defined. Indices used in this investigation are described in Materials and methods section, and results are presented in Table 6.

Although there are statistically significantly differences between the values of all indices between different groups, only Ca/Cit and BI can distinguish between both female and male patients and controls, while Ca/Mg and Tisselius index can distinguish only between female patient and controls. None of indices can distinguish between male and female patients and/or male and female control groups.

Statistically significant differences in Ca/Cit ratio between corresponding patients and control groups indicate equilibrium disorder in favor of promoting factors, which leads to increased supersaturation and lowered inhibitory urine potential.

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Ca/Mg ratio was significantly higher for female patients in comparison with control group, and also higher (but not significantly) for male patients in comparison with control groups. Similarly to Ca/Cit ratio this also indicates equilibrium disorder in favor of promoting factors.

TABLE 5
FREQUENCY OF METABOLIC DISORDERS (NUMBER OF SUBJECTS WITH DIFFERENT TYPES OF METABOLIC DISORDER / TOTAL NUMBER OF MALE OR FEMALE CONTROLS OR PATIENTS) IN MALE AND FEMALE SUBJECTS

Metabolic disorder	Male		Female	
	Controls	Patients	Controls	Patients
HCa		4/31	1/19	5/31
HOx	1/16	2/31	1/19	
HU	2/16	2/31	1/19	
hCit		6/31	2/19	4/31
hMg			2/19	2/31
HCa, HOx	2/16		2/19	
HCa, HU				1/31
HCa, hCit		1/31		1/31
HOx, hCit		1/31		1/31
HOx, HU		1/31	1/19	2/31
hCit, hMg	1/16	2/31	1/19	4/31
HCa, HOx, HU				2/31
HCa, HU, hCit				1/31
HU, HOx, hCit		1/31		
none	8/16	11/31	8/19	8/31

HCa – hypercalciuria, HOx – hyperoxaluria, HU – hyperuricosuria, hCit – hypocitraturia, hMg – hypomagnesiuria

TABLE 6
UROLITHIASIS RISK INDICES ($\bar{X}\pm$SD) FOR PATIENT AND CONTROL GROUPS (MALE AND FEMALE). VALUES IN THE SAME ROW WITH DIFFERENT SUPERSCRIPTS ARE STATISTICALLY DIFFERENT.

Index	Patients		Controls		p>F
	Male	Female	Male	Female	
Ca/Cit	3.135±2.784[A]	2.317±2.233[A,B]	1.504±1.209[B,C]	1.142±0.872[C]	< 0.001
Ca/Mg	1.399±0.623[A]	1.546±0.81[A]	1.179±0.714[A,B]	0.917±0.501[B]	0.001
IAP(COM) × 10⁻⁸	1.979±1.310[A]	1.521±0.809[A,B]	1.471±1.092[A,B]	1.000±0.944[B]	0.008
Ogawa index × 10⁻⁸	0.892±0.556[A]	0.739±0.423[A,B]	0.816±0.559[A,B]	0.461±0.383[B]	0.014
Tiselius index	491.7±246.4[A,B]	567.7±406.4[A]	331.2±253.6[A,B]	375.8±305.7[B]	0.006
Baggio index	731.3±847.1[A]	404.0±379.1[A]	162.4±164.8[B]	186.0±210.9[B]	< 0.001

IAP – ionic activity product

IAP (COM) and Ogawa index are higher, but not significantly, for patients than for corresponding control groups. This is in accordance with previous studies[22,24], and also indicates higher patients urine supersaturation.

Female patients had statistically higher RI than control groups. Male patients also had higher values, but not significantly higher. This is in accordance with earlier studies[22].

Baggio index was significantly higher in both patient groups than in corresponding control groups. Literature data show that over 80% of stone formers can be distinguished from nonstone formers using this index. In addition it enables the use of fasting urine and avoids the problems connected with 24-urine collection and diet restrictions[25].

Correlation between IAP (COM) and risk indices

The IAP (COM) values were correlated with other indices for each group of the subjects. Significant correlations were established with Ogawa index for all groups, Tiselius index for all but male patients, Ca/Cit and Ca/Mg ratios for both control groups and Baggio index for female control groups (Table 7).

Pearson coefficient is a measure of linear correlation of the variables. Therefore, from a purely statistical point of view, lack of significant correlation between IAP (COM) and Baggio index for patient and male control groups, Ca/Cit and Ca/Mg ratio for patient groups, is a little bit surprising, because all those indices contain one common variable, calcium or oxalate concentration. In this respect, lack of significant correlation would be more easily expected for Tisselius and Ogawa indices, because they are not linear in calcium and oxalate concentrations.

These observations point to the importance of the interplay between promoting and inhibiting urinary constituents in kidney stone formation. Therefore several methods for the determination of the urinary inhibitory activity to CaOx precipitation[40–42] and calcium binding capacity[43] have already been proposed, and used[40] in the follow up of patients with recurrent urolithiasis[44].

TABLE 7
PEARSON CORRELATION COEFFICIENTS AND PROBABILITIES FOR THE CORRELATION OF CALCIUM OXALATE MONOHYDRATE IONIC ACTIVITY PRODUCT (IAP(COM)) WITH OTHER RISK INDICES

Index	IAP(COM) EQ x10⁻⁸			
	Patients		Controls	
	Male	Female	Male	Female
Ca/Cit	0.0429	0.195	0.575	0.672
	0.819 NS	0.292 NS	0.020	0.002
Ca/Mg	0.179	0.228	0.582	0.504
	0.336 NS	0.217 NS	0.018	0.028
Ogawa index × 10⁻⁸	0.963	0.890	0.891	0.96239
	<0.001	<0.001	<0.001	<0.001
Tiselius index (RI)	0.287	0.414	0.508	0.743
	0.118 NS	0.021	0.045	0.001
Baggio index	–0.082	–0.012	0.122	0.497
	0.662 NS	0.951 NS	0.651 NS	0.030

NS – Not statistically different

Conclusion

In order to successfully deal with problems connected with urinary stone formation it is of utmost importance to be able to differentiate between possible stone formers and non-stone formers. Although 24-hours urine is considered to be golden standard in this sense, problems connected with its collection render its applicability. The results of this study are yet another support in qualifying first morning urine as easily collectable and valuable specimen for stone former discrimination. However, more investigations on lager number of subjects are needed, because results are pointing to a redefinition of risk indices for first morning urine in order for it to be successfully applied. Correct first morning urine risk indices would also facilitate targeted treatment of the patients enabling better prevention of urinary stone formation.

Acknowledgement

R E F E R E N C E S

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METABOLIČKI I FIZIKALNO-KEMIJSKI PARAMETRI UROLITIJAZE U PRVOM JUTARNJEM URINU

S A Ž E T A K

24-satni urin je »zlatni standard« za metaboličku procjenu stvaranja kamenaca. Međutim, s obzirom na poteškoće prilikom sakupljanja urina, gotovo 1/3 uzoraka ne može se koristiti za analize. Zbog toga smo analizirali prvi jutarnji urin i računali različite indekse rizika, s namjerom da ukažemo na mogućnost njegove upotrebe u određivanju rizika urolitijaze. Ispitanici su bili podijeljeni u 4 skupine: muškarci (n=31, dobi 18–64 godine), žene (n=31, dobi 25–63 godine), muška kontrolna skupina (n=16, dobi 25–64 godine) i ženska kontrolna skupina (n=9, dobi 21–65 godina). U prvom jutarnjem urinu određeni su pH, koncentracije kalcija, magnezija, fosfata, natrija, kalija, klorida, citrata, urata, oksalata, kreatinina i glikozaminoglikana. Temeljem ovih podataka računalnim programom EQUIL 2 izračunate su ionske koncentracije i aktivni produkti kalcijeva oksalata i fosfata, a dodatno su izračunati i različiti indeksi rizika.

Rezultati su pokazali da skupine bolesnika, kao i kontrolne skupine, imaju metaboličke poremećaje, ali učestalost pojave je statistički neovisna. Značajna razlika u koncentracijama mokraćnih parametara između odgovarajućih skupina bolesnika i kontrolnih skupina ustanovljena je samo za glikozaminoglikane u žena. Odnos Ca/Cit i Baggio indeks mogu razlikovati skupinu bolesnika od kontrolne skupine. Međusobno djelovanje inhibitora i promotora stvaranja kamenaca može biti odgovorno za nastajanje kamenaca a prvi jutarnji urin može se koristiti u određivanju rizika od urolitijaze i prilikom njene prevencije.