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Research Article

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Bacteriological evaluation of the non-struvite nephrolithiasis and its association with urinary tract infections

Evaluarea bacteriologică a nefrolitiazei non-struvitice și asocierea ei cu infecții ale tractului urinar

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Abstract

Objective: *To evaluate the bacteriological features in non-struvite nephrolithiasis and in its associated urinary tract infection, and to establish the relationship between the two pathologies.*

Methods: *The non-struvite calculi from 132 patients were aseptically extracted by percutaneous nephrolithotomy (PNL). The midstream urine and calculi were bacteriologically and biochemically processed.*

Results: *Most calculi (78%) were located to renal pelvis, associated with hydronephrosis, the biochemical composition confirming the lack of struvite and revealing the predominance of calcium oxalate. The females presented significantly more colonized calculi (50%) than males (21.9%), with higher bacteriological diversity. There is a significant relation between the presence of colonized calculi and urinary tract infections, 24.2% of calculi and 25.8% of the urine samples presenting positive cultures. In 70.4% of cases, we found the same antibiotic resistance pattern between the pathogens isolated from calculi and urine, thus considering them identical strains. The Enterobacteriaceae represented the most predominant bacteria both from calculi (62.5%) and urine (63.6%), approximatively 30% being resistant to cephalosporins and over 50% resistant to fluoroquinolones, ampicillin and tetracycline. There were 3.8% of cases in which the calculi were colonized but the urine was sterile, the bacteria being sensitive to cephalosporins that are used as prophylaxis.*

Conclusions: *In all the cases, the same bacterial species was found both in calculi and urine, and 70.4% of them were phenotypically identical. The resistance to the second generation cephalosporins is lower than in the case of other antibiotics, which makes them the most suitable for prophylaxis in PNL.*

Keywords: *nephrolithiasis, non-struvite calculi, percutaneous nephrolithotomy, phenotypic similarity, chemical composition*

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Rezumat

Obiectiv: *Evaluarea bacteriologică în nefrolitiaza non-struvitică și în infecțiile tractului urinar asociate nefrolitiazei, precum și stabilirea relației dintre cele două patologii.*

Metode: *Calculii non-struvitici de la 132 de pacienți au fost extrași în mod aseptic prin nefrolitotomie percutanată (NLP). Probe de urină din jetul mijlociu, alături de calculii extrași, au fost procesate bacteriologic și biochimic.*

Rezultate: *Cei mai mulți calculi (78%) au fost localizați la nivelul bazinetului, asociindu-se cu hidronefroză, compoziția biochimică confirmând lipsa struvitului și relevând predominanța oxalatului de calciu. Femeile au prezentat un grad de colonizare a calculilor semnificativ mai mare decât bărbații (50% versus 21,9%), dar și cu o diversitate bacteriologică mai mare. S-a identificat o relație semnificativă între prezența calculilor colonizați și infecțiile tractului urinar, 24,2% din calculi și 25,8% din probele de urină prezentând culturi pozitive. În 70,4% dintre probe s-a găsit aceeași tablou de susceptibilitate față de antibiotice la microorganismele izolate din calculi și la cele din urină, considerându-le astfel tulpini identice. Bacteriile din familia Enterobacteriaceae au reprezentat flora predominantă izolată atât din calculi (62,5%) cât și din urină (63,6%), aproximativ 30% fiind rezistente la cefalosporine și peste 50% rezistente la fluorochinolone, ampicilină și tetraciclină. În 3,8% din cazuri, calculii au fost colonizați, iar urina sterilă, bacteriile identificate fiind sensibile la cefalosporinele folosite în profilaxie.*

Concluzii: *În toate cazurile, aceleași bacterii s-au găsit atât în calculi cât și în urină, iar 70,4% dintre ele au fost fenotipic identice. Rezistența la cefalosporinele de generația a doua este mai mică decât în cazul altor antibiotice, ceea ce le face cele mai potrivite pentru profilaxia din cadrul NLP.*

Cuvinte cheie: *nefrolitiază, calculi non-struvitici, nefrolitotomie percutanată, similaritate fenotipică, compoziție chimică*

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Introduction

Nowadays, the lithiasis disease is one of the most common pathologies in urological praxis, having been described since antiquity. The main process of lithiasis takes place in the kidneys, after which the calculi can migrate along the ureter towards the bladder and finally be eliminated through the urethra. Sometimes the urinary tract infections (UTI) facilitate the lithogenesis, or the lithiasis can coexist with the infection. In some cases the calculi are infection related with struvite or carbonate apatite composition (1). Urological practice has demonstrated the existence of struvite calculi (magnesium ammonium phosphate) in the urinary tract, mainly due to their production by the Gram-negative bacteria; however, we have little data regarding the situation of other types of calculi and their relation to the UTI, especially if these calculi are infected. Previous studies showed that calcium oxalate, cystine and uric acid can be present within UTI (2).

Some clinical issues can be developed by urinary calculi, such as pyonephrosis, UTI with sepsis or renal deterioration (3,4). The persistence of upper urinary tract lithiasis can lead to hydronephrosis, which promotes local kidney complications such as total parenchyma destruction, including infections (5). Because of these consequences, a close medical follow-up of the patients is mandatory, with complete antibiotic prophylaxis and removal of the calculi (6).

The calculi produced by urinary tract infections are described to be in conjunction with some urease producing bacteria such as *Klebsiella* spp. and especially *Proteus* spp. which has the ability to form crystals inside the host cells (7), but other bacterial species such as *Pseudomonas* spp., *Escherichia coli* or *Staphylococcus aureus* are also involved in nephrolithiasis (8). After calculi development, the germs can survive in the inorganic matrix, where the antibiotics do not penetrate, thus the persistent infection can determine the growth of calculi in all the kidney cavities (calyx, pelvis) in time of weeks or months (9). Several studies showed that the urinary lithiasis can be induced by chronic or persistent UTI (so-called "infection-induced stones"). In contrast, there is a similar strong evidence that the presence of calculi are risk factors for UTI (so-called "stones with subsequent infections") (7,8,10). In these situations, the bacteria from calculi and urine are the same. Of course, there is the possibility for the same patient to have different germs in midstream urine and in calculus.

Purpose

The main purpose was to assess the germ discrepancy/similarity in calculus vs urine culture for patients who underwent percutaneous nephrolithotomy (PNL) for non-struvite nephrolithiasis.

Material and methods

In our prospective study, we evaluated patients with renal calculi, who underwent minimal invasive treatment for nephrolithiasis in the Urology Clinic of The Clinical County Hospital of Tîrgu Mureș, over a period of 12 months, from February 2013 to January 2014. The study was conducted according to the Declaration of Helsinki, being approved by the local hospital administration and by the patients, the surgical procedure being part of the nephrolithiasis management.

We have included 132 adult Caucasian patients residing in our geographic region, with de novo or recurrent renal lithiasis, subjects for PNL, who presented symptoms of nephrolithiasis (flank pain) associated or not with uncomplicated lower UTI (dysuria, frequency and urgency) (11). We have excluded 12 cases that were subjected for PNL, due to the presence of indwelling catheter (such as ureteral double 'j' or uretro-vesical catheter), of struvite calculi or with prior antibiotic use (last two weeks), as well as 5 cases with associated lower urinary tract lithiasis, as a possibly associated transient asymptomatic bacteriuria could lead to upper calculi colonization. Because of the high risk of sepsis or bacteraemia following the surgical intervention, a perioperative prophylactic treatment was performed according to the European Guidelines of Urology (12), using a second generation cephalosporin, which was administered intravenously at the time of the induction of the anaesthesia. Due to the risk of fever associated to infective complications following nephrolithotomy, even with sterile preoperative urinary culture and perioperative antibiotic prophylaxis (13), the same antibiotic was administered until the bacteriological urine culture results were received.

The PNL was chosen as a therapeutic method, as it also allowed us to harvest the renal stones in aseptic conditions. Basically, after an indwelling ureteral catheter was set, with the patient in prone position, we punctured the postero-inferior calyx of the kidney under fluoroscopic control; the contrast substance and 10% methylene blue solution were simultaneously injected through the ureteral catheter. The presence of methylene blue in the puncture liquid signified a proper procedure. Afterwards, we created a nephrostomy pathway, and then we performed the lithotripsy in situ with the nephroscope and extracted the resulted calculi fragments. At the end of the intervention, a nephrostomy catheter was set to be removed after 2 or 3 days. The collected calculi fragments were gently washed several times in sterile saline, in order to remove the methylene blue, which could interfere with the bacteriological results by inhibiting the bacterial growth; the calculi were then processed for bacteriological examination and chemical analysis. Based on the chemical analysis results, the patients with struvite urolithiasis were excluded.

The chemical analysis of calculi was performed by using macro-and microscopic examination (Elerom photomicroscope, 3,4X) followed by their chemical processing. This analysis was performed in glass test tubes or porcelain capsules, using the powder obtained by smashing the stones in a mortar with a pestle. The following compounds of the calculi were identified by colour changes in the mixed substances: oxalate (discoloration of violet solution of 1 mL 5% H_2SO_4 and 2 drops of 1‰ $KMnO_4$ after heating), phosphate (yellow precipitate after adding and heating a few drops of HNO_3 1.42 g/mL and 1 mL of 5% ammonium molybdate), urate (red color after adding a few drops of HNO_3 1.42 g/mL, then violet after adding a drop of 25% NH_3 and a drop of 10% NaOH), xanthine (yellow color after adding a few drops of HNO_3 1.42 g/mL, and no color change after adding NaOH) and cystine (black precipitate adding and boiling 1 mL 10% NaOH and 2 drops of $Pb(CH_3COO)_2$).

Mid-stream urine samples were also collected from each patient, before administrating any antibiotics, in the same day with the surgical intervention.

The calculi and urine samples were analyzed in the suitable culture media for identification of aerobic bacteria. Each calculus fragment was vortexed in nutrient broth and then inoculated on agar plates with 10 µl sterile loop. The urine samples were processed according to the urine culture internal protocol. The bacteriological results were considered positive for urine in case of growth over 100,000 CFU/mL after 24h of incubation. We excluded all the results with more than three bacterial types from urine, suspecting contamination. The calculi from which no growth was achieved after direct inoculation, were examined again after enrichment in nutrient broth for up to five days. All bacteria isolated from renal calculi, regardless of their number, were identified.

The bacterial identification was performed using standard biochemical methods and when necessary by Biomerieux® Vitek 2 Compact system. The antibiotic susceptibility profile was evaluated for each clinically-relevant isolated bacteria using the CLSI 2013 standard, by disk diffusion and by Biomerieux® Vitek 2 Compact system when necessary.

We followed aspects regarding the proportion of the urinary tract infections, the infected calculi and their etiological correlation, antibiotic susceptibility, and clinical findings such as the degree of hydronephrosis or the calculi localization.

The phenotypic similarity was achieved by comparing the antibiotic susceptibility pattern of the bacterial isolates from calculi and urine, with a relatively good discrimination power (14). We considered that two bacterial strains are likely identical when the antibiotic susceptibility pattern concordance was over 85% (different susceptibility reported in no more than one antibiotic) or identical when the concordance was 100%.

The urinalysis was used in order to support the UTI diagnosis and differentiate it by the asymptomatic bacteriuria or urine contamination. The urinalysis was performed using LabStrip, U11Strip tests.

The statistical tests (chi-square, comparison of proportions) were calculated using GraphPad InStat3 and Medcalc software, two-tailed, with a significance level alpha of 0.05.

Results

We evaluated 132 patients with renal non-struvite calculi. Most calculi were located to renal pelvis site (103 cases; 78%), renal pelvis + inferior calyx (ICX) (13 cases; 9.8%) and ICX solely (12 cases; 9.1%). Other locations such as renal pelvis + medium calyx (MCX), MCX, ICX-+MCX and superior calyx (SCX) hosted calculi in one case each (0.8%). The calculi sizes were between 2 and 5 cm, with a mean of 3.4±0.9 cm. All cases were complicated with hydronephrosis in different stages, the most predominant being the 2^{nd} and 3^{rd} stage: 58 cases (43.9%) and 56 cases (42.4%) respectively.

The genders were almost equally represented, with a slight predominance of females (68 cases; 51.5%). However, the percentage of contaminated calculi was higher in females than in males (34 cases; 50% vs 14 cases; 21.9%), with $p < 0.05$ (OR = 3.571; 1.670 – 7.636 at 95% Confidence Interval). In females, we also found a higher bacteriological diversity (10 bacterial and yeast species) than in males (4 bacterial species).

The renal lithiasis was more predominant in the 60-69 year age group (40 cases; 30.3%) followed by 40-49 year (35 cases; 26.5%) and 50-59 year (29 cases; 22%) age groups. The average age was similar among genders (53 years old) with wider extremities in females (20 to 80 years old).

From the total of 132 calculi, 84 (63.6%) showed no bacterial growth after 5 days of incubation in nutrient broth, whereas 48 (36.4%) presented positive cultures, with high microbial diversity (12 genera consisting in Gram-negative and -positive bacteria, but also yeasts). As we will state in the discussions section, we considered part of the isolated bacteria as contaminants due to their growth only after enrichment, at 5 days of incubation. Thus, 32 calculi (24.2%) were considered infected; the actual situation regarding the pathogens found in urine/calculi can be followed in Table I. The total number of positive cultures was 34 for urine (25.8% of total urine samples). The Enterobacteriaceae family represented the most predominant bacteria both from calculi (20 cases; 62.5%) and urine culture (21 cases; 63.6%).

There is a significant relation between the presence of colonized calculi and UTI ($p < 0.05$). In 27 cases (20.5% of all cases or 84.4% of the calculi with positive culture) the presence of colonized calculi was associated with positive urine samples, and within these, the same bacterial species were identified (27 cases; 100%). From these, the phenotypic similarity showed likely identical bacteria in 24 cases and identical bacteria in 19 cases (88.9%, respectively 70.4% of the cases with positive culture from calculi and urine).

Table I. Clinically relevant bacterial species identified from calculi and urine (excluding contaminants)

	Positives samples from calculi		**Positives samples from urine**	
	No	**%**	**No**	**%**
Escherichia coli	**10**	**31.3%**	**12**	**35.3%**
Pseudomonas aeruginosa	**9**	**28.1%**	**8**	**23.5%**
Klebsiella pneumoniae	**3**	**9.4%**	**3**	**8.8%**
Proteus mirabilis	**3**	**9.4%**	**2**	**5.9%**
Enterobacter spp.	**2**	**6.3%**	**2**	**5.9%**
Enterococcus faecalis	**1**	**3.1%**	**2**	**5.9%**
Candida albicans	**1**	**3.1%**	**1**	**2.9%**
Citrobacter spp.	**1**	**3.1%**	**1**	**2.9%**
Serratia marcescens	**1**	**3.1%**	**1**	**2.9%**
Staphylococcus cohnii	**1**	**3.1%**	**1**	**2.9%**
Staphylococcus saprophyticus	**0**	**0%**	**1**	**2.9%**
TOTAL	**32**	**100%**	**34**	**100%**

In a small number (7 cases; 5.3% of total samples), the urine culture was positive with sterile calculi, the identified bacteria being *Escherichia coli* (3 cases) and one of each: *Enterococcus faecalis, Candida albicans, Pseudomonas aeruginosa and Staphylococcus saprophyticus*. Conversely, negative urine cultures with positive calculi culture were found in 5 cases (3.8% of total samples): *Pseudomonas aeruginosa* (2 cases) and singular cases of the following: *Candida albicans*, *Escherichia coli* and *Proteus mirabilis*.

The remaining 93 cases (70.4%) were considered sterile both for calculi and urine, as 14 CoNS, one *Chryseobacterium indologenes* and *Leuconostoc pseudomesenteroides* were isolated and identified from calculi only after 5 days of incubation in enrichment media, thus being considered contaminants.

The antibiotic susceptibility of enterobacteria showed a mild to low resistance profile, with the highest resistance towards ampicillin and tetracycline, both for the isolates from calculi and urine (Figure 1). Small differences were found in the antibiotic resistance patterns between the isolates from calculi and urine (Table II). The enterobacteria from calculi were more resistant to fluoroquinolones and trimethoprim-sulfamethoxazole, while those from urine were more resistant to cephalosporins. In one case, *Klebsiella pneumoniae* was identified in both sites, but with extended spectrum beta-lactamase (ESBL) profile from urine, with a phenotypic similarity of 54.5%.

One patient presented methicillin-resistant CoNS: *S. cohnii* isolated both from calculi and urine, with sensitivity to gentamycin, levofloxacin, nitrofurantoin, vancomycin and linezolid.

Discussions

The bacteriological examination of calculi is not a routine procedure in our clinic; this might be because the presence of bacteria in the urinary tract system is commonly evaluat-

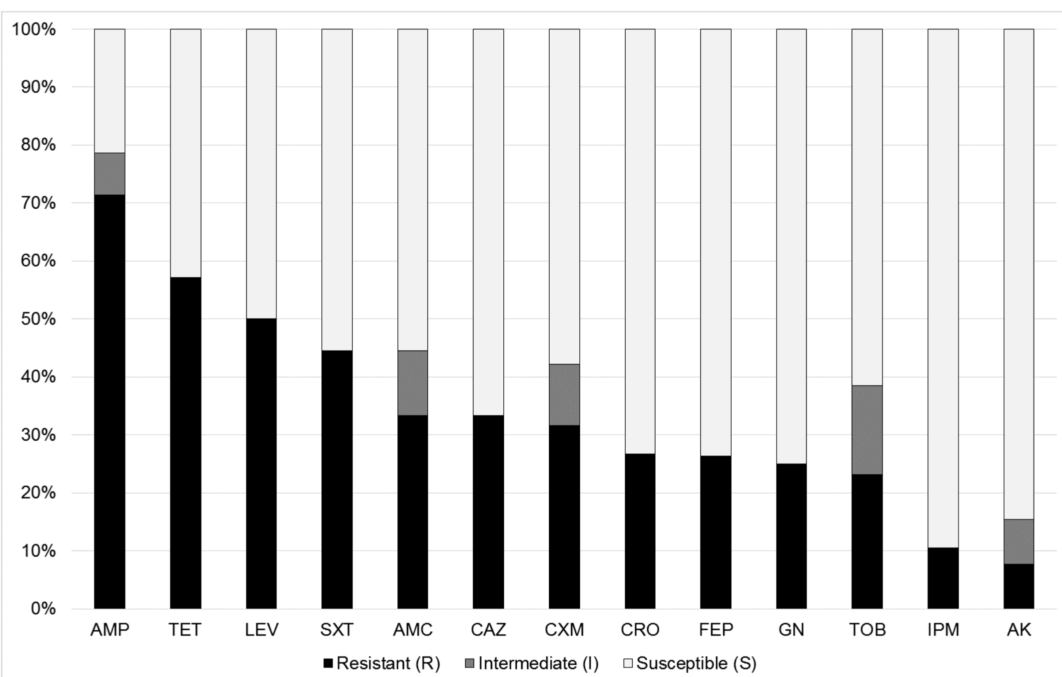

Figure 1. Antibiotic susceptibility in Enterobacteriaceae isolated from calculi

Table II. Resistance profile of the Enterobacteriaceae isolated from calculi and urine

Antibiotic	%R in calculi	%R in urine	Difference in percentage points	p
SXT	44.4%	33.3%	11.1%	0.631
AK	7.7%	0.0%	7.7%	0.337
TET	57.1%	50.0%	7.1%	0.776
LEV	50.0%	47.1%	2.9%	0.859
TOB	23.1%	22.2%	0.9%	0.956
GN	25.0%	25.0%	0.0%	1.000
AMC	33.3%	35.3%	-2.0%	0.900
IPM	10.5%	14.3%	-3.8%	0.795
AMP	71.4%	76.9%	-5.5%	0.722
FEP	26.3%	33.3%	-7.0%	0.640
CXM	31.6%	38.9%	-7.3%	0.656
CAZ	33.3%	41.2%	-7.8%	0.624
CRO	26.7%	40.0%	-13.3%	0.450

ed through urine culture. However, we consider that the microbiological investigation of the calculi may be an important investigation, as the bacteria that colonize the calculi can induce bacteriuria/UTI, or even inflammatory response syndrome and sepsis when certain conditions are met (15). The presence of this association, left without an adequate treatment (such as the calculi-free status and proper antibiotherapy) can lead patients to develop recurrence of urolithiasis or even struvite urolithiasis, with well-known consequences for the urinary system and for the entire human body. There are reviews that confirm the development of symptomatic bacteriuria after extracorporeal lithotripsy, were the single possible bacterial source was the fragmented calculi (16,17).

The results in our survey revealed about 24% of calculi as infected and about 25% positive urine samples at the time of the surgical procedure, with women patients being the most affected, as it was also shown by Roushani et al (18). Though there is a significant relation between the presence of calculi and UTI, it is not certain which one is the cause and which is the effect, as in the principle "which was the first: the chicken or the egg?". In some situations the chemical contents of calculi may indicate the etiology of calculi, as a chronic UTI can induce the development of magnesium ammonium phosphate based calculi, whereas newer studies presented other types of calculi as well, following UTI (10,19). The urinary calculi are developed mostly de novo in renal site (20). The bladder calculi are specific in elderly patients, with urinary retention due to enlarged prostate or neurogenic bladder (21), while our patients were middle-aged to 53.

More often, bacteria reach the renal site (pelvis, calyx) by retrograde pathway such as the ureter, in lower UTI (cystitis) or secondary to endoscopic interventions (22,23). The hematological dissemination as antegrade pathway is described mostly within yeast bacteremia (24). As the antibiotic therapy and prophylaxis is widely used nowadays, the hematological dissemination of bacteria in patients with bacteremia towards renal sites is practically absent (22).

Most of the CoNS were identified from calculi only after enrichment in the nutrient broth, both the primary calculi cultures and urine cultures being negative. Only in one case, in which methicillin-resistant *Staphylococcus cohnii* was identified both from urine and calculi, the antibiotic susceptibility pattern showed a similarity of 100% and positive urine markers (positive leukocytes, red blood cells and proteins). This made us consider that all the CoNS except for the one previously described were external contaminants of the calculi. Nevertheless, there are few studies which found CoNS as real etiological agents in UTI and calculi, especially when prosthetic devices were inserted (25,26). Similar to CoNS, *Chryseobacterium indologenes* and *Leuconostoc pseudomesenteroides* were identified only after enrichment, so we also interpreted them as external contaminants. In the one case of colonized calculus with *Candida albicans*, the culture was positive after 24 hours from primary inoculation. This calculus had a particular macroscopic aspect in comparison to the rest of the calculi: it was porous and brittle, composed only of calcium phosphate, was located in renal pelvis and associated with grade III hydronephrosis. It is known that Candida is among the few microorganisms that can induce antegrade UTI from the bloodstream (24), thus it could have led to calculus colonization in our case. Multiple colonization is also possible, as in one described case in which *E. coli*, *Pseudomonas* spp., *Enterococcus* spp., and *Enterobacter cloacae* were all together found from direct calculus culture (27).

Thus, excluding the possible contaminants, the top bacteria with clinical importance recovered from calculi became *E. coli* and *Pseudomonas* spp. A similar study in our area from 2011 revealed the same etiology (28). Interestingly, *E. coli* and *Pseudomonas* spp., which are bacteria without urease activity are the most frequently found within our patients. As a limitation of the study we have to mention that we did not use additional diagnostic methods (Ureaplasma/Mycoplasma identification systems, molecular biology), thus the results will reflect only the statistics regarding the classical diagnostic methods. Nevertheless, our results are similar to those presented in other studies (10), but Shafi et al. who assessed the non-cultivable germs, described *Ureaplasma urealyticum* as the main microorganism that caused UTI associated to urolithiasis (29). Additional procedures, as Gram stained smears from calculi, may help to confirm the positive cultures, as this method seems to have a good specificity (30).

Following the urine cultures in the context of urolithiasis, the calculi were either colonized with the same bacteria found in urine or were sterile. The antibiogram typing is shown to have a relatively good discrimination power and can be used in preliminary statistics, prior to more specific methods as biotyping, ribotyping or other molecular typing methods (14). There was a good similarity between the antibiotic susceptibility pattern of the bacteria found in calculi and urine, of over 70%, but there were also some phenotypical differences, even if the bacterial species were the same; thus, the antibiotic susceptibility testing only from urine samples may not be enough for adequate management of infectious calculi and UTI. By leaving out the samples that became positive only after enrichment in the nutrient broth, only a few cases remain with sterile urine and colonized calculi; this makes us consider that initially the calculi were sustaining an upper UTI, and following it, some calculi may have remained colonized (by the persistence of bacteria in the inorganic matrix of the calculi) even after the treatment of UTI. As previously mentioned, these colonized calculi could be a trigger for further UTI, spontaneously or after non-invasive procedures such as extracorporeal lithotripsy. Thus, the study brings some arguments for the need of an adequate antibiotic therapy and perioperative prophylaxis, with efficacy on bacteria both from calculi and urine, in order to prevent the recurrence or development of new urinary infectious episodes with calculi starting point, as well as the formation of new renal calculi. Though we have found 31% resistant enterobacteria to 2nd generation cephalosporins, this class of antibiotics is the best choice for prophylaxis; according to our results, an alternative would be the aminoglycosides, but not the fluoroquinolones. Further studies are required to establish if a protocol adaptation on PNL prophylaxis is needed in our area.

In Romania there are limited studies that evaluate the presence of bacteria simultaneously in upper and lower urinary tract in patients with urolithiasis and the concordance between urinary tract infection and renal lithiasis. Thus, this study, even with the limitation of using phenotypical methods for bacterial similarity checking, brings new and clinically relevant information in urolithiasis field.

Conclusions

The data from our study revealed the presence of calculi infection even if the composition is not struvite. The presence of bacteria both in calculi and urine at the same patient may or may not require multiple antibiotherapy, depending on the each bacteria's antibiotic susceptibility. We found that in most of the cases, the same bacteria is found both in calculi and urine, and 70.4% of them were phenotypically identical. We also found that in 3.8% of cases, the calculi are infected/colonized and the urine is sterile. Therefore, the bacteriological examination of calculi associated with bacteriological examination of urine samples has a major implication in the proper treatment and prophylaxis of UTI and renal calculi. This aspect is an important one, especially for the patients with recurrence of this kind of pathologies. Further studies, based on larger groups of patients with urolithiasis, are required to obtain more precise information upon the association of UTI and calculi and to assess the proper prophylaxis regimen in our geographic area.

Abbreviations

AK	Amikacin
AMC	Amoxicillin/Clavulanic acid
AMP	Ampicillin
CAZ	Ceftazidime
CoNS	Coagulase-negative staphylococci
CRO	Ceftriaxone
CXM	Cefuroxime
FEP	Cefepime
GN	Gentamicin
IPM	Imipenem
LEV	Levofloxacin
PNL	Percutaneous nephrolithotomy
SXT	Trimethoprim/Sulfamethoxazole
TET	Tetracycline
TOB	Tobramycin
UTI	urinary tract infections

Acknowledgements

There is no conflict of interest regarding this study.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

References

1. Margaret SP, Yair L. Urinary lithiasis: Etiology, epidemiology, and pathogenesis. In: Campbell-Walsh Urology 10th Edition Review. Elsevier Health Sciences;

2011. p.1257–60.
2. Sakhaee K, Maalouf NM, Sinnott B. Clinical review. Kidney stones 2012: pathogenesis, diagnosis, and management. J Clin Endocrinol Metab. 2012 Jun;97(6):1847–60. DOI: 10.1210/jc.2011-3492
3. Li AC, Regalado SP. Emergent Percutaneous Nephrostomy for the Diagnosis and Management of Pyonephrosis. Semin Interv Radiol. 2012 Sep;29(3):218–25. DOI: 10.1055/s-0032-1326932
4. Tanwar R, Singh SK, Pawar DS. Pyelo-hepatic abscess caused by renal calculi: A rare complication. Indian J Urol. 2013;29(3):249–50. DOI: 10.4103/0970-1591.117260
5. Urinary Tract Obstruction: Obstruction of the Urinary Tract: Merck Manual Home Edition [Internet]. [cited 2014 Jun 22]. Available from: http://www.merckmanuals.com/home/kidney_and_urinary_tract_disorders/obstruction_of_the_urinary_tract/urinary_tract_obstruction.html
6. Zanetti G, Paparella S, Trinchieri A, Prezioso D, Rocco F, Naber KG. Infections and urolithiasis: current clinical evidence in prophylaxis and antibiotic therapy. Arch Ital Urol Androl. 2008 Mar;80(1):5-12.
7. Torzewska A, Budzyńska A, Białczak-Kokot M, Różalski A. In vitro studies of epithelium-associated crystallization caused by uropathogens during urinary calculi development. Microb Pathog. 2014 Jul;71-72:25–31. DOI: 10.1016/j.micpath.2014.04.007
8. Miano R, Germani S, Vespasiani G. Stones and urinary tract infections. Urol Int. 2007;79 Suppl 1:32–6. DOI: 10.1159/000104439
9. McLean RJ, Nickel JC, Beveridge TJ, Costerton JW. Observations of the ultrastructure of infected kidney stones. J Med Microbiol. 1989 May;29(1):1–7. DOI: 10.1099/00222615-29-1-1
10. Tavichakorntrakool R, Prasongwattana V, Sungkeeree S, Saisud P, Sribenjalux P, Pimratana C, et al. Extensive characterizations of bacteria isolated from catheterized urine and stone matrices in patients with nephrolithiasis. Nephrol Dial Transplant. 2012 Nov 1;27(11):4125–30. DOI: 10.1093/ndt/gfs057
11. Grabe M, Bartoletti R, Bjerklund Johansen T, Cai T, Çek M, Köves B, et al. Cystitis and pyelonephritis in adults. In: Guidelines on Urological Infections [Internet]. European Association of Urology; 2015. p. 14. Available from: http://uroweb.org/guideline/urological-infections/
12. Grabe M, Bartoletti R, Bjerklund Johansen T, Cai T, Çek M, Köves B, et al. Perioperative antibacterial prophylaxis in urology. In: Guidelines on Urological Infections [Internet]. European Association of Urology; 2015. p. 53. Available from: http://uroweb.org/guideline/urological-infections/
13. Türk C, Knoll T, Petrik A, Sarica K, Skolarikos A, Straub M, et al. Complications following PNL. In: Guidelines on Urolithiasis [Internet]. European Association of Urology; 2015. p. 21. Available from: http://uroweb.org/guideline/urolithiasis/
14. Struelens MJ. Consensus guidelines for appropriate use and evaluation of microbial epidemiologic typing systems. Clin Microbiol Infect. 1996 Aug;2(1):2–11. DOI: 10.1111/j.1469-0691.1996.tb00193.x
15. Koras O, Bozkurt IH, Yonguc T, Degirmenci T, Arslan B, Gunlusoy B, et al. Risk factors for postoperative infectious complications following percutaneous nephrolithotomy: a prospective clinical study. Urolithiasis. 2014 Oct 1;1–6.
16. Salem S, Mehrsai A, Zartab H, Shahdadi N, Pourmand G. Complications and outcomes following extracorporeal shock wave lithotripsy: a prospective study of 3,241 patients. Urol Res. 2010 Apr;38(2):135–42. DOI: 10.1007/s00240-009-0247-8
17. Honey RJD, Ordon M, Ghiculete D, Wiesenthal JD, Kodama R, Pace KT. A prospective study examining the incidence of bacteriuria and urinary tract infection after shock wave lithotripsy with targeted antibiotic prophylaxis. J Urol. 2013 Jun;189(6):2112–7. DOI: 10.1016/j.juro.2012.12.063
18. Roushani A, Falahatkar S, Sharifi SHH, Mahfoozi L, Saadat SMS, Allahkhah A, et al. Intra-operative stone culture as an independent predictor of systemic inflammatory response syndrome after percutaneous nephrolithotomy. Urolithiasis. 2014 Oct 1;42(5):455–9. DOI: 10.1007/s00240-014-0688-6
19. Bichler K-H, Eipper E, Naber K, Braun V, Zimmermann R, Lahme S. Urinary infection stones. Int J Antimicrob Agents. 2002 Jun;19(6):488–98. DOI: 10.1016/S0924-8579(02)00088-2
20. Evan AP. Physiopathology and etiology of stone formation in the kidney and the urinary tract. Pediatr Nephrol Berl Ger. 2010 May;25(5):831–41. DOI: 10.1007/s00467-009-1116-y
21. Board ADAME. Bladder stones [Internet]. PubMed Health. 2012 [cited 2014 Jun 22]. Available from: http://

www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002254/

22. Coman I. Infectiile tractului urinar. In: Tratat de urologie. Editura Medicală; 2008. p. 889–92.
23. Heckler AM, Sung J, Watters S, Martinez Acevedo A, Conlin M, Skoog S. The Long-term Incidence of Urinary Tract Infection After Endoscopic Management of Vesicoureteral Reflux. Urology. 2014 Jun 1;83(6):1383–7. DOI: 10.1016/j.urology.2013.12.045
24. Fisher JF, Kavanagh K, Sobel JD, Kauffman CA, Newman CA. Candida Urinary Tract Infection: Pathogenesis. Clin Infect Dis. 2011 May 15;52(suppl 6):S437–51. DOI: 10.1093/cid/cir108 DOI: 10.1093/cid/cir110 DOI: 10.1093/cid/cir112
25. Fowler J, Jackson E. Staphylococcus saprophyticus as the Cause of Infected Urinary Calculus. Ann Intern Med. 1985 Mar 1;102(3):342–3. DOI: 10.7326/0003-4819-102-3-342
26. Becknell B, Carpenter AR, Bolon B, Asplin JR, Ingraham SE, Hains DS, et al. Struvite Urolithiasis and Chronic Urinary Tract Infection in a Murine Model of Urinary Diversion. Urology. 2013 May;81(5):943–8. DOI: 10.1016/j.urology.2013.02.003
27. Mufarrij PW, Lange JN, Assimos DG, Mirzazadeh M, Holmes RP. Multibacterial Growth From a Surgical Renal Stone Culture: A Case Report and Literature Review. Rev Urol. 2012;14(3-4):108–14.
28. Tudor B, Toma F, Boja R, Oșan V, Cighir T, Szavuj J, et al. Bacteriological Study of Urinary Stones. Acta Medica Marisiensis. 2011 Jan 5;57(2):133–5.
29. Shafi H, Shahandeh Z, Heidari B, Sedigiani F, Ramaji AA, Pasha YRY, et al. Bacteriological study and structural composition of staghorn stones removed by the anatrophic nephrolithotomic procedure. Saudi J Kidney Dis Transplant Off Publ Saudi Cent Organ Transplant Saudi Arab. 2013 Mar;24(2):418–23. DOI: 10.4103/1319-2442.109623
30. Cockerill PA, Rivera ME, Krambeck AE. Analysis of the Utility of Stone Gram Stain in Urolithiasis Treated With Percutaneous Nephrolithotomy. Urology. 2014 Jun 1;83(6):1254–7. DOI: 10.1016/j.urology.2013.12.043