Brief Original Article | Iran J Med Microbiol. 2023; 17(3): 369-372

10.30699/ijmm.17.3.369

Iranian Journal of Medical Microbiology | ISSN:2345-4342

Urolithiasis – Do Ureaplasmas Play a Role in Etiology

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ABSTRACT

Background and Aim: Urinary tract infections (UTIs) caused by urease-producing organisms, including ureaplasmas, may contribute to urolithiasis formation. We aimed to determine the frequency of *Ureaplasma parvum* and *Ureaplasma urealyticum* among urology hospital patients with urinary stones.

Materials and Methods: The study group included 30 men with urolithiasis from Katowice, Poland. Urine samples were examined routinely for bacteria and by RT-PCR for ureaplasma DNA. Statistical analysis was done by chi-square and Fisher test ($p<0.05$ was statistically significant).

Results & Conclusion: In patients with urolithiasis, DNAs of *Ureaplasma* spp. were detected 2 times more frequently (20%) compared with controls (10%). We suggest including the detection of *Ureaplasma* spp. in the group of patients with urolithiasis and sterile leukocyturia.

Keywords: *Ureaplasma parvum, Ureaplasma urealyticum*, Urolithiasis, Infection

Received: 2022/10/22; **Accepted**: 2023/01/11; **Published Online:** 2023/06/26

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Smolec D, Gofron Z, Ekiel A. Urolithiasis – Do Ureaplasmas Play a Role in Etiology. Iran J Med Microbiol. 2023; 17(3):369-72.

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1. Introduction

Urinary stones may crystallize as a result of urinary tract infections (UTIs) **(1, 2)**. Infectious stones account for ~ 15% of urinary stone disease (USD), composed of struvite and/or carbonate apatite. Some bacterial species as *Proteus*, *Klebsiella, Pseudomonas* and *Staphylococcus* species split urea into ammonia and CO_2, causing alkaline urinary pH and the formation of stones which can lead to urinary tract obstruction **(3, 4)**. Ureaplasmas found in the human urogenital tract belong to *Ureaplasma parvum* and *Ureaplasma urealyticum*, before 1999 constituted one species – *U. urealyticum.* Identification of these species is possible only by molecular methods **(5)**. Contrary to *U. parvum*, in most cases, presence is only colonization, *U. urealyticum* is studied to be a possible etiological agent of infections, especially in symptomatic patients with NGU (*nongonococcal urethritis*) and NCNGU (*non-chlamydial, nongonococcal urethritis*) **(6, 7)**.

Usually, the routine diagnostic procedure does not include the detection of ureaplasmas. This study aimed to estimate the frequency of ureaplasma DNA in selected group of patients.

2. Materials and Methods

Thirty men with active kidney stones disease (mean age 49±11.6 yr) attending the Med Holding E. Michalowski Specialist Hospital (urology hospital) in Katowice, Poland were enrolled into this study. The samples were collected between October 2021 and April 2022. Basic laboratory tests were performed on all patients: morphology, urinalysis and urine culture test. Data on patients from the study group are presented in Table 1. Controls include thirty sexually active, healthy men without urinary tract infections (mean age 49±14.1 yr). All men gave consent to participate in this study and were informed how to

collect urine. Patients and controls were not under antibiotic and/or chemo- and antifungal therapy were not diagnosed STI and had not undergone any medical procedures for at least 4 weeks prior to this study.

FVU (*first void urine*) samples were collected (5-10 mL) in sterile plastic container and transported at + 4ºC to the Department of Medical Microbiology. Isolation of ureaplasma DNA from urine after centrifugation of urine samples at 15 000 g for 30 min was done by Bacterial & Yeast Genomic DNA Purification Kit (EURx), according to the manufacturer's instructions. Detection of *U. parvum* and *U. urealyticum* DNAs was performed by real time (RT-PCR) using MutaPLEX *Ureaplasma urealyticum /parvum* real-time PCR kit (Immundiagnostik AG, Germany) microplate system (e.g. LightCycler 96 [Roche]). Statistical analysis was done by chi-square and Fisher test ($p<0.05$ was statistically significant).

Table 1. The characteristics of patients.

	Men with urolithiasis [n=30]		
Age [years]	49±11.6		
Selected laboratory parameters			
Urine		Blood	
Leukocyturia >5	13*	Leukocytosis N: >11000/µL	2
Urine culture test-sterile	27	Creatinine >0,9 mg/dl	10
Urine culture test-not sterile	3 (*E.coli*)	GFR <60 ml/min/1,73 m^2	2
Others diseases			
Hypertension	5		
Smoking	4		
Type 2 diabetes	2		

* including: 6 men with ureaplasmas infection, 3 men with *E. coli* infection, 4 men with no detected bacteria in urine

3. Results and Discussion

The occurrence of ureaplasmas (*U. parvum* and *U. urealyticum)* was performed more frequently in FVU of the study group of men than in control – 20% vs. 10%, respectively ($p>0.05$). DNA of *U. urealyticum* was detected in 3/30 patients with urolithiasis (10%) and only in 1/30 men (3.3%) from the control group. *U. parvum* was also frequently isolated from FVU patients in the study group than in controls (10% vs. 6%, respectively) (Table 2). However, these differences were not statistically significant.

Table 2. Occurrence of *U. parvum* and *U. urealyticum* in the study groups.

	Men with urolithiasis [n=30]	**Control group** [n=30]	**P value**
	N (%)		
U. urealyticum	3 (10)	1 (3.3)	0.3060
U. parvum	3 (10)	2 (6)	0.5000
Total	6 (20)	3 (10)	0.2716

Bacterial infections were noted in 9 men from the study group; in 6 of them, *Ureaplasma* spp. DNA was detected and in 3 men – *Escherichia coli*. In all infected patients (9/9) leukocyturia was found. Among 21 patients from study group with no bacterial infection, leukocyturia was presented only in 4 men (4/21). This difference was statistically significant ($p=0.00005$). Leukocyturia was also significantly more frequent ($p=0.00289$) in men with ureaplasma infection (6/6) compared to the remaining 24 men from the study group without *Ureaplasma* spp. (7/24). No relationship was found between the rest of the laboratory test results or others diseases in the study group (Table 1).

Potentially, microorganisms cultured from stones (urine also), with or without a clinically apparent UTI, could cause kidney inflammation and turn potentiate crystal retention and stone formation **(8-10)**. According to medical literature, *E. coli* as the most common microorganism typically related to urinary stones, followed by the urease-producing bacteria typically involved in struvite stone formation **(11, 12)**. However, the standard urine culture protocols do not include fastidious and slow growing bacteria, such as *Ureaplasma* spp **(13)**. Meanwhile, the role of *Ureaplasma* spp. in the development of urinary stones was shown *in vivo* in rats **(9, 14)**. In Mobarak and Tharwat's study, the results of urine culture tests from 30 patients with urinary infection stones were performed: 86.7% of patients were infected with *E. coli* (46.7%), *Klebsiella* spp. (30%), *Proteus* spp. (6.7%), *Pseudomonas* spp. (3.3%), 26.7% positive results were obtained for *U. urealyticum* **(15)**. Our study found ureaplasma DNA in 20% of study group patients. A similar frequency of ureaplasma infections was observed in men with urethritis. Maeda et al. detected *U urealyticum* and *U. parvum* in 16.3% and 7.8% of men with NGU, respectively. In NCNGU patients, the frequency of ureaplasmas was 18.8% and 8.8%, respectively **(16)**. Although a higher incidence of Ureaplasma spp. in infertile men was demonstrated in a study by Zhou et al., the occurrence of *Ureaplasma* spp. in semen specimens was 39.6% (214/540) **(17)**. In patients with urolithiasis, leukocyturia occurs in ~3% of patients, mostly due to urinary tract infection (UTI) **(18)**. Vlasic-Matas et al. found that in patients with uncomplicated recurrent urinary tract infections, leukocyturia was more frequent with *U. urealyticum* infection than in patients with *C. trachomatis* **(19)**. In our study, leukocyturia was also significantly more frequent in men with ureaplasma infection. Twenty % of positive results for ureaplasma DNA (p=0.2716) were observed in men with urolithiasis.

4. Conclusion

We suggest a possible role of ureaplasmas in urolithiasis and the necessity to include detection of *Ureaplasma* spp. in the group of patients with urolithiasis and sterile leukocyturia.

This study will be continued with the larger number of patients in the studied groups.

Acknowledgment

None.

Ethics approval & Consent to Participate

The study was approved by the Bioethical Committee of the Medical University of Silesia in Katowice (KNW/0022/KB1/48/II/14/16/17).

Authors' contributions

Study concept and design DS and AE. Analysis and interpretation of data: DS and AE. Drafting of the manuscript: DS and AE. Material's collection: ZG and DS. Critical revision of the manuscript for important intellectual content: AE. Statistical analysis: DS. The corresponding author was responsible for the manuscript's final content and the decision to submit it for publication.

Funding

This study was supported by Grant number PCN-2-O36/N/9/N and KNW-1-126/K/0/I of Medical University of Silesia, Katowice, Poland.

Conflict of Interest

The authors declare no conflicts of interest.

Reference

1. Edvardsson VO, Indridason OS, Haraldsson G, Kjartansson O, Palsson R. Temporal trends in the incidence of kidney stone disease. Kidney Int. 2013;83(1):146-52. [DOI:10.1038/ki.2012.320] [PMID]
2. Türk C, Knoll T, Petrik A, Sarica K. Guidelines on Urolithiasis. Eur Assoc Urol. 2015(8).
3. Bichler KH, Eipper E, Naber K, Braun V, Zimmermann R, Lahme S. Urinary infection stones. Int J Antimicrob Agents. 2002;19(6):488-98. [DOI:10.1016/S0924-8579(02)00088-2] [PMID]
4. de Cógáin MR, Lieske JC, Vrtiska TJ, Tosh PK, Krambeck AE. Secondarily Infected Nonstruvite Urolithiasis: A Prospective Evaluation. Urology. 2014;84(6):1295-300. [PMID] [PMCID] [DOI:10.1016/j.urology.2014.08.007]
5. Kong F, Ma Z, James G, Gordon S, Gilbert GL. Species identification and subtyping of Ureaplasma parvum and Ureaplasma urealyticum using PCR-based assays. J Clin Microbiol. 2000;38(3):1175-9. [DOI:10.1128/JCM.38.3.1175-1179.2000] [PMID] [PMCID]
6. Ondondo RO, Whittington WLH, Astete SG, Totten PA. Differential association of ureaplasma species with non-gonococcal urethritis in heterosexual

men. Sex Transm Infect. 2010;86(4):271-5. [DOI:10.1136/sti.2009.040394] [PMID] [PMCID]

7. Beeton ML, Payne MS, Jones L. The role of Ureaplasma spp. in the development of nongonococcal urethritis and infertility among men. Clin Microbiol Rev. 2019;32(4):e00137-18. [DOI:10.1128/CMR.00137-18] [PMID] [PMCID]
8. Kramer G, Klingler HC, Steiner GE. Role of bacteria in the development of kidney stones. Curr Opin Urol. 2000;10(1). [PMID] [DOI:10.1097/00042307-200001000-00009]
9. Reyes L, Alvarez S, Allam A, Reinhard M, Brown Mary B. Complicated Urinary Tract Infection Is Associated with Uroepithelial Expression of Proinflammatory Protein S100A8. Infect Immun. 2009;77(10):4265-74. [DOI:10.1128/IAI.00458-09] [PMID] [PMCID]
10. Boonla C, Krieglstein K, Bovornpadungkitti S, Strutz F, Spittau B, Predanon C, et al. Fibrosis and evidence for epithelial-mesenchymal transition in the kidneys of patients with staghorn calculi. BJU Int. 2011;108(8):1336-45. [PMID] [DOI:10.1111/j.1464-410X.2010.10074.x]
11. Golechha S, Solanki A. Bacteriology and chemical composition of renal calculi accompanying urinary tract infection. Indian J Urol. 2001;17(2):111.
12. 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;27(11):4125-30. [DOI:10.1093/ndt/gfs057] [PMID]
13. Schwaderer AL, Wolfe AJ. The association between bacteria and urinary stones. Ann Transl Med. 2017; 5(2):32. [DOI:10.21037/atm.2016.11.73] [PMID] [PMCID]
14. Yüce A, Yücesoy M, Yücesoy K, Canada T, Fadiloğlu M, Güre A, et al. Ureaplasma urealyticum-induced urinary tract stones in rats. Urol Res. 1996;24(6): 345-8. [DOI:10.1007/BF00389791] [PMID]
15. Mobarak A, Tharwat A. Ureaplasma urealyticum as a causative organism of urinary tract infection stones. J Egypt Public Health Assoc. 1996;71(3-4): 309-19.
16. Maeda S-I, Deguchi T, Ishiko H, Matsumoto T, Naito S, Kumon H, et al. Detection of Mycoplasma genitalium, Mycoplasma hominis, Ureaplasma parvum (biovar 1) and Ureaplasma urealyticum (biovar 2) in patients with non-gonococcal urethritis using polymerase chain reaction-microtiter plate hybridization. Int J Urol. 2004; 11(9):750-4. [PMID] [DOI:10.1111/j.1442-2042.2004.00887.x]
17. Zhou YH, Ma HX, Shi XX, Liu Y. Ureaplasma spp. in male infertility and its relationship with semen quality and seminal plasma components. J Microbiol Immunol Infect. 2018;51(6):778-83. [DOI:10.1016/j.jmii.2016.09.004] [PMID]
18. Szczeklik A, Gajewski P. Interna Szczeklika. Publisher: MP Cracow. 2017.
19. Vlasic-Matas J, Raos H, Vuckovic M, Radic S, Capkun V. Prevalence of Ureaplasma urealyticum, Mycoplasma hominis and Chlamydia trachomatis in patients with uncomplicated recurrent urinary tract infections. Nephrol Renal Dis. 2019;4:1-4. [DOI:10.15761/NRD.1000150]