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Major article

# Bacteriuria and urinary tract infection after female urodynamic studies: Risk factors and microbiological analysis

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*Key Words:*
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***Background:*** This study was conducted to determine risk factors for infectious complications after urodynamic study (UDS) in women, which can assist clinicians in identifying high-risk subjects who would benefit from antibiotic prophylaxis before UDS.

***Methods:*** In this prospective cohort study, we studied 232 women who underwent UDS at Santa Casa de São Paulo School of Medical Sciences between June 2013 and June 2014. Women ranging in age from 26 to 84 years who had urinary incontinence, pelvic organ prolapse, or voiding dysfunction were required to collect urine samples at 7 days before, on the day of, and 3-5 days after UDS. Urine cultures with >100,000 CFU/mL were considered positive. Risk factors associated with bacteriuria and urinary tract infection (UTI) after UDS were evaluated using multivariate analysis with multiple logistic regression.

***Results:*** Two hundred thirty-two out of 257 women were subjected to further analysis. The incidence of bacteriuria, transient bacteriuria, and UTI after UDS was 11.6%, 7.3%, and 4.3%, respectively. On multivariate analysis, hypothyroidism ($P = .04$), body mass index (BMI) >30 ($P = .025$), and advanced pelvic organ prolapse ($P = .021$) were associated with a significantly increased risk of bacteriuria; however, only BMI >30 ($P = .02$) was associated with an increased risk for UTI.

***Conclusions:*** The rate of infectious complications after UDS was low, and advanced pelvic organ prolapse and hypothyroidism increased the risk for bacteriuria. However, only BMI >30 was associated with bacteriuria and UTI after UDS.



Urologic procedures may cause trauma to the urinary tract epithelium and consequently infectious complications may occur, with bacteriuria developing in 1%-5% of patients subjected to a single urinary catheterization episode.[1] A urodynamic study (UDS) has been frequently indicated for evaluating lower urinary tract dysfunction, such as urinary incontinence.[2] A UDS involves urinary catheterization, which may increase the risk of urinary tract infection (UTI).[2,3] The incidence of bacteriuria or UTI after UDS in women is not yet well established, reportedly ranging from 1.5% to 30% after cystometry[4,5]; consequently, information regarding the safety of UDS and the need for routine antibiotic prophylaxis remains limited. In previous studies, advanced age,[3,4] recurrent UTI, and previous urologic surgery were the risk factors most often associated with the development of UTI after UDS.[2,6]

Studies have shown that the natural history of UDS-related bacteriuria is not well understood. It is often asymptomatic and transient, with *Escherichia coli* the most prevalent microorganism identified from urine cultures.[2,3,6-8] The consequences of UTI may be serious; however, in most women, it manifests in the form of cystitis which is easily recognized and treated with oral antibiotics. In a small group of patients (2.6%), the urinary pathogen can ascend through the urinary tract and cause life-threatening infections, such as pyelonephritis and severe sepsis, which require hospitalization.[2]

Given the divergence in the rates of bacteriuria and UTI and possible predisposing factors associated with infectious complications after UDS, the present study aimed to determine the incidence of bacteriuria after UDS in women, as well as to identify the risk

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factors, most prevalent microorganisms, and antimicrobial susceptibility profile.

## PATIENTS AND METHODS

### *Study population*

A prospective cohort study was conducted with 257 women who underwent UDS between June 2013 and June 2014 at the Obstetrics and Gynecology Department, Santa Casa de São Paulo School of Medical Sciences. The study included women aged 26-84 years who had urinary incontinence and advanced pelvic organ prolapse with suspected occult urinary incontinence and voiding dysfunction. Subjects who had bacteriuria before the test, had used an indwelling urinary catheter, had been submitted to intermittent catheterization, had taken systemic antibiotics in the preceding 15 days, had a neurogenic bladder, or who refused participation were excluded from the study. All included subjects provided informed signed consent before participating in the study. The study was reviewed and approved by the school's Institutional Review Board.

### *Diagnosis of bacteriuria, transient bacteriuria, asymptomatic bacteriuria, and UTI*

Bacteriuria was defined as a bacterial count in urine culture of $\geq$100,000 colony- forming units (CFU)/mL. Transient bacteriuria was defined as a bacterial count $\geq$100,000 CFU/mL in an asymptomatic patient in a single urinalysis. Asymptomatic bacteriuria was defined as a bacterial count $\geq$100,000 CFU/mL in an asymptomatic patient in at least 2 urinalyses performed within a 1-week period. UTI was diagnosed in symptomatic subjects (dysuria, polyuria, urinary urgency) with a urine culture containing $\geq$100,000 CFU/mL in at least 1 urinalysis.

### *Collection of urine samples and microbiological analysis*

Urine samples were collected for culture 7 days before the test. When the first urine sample was negative, subjects were asked to collect a new sample on the day of the test and another sample at 3-5 days after the UDS. Subjects were asked to collect urine samples themselves, after reading a guide on vulvar hygiene and the proper procedure for collecting urine in a sterile container. After urine collection, the samples were sent to a local microbiology laboratory for analysis. After homogenization with a calibrated (0.01 μL) sterile loop, each sample was inoculated into chromogenic medium for identification of urinary pathogens (CPS ID3; bioMérieux, Durham, NC). The chromogenic medium was incubated for 48 hours at $35 \pm 2^{\circ}$C in ambient air, the Petri dishes were examined daily for bacterial growth, and bacterial counts were recorded (in CFU/mL). The susceptibility test was performed in accordance with Clinical Laboratory Standards Institute guidelines, as were the tests carried out on the antimicrobialsfor different bacterial species.

### *UDS*

Before the scheduled examination, each subject completed a questionnaire inquiring about age, body mass index (BMI), parity, menopausal status, sexual activity, comorbidities, previous urinary incontinence surgery, history of recurrent UTI history, and pelvic organ prolapse. The subject was instructed to have full urinarybladder for UDS. The urinary flow rate was measured, and the subject was encouraged to completely empty her bladder. The subject was placed in the gynecologic position, and vulvar, external urethral meatus, and perineal region disinfection was performed with aqueous 2% chlorhexidine. After adequate lubrication with sterile jelly lubricant, a bladder pressure catheter (6 F) and bladder filling catheter (8 F) were inserted into the bladder, and a 10 F rectal balloon catheter was inserted into the rectum to measure intra-abdominal pressure.

Next, the subject was seated on a chair with a flow meter along with the pressure catheters connected to the transducers and the infusion catheter connected to the saline solution equipment. The set of transducers was positioned at the level of the subject's pubic symphysis, and the equipment was calibrated. The UDS was performed using the urodynamic Uranus (Alacer Biomédica, São Paulo, Brazil) and consisted of 3 steps: uroflowmetry, cystometry, and flow/pressure study, according to the guidelines of the International Continence Society.[9] The examination was performed with the subject placed according to local protocol.[10] After UDS, the subject was informed about the possibility of local irritation symptoms and the need for oral hydration. She was instructed to contact the outpatient clinic if there no spontaneous improvement of local symptoms occurred or if such symptoms as fever, dysuria, suprapubic pain, or hematuria developed.

### *Follow-up*

One week after UDS, subjects were actively contacted by telephone, to inform them of the results of their urine tests and to investigate the possible appearance of new signs or symptoms of UTI. Subjects presenting with a UTI were treated with antibiotics according to the results of the susceptibility tests.

### *Statistical analysis*

This analysis was performed using the presence or absence of bacteriuria as the primary outcome variable and considering the following qualitative variables: sexual activity, menopausal status, recurrent UTI, and pelvic organ prolapse—the most influential factors in the primary outcome. The sample size was set at a total of 220 participants; the tests were executed with a significance level of $\alpha = 0.05$ (5%) and with 80% power ($\beta = 0.80$). In anticipation of a 15% follow-up loss, 257 patients were included in the study. Qualitative variables are described by absolute (n) and relative (%) frequencies; quantitative variables are presented as mean, median, and standard deviation (SD). The associations among the qualitative variables were analyzed using analysis of variance (ANOVA) and the test for equality of 2 proportions. Odds ratio (OR) and 95% confidence interval (CI) were calculated for all outcomes. All *P* values were 2-tailed, and the level of statistical significance was set at $P < .05$. We also evaluated the risk factors associated with the presence of bacteriuria and UTI, using multivariate analysis with multiple logistic regression. All analyses were performed with SPSS 17.0 (SPSS, Chicago, IL) and Minitab 16 (Minitab, State College, PA).

## RESULTS

A total of 257 women who underwent UDS were enrolled in the study. Twenty-two subjects with no urine sample collected after UDS and 3 subjects with bacteriuria at the time of the UDS were excluded. Two hundred and thirty-two subjects (90%) were analyzed, with a mean age of 56 (range, 26-84 years). After UDS, bacteriuria was detected in 27 women (11.6%), transient bacteriuria was diagnosed in 17 women (7.3%; 95% CI, 4.0%-10.6%), and UTI was diagnosed in 10 women (4.3%; 95% CI, 1.6%-6.9%). Asymptomatic bacteriuria was not detected in any subject. Tables 1 and 2 summarize the demographic and clinical characteristics of the 232 subjects based on the presence or absence of bacteriuria and UTI after UDS.

**Table 1**
Clinical and demographic characteristics of the 232 subjects with or without bacteriuria after UDS

| Characteristic | Bivariate analysis | | | | Multivariate analysis | |
|---|---|---|---|---|---|---|
| | With bacteriuria (n = 27) | Without bacteriuria (n = 205) | OR (95% CI) | *P* value | OR (95% CI) | *P* value |
| Age, y, mean (range) | 60 (41-83) | 56 (26-84) | — | .062 | — | — |
| BMI, mean (range) | 30.6 (23.2-43.6) | 28.8 (16-3.3) | — | .089 | **1.10 (1.01-1.20)** | **.025** |
| Parity, mean (range) | 4.2 (0-10) | 3.6 (0-13) | — | .152 | — | — |
| Clinical characteristics, n (%) | | | | | | |
| Previous urinary incontinence surgery | 4 (14.8) | 27 (13.2) | 1.15 (0.37-3.57) | .813 | — | — |
| Dyslipidemia | 5 (18.5) | 25 (12.2) | 1.64 (0.57-4.71) | .357 | — | — |
| Diabetes | 7 (25.9) | 40 (19.5) | 1.44 (0.57-3.65) | .436 | — | — |
| Hypertension | 15 (55.6) | 84 (41) | 1.80 (0.80-4.04) | .150 | — | — |
| Hypothyroidism | 6 (22.2) | 15 (7.3) | **3.62 (1.27-10.33)** | **.011** | **3.44 (1.03-11.43)** | **.044** |
| Recurrent UTI | 2 (7.4) | 16 (7.8) | 0.95 (0.21-4.36) | .942 | — | — |
| Menopause | 20 (74.1) | 126 (61.5) | 1.79 (0.72-4.43) | .202 | — | — |
| Active sexual life | 16 (59.3) | 121 (59) | 1.01 (0.45-2.28) | .981 | — | — |
| Advanced pelvic organ prolapse | 8 (29.6) | 24 (11.7) | **3.18 (1.25-8.04)** | **.011** | **3.67 (1.21-11.08)** | **.021** |

Note: bold indicates statistic significance $P < .05$.
All percentages are relative to the number of subjects with or without bacteriuria. Patient characteristics were compared using ANOVA. All tests were 2-tailed, and $P < .05$ was considered significant.

**Table 2**
Clinical and demographic characteristics of the 232 subjects with or without UTI after UDS

| Characteristic | With UTI (n = 10) | Without UTI (n = 222) | OR (95% CI) | *P* value |
|---|---|---|---|---|
| Age, y, mean (range) | 58.6 (41-78) | 56.1 (26-84) | — | .487 |
| BMI, mean (range) | 31.8 (24.7-43.6) | 28.9 (16-53.3) | — | .087 |
| Parity, mean (range) | 4.3 (1-9) | 3.6 (0-13) | — | .344 |
| Clinical characteristics, n (%) | | | | |
| Previous urinary incontinence surgery | 2 (20) | 29 (13.1) | 1.66 (0.34-8.22) | .528 |
| Dyslipidemia | 2 (20) | 28 (12.6) | 1.73 (0.35-8.57) | .496 |
| Diabetes | 4 (40) | 43 (19.4) | 2.78 (0.75-10.27) | .112 |
| Hypertension | 5 (50) | 94 (42.3) | 1.36 (0.38-4.84) | .632 |
| Hypothyroidism | 2 (20) | 19 (8.6) | 2.67 (0.53-13.49) | .217 |
| Recurrent UTI | 0 (0) | 18 (8.1) | ND | .348 |
| Menopause | 7 (70) | 139 (62.6) | 1.39 (0.35-5.54) | .636 |
| Active sexual life | 7 (70) | 130 (58.6) | 1.65 (0.42-6.55) | .472 |
| Advanced pelvic organ prolapse | 3 (30) | 29 (13.1) | 0.5 (0.09-1.43) | .129 |

*ND*, not done; no statistical test could be applied.
All percentages are relative to the number of women with and without bacteriuria. Patient characteristics were compared using ANOVA. All tests were 2-tailed, and $P < .05$ was considered significant.

In the bivariate analysis, only the presence of hypothyroidism ($P = .011$) and the presence of advanced pelvic organ prolapse ($P = .011$) were significantly associated with bacteriuria after UDS, and no risk factor was identified for the presence of UTI. However, the multivariate analysis identified hypothyroidism ($P = .044$), BMI $\geq$30 kg/m$^2$ ($P = .025$), and advanced pelvic organ prolapse ($P = .021$) were significant risk factors for bacteriuria (Table 1), whereas only BMI $\geq$ 30 kg/m$^2$ was significantly associated with UTI after UDS (OR, 1.16; 95% CI, 1.01-1.32; $P = .02$).

Irritative lower urinary tract symptoms, mainly dysuria, were observed in 122 subjects (52%). These symptoms persisted for 1-5 days (average, 1.5 days) in 108 subjects (89%). Fourteen women required therapy for symptom relief, 10 (8%) needed antibiotics for UTI, and 4 (3%) were treated with analgesic drugs.

Table 3 summarizes the microorganisms identified in urine cultures of 27 subjects with bacteriuria and 10 subjects with UTI. Gram-negative bacilli were highly predominant, with *Klebsiella* spp, *Escherichia coli*, and *Proteus* spp the most frequently isolated. *Candida* spp were identified in only 1 subject presenting with bacteriuria. The most commonly identified microorganism in subjects presenting with UTI was *E coli*. Fig 1 shows the antimicrobial susceptibility of Enterobacteriaceae identified in 25 subjects with bacteriuria after UDS.

## DISCUSSION

It is well established that urethral manipulation may increase the risk of bacteriuria and UTI in women,[11,12] with the reported rate of infection after UDS ranging from 3% to 20%.[13,14] Previous studies have shown that the natural history of UDS-associated bacteriuria is most often asymptomatic and transient, but incompletely understood; its occurrence can result either from urethral manipulation or from catheterization-related trauma of the urethral mucosa, increasing susceptibility of the urinary tract to delayed UTI.[3,4,6,8,15] The incidence of UDS-associated bacteriuria in our cohort was in accordance with previously published data; transient bacteriuria and UTI were detected at acceptable rates (7.3% and 4.3%, respectively) at 3-5 days after UDS. Interestingly, neither of the subjects presented with asymptomatic bacteriuria. Rates of UDS-associated infections were reported by Choe et al[6] as 6.2% for bacteriuria and 2.9% for UTI, and by Bombieri et al[4] as 8% for bacteriuria and only 0.5% for UTI. However, Quek et al[7] reported rates as high as 14% for bacteriuria, 2% for UTI, 7.6% for transient bacteriuria, and 4.6% for asymptomatic bacteriuria at 3-7 days after UDS. Tsai et al[14] and Okorocha et al[11] found a much higher rate (20%) of UTI after UDS. Compared with these previously published data, the discrepancies in the rates of bacteriuria and UTI in women after UDS found in our cohort may be related to urine sample collection either too early or too late after UDS, differences in our study population, or even modifications in urinary catheterization techniques.[4,11]

Regarding irritative symptoms that frequently occur after UDS,[12] urinary signs and symptoms were reported by one-half of the subjects, but most had a spontaneous resolution. In fact, such symptoms were mild and transient, and no correlation with the development of bacteriuria or UTI was observed. Quek and Tay

**Table 3**
Distribution of microorganisms identified urine culture in 27 subjects with bacteriuria after UDS

| | Bacteriuria (n = 27) | | UTI (n = 10)* | |
|---|---|---|---|---|
| Microorganism | n | % | n | % |
| *Klebsiella* spp | 8 | 30 | 2 | 20 |
| *Escherichia coli* | 7 | 26 | 4 | 40 |
| *Proteus* spp | 7 | 26 | 2 | 20 |
| *Citrobacter* spp | 3 | 11 | 2 | 20 |
| *Pseudomonas aeruginosa* | 1 | 4 | 0 | 0 |
| *Candida* spp | 1 | 4 | 0 | 0 |

*Microorganisms causing UTI.

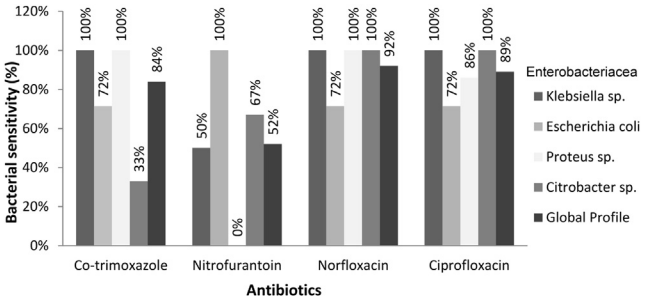


**Fig 1.** Susceptibility profile of Enterobacteriaceae identified in 25 subjects with bacteriuria after UDS.

(2004)[7] reported irritative symptoms in 25% of their subjects after UDS, however, spontaneous resolution occurred after 5 days. Bombieri et al (1999)[4] reported comparable results, with symptoms in 34% of patients after UDS, with spontaneous resolution within 2 days.

The identification of risk factors associated with the development of urinary complications after UDS is crucial for improving the knowledge of individuals, who should always by advised regarding the predisposition to develop bacteriuria and UTI after UDS. Advanced age, recurrent UTI, and previous urinary incontinence surgery have been identified as predisposing patient-related factors for bacteriuria and UTI after UDS.[2-4,6] Interestingly, in the present study we identified different patient-related factors for UDS-associated bacteriuria, including hypothyroidism, BMI >30, and advanced pelvic organ prolapse. Before this study, only BMI >30 had been independently associated with UTI after UDS. Bombieri et al,[4] Yip et al,[2] and Dass et al[3] identified advanced age as a well-defined risk factor for bacteriuria related to urinary catheterization; however, we found no significant correlation between advanced age and either bacteriuria or UTI after UDS. So far, there has been no report of correlations between hypothyroidism and infectious complications after UDS. We hypothesized that most patients with hypothyroidism may have had Hashimoto's thyroiditis, an autoimmune disease determinant of immunosuppression that might have increased the incidence of bacteriuria.[16,17] Nevertheless, this variable showed a risk factor association with transient bacteriuria in the bivariate and multivariate analyses. We found that patients with advanced pelvic organ prolapse were at greater risk for developing bacteriuria and UTI; these patients often have incomplete bladder emptying and increased residual volume, which have been associated with lower urinary tract infection and could explain the increased risk of infection.[18] In agreement with a previous study,[19] we found an association between higher BMI and UTI; however, the pathophysiology of this association remains unclear, owing to the lack of studies addressing this issue. As speculated by Semins et al,[19] we also argue that an association between obesity and other comorbidities may increase the risk of infectious complications, such as UTI.

The microbial spectrum identified in urine cultures of our subjects with bacteriuria after UDS was slightly different from that reported by other authors. Our results identified *Klebsiella* spp as the most common pathogen detected, followed by *E coli*, *Proteus* spp, and *Citrobacter* spp. Bombieri et al,[4] Quek and Tay,[7] and Yip et al[2] reported a predominance of *E coli* in bacteriuria and UTI, followed by other Enterobacteriaceae, including *Klebsiella* spp. In accordance with many other authors, we identified *E coli* as the most common pathogen in women with UDS-associated UTI.[3,5,6,20] Importantly, the susceptibility profiles of community-acquired UTI (CA-UTI) of *E coli* and *Klebsiella* spp have changed in recent decades, showing a significant increase in extended-spectrum β-lactamase (ESBL) producers.[21] Recently, Salles et al reported that in Latin American countries, including Brazil, there has been an increasing prevalence of ESBL-producing *E coli* causing CA-UTI with resistance to cotrimoxazole, quinolones, and second-generation cephalosporins.[21] According to our data, the overall susceptibility profile of Enterobacteriaceae is highly variable, with a worrisome resistance profile to nitrofurantoin and acceptable susceptibility to cotrimoxazole and quinolones. *Proteus* spp and *Citrobacter* demonstrated complete and intermediate levels of resistance to nitrofurantoin, respectively. On the other hand, *E coli* already exhibited an alarming rate of resistance to quinolones and cotrimoxazole.

Our study had some limitations. The time to urine sample collection after UDS ranged from 3 to 5 days; however, samples collected after 7 days could identify later infections, which in turn could show a higher number of infectious complications. Another limitation was the lack of control over the aseptic conditions in which the urine samples were collected, because they were collected by the subjects themselves. A recent systematic review assessed the impact of antibiotic prophylaxis to reduce infectious complications after UDS, and concluded that the use of antibiotics reduces only bacteriuria, but not UTI.[1] That study has also concluded that antibiotic prophylaxis would be beneficial after UDS only if UTI rates were expected to exceed 10%.[1] We detected a low rate of UTI after UDS, which led us to conclude that antibiotic prophylaxis for women before UDS should be discouraged for ordinary procedures. All patients with risk factors should be warned that complications could occur owing to the possibility of a delayed UTI after UDS.

In conclusion, UDS appears to be a safe medical procedure associated with a low incidence of UTI, and women with a BMI >30 may benefit from antibiotic prophylaxis before UDS. Further studies addressing this issue should be encouraged to confirm our results.

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