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Major article

Catheter-associated candiduria: Risk factors, medical interventions, and antifungal susceptibility

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Background: Catheter-associated candiduria is a common clinical finding in hospitalized patients, especially in the intensive care unit. The objective of this study was to obtain demographic and clinical data regarding the prevalence of *Candida* spp in catheterized in-patients and the medical interventions provided to these patients in a northern Israeli hospital between 2011 and 2013.

Methods: Isolation and identification of microorganisms were performed on 1,408 urine culture samples 48 hours after catheter insertion. Antifungal Etest susceptibility tests were carried out on every *Candida*-positive urine sample. Demographic and clinical data were gathered to determine risk factors and medical interventions.

Results: Candiduria was detected in 146 catheterized in-patients out of the 1,408 patients included in this study. *C albicans* was detected in most cases (69.1%). Fever was observed in 52 (35.61%) patients, and leukocyturia was observed in 48 cases (32.87%). Diabetes mellitus was associated with *C albicans* candiduria. There were 93 patients (63.69%) who did not receive any medical intervention for their candiduria.

Conclusion: *Candida* is the second leading pathogen causing catheter-associated urinary tract infection or asymptomatic colonization, whereas previous studies showed *Candida* as the third leading pathogen. Clinical signs and symptoms, such as fever and laboratory tests, cannot distinguish between asymptomatic colonization and infection. Because the management of catheter-associated candiduria is still controversial, additional studies should be carried out.

The presence of microorganisms such as *Candida* spp in urine samples of hospitalized patients is a common clinical finding. *Candida*, a saprophytic yeast, colonizes the mucosal surfaces and external genitalia of both men and women, especially in premenopausal women's urethral meatus area. In the general population, >1% of urine samples contain *Candida* in a measurable quantity; however, in hospitalized patients this rate is 5-10 times higher. Most hospitalized patients diagnosed with candiduria or *Candida* urinary tract infection (UTI) were treated at intensive care units (ICUs) or had a urethral catheter.[1]

Candida spp account for 20% of the UTIs in the setting of ICUs. They are considered to be the second leading pathogen causing UTI in ICUs after *Escherichia coli*.[2]

Most cases of candiduria are nosocomial because of the use of catheters and antibiotic therapy. Women are more likely to develop candiduria. Advanced age, ICU hospitalization, surgery, and preexisting diabetes mellitus are other known risk factors for candiduria.[3]

Candiduria has 3 categories of severity: (1) colonization or contamination—asymptomatic (most common presentation[4]), (2) UTI—cystitis or pyelonephritis, and (3) systemic infection, mostly in immunocompromised patients.

Catheter-associated urinary tract colonization is the leading cause of secondary nosocomial infection in hospitalized patients. Candiduria is unavoidable in 50% of patients with urethral catheters for >5 days.[5]

Catheter-associated UTI can be extraluminal (entrance of microorganisms through the catheter biofilm to the urine bladder), as in most cases, or intraluminal (urine stasis caused by drainage

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Conflicts of interest: None to report.

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Table 1
Organisms that were specified in all positive urine cultures

Organism	n (%)
Escherichia coli	294 (39.25)
Candida	146 (19.49)
C albicans	101 (69.17)
C parapsilosis	14 (9.58)
C krusei	11 (7.53)
C tropicalis	9 (6.16)
C glabrata	7 (4.79)
Other *Candida*	4 (2.73)
Pseudomonas	114 (15.22)
Enterococcus	76 (10.15)
Klebsiella	68 (9.08)
Proteus	30 (4.01)
Other	21 (1.49)

Table 2
Clinical features of catheter-associated candiduria

Clinical feature	n (%)
Fever	52 (35.61)
Leukocyturia	48 (32.87)
Bacterial coinfection and colonization	17 (11.64)
Candida in urine sediment	41 (28.08)
Antibiotic use	68 (46.57)
Immunosuppression	13 (08.90)
Diabetes mellitus	19 (13.01)
Malignancy	9 (06.16)
Candidemia	0 (0)

failure or ascending infection caused by contamination of the urine collection bag).[6]

The lower urinary tracts are commonly the primary infection site.[3] In rare conditions, the infection can spread toward the kidneys and damage their parenchyma and cause candidemia. This can happen in the setting of urinary tract obstruction. Hematogenous spread of *Candida* to the kidneys is possible in immunocompromised patients.[7-9]

The decision whether to treat catheter-associated candiduria is controversial because candiduria can be a sign of colonization where treatment is not required or upper or lower UTI where treatment is mandatory. Previous studies[10] and current guidelines[11] recommend catheter removal (or replacement) and controlling other risk factors as first-line therapy in asymptomatic colonization. Postcatheterization asymptomatic candiduria usually resolves without specific antifungal therapy. Current recommendations are to not administer antifungal agents unless the patient is symptomatic or at high risk for dissemination, such as postrenal transplant patients, low birth weight infants, and patients who are undergoing urinary tract instrumentation. When antifungal treatment is considered, amphotericin B, fluconazole, and voriconazole are the recommended antifungal agents.[12-14]

The aim of this study is to obtain demographic and clinical data regarding the prevalence of *Candida* spp in catheterized in-patients and the medical interventions provided to these patients in a northern Israeli hospital between 2011 and 2013. In addition, susceptibility of *Candida* spp obtained from catheterized patients to common antifungal agents was tested.

MATERIALS AND METHODS

Patient characteristics

There were 1408 hospitalized patients with urethral catheters included in this study. All patients were hospitalized between 2011 and 2013 at our medical center, a 300-bed general hospital in northern Israel. Pediatric patients were not included in this study. Of the patients, 506 were women (36%), and 902 were men. The mean age was 58.5 years. At least 1 urinary sample was obtained from each patient 48 hours after urinary catheter installation. All demographic and medical data were obtained from the hospital's digital medical records.

Culture and antifungal susceptibility tests

Every urine sample was sent to the clinical microbiology laboratory in a sterile container. All samples were refrigerated up to 12 hours from the time they were obtained. Samples were inoculated using a 1-μL calibrated loop on CHROMagar Orientation (BD Diagnostics, Sparks, MD), which is a chromogenic agar that allows the preliminary identification of uropathogens. Plates were examined after incubation of 24 and 48 hours at 37°C. Significant candiduria was defined as the growth of ≥10,000 colony forming units/mL. *Candida* growth was initially identified by microscopic examination of suspected colonies. Later, those colonies were transformed to CHROMagar Candida agar (hy-labs, Rehovot, Israel), which allows *Candida* specification by colony color: *C albicans* (light to medium green), *C krusei* (mauve to rose pink), and *C tropicalis* (dark blue to metallic blue, with or without halos). The VITEK 2 (bioMérieux, Marcy l'Etoile, France) automated microorganism identification system was used to specify colonies that were not categorized.

Candida Etest susceptibility examinations to antifungal agents fluconazole, voriconazole, and amphotericin B were carried out on RPMI 1640 Agar with MOPS and 2% Glucose (hy-labs, Rehovot, Israel). The *Candida* colony was fluidized in a 0.85% NaCl solution creating a 0.5 McFarland standard solution. Plates were incubated in 35°C for 48 hours until susceptibility results were noted. *Candida* was considered susceptible to antifungal agents according to the Clinical and Laboratory Standards Institute and European Committee on Antimicrobial Susceptibility Testing breakpoints.[15,16]

Statistical analysis

Student *t* test was used to determine the difference of risk factors between *C albicans* and nonalbicans *Candidas*. $P < .05$ was considered significant.

RESULTS

Out of the 1,408 patients that were included in this study, 749 had a positive urine culture (53.20%), 603 were positive for bacteria (80.51%), and 146 grew *Candida* (19.49%). *Candida* was the second most prevalent organism in urine cultures (after *E coli*) (Table 1). *C albicans* was identified in 101 (69.17%) of all *Candida* positive samples. The mean age of patients with *Candida* positive urine culture was 63.7 years. Of the patients, 94 (67.1%) were women.

Most of the patients were hospitalized in the ICU (n = 67, 46%) and in the internal medicine departments (n = 59, 40%). The other patients were hospitalized in the surgery-urology department (n = 16, 11%) and obstetrics and gynecology department (n = 4, 3%).

Fifty-two patients (35.61%) had fever and 48 patients (32.87%) had leukocytes in their urine sample. *Candida* spp were visible in the urine sediment of 41 patients (28.08%). Seventeen patients (11.64%) had fungal-bacterial coinfection and colonization. Sixty-eight (46.57%) of the patients received antibiotics. Nineteen patients (13.01%) had pre-existing diabetes mellitus, 13 patients (8.9%) were immunosuppressed, and 9 patients (6.16%) had cancer. No candidemia cases were reported in the patients included in this study. Table 2 summarizes the clinical features of all catheter-associated candiduria.