

Candida Urinary Tract Infections—Epidemiology

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Candiduria is rarely present in healthy individuals. In contrast, it is a common finding in hospitalized patients, especially those in intensive care units (ICUs) who often have multiple predisposing factors, including diabetes mellitus, indwelling urinary catheters, and exposure to antimicrobials. Candiduria occurs much less commonly in the community setting. In a majority of episodes in adult patients in critical care facilities candiduria represents colonization, and antifungal therapy is not required. However, the presence of yeast in the urine can be a sign of a disseminated infection. In the critically ill newborn, candiduria often reflects disseminated candidiasis and is accompanied by obstructing fungus ball formation in the urinary tract. In ICU patients, although candiduria is a marker for increased mortality, it is only rarely attributable to *Candida* urinary tract infection.

Candiduria, the presence of *Candida* species in urine, is a common clinical finding, particularly in hospitalized patients. Since the 1980s there has been a marked increase in opportunistic fungal infections involving the urinary tract, of which *Candida* species are the most prevalent [1–3]. Yeast belonging to the genus *Candida* exist as saprophytes, colonizing mucosal surfaces and external genitalia of humans of either gender, but especially near the urethral meatus of healthy, premenopausal women. *Candida* species in measurable quantities in the urine (candiduria) are found in < 1% of clean voided specimens in healthy persons [4] but account for 5% of all urine culture results in the general hospital setting and 10% of urine isolates in tertiary care facilities [5]. All common *Candida* species are capable of causing urinary tract infections (UTIs), and in many centers worldwide non-*albicans* *Candida* species now predominate.

CANDIDURIA IN ADULTS

Most UTIs due to *Candida* or episodes of candiduria occur in hospitalized patients with indwelling bladder

catheters [3, 6–12, Table 1]. Within the hospital setting, candiduria is especially common in intensive care units (ICUs) and may represent the most frequent UTIs encountered in adult surgical ICUs [3, 6–12]. Multiple studies indicate that at least 10%–15% of hospital-acquired UTIs are caused by *Candida* species [3, 8, 12–21]. The percentage of nosocomial UTIs due to *Candida* species increased from 22% for the period 1986–1989 to almost 40% for the period 1992–1997 [6, 7].

Shay and Miller [18] estimated in 2004 that the incidence of candiduria was ~25,000 cases per year in the United States. Moreover, approximately one-third of hospitalized patients with urine cultures yielding *Candida* were in the ICU where bladder catheter use was high. However, as early as 1986 Platt and colleagues [2] reported that 26.5% of all UTIs with bladder catheter usage were due to *Candida* species. This observation was later substantiated by others who found that 90% of *Candida* UTIs in a large tertiary care center in the United States were related to bladder catheters [16]. On a national scale, surveillance studies have indicated that ~25% of all UTIs in ICUs are caused by *Candida* species [22, 23] and the length of stay (LOS) in such units influences the incidence significantly. However, in all of the above studies, whether these patients had UTIs or merely colonization is not clear.

As observed in a large multicenter study in Spain, 22% percent of critically ill patients hospitalized for more than 7 days in an ICU developed candiduria [11].

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Clinical Infectious Diseases 2011;52(S6):S433–S436

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1058-4838/2011/52S6-0002\$14.00

DOI: 10.1093/cid/cir109

In a similar study from France, the mean incidence of candiduria was 27.4/1000 ICU admissions, and it occurred late with a mean interval between ICU admission and onset of candiduria of 17.2 ± 1.1 days [15]. Noteworthy was the observation that the incidence observed in the burn unit was 3 times higher than those reported in medical and surgical ICUs [15]. *Candida* urinary isolates are second only to *Escherichia coli* in combined medical-surgical ICUs [6]. Another group of patients with high rates of candiduria are renal transplant recipients, especially during the early post-transplant period when both bladder drainage catheters and ureteral stents are still present [24].

As indicated above, candiduria occurs most commonly among catheterized patients. Bouza et al [25] found that the overall percentage of nosocomial UTIs among catheterized individuals was as high as 37%, of whom 16.4% had infections due to *Candida* species. In this same study the incidence of candiduria in non-catheterized subjects was only 6.6%.

There are few data regarding the epidemiology of candiduria in settings other than medical facilities, but in such settings candiduria remains uncommon [23, 24]. In one study, of predisposing factors for community-acquired candiduria, several differences were noted when compared with nosocomial candiduria [26]. Risk factors included diabetes mellitus (28.8%), bedridden status (46.4%), and recent administration of antimicrobials. A significantly higher percentage of pregnant women had community-acquired candiduria. However, the case definition required only one positive *Candida* culture, regardless of how the sample was procured, and it is possible that many of these cultures reflected urine specimen contamination by periurethral or vulvovaginal colonizing yeast [26].

Candiduria, particularly when symptomatic, is rare in otherwise healthy individuals of all ages who lack recognized risk factors (Table 1), and the incidental finding of yeast in the urine represents procurement contamination in the vast majority of instances. Unfortunately, this fact is frequently not recognized by clinicians who treat asymptomatic candiduria without repeating urine cultures and taking steps to prevent specimen contamination [27]. In 2000, a multicenter US study reported that 43% of instances of candiduria were treated, likely reflecting overzealous antifungal use [3].

CANDIDURIA IN NEONATES AND CHILDREN

Yeast-related UTIs are rare in healthy newborns. In contrast, candiduria and candidemia occur commonly in neonatal and pediatric ICUs and particularly in premature infants [5, 9, 18, 22, 23, 28–30]. Risk factors are similar to those associated with adults acquiring candiduria but usually develop in an antegrade fashion from sources such as candidemia and renal candidiasis. In addition, candiduria is also reported to complicate urological surgery following the placement of prosthetic devices for major

Table 1. Predisposing Factors for Candiduria and *Candida* Urinary Tract Infections

Diabetes mellitus	Renal transplantation
Extremes of age	Instrumentation of the urinary tract
Female sex	Concomitant bacteriuria
Prolonged hospitalization	Congenital abnormalities of the urinary tract
ICU admission	Structural abnormalities of the urinary tract
Broad-spectrum antibiotics	Indwelling urinary tract devices
Bladder dysfunction	Bladder stones
Urinary stasis	
Nephrolithiasis	

congenital urological malformations. Considered medical oddities in adults, fungal bezoars are particularly common in the urinary tracts of critically ill neonates regardless of the route of infection. Further complicating the management of these children are pharmacokinetic and toxicity considerations, which are special to this population.

MICROBIOLOGY OF CANDIDURIA

Virtually any *Candida* species may be associated with candiduria, and widely variable prevalence data regarding such *Candida* species and candiduria have been reported [12]. It is important that the specific species responsible for symptomatic infection is identified, given the differences in antimicrobial susceptibility among *Candida* species [12]. Although *C. albicans* is frequently reported as the most prevalent species infecting the urinary tract, non-*albicans Candida* species appear better adapted to the urinary tract environment with many studies reporting that >50% of urinary *Candida* isolates belong to non-*albicans* species [10, 12]. For example, reports from some institutions have identified *C. tropicalis* as the most prevalent fungal isolate [31], while others have identified *C. glabrata* as the dominant species [12]. *C. glabrata* apparently adapts well to selected urine properties such as substrate availability, osmolality, and pH (see pp. S437–S451 of Pathogenesis section). Other additional predisposing factors have been reported [32].

Polymicrobial infections, not only with bacteria but also with several yeast species occur in 5%–10% of *Candida* UTIs. In these circumstances, *C. glabrata* appears to be a frequent pathogen, often in combination with *C. albicans* and sometimes with other *Candida* species [33].

From the foregoing data it is apparent that candiduria is an increasingly difficult problem for modern physicians to recognize and manage. What is often not appreciated is the fact that candiduria is also associated with high crude mortality, especially in patients with comorbidities [3, 12, 33, 34]. However, the specific contribution of UTIs caused by *Candida* species to

attributable mortality is considerably lower than crude mortality figures would indicate. Many regard candiduria simply as a “red flag” or surrogate marker for associated high mortality without direct attribution [12]. In part this may be related to the low percentages of concomitant candidemia detectable in patients with candiduria [12, 35]. In a recent large, prospective study in France conducted in multiple ICUs, only 18 patients had both ICU-acquired candidemia and candiduria [15], and only 5 of the 18 were of the same species. The ICU total mortality for all patients in this study was 61.8% for those with candidemia and 31.3% for those with candiduria. The site of the initial *Candida* infection is often not evident in such investigations. However, the authors of another study of 23 ICU patients with concomitant candidemia and candiduria concluded that in the majority of patients the urinary tract was not the source of candidemia [36]. Nevertheless, in the surgical ICU setting candiduria detected at anytime has been shown to be independently associated with mortality [34].

SUMMARY AND CONCLUSIONS

Medical progress over the last 30 years has been attended by a concomitant increase in the prevalence of candiduria as well as in the incidence of *Candida* UTIs. Although occasionally community-acquired in persons who are pregnant, diabetic, bedridden, and/or have received antibacterial agents, most *Candida* UTIs are nosocomial and commonplace in ICUs where bladder catheters are employed almost routinely. In a majority of episodes in adult patients in the critical care setting, candiduria represents colonization or contamination of the specimen cultured rather than infection and most patients are asymptomatic. Rarely is antifungal therapy required. However, occasionally the presence of yeast in the urine is a sign of a disseminated infection or candidemia and may serve as a marker for increased mortality, especially in critically ill surgical patients with comorbidities. In contrast to that which occurs in adults in the medical and surgical ICU settings, candiduria in the critically ill newborn very often reflects candidemia or disseminated candidiasis and in addition may be accompanied by obstructing, urinary tract fungus ball formation.

For many years *C. albicans* was the most prevalent species isolated from the urinary tract. With the advent and increasing use of fluconazole, non-*albicans* *Candida* species have emerged and are now dominant. These non-*albicans* species may not only be well adapted to the kidney and collecting system but also more difficult to eradicate than *C. albicans*.

Acknowledgments

Supplement sponsorship. This supplement was sponsored through research funds of Georgia Health Sciences University, Medical College of Georgia, Augusta, Georgia.

Potential conflicts of interest. J. F. received payment from speaker's bureaus for Continuing Education Company and Southern Medical Association. C. K. received grant support from Merck, royalties from Springer Publishing and UpToDate, and payment from Pfizer for chairing Data Adjudication Committee for Aniduafungin study. J. S. received payment from the speaker's bureau for Astellas and Pfizer; his institution has received grant support from Merck. C. N.: no conflicts.

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