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Original article

Epidemiological profile of patients hospitalized with candiduria in the Central-Western region of Brazil

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ABSTRACT

Background: *Candida* yeasts are considered the main agents of nosocomial fungal infections.
Aims: This study aimed to establish the epidemiological profile of patients with candiduria hospitalized in the capital of the State of Mato Grosso, in the Central-Western region of Brazil.
Methods: Patients from three private hospitals and a public hospital participated in the study. This was an observational and cross-sectional study including analysis of patients mortality. It was carried out from March to August 2015.
Results: A total of 93 patients with candiduria were evaluated. *Candida tropicalis* was found most commonly (37.6%; *n* = 35), followed by *Candida albicans* (36.6%; *n* = 34), *Candida glabrata* (19.3%; *n* = 18), *psilosis* complex (4.3%; *n* = 4), *Candida lusitaniae* (1.1%; *n* = 1) and *Candida krusei* (1.1%; *n* = 1). Antibiotic therapy (100%) and the use of an indwelling urinary catheter (89.2%; *n* = 83) were the most frequent predisposing factors. Antifungal treatment was given to 65.6% of the patients, and anidulafungin was the most used antifungal. Mortality rates were 48% higher among patients with candiduria who had renal failure. Micafungin was the antifungal most prescribed among the patients who died. Candidemia concomitant with candiduria occurred in eight (8.6%; *n* = 8) cases. Considering the species recovered in the blood and urine, only one patient had genetically distinct clinical isolates.
Conclusions: Non-*C. albicans Candida* species were predominant, with *C. tropicalis* being the most responsible for most cases of candiduria.

Perfil epidemiológico de pacientes hospitalizados con candiduria en la región centro-oeste de Brasil

Palabras clave:
Candiduria
Infección nosocomial
Perfil epidemiológico
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RESUMEN

Antecedentes: Las levaduras del género *Candida* están consideradas los principales agentes de infecciones micóticas nosocomiales.
Objetivos: El objetivo del presente estudio fue establecer el perfil epidemiológico de los pacientes con candiduria hospitalizados en la capital de Mato Grosso, estado situado en la Región centro-oeste de Brasil.
Métodos: Participaron en el estudio pacientes de tres hospitales privados y un hospital público. Se trataba de un estudio observacional y transversal que incluía el análisis de la mortalidad de los pacientes. Se llevó a cabo de marzo a agosto de 2015.

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Resultados: Se incluyó en el estudio a un total de 93 pacientes con candiduria. *Candida tropicalis* se encontró con mayor frecuencia (37,6%; n = 35), seguida por *Candida albicans* (36,6%; n = 34), *Candida glabrata* (19,3%; n = 18), *Candida psilosis complex* (4,3%; n = 4), *Candida lusitaniae* (1,1%; n = 1) y *Candida krusei* (1,1%; n = 1). El tratamiento antibiótico (100%) y el uso de una sonda urinaria permanente (89,2%; n = 83) fueron los factores predisponentes más frecuentes. Se prescribió tratamiento antimicótico al 65,6% de los pacientes y la anidulafungina fue el antimicótico utilizado con más frecuencia. Las tasas de mortalidad fueron un 48% superiores entre los pacientes con candiduria con insuficiencia renal. Los pacientes que murieron presentaron la mayor proporción de prescripción del antimicótico micafungina. La candidemia concomitante con candiduria se produjo en ocho casos (8,6%; n = 8). Si se tienen en cuenta las especies recuperadas en sangre y orina, solo en un paciente se encontraron aislamientos clínicos genéticamente diferentes.
Conclusiones: Las especies de *Candida* no *C. albicans* fueron predominantes. *C. tropicalis* fue la responsable de la mayoría de los casos de candiduria.

The presence of *Candida* yeasts in urine (candiduria) has been an increasingly common event in hospitalized patients. *Candida* is considered the second most frequent microorganism in urinary tract infections in intensive care units.[29,35] *Candida* spp. are commensal yeasts of the urogenital tract. Their transformation into pathogenic microorganisms is mainly related to invasive procedures and the extensive use of broad-spectrum antibiotics.[15,41,59] It is estimated that 50% of the patients using indwelling urinary catheters for more than five days develop candiduria.[19] Women are more affected because, in addition to having a shorter urethra, they may have vulvovaginal colonization by *Candida*.[32,33] The infection commonly occurs by the ascending route, via the migration of yeasts from the periurethral area to the bladder. Kidney infections usually occur via a hematogenic route; however, retrograde infections from the bladder to the kidneys may occur, especially in the presence of urinary outflow obstruction.[25,38]

Although it is frequently seen in hospitalized patients, there is still no laboratory diagnostic protocol and treatment for candiduria, since the presence of *Candida* in the urine often represents only colonization.[27,49] However, candiduria associated with several underlying conditions in patients of the intensive care unit (ICU) may progress to candidemia, increasing the risk of death.[2,33,57] Candiduria, which does not necessarily involve the presence of signs and/or symptoms of urinary tract infection, may be defined as the growth of *Candida* in culture from urine collected by suitable techniques.[21] It is a very common event among patients exposed to risk factors, and 20% of hospitalized patients may have candiduria throughout his hospitalization, particularly patients in intensive care unit.[25] This laboratory finding is controversial regarding its interpretation, as may correspond to simple contamination of the urine collection, asymptomatic cystitis or pyelonephritis, primary renal candidiasis, ureteropelvic fungal ball or disseminated candidiasis with renal manifestation.[26,53]

In view of the controversies regarding the relevance and clinical interpretation of candiduria, it is important to conduct studies aimed at elucidating its global epidemiological presence, and establishing prophylactic and therapeutic actions more specific to each region. This study aimed to evaluate the clinical and epidemiological profile of patients with candiduria hospitalized in four hospitals in the capital of Mato Grosso, a State located in the Central-Western region of Brazil.

Methods

Type of study and population

This was an observational and cross-sectional study including analysis of patients mortality. It was carried out from March to August 2015 and involved four hospitals in the capital of Mato Grosso, a State located in the Central-Western region of Brazil. A total of 93 patients with candiduria were analyzed.

Urinary sediment and culture were requested by physicians as part of the routine care to achieve a diagnosis and provide the proper clinical management to the patients. After the collection of urine samples by the nursing team, they were sent to the clinical analysis laboratory and were examined by the professionals responsible. After the laboratory analysis of each sample, the isolates were sent to the Laboratory of Mycology of the Federal University of Mato Grosso to identify them. Data such as sex, age, and predisposing factors, including comorbidities, length of hospital stay, treatment, and mortality, were obtained from the medical records of each patient. Data on urinary sediment analysis and colony counts were acquired by the operating system of each clinical laboratory.

Patients were included when the number of colony-forming units (CFU) were greater than or equal to 10^3 CFU/ml.[20] Patients with more than one positive sample were included only once. Patients who had been treated for genital candidiasis during hospitalization were not considered in the study due to the risk of contaminating the urine sample. Candiduria cases that occurred before the collecting of samples were also excluded from the study.

In compliance with Resolution 196/96 of the National Health Council, this study began after the evaluation and approval of the Research Ethics Committee of Plataforma Brasil under the number 38452914.1.0000.5541.

Microbiological and statistical analysis

Samples were cultured on Sabouraud dextrose agar (BD Difco® – USA), and the colonies obtained were transferred to a chromogenic agar (BD Difco® – USA) to check the purity of the colonies and to achieve a presumptive identification. The yeasts were identified by germ tube and micromorphologic analysis in cornmeal agar – Tween 80.[28] Confirmation of the species was carried out using the Vitek® system (bioMérieux – France). The species recovered from the blood and urine of patients who had candiduria concomitant with candidemia were identified by PCR (polymerase chain reaction) and sequencing of the ITS (internal transcribed spacer) region.

All statistical analyses were performed using the Stata Statistical Software (v.12). To verify the existence of an association between mortality and categorical variables, Pearson's chi-square test was used. In order to estimate the strength of the association, the prevalence ratio (PR) was used. The independent effect of the exploratory variables on the response variable was determined by Poisson regression with robust variance.[4] Variables with p-value <0.2 in

Table 1
Frequency distribution of the predisposing factors found among the patients with candiduria.

Exposure factors	Number of patients (%)
Antibiotic therapy	93 (100%)
Indwelling urinary catheter	83 (89.2%)
Diabetes mellitus	32 (34.4%)
Immunosuppressive disease	15 (16.1%)
Immunosuppressive therapy	43 (46.2%)
Parenteral nutrition	17 (18.3%)
Kidney failure	28 (30.1%)
Abdominal surgery	10 (10.7%)

the bivariate analysis were included in the model. Results were considered significant when $p < 0.05$ in the two-tailed test. Considering the time elapsed between the diagnosis of candiduria and the death of the patient, a Kaplan–Meier curve was made to evaluate the probability of survival.

Results

A total of 132 isolates were obtained from the urine of 93 patients with candiduria. Considering the first species recovered from each patient, *Candida tropicalis* (37.6%; $n = 35$) was the most frequent microorganism isolated, followed by *Candida albicans* (36.6%; $n = 34$), *Candida glabrata* (19.3%; $n = 18$), *psilosis* complex (4.3%; $n = 4$), *Candida lusitaniae* (1.1%; $n = 1$), and *Candida krusei* (1.1%; $n = 1$). Mixed infections involving *C. glabrata* and *C. albicans* occurred in two cases, with significant growth rates ($\geq 10^5$ CFU/ml) for both species.

From the patients evaluated, 57% ($n = 53$) were females and 43% ($n = 40$) males. Two patients were from neonatal ICU. The most common species in female patients was *C. albicans* (37.7%; $n = 20$), and the most common species in male patients was *C. tropicalis* (45%; $n = 18$). The average age of patients with candiduria was 63.1 years (confidence interval [95% CI] = 58.7–67.5). Among the different predisposing factors, the most frequent were antibiotic therapy (100%) and the use of an indwelling urinary catheter (89.2%; $n = 83$) (Table 1).

Candidemia concomitant with candiduria was observed in 8.6% of cases ($n = 8$). Molecular analysis of the isolates obtained from the blood and urine showed only one case in which the species were different. The species isolated from blood cultures were *C. albicans* ($n = 2$), *C. tropicalis* ($n = 3$), *Candida parapsilosis* ($n = 2$) and *Candida orthopsilosis* ($n = 1$). Two patients had positive catheter tip cultures for the same species isolated from the blood and urine.

The average time after hospitalization for the occurrence of the first episode of candiduria was 19.9 days (95% CI = 15.3–24.5). Nine patients had positive cultures on the first day of hospitalization. The average time for the onset of candiduria after the introduction of an indwelling urinary catheter was 16 days (95% CI = 11.2–20.8). The replacement or removal of the catheter occurred in 6.2 days on average (95% CI = 4.3–8.2) after the diagnosis of candiduria. The analysis of the urinary sediment was performed in 65 patients. Fifty one (78.4%) of them had leukocyturia and 46 (69.2%) suffered hematuria. The presence of pseudohyphae was reported in only one case.

Antifungal treatment was prescribed in 61 (65.6%) patients. Therapy prescription was 26% higher in patients who had urine cultures with colony counts $\geq 10^5$ CFU/ml (PR = 1.26; $p = 0.035$). Anidulafungin was the most commonly used antifungal in private hospitals, and so was micafungin in the public hospital. Among the patients who had an indwelling catheter during candiduria and received treatment, 38.6% ($n = 22$) did not have the catheter replaced or removed when starting the antifungal therapy.

Considering mortality rates in the patients with candiduria, univariate analysis showed that the use of an indwelling catheter ($p = 0.003$), kidney failure ($p = 0.002$), antifungal treatment ($p = 0.02$), use of anidulafungin ($p = 0.01$), and use of micafungin ($p = 0.007$) were statistically significant associations (Table 2). The mortality among patients with candiduria was 48% higher when renal failure was present and 51% lower among those receiving micafungin treatment (Table 3).

Kaplan–Meier survival analysis showed a statistically significant difference ($p = 0.0004$) between the elapsed time from diagnosis of candiduria to death for patients who underwent the replacement of the indwelling urinary catheter after diagnosing candiduria (Fig. 1). There was no statistical difference between the survival functions for the other variables.

Discussion

Despite the high prevalence in hospitalized patients, the presence of *Candida* in the urine still has uncertain significance due to the lack of well-established criteria to aid diagnosis.[40] Several predisposing factors are related to candiduria. As in several previously published studies, antibiotic therapy and the use of an indwelling urinary catheter were the most frequent predisposing factors in patients with candiduria[2,27,41,52] in our study. When suppressing the bacterial flora of the gastrointestinal tract and lower genital tract, antibiotics favor fungal colonization of the epithelial surface, facilitating the entrance to the urinary tract, especially in the presence of permanent catheters.[22] According to the literature, cases of candiduria are more frequent in patients above 60 years old (67.7%). The greater predisposition of the elderly is related to immunological factors, long-stay hospitalizations, and clinical procedures that may increase the risk of infection.[16,26]

Unlike studies conducted in other Brazilian regions in which *C. albicans* was reported as the most frequent species in cases of candiduria, less cases due to this species were found in our study, with 63.4% of the isolates identified as non-*C. albicans Candida* species, highlighting *C. tropicalis* as the most prevalent species in 37.6% of the cases.[6,41,51] *C. tropicalis* has been reported in previous studies as the most prevalent species in candiduria with reported prevalences varying from 43% to 57.3%.[40,42,52] This difference may be explained by the inversion of the profile of *Candida* species (*C. albicans* versus non-*C. albicans Candida* species) that has occurred over the course of the last few years.[36] Moreover, the distribution of species varies according to the characteristics of each demographic region and group of subjects studied. A study in another State in the Central-Western region of Brazil (Mato Grosso do Sul) reported a similar proportion of non-*C. albicans Candida* species (60.4%), although the frequency of *C. albicans* (39.6%) was slightly higher than that of *C. tropicalis* (31.1%).[31]

As in other studies, candiduria was more frequent in female patients.[8,27,41] The higher incidence in women is due to the shorter urethra compared with men, as well as vulvovaginal colonization by *Candida*, which facilitates reaching the bladder via the ascending route.[32,33] This hypothesis was suggested by Febré et al.,[14] who found *Candida* in the urine of five women from a group of eight whose vaginal secretions taken previously were positive for the same species of *Candida*. According to the literature, there has been an increase in vaginal candidiasis by non-*C. albicans Candida* species, especially *C. glabrata*.[11,18] In this study, 18 patients were infected with this species, among whom 14 were women. As observed in our study, *C. glabrata* is reported in the literature as an emerging and frequently species in elderly patients.[9,34] Except for one case, all cases of *C. glabrata* candiduria were diagnosed in patients over 60 years old. Yeasts belonging to the *psilosis* complex

Table 2
Univariate analysis between the explanatory variables and mortality among patients with candiduria admitted to tertiary hospitals in Mato Grosso.

Variables	Death		Total $n=93$	p
	No	Yes		
Gender				
Male	17	23	40	0.40
Female	18	35	53	
Age				
≤15 years old	1	2	3	
16–30 years old	3	2	5	0.32
31–59 years old	11	11	22	
≥60 years old	20	43	63	
Antibiotic therapy	35	58	93	–
Indwelling urinary catheter	27	56	83	0.003
Diabetes mellitus	10	22	32	0.35
Kidney failure	4	24	28	0.002
Parenteral nutrition	4	13	17	0.18
Abdominal surgery	1	9	10	0.05
Immunosuppressive therapy	13	30	43	0.17
Immunosuppressive disease	5	10	15	0.71
Candidemia	1	7	8	0.12
Leukocyturia	17	34	51	0.51
Hematuria	15	30	45	0.60
Colony-forming units/ml				
10,000–100,000 CFU/ml	8	10	18	0.51
≥100,000 CFU/ml	27	48	75	
Antifungal treatment	18	43	61	0.02
Fluconazole	12	11	23	0.09
Anidulafungin	7	26	33	0.01
Caspofungin	1	2	3	0.87
Micafungin	1	14	15	0.007
Amphotericin B	2	4	6	0.82

Table 3
Statistically significant results of the Poisson regression with robust variance in relation to mortality among hospitalized patients with candiduria in tertiary hospitals in Mato Grosso.

Associated factors	PR	95% CI	p
Kidney failure	1.48	1.11–1.97	0.006
Micafungin treatment	0.49	0.31–0.78	0.003

CI: confidence interval; PR: prevalence ratio. Model adjusted by sex, age, use of indwelling urinary catheter, parenteral nutrition, abdominal surgery, immunosuppressive therapy, candidemia, antifungal therapy, treatment with anidulafungin and fluconazole.

have not been reported as a frequent cause of urinary tract infections. It is a group of yeasts that primarily affects infants and is more related to candidemias.[30,44] Although only two infants were included in this study, *psilosis* complex species were not the etiological agents of candiduria in these patients. The four cases of candiduria caused by this group of yeasts occurred in adult men.

In a multivariate analysis, renal failure increased mortality by 48% in patients with candiduria when compared to patients with candiduria but without renal failure. In pediatric patients hospitalized in an intensive care unit who developed candidemia, candiduria increased mortality by almost five-fold.[23] In neonates born with extremely low birth weight, mortality after discharge was two-fold higher among those who developed candiduria when compared to those with no proven infection.[60]

Candiduria may increase the risk of candidemia by non-*C. albicans Candida* species by up to 15 times,[12] probably due to upper urinary tract involvement and translocation to renal blood vessels. Patients with candiduria and renal failure had a three-fold higher risk of death than patients with candiduria but without renal failure.[43] Among patients with candiduria, antifungal treatment with micafungin reduced mortality by 51% in a multivariate analysis. In a study by Gabardi et al., this antifungal was associated with short-term and long-term urine sterilization, regardless the catheter was removed or not, and the cause of candiduria were both *C. albicans* or non-*C. albicans Candida* species.[17] In a cohort study of 280 patients aged 18–75 years a 6-fold all-cause mortality rate among patients with candiduria was found.[46] When compared with the antifungal anidulafungin, micafungin reduced the mortality rate by 27% after 90 days in patients with invasive candidiasis.[58]

As in other studies, candiduria cases occurred, on average, 20 days after hospitalization.[2,27] Some studies have reported the appearance of yeasts in the urine within the first two weeks of hospitalization.[39,50] Among patients who used an indwelling urinary catheter, candiduria occurred, on average, 16 days after inserting the device. Another study reported that candiduria developed, on average, 11 days after catheterization.[56] Considering the hospitals evaluated in this study, we observed that the catheter was replaced every 20 days in most patients. Thus, it would be possible to reduce colonization by yeasts if the replacements were more frequent. Even if such a practice causes higher costs for the hospital, the potential savings of not requiring antifungal treatment and their consequent potential adverse effects should also be considered. However, in order to assess this change in practice, clinical studies with specific designs for this hypothesis are required, such as randomized controlled trials, cohort studies, or case–control studies aimed at evaluating and comparing groups of patients with candiduria following different replacement intervals for an indwelling catheter.

The higher likelihood of survival among patients who had the urinary catheter replaced after the diagnosis of candiduria, as evidenced by Kaplan–Meier analysis, highlights the benefits that continuous catheter replacement can bring to the patient. Despite the design limitations of this study in testing this hypothesis, a statistically significant difference was found in the mortality rates

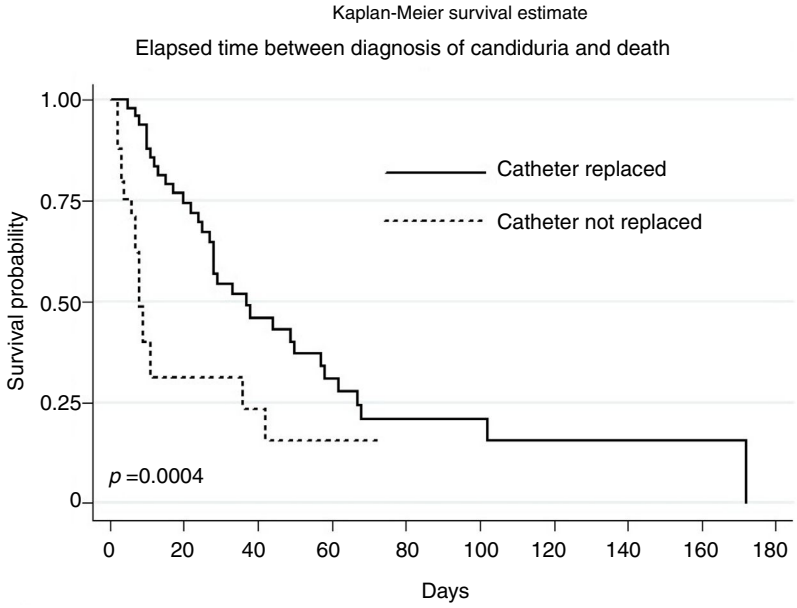

Fig. 1. Comparison of the Kaplan–Meier survival curves after the diagnosis of candiduria, according to the replacement of the indwelling urinary catheter.

between patients in whom the catheter was replaced and those in whom the urinary catheter was not replaced after the diagnosis of candiduria. Studies addressing issues specifically related to the urinary catheter replacement regimen in these patients might provide better evidence of the importance of catheter replacement as a non-therapeutic intervention factor for candiduria cases.

Candidemia concomitant with candiduria is reported in the literature as a low occurrence event.[8,52,54] In the present study, eight patients (8.6%) out of the 84 patients with candiduria had concomitant candidemia. A similar rate was found by Storfer et al.[56] Some genetic studies have been conducted showing identical genotypic patterns among yeasts recovered in the urine and blood.[1,5,7] In the present study, the molecular analysis of urine and blood isolates obtained from patients who had candiduria concomitant with candidemia demonstrated only a single case in which *Candida* species were different in the two samples. However, despite the studies showing the same species of *Candida* present in the blood and urine, there are difficulties in establishing which event occurred first due to the low sensitivity of blood cultures in detecting candidemias.[13,57] Thus, some authors believe that candiduria is an event that should never be ignored because it may be the first indication of systemic or invasive infection.[37,51,53]

Some studies have reported that most cases of candiduria are untreated.[3,6,25] In the present study more than half of the patients (65.6%) received treatment. In most cases, the treatment was based on a single positive culture. Only 34.4% of the treated patients were taken a second sample taken after the detection of candiduria. The same behavior was observed by a group of researchers in Parana, a State located in the Southern Region of Brazil.[6] Many authors do not recommend the antifungal treatment in patients with a permanent urinary catheter due to an increase in the resistance to antifungal drugs, since the formation of biofilms complicates the eradication of the microorganisms.[47,48] In this study, 22 (38.6%) out of the 57 patients who had indwelling catheter and received treatment had no replacement or removal of the urinary catheter. Similar results were found by Dalen et al.[10] who, when assessing the practice in asymptomatic patients using urinary catheters, found in only half of the cases the replacement or removal of the device.

Fluconazole is reported in the literature as the best antifungal drug for the treatment of candiduria due to the high active concentration of the drug in the urine. However, it is known that its use is limited in urinary tract infections caused by *C. krusei* due to its intrinsic resistance to the mentioned antifungal agent, and *C. glabrata* due to its dose-dependent susceptibility.[24,45,55] However, a major problem faced by most hospitals is the lack of laboratory results enabling an appropriate antifungal drug to treat patients with candiduria. From the hospitals involved in this study, only the public hospital could analyze urine cultures by identifying the yeast species and assessing their susceptibility to antifungal drugs. Thus, anidulafungin was the drug most frequently used by private hospitals since the laboratory results were insufficient to guarantee an optimal antifungal activity of fluconazole.

However, it should be noted that, given the different difficulties related to the diagnosis of candiduria, more discerning measures are required for detecting the presence of *Candida* in urine. Any event diagnosed as candiduria, considering clinical and laboratory criteria, should be investigated to evaluate the risk of progression from colonization to disease. Thus, any replacement of an indwelling urinary catheter and any antifungal treatment should be evaluated with subsequent urine cultures in order to better monitor candiduria cases.

Competing interests

The authors declare that they have no competing interests.

References

1. Ahmad S, Khan Z, Mustafa AS, Khan ZU. Epidemiology of *Candida* colonization in an intensive care unit of a teaching hospital in Kuwait. Med Mycol. 2003;41:487–93.
2. Alvarez-Lerma F, Nolla-Salas J, León C, Palomar M, Jordá R, Carrasco N, et al. Candiduria in critically ill patients admitted to intensive care medical units. Intensive Care Med. 2003;29:1069–76.
3. Ayeni O, Riederer KM, Wilson FM, Khatib R. Clinicians' reactions to positive urine culture for *Candida* organisms. Mycoses. 1999;42:285–9.
4. Barros AJD, Hirakata V. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. BMC Med Res Methodol. 2003;3:21.
5. Binelli CA, Moretti ML, Assis RS, Sauaia N, Menezes PR, Ribeiro E, et al. Investigation of the possible association between nosocomial candiduria and candidemia. Clin Microbiol Infect. 2006;12:538–43.
6. Carvalho M, Guimarães CM, Mayer-Junior JR, Bordignon GPF, Queiroz-Telles F. Hospital-associated funguria: analysis of risk factors, clinical presentation and outcome. Braz J Infect Dis. 2001;5:313–8.

7. Chen YC, Chang SC, Tai HM, Hsueh PR, Luh KT. Molecular epidemiology of *Candida* colonizing critically ill patients in intensive care units. J Formos Med Assoc. 2001;100:791–7.
8. Chen SCA, Tong ZS, Lee OC, Halliday C, Playford EG, Widmer F, et al. Clinican response to *Candida* organisms in the urine of patients attending hospital. Eur J Clin Microbiol Infect Dis. 2008;27:201–88.
9. Colombo AL, Garnica M, Aranha Camargo LF, Da Cunha CA, Bandeira AC, Borghi D, et al. *Candida glabrata*: an emerging pathogen in Brazilian tertiary care hospitals. Med Mycol. 2013;51:38–44.
10. Dalen DM, Zvonar RK, Jessamine PG. An evaluation of the management of asymptomatic catheter-associated bacteriuria and candiduria at The Ottawa Hospital. Can J Infect Dis Med Microbiol. 2005;16:166–70.
11. Del Palacio A, Sanz F, Sánchez-Alor G, Garau M, Calvo MT, Boncompte E, et al. Double-blind randomized dose-finding study in acute vulvovaginal candidosis. Comparison of flutrimazole site-release cream (1, 2 and 4%) with placebo site-release vaginal cream. Mycoses. 2000;43:355–65.
12. Dimopoulos G, Ntziora F, Rachiotis G, Armaganidis A, Falagas ME. *Candida albicans* versus non-*albicans* intensive care unit-acquired bloodstream infections: differences in risk factors and outcome. Anesth Analg. 2008;106:523–9.
13. Eggimann P, Garbino J, Pittet D. Epidemiology of *Candida* species infections in critically ill non immunosuppressed patients. Lancet Infect Dis. 2003;3:685–702.
14. Febré N, Silva V, Medeiros EA, Wey SB, Colombo AL, Fischman O. Microbiological characteristics of yeasts isolated from urinary tracts of intensive care unit patients undergoing urinary catherization. J Clin Microbiol. 1999;37:1584–6.
15. Fisher JF, Kavanagh K, Sobel JD, Kauffman CA, Newman CA. *Candida* urinary tract infection: pathogenesis. Clin Infect Dis. 2011;52:437–51.
16. Fraisse T, Lachaud L, Sotto A, Lavigne JP, Cariou G, Boiteux JP, et al. Recommendations of the Infectious Disease Committee of the French Association of Urology. Diagnosis, treatment and monitoring candiduria. Prog Urol. 2011;21:314.
17. Gabardi S, Martin S, Sura M, Mohammed A, Golan Y. Micafungin treatment and eradication of candiduria among hospitalized patients. Int Urol Nephrol. 2016;48:1881–5.
18. Gonçalves B, Ferreira C, Alves CT, Henriques M, Azeredo J, Silva S. Vulvovaginal candidiasis: epidemiology, microbiology and risk factors. Crit Rev Microbiol. 2015;21:1–23.
19. Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA. Healthcare Infection Control Practices Advisory Committee Guideline for prevention of catheter-associated urinary tract infections 2009. Infect Control Hosp Epidemiol. 2010;31:319–26.
20. Grabe M, Bartoletti R, Bjerklund Johansen TE, Cai T, Çek M, Koves T, et al. Guidelines on urological infections. European Association of Urology; 2015.
21. Guimarães T, Colombo AL. Candiduria: uma abordagem clínica e terapêutica. Rev Soc Bras Med Trop. 2007;40:332–7.
22. Guler S, Ural O, Findik D, Arslan U. Risk factors for nosocomial candiduria. Saudi Med J. 2006;27:1706–10.
23. Hegazi M, Abdelkader A, Zaki M, El-Deek B. Characteristics and risk factors of candidemia in pediatric intensive care unit of a tertiary care children's hospital in Egypt. J Infect Dev Ctries. 2014;8:624–34.
24. Hollenbach E. To treat or not to treat – critically ill patients with candiduria. Mycoses. 2008;51:12–24.
25. Kauffman CA, Vazquez JA, Sobel JD, Gallis HA, McKinsey DS, Karchmer AW, et al. Prospective multicenter surveillance study of funguria in hospitalized patients. Clin Infect Dis. 2000;30:14–8.
26. Kauffman CA. Diagnosis and management of fungal urinary tract infection. Infect Dis Clin North Am. 2014;28:61–74.
27. Kobayashi CC, De Fernandes OF, Miranda KC, De Sousa ED, Silva Mdo R. Candiduria in hospital patients: a study prospective. Mycopathologia. 2004;158:49–52.
28. Kwon-Chung KJ, Bennett JE. Medical mycology. Philadelphia: Lea & Febiger; 1992.
29. Laupland KB, Baqshaw SM, Gregson DB, Kirkpatrick AW, Ross T, Church DL. Intensive care unit-acquired urinary tract infections in a regional critical care system. Crit Care. 2005;9:60–5.
30. Levy I. Emergence of *Candida parapsilosis* as the predominant species causing candidemia in children. Clin Infect Dis. 1998;26:1086–8.
31. Lima GME, Master Thesis (Graduate Program in Health and Development of the Midwest) Analysis of cases of candiduria in adults admitted to the university hospital – UFMS, Campo Grande/MS. 75f. Campo Grande: Federal University of Mato Grosso do Sul; 2014.
32. Lundstrom T, Sobel J. Nosocomial candiduria: a review. Clin Infect Dis. 2001;32:1602–7.
33. Magill SS, Swoboda SM, Johnson EA, Merz WG, Pelz RK, Lipsett PA, et al. The association between anatomic site of *Candida* colonization, invasive candidiasis and mortality in critically ill surgical patients. Diagn Microbiol Infect Dis. 2006;55:293–301.
34. Malani A, Hmoud J, Chiu L, Carver PL, Bielaczyc A, Kauffman CA. *Candida glabrata* fungemia: experience in a tertiary care center. Clin infect Dis. 2005;41:975–81.
35. Manisha J, Vinita D, Bibhabati M, Archana T, Poonam SL, Aradhana B. Candiduria in catheterized intensive care unit patients: emerging microbiological trends. Ind J Path Microbiol. 2011;54:552–5.
36. Méan M, Marchetti O, Calandra T. Bench-to-bedside review: *Candida* infections in the intensive care unit. Crit Care. 2008;12:204.
37. Nassoura Z, Ivatury RR, Simon RJ, Jabbour N, Stahl WM. Candiduria as an early marker of disseminated infection in critically ill surgical patients: the role of fluconazole therapy. J Trauma. 1993;35:290–5.
38. Nishikawa T, Tokunaga S, Fuse F, Takashima M, Noda T, Ohkawa M, et al. Experimental study of ascending *Candida albicans* pyelonephritis focusing on the hyphal form and oxidant injury. Urol Int. 1997;58:131–6.
39. Occhipinti DJ, Gubbins PO, Schreckenberger P, Danziger LH. Frequency pathogenicity and microbiologic outcome of non-*Candida albicans* candiduria. Eur J Clin Microbiol Infect Dis. 1994;13:459–67.
40. Oliveira RDR, Maffei CML, Martinez R. Hospital urinary infection by *Candida* spp. Rev Assoc Med Bras. 2001;47:231–5.
41. Passos XS, Sales WS, Maciel PJ, Costa CR, Miranda KC, Lemos JA, et al. *Candida* colonization in intensive care unit patients' urine. Mem Inst Oswaldo Cruz. 2005;100:925–8.
42. Paul N, Mathai E, Abraham OC, Mathai D. Emerging microbiological trends in candiduria. Clin Infect Dis. 2004;39:1743–4.
43. Paul N, Mathai E, Abraham OC, Michael JS, Mathai D. Factors associated with candiduria and related mortality. J Infect. 2007;55:450–5.
44. Pfaller MA. Nosocomial candidiasis: emerging species, reservoirs, and modes of transmission. Clin Infect Dis. 1996;22:89–94.
45. Pfaller MA, Diekema DJ, Gibbs DL, Newell VA, Nagy E, Dobiasova S, et al. *Candida krusei*, a multidrug-resistant opportunistic fungal pathogen: geographic and temporal trends from the ARTEMIS DISK antifungal surveillance program, 2001 to 2005. J Clin Microbiol. 2008;46:515–21.
46. Radosevich JJ, Nix D, Erstad BL. Evaluation of the treatment of candiduria at an Academic Medical Center. Am J Ther. 2016;23:e1774–80.
47. Saint S, Chenoweth CE. Biofilms and catheter-associated urinary tract infections. Infect Dis Clin North Am. 2003;17:411–32.
48. Sedor J, Mulholland SG. Hospital-acquired urinary tract infections associated with the indwelling catheter. Urol Clin North Am. 1999;26:821–8.
49. Seifi Z, Azish M, Salehi Z, Zarei Mahmoudabadi A, Shamsizadeh A. Candiduria in children and susceptibility patterns of recovered *Candida* species to antifungal drugs in Ahvaz. J Nephropathol. 2013;2:122–8.
50. Sellami A, Sellami H, Makni F, Bahloul M, Cheikh-Rouhou F, Bouaziz M, et al. La candidurie en milieu de réanimation: signification et intérêt de la numération des levures dans les urines. Ann Fr Anesth Reanim. 2006;25:584–8.
51. Silva EH, Ruiz LS, Matsumoto FE, Auler ME, Giudice MC, Moreira D, et al. Candiduria in a public hospital of São Paulo (1999–2004): characteristics of the yeast isolates. Rev Inst Med Trop S Paulo. 2007;49:349–53.
52. Singla N, Gulati N, Kaistha N, Chander J. *Candida* colonization in urine samples of ICU patients: determination of etiology, antifungal susceptibility testing and evaluation of associated risk factors. Mycopathologia. 2012;174:149–55.
53. Sobel JD. Management of asymptomatic candiduria. Int J Antimicrob Agents. 1999;11:285–8.
54. Sobel JD, Kauffman CA, McKinsey D, Zervos M, Vazquez JA, Karchmer AW, et al. Candiduria: a randomized, double-blind study of treatment with fluconazole and placebo. Clin Infect Dis. 2000;30:19–24.
55. Sobel JD, Lundstrom T. Management of candiduria. Curr Urol Rep. 2001;2:321–5.
56. Storfer SP, Medoff G, Fraser VJ, Powderly WG, Dunagan WC. Candiduria: retrospective review in hospitalized patients. Infect Dis Clin Pract. 1994;3:23–9.
57. Toya SP, Schraufnagel DE, Tzelepis GE. Candiduria in intensive care units: association with heavy colonization and candidaemia. J Hosp Infect. 2007;66:201–6.
58. Van der Geest PJ, Hunfeld NGM, Ladage SE, Groeneveld ABJ. Micafungin versus anidulafungin in critically ill patients with invasive candidiasis: a retrospective study. BMC Infect Dis. 2016;16:490.
59. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Hospital-acquired candidemia. The attributable mortality and excess length of stay. Arch Intern Med. 1988;148:2642–5.
60. Wynn JL, Tan S, Gantz MG, Das A, Goldberg RN, Adams-Chapman I, et al. Outcomes following candiduria in extremely low birth weight infants. Clin Infect Dis. 2012;54:331–9.