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ARTICLE

Community-acquired and hospital-acquired candiduria: comparison of prevalence and clinical characteristics

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Abstract Hospital-acquired candiduria (HAC) is a well-known finding, related to severely ill patients, prolonged antibiotic treatment, use of catheters, and invasive procedures. However, the risk factors and clinical significance of community-acquired candiduria (CAC) has not yet been described. In this study, the prevalence and clinical characteristics of CAC and HAC were compared. Demographic and clinical data from all patients with positive urinary cultures sent to the bacteriology laboratory of the Haemek Medical Center, Israel, between May 2005 and October 2006 which grew *Candida* spp. were collected and analyzed. A total of 100,522 urine samples were received, 19,611 (19.5%) of which grew uropathogens. Among them, 204 (125 community-acquired and 79 hospital-acquired) grew *Candida* spp. (1% of all positive and 0.2% of all samples). Patients with CAC were younger than those with HAC (mean 50.5 years vs. 68.3 years). Pregnant women and bed-ridden patients were more prevalent in CAC (22.5% vs. 1.9% and 46.8% vs. 18.55%, respectively). More patients with HAC suffered from renal failure (27.8% vs. 11.2%) and fever (62.0% vs. 25.6%), had urinary catheters (32.9% vs. 15.2%), and received antibiotic or immunosuppressive therapy in the last month (73.4% vs. 46.4% and 10.1% vs. 3.2%). Most candiduria cases were not treated medically and no further investigation was conducted. Significant differences between patients with CAC and HAC were found. Our results confirm that candiduria (nosocomial as community-acquired) infrequently requires intervention. However, the identification of high-risk patients is desirable and questions regarding the management of candiduria, both CAC and HAC, still remain unresolved.

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Introduction

Hospital-acquired candiduria (HAC) is a well-known finding, and risk factors for acquisition, clinical characteristics, and significance have been extensively published. HAC have been mainly related to severely ill patients, prolonged antibiotic treatment, use of urinary catheters, and invasive procedures [1–3]. However, the risk factors and clinical significance of community-acquired candiduria (CAC) has not yet been described. In this study, the prevalence, risk factors for acquisition, and clinical characteristics of both CAC and HAC were compared.

The comparison was based on the analysis of clinical records of all patients presenting with candiduria, whose urine cultures were processed at the microbiology laboratory of the Haemek Medical Center, a facility serving a 500-bed regional hospital and a net of outpatient clinics with a total population of 500,000 inhabitants in the northeast region of Israel. All urine cultures from this population are processed exclusively in this laboratory.

Materials and methods

All patients whose urinary cultures were sent to the bacteriology laboratory of the Haemek Medical Center between May 2005 and October 2006 and grew *Candida* spp. were included in the study. The study included two phases: a retrospective phase, where demographic and clinical data were collected from clinical records of patients with candiduria between May 2005 and May 2006, and a prospective phase between May 2006 and October 2006, where *Candida* strains isolated were identified to the species level, in addition to the analysis of the demographic and clinical data.

Significant candiduria was defined as the growth of ≥10,000 colony forming units (CFU)/mL for women and ≥5,000 CFU/mL for men.

Patients with candiduria were divided in two groups: CAC and HAC. HAC was defined as candiduria developed after 48 h of hospitalization.

Demographic and clinical data, including age, gender, diabetes mellitus, renal failure (blood creatinine level >2 mg/dL), pregnancy, presence of urinary catheter, recurrent urinary tract infection (UTI-3 or more events in the last year), and antibiotic or immunosuppressive treatment during the last month, were recorded from medical records in the hospital and outpatient clinics. Clinical signs, symptoms, and laboratory findings were recorded, including fever, abdominal or lumbar pain, urinary complaints (frequency, urgency, dysuria), leucocyturia, and culture results.

At the laboratory, urine culture was performed as follows: fresh urine samples obtained by the clean-catch midstream method were refrigerated and delivered to the laboratory within a maximum of 12 h. Samples were inoculated using a 1-μl calibrated loop on Uriselect agar (Novamed Ltd., Jerusalem, Israel), which is a chromogenic agar that allows the preliminary identification of uropathogens [4].

Plates were examined following incubation of 24 and 48 h at 36°C. *Candida* spp. strains were identified by the appearance of colonies in Uriselect agar according to manufacturer's instructions and confirmation by Gram stain.

In the prospective phase of the study, *Candida* spp. strains isolated from all patients recruited between May 2006 and October 2006 were identified to the species level using API 32C (Biomerieux, France).

Statistical analysis

Variants from both groups were compared using the χ^2 statistic and Student's *t*-test. *p*-values≤0.05 were considered to be statistically significant.

Results

During the 18-month period of the study, a total of 100,522 urine cultures were received at the microbiology laboratory of the Haemek Medical Center; 91,747 (91.3%) and 10,253 (10.2%) from hospitalized and outpatients, respectively. Among them, 19,611 (19.5%) were considered as positive and grew uropathogens in significant numbers. *Candida* spp. was isolated in 204 cases (0.2% of all cultures or 1.0% of all positive cases); 125 from CAC (0.14% of all cultures in this group) and 79 from HAC (0.77% of all cultures in this group) ($p<0.0001$).

Table 1 shows demographic characteristics of both groups of patients (CAC and HAC). One hundred and fifty four patients (154, 75.5%) with candiduria were women. In the CAC group, there were more women in general, more pregnant women, and patients were significantly younger compared to the HAC group (Table 1).

Signs and symptoms characterizing both groups of patients are also presented in Table 1. The CAC group included significantly more bed-ridden patients, patients suffering from abdominal pain, and dysuria. However, significantly higher rates of diabetes mellitus, renal failure, presence of permanent catheter, antibiotic or immunosuppressive therapy in the last month, fever, and the presence of yeasts in urine sediment were seen in the HAC group. The mortality rate was also higher in this group. However, the death rate attributable to the presence of *Candida* in urine could not be established.

Table 2 shows the physician's decision on management as a consequence of a positive culture growing *Candida* spp. As can be seen, significant differences between groups regarding the performance of recurrent cultures, removal of catheters, and imaging requests were not observed. Moreover, in the majority of the cases (81.4%), nothing was done. However, significantly more patients in the HAC group received antifungal therapy following positive cultures.

The species distribution of the 51 strains isolated in the prospective phase of the study is shown in Table 3. As shown in the table, *Candida albicans* was isolated in half of the cases, and significant differences between groups regarding the prevalence rates of species were not observed.

Discussion

The prevalence of *Candida* infection in general and hospital candiduria in particular is on the rise worldwide, mainly due to the increasing use of immunosuppressive and antibiotic therapy and invasive procedures. Although data is available regarding the hospitalized patient, CAC has not yet been sufficiently investigated. The goals of the present

Table 1 Demographic characteristics, signs, and symptoms in both groups

	CA	HA	Total	*p*
Age mean: years (range)	46 (16–97)	72 (12–96)	62 (12–97)	<0.001
Gender (male): *n* (%)	23 (18.4)	27 (34.2)	50 (24.5)	<0.01
LTCF: *n* (%)	12 (9.5)	12 (15.0)	24 (11.7)	ns
Bed-ridden: *n* (%)	37 (46.8)	23 (18.5)	60 (29.4)	0.001
Pregnancy: *n* (%)	23 (22.5)	1 (1.9)	24 (15.6)	0.001
Diabetes mellitus: *n* (%)	36 (28.8)	35 (44.3)	71 (34.8)	0.02
Renal failure: *n* (%)	14 (11.2)	22 (27.8)	36 (17.6)	0.002
Permanent catheter: *n* (%)	19 (15.2)	26 (32.9)	45 (22.1)	0.003
Recurrent UTI: *n* (%)	45 (36.0)	23 (29.1)	68 (33.3)	ns
Nephrolithiasis: *n* (%)	15 (12.0)	7 (8.9)	22 (10.8)	ns
Malignancy: *n* (%)	13 (10.4)	10 (12.7)	23 (11.3)	ns
AB Tx: *n* (%)	58 (46.4)	58 (73.4)	116 (56.9)	0.001
IMM Tx: *n* (%)	4 (3.2)	8 (10.1)	12 (5.9)	0.04
Fever: *n* (%)	32 (25.6)	49 (62.0)	81 (39.7)	<0.001
Abdominal pain: *n* (%)	48 (46.6)	10 (21.3)	58 (38.7)	0.003
Dysuria: *n* (%)	56 (54.4)	5 (10.9)	61 (40.9)	<0.001
Leucocyturia: *n* (%)	54 (65.1)	35 (56.5)	89 (61.4)	ns
Candida seen in urine sediment: *n* (%)	8 (6.4)	11 (13.9)	19 (9.3)	0.009
Death: *n* (%)	3 (2.4)	21 (26.6)	24 (11.8)	<0.001

CA=community-acquired; HA=hospital-acquired; LTCF=living at long-term care facility; ns=not statistically significant; AB Tx=antibiotic treatment during the last month; IMM Tx=immunosuppressive therapy during the last month

study were to determine the prevalence of CAC and HAC among all urine cultures sent to our facility, to compare the risk factors for acquirement, and examine the clinical significance of both.

Candiduria, a clinical situation defined as the presence of *Candida* spp. in significant numbers in urine, has been extensively reported in the last 20 years [1–3]. Most of the candiduria cases are nosocomial, as a result of a catheter insertion or other invasive procedures in the urinary tract, or following prolonged antibiotic therapy. *Candida* species have been reported as being the cause of up to 20% of UTI episodes in intensive care units, being the most prevalent organism after *Escherichia coli* [5]. In contrast, CAC is a much less common clinical entity, and has been scarcely investigated [6].

The presence of candiduria may be classified into three different categories:

1. Colonization/contamination: colonization of the urinary tract by *Candida* spp. without any clinical significance or contamination of permanent catheters. In a study by Schönebeck and Anséhn [7], *Candida* spp. have been recovered from the urine of 2.2% of healthy asymptomatic non-hospitalized patients.
2. Urinary tract infection: as other pathogens, *Candida* spp. can cause lower (cystitis) and upper (pyelonephritis) UTI. The latter may lead to a complicated situation called "fungus ball," a fungal mass in the urinary tract [8].
3. Candiduria as a consequence of systemic infection: mostly in immunocompromised patients.

C. albicans causes 50–70% of all cases of candiduria [9, 10], *C. glabrata* is next (25%) [11, 12], followed by *C. parapsilosis* and *C. tropicalis* in descending order. *C. parapsilosis* frequently causes candiduria in neonates systemically infected with this yeast [13]. In about 2% of candiduria cases, more than one species of *Candida* are isolated at the same specimen [14].

Candiduria is mostly asymptomatic; Kauffman et al. [14] reported that, among 861 patients with HAC, 2% were symptomatic and only 1.3% of the immunocompromised

Table 2 Physician's decision on management

Physician's decision	CA *n* (%)	HA *n* (%)	Total *n* (%)	*p*
Repeat culture	18 (14.4)	6 (7.6)	24 (11.8)	ns
Removal of catheter	0 (0)	2 (2.5)	2 (0.98)	ns
Antifungal treatment	5 (4.0)	9 (11.4)	14 (6.9)	0.04
Renal ultrasonography or CT	1 (0.8)	1 (1.3)	2 (0.98)	ns
No intervention	101 (80.8)	65 (82.3)	166 (81.4)	ns

CA=community-acquired; HA=hospital-acquired; CT=computed tomography; ns=not statistically significant

Table 3 Species distribution of 51 *Candida* isolates

Species	CA *n* (%)	HA *n* (%)	Total *n* (%)	*p*
C. albicans	14 (51.9)	11 (45.8)	25 (49.0)	ns
C. glabrata	4 (14.8)	6 (25.0)	10 (19.6)	ns
C. tropicalis	5 (18.5)	4 (16.7)	9 (17.6)	ns
C. parapsilosis	2 (7.4)	2 (8.3)	4 (7.8)	ns
Other	2 (7.4)	1 (4.2)	3 (5.9)	ns
Total	27 (100)	24 (100)	51 (100)	

CA=community-acquired; HA=hospital-acquired; ns=not statistically significant

patients developed candidemia. On the other hand, candiduria in immunocompromised patients is frequently a consequence of systemic infection [15, 16], and it is present in about 10% of candidemia cases [17, 18].

In general, the clinical significance of candiduria is controversial. Candiduria is mostly related to contamination, colonization, or benign infection of the lower urinary tract [11, 14, 19, 20]. Unfortunately, clinical features are not specific, and in critically ill patients in intensive care units, fever and leukocytosis may have several other causes. In contrary to bacterial infection, pyuria and colony counts are not always helpful in discriminating between contamination, colonization, and true *Candida* infection. The presence of pyuria in catheterized patients has not been shown to be helpful in differentiating infection from colonization, as an indwelling catheter may itself lead to pyuria due to mechanical irritation of bladder mucosa and because of concomitant bacteriuria [21]. Moreover, the clinical significance of candiduria in pregnant women is also still unclear and should be evaluated. Imaging by ultrasonography (US) or computed tomography (CT) are helpful tools in diagnosing fungus ball, a clinical situation that requires a more aggressive treatment approach [22], but not in other situations.

The incidence of candiduria among hospitalized patients could reach values higher than 20%, especially in critically ill patients [23, 24]. In contrast, in the present study, we found much lower values: from 10,253 urine cultures from hospitalized patients, only 0.77% grew *Candida* spp., and 0.14% of 91,747 cultures from outpatients did so.

According to these findings, candiduria seems to be a very infrequent uropathogen in our region in general and in our hospital particularly.

Risk factors for the acquirement of HAC have been analyzed in a number of case–control and prospective surveillance studies, and are well characterized. Remarkably, all studies presented similar findings: increased age, female gender, use of long-term indwelling urethral catheters or other urinary drainage devices, stay at intensive care units, previous use of antibiotics, surgical procedures, and diabetes mellitus [3, 14, 22, 25]. However, data regarding risk factors for CAC was not found in an extensive Medline search.

In our study, we compared possible risk factors between the two groups. Our findings showed (Table 1) that patients in the CAC group were significantly younger than those in the HAC group, and there was a higher percentage of females with CAC compared with HAC ($p<0.01$). A possible explanation to this finding may be the increased use of antibiotics by women with recurrent UTI and the use of hormones, which increase the colonization of *Candida* in the urogenital tract. Unfortunately, data regarding the use of such drugs as long-term therapy was not available in this study.

Significantly higher percentages of pregnant women and bed-ridden patients were observed in the CAC group compared to the HAC group. The latter could be probably explained by the use of permanent urinary catheters or stay in long-term care facilities (LTCF).

As expected, diabetes mellitus, renal failure, permanent catheter, previous antibiotic or immunosuppressive treatment in the last month, and fever were observed in both groups, but were significantly more frequent in patients with HAC. However, significantly more patients with CAC presented with abdominal pain or dysuria.

The majority of the urine cultures from hospitalized patients are requested as a part of source-of-fever investigation, even in the absence of any urinary complaints. This could explain the higher percentage of fever in the HAC group and the presence of more urinary signs, like abdominal pain and dysuria, in CAC patients.

Accordingly, the clinical significance of candiduria seems to be very poor, especially in the asymptomatic patient. As can be seen in Table 2, in the vast majority of cases (81.4%), physicians decided carry out any intervention, treatment, or further diagnostic procedures related to candiduria findings. Moreover, only in 14.4% and 7.6% of the cases in CAC and HAC, respectively, was a new urine culture was requested. As expected, more patients in the HAC group were treated with antifungals following a positive culture, but this was the unique significant difference between groups regarding management decision.

In early reports on HAC [1–3], the prevalence rates of *C. albicans* were much higher than in recent studies, this due to the fact that the prevalence of non-*albicans* species is on the rise worldwide. As has been reported by other authors [3, 14], in the prospective phase of our study, we found that the most frequent species isolated were *C. albicans*, *C. glabrata*, and *C. tropicalis* (Table 3). These three species

were the most frequent in both groups, and, in fact, no significant differences were found between groups regarding the frequency of all species.

In conclusion, we compared the characteristics of CAC to those of HAC. However, the main limitation of this work was the lack of a control group including outpatients without candiduria. The inclusion of such group of patients would allow a multivariate analysis in order to define independent risk factors for CAC.

An interesting finding was that, in the great majority of the cases, the isolation of *Candida* spp. from urine cultures did not affect the physician's decision on patient management.

The clinical significance of CAC remains unclear and should be investigated in future studies.

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