Candidemia Distribution, Associated Risk Factors, and Attributed Mortality at a University-Based Medical Center

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***Candida* is the fourth most common cause of nosocomial bloodstream infections (BSI), being *Candida albicans* the most common species. This study evaluated the distribution of *Candida spp* isolates at a tertiary care medical center. The associated factors and outcome of patients with candidemia at the Puerto Rico Medical Center (PRMC) were evaluated. Laboratory data from May 2005 to April 2006 was reviewed. Blood cultures reported as positive for *Candida spp* were identified and records were reviewed. Two hundred and four blood cultures were reported with *Candida spp*, corresponding to 85 different episodes of candidemia in 82 patients: 3 patients presented more than one candidemia episode with two different *Candida spp*. In seventy-two percent (61/85) of candidemia episodes, the organism isolated was a non-albicans Candida, being *C. parapsilosis* the most common species isolated with 49% (42/85). Sixty five records were evaluated; of which 45 cases were reviewed (20 cases were excluded from the study due to incomplete information). The predominant factors identified were being on broad spectrum antibiotics 95.6% (43/45), central catheter placement 97.8% (44/45), mechanical ventilation 64.4% (29/45), and urinary catheter placement 73.3% (33/45). The mortality among the reviewed cases was 48.9% (22/45). [*P R Health Sci J 2010;1:26-29*]**

Key words: Candidemia, Non-albicans candida, Candida albicans, Candida parapsilosis

Nosocomial bloodstream infections (BSI) are an important cause of morbidity and mortality in hospitalized patients. *Candida* infections account for the fourth most common pathogen in patients admitted to critical care units as evidenced in a multi-center study performed in 49 hospitals in the United States (1). A multicenter prospective observational study conducted at several tertiary care centers in the United States revealed that *C. albicans* was the most common *Candida* species isolated in BSI (2). Similar surveillance studies had reported an increasing trend of candidemias secondary to non-albicans *Candida* (NAC) (3).

NAC presents a therapeutic challenge in view of increased incidence of azole-resistance when compared to *C. albicans* species. *C. glabrata* and *C. krusei* are usually considered to be resistant to azoles (4). On the other hand, important virulence factors, such as adhesion and biofilm formation affecting indwelling devices, may be responsible for *C. parapsilosis* infections (5-7).

The Puerto Rico Medical Center (PRMC) at San Juan, Puerto Rico, provides medical care to an underserved population with a wide variety of conditions. At our institution, which is a tertiary care hospital and a referral center for the Caribbean, the distribution of fungal BSI has not been documented. The aim of this study was to evaluate the distribution of *Candida spp* at our center. Additional information such as demographics, comorbidities, presence of artificial medical devices, and outcome were also obtained to evaluate associated risk factors present in our patients' population.

Methods

This study is a retrospective review of positive blood cultures with *Candida spp* reported by the bacteriology division of patients admitted to the PRMC from May 2005 to April 2006. Identification was performed at the laboratory according to standard microbiological techniques. Records were reviewed in order to evaluate patients' demographics, potential risk factors, and outcome. Candidemia was defined as the presence of at

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least one positive blood culture with *Candida spp*. Mortality was defined as death during hospitalization.

Statistical analysis was performed using the statistical package for the social science (SPSS version 16.0 for Windows). Summary statistics were performed using measures of central tendency and dispersion. Categorical variables were summarized using proportions and percentages. Pearson X2 and Fisher's exact test statistics were employed to compare differences between survived and deceased patients.

Results

The frequency of different *Candida* species in the 82 patients with BSI is shown in Figure 1. Two-hundred and four isolates were reported during the evaluated period, corresponding to 85 different episodes of candidemia in 82 patients. The evaluated isolates corresponding to 85 candidemia episodes were identified as: 42 (49%) *C. parapsilosis*, 24 (28%), *C. albicans*, 14 (17%) *C. tropicalis*, 3 (4%) *C. glabrata*, 1 (1%) *C. krusei*, and 1 (1%) *C. rugosa*. Three patients presented two different *Candida spp* isolated during hospitalization representing different candidemia episodes: one patient presented with *C. parapsilosis* and *C. tropicalis*; and the other two patients presented with *C. tropicalis* and *C. albicans*.

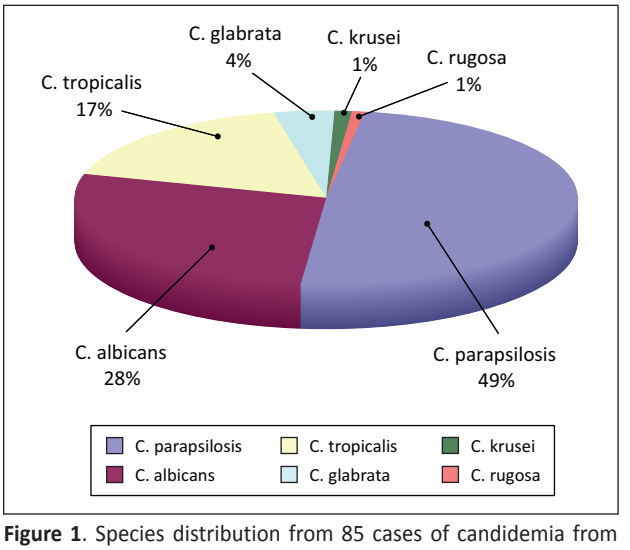

Figure 1. Species distribution from 85 cases of candidemia from May 2005 to April 2006

The distribution of the identified *Candida* cases is shown in Figure 2; 22 were from general medicine (27%), 14 from the adult intensive care unit (17%), 20 from the pediatric intensive care unit (24%), 10 from general pediatrics (12%), 4 from the trauma unit (5%), 8 from surgery units (10%) (orthopedic, neurosurgery, and general surgery), and 4 from the hematology-oncology unit (5%). Overall, 41% of the patients belonged to an intensive care unit; including the three patients with two different *Candida spp* identified (1 in adult intensive care unit and 2 in pediatric intensive care unit).

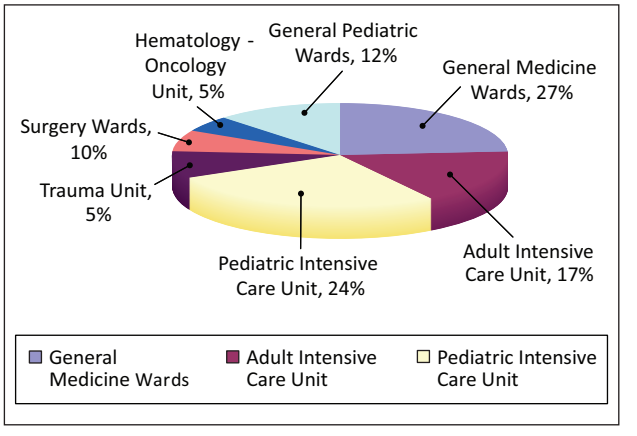

Figure 2. Distribution of the 82 patients with candidemia per ward

Sixty-five records from the identified cases were evaluated. Forty-five cases were analyzed and the remaining twenty records were excluded from the study due to incomplete information. Demographics at the time of diagnosis were 16 females (35.6%) and 29 males (64.4%). Our population consisted of 34 adults (75.6%) with a mean (s.d) age of 55.2 (15.5); and 11 pediatric patients (24.4%) of which 9 were premature infants. Review of potential predisposing factors revealed that 97.8% of the cases had central venous catheters, 73.3% had a urinary catheter, 64.4% required mechanical ventilation, and 95.6% had received broad spectrum antibiotics. The average number of antibiotics used prior to the development of candidemia was 3 (range 0 to 7) in the survival group and 4 (range from 0 to 8) in the deceased group. The mortality was 48.9%. Other evaluated factors included past medical history, such as history of malignancy (18%), diabetes mellitus (22.2%), steroid administration (15.6%), HIV (8.9%), recent trauma (11.1%), abdominal surgery (17.8%), recent hospitalization (31.1%), total parenteral nutrition (46.7%), and hemodialysis (22.2%).

A comparison of clinical characteristics between the patients who survived (n=23) and those who died (n=22) is summarized in Table 1. Statistical analysis of the most common identifiable risk factors revealed that there exists a positive correlation between mortality of candidemia and early onset during admission (p=0.048). When analyzed by age groups (infants and adults), the same mortality was observed in this study. In the infant group, it was seen that 10 out of 11 patients (90.9%) had a strong evidence of TPN being a risk factor for candidemia and mortality (p=0.001). The presence of a urinary catheter (p=0.06) and mechanical ventilation (p=0.08) suggests an increased risk for mortality, but more data would be needed to verify this conclusion. From the analysis, there was insufficient evidence to conclude that there is a relationship between mortality and hemodialysis (p=0.13). Despite the presence of

central catheters in 97.8% of the patients in this study, statistical analysis failed to establish a correlation between this risk factor and mortality (p=0.99).

Table 1. Demographical data, risk factors, and mortality obtained from record review of patients with systemic candidiasis.

Cases Reviewed (N)	Total (%) 45	Survived (%) 23 (51.1)	Deceased (%) 22 (48.9)	p-value
Adults	34 (75.6)	17 (50)	17 (50)	0.99
Pediatric	11 (24.4)	6 (54.5)	5 (45.5)	0.55
Female	16 (35.6)	6 (37.5)	10 (62.5)	0.16
Male	29 (64.4)	17 (58.6)	12 (41.4)	0.25
Previous Antibiotic Administration	43 (95.6)	22 (51.2)	21 (48.8)	0.99
Cancer/Hematologic malignancy	8 (17.8)	3 (37.5)	5 (62.5)	0.38
Diabetes mellitus	10 (22.2)	4 (40)	6 (60)	0.42
HIV	4 (8.9)	2 (50)	2 (50)	0.99
Steroid administration	7 (15.6)	4 (57.1)	3 (42.9)	0.78
Recent Trauma	5 (11.1)	2 (40)	3 (60)	0.60
Surgical intervention				
Orthopedic	4 (8.9)	1 (25)	3 (75)	0.27
Abdominal	8 (17.8)	5 (62.5)	3 (37.5)	0.43
Pelvic	1 (2.2)	1 (100)	0 (0)	0.99
Neurosurgical	5 (11.1)	4 (80)	1 (20)	0.20
Recent hospitalization	14 (31.1)	4 (28.6)	10 (71.4)	0.048
Total Parenteral Nutrition	21 (46.7)	12 (57.1)	9 (42.9)	0.46
Central Catheter	44 (97.8)	22 (50)	22 (50)	0.99
Urinary Catheter	33 (73.3)	14 (42.4)	19 (57.6)	0.06
Mechanical Ventilation	29 (64.4)	12 (41.4)	17 (58.6)	0.08
Hemodialysis	10 (22.2)	3 (30)	7 (70)	0.13

Conclusions

The incidence of *Candida BSI* has considerably increased since the early 1980's (8). Candidemia is the fourth most common source of BSI and represents 8-15% of all nosocomial sepsis in USA (1). The incidence of *Candida* related BSI in Puerto Rico has not been studied.

The PRMC is a supra-tertiary institution providing services to an underserved population and is also a referral center for medical, pediatric, gynecologic, and surgical patients, including its sub-specialties. It is also the leading trauma center in the Caribbean. Our center provides medical care to hematologic malignancy patients and has the only leukemia/bone marrow transplant unit available in the Island. The severity of illness present in a considerable amount of patients, especially those admitted to Medicine wards and intensive care units, could be a contributing factor to the high incidence of candidemia observed in these groups (27% in the Medicine wards and 41% in intensive care units). In contrast to current data, which presents *C. albicans* as the primary pathogen causing fungemia across the world, *C. parapsilosis* was identified as the leading species at our center. To our knowledge, this finding has only been reported by another center in Osaka, Japan (9). Several studies have suggested an increased incidence of *C. parapsilosis* in Latin America, which might in part explain our findings (5, 7, 10).

Antifungal prophylaxis and empirical therapy is commonly used in patients with acute myelogenous leukemia receiving standard chemotherapy leading to neutropenia, in allogeneic bone marrow transplant, and in high risk autologous bone marrow transplant (4). This approach to the hematologic malignancy patient, which is also practiced at our institution, might explain the low incidence of candidemia in this group (5% of the samples studied). Taking into consideration that *C. albicans*, which was the only species isolated in this group, is repeatedly reported in literature as being susceptible to fluconazole (7-8), the use of this medication as preemptive or prophylactic therapy should be adequate for our patients and could be considered as the first choice antifungal agent when therapy for candidemia is required at our center.

The risk factors identified for the development of candidemia in our study were similar to those described in the literature (6-8, 11-16). The majority of patients had a central venous catheter (97.8%), a urinary catheter (73.3%), was on mechanical ventilation (7, 8, 11-13) (64.4%) or had received broad spectrum antibiotics (95.6%). *C. parapsilosis* is an exogenous pathogen that may be found on the skin and is known to form biofilms on catheters and other medical devices. Infections with this organism have been associated with hyperalimentation, poor catheter care, and breaks in infection control practices (6-7). Further studies regarding infection control techniques at our institution need to be considered in order to determine if these factors influenced our findings.

The mortality in our study was 48.9%, which correlates with the range reported in literature of 40-60% (1, 11, 17-20). Evaluation of risk factors in our population leads to suggest that the presence of a urinary catheter or exposure to mechanical ventilation, which are usually present in critically ill patients with guarded prognosis, contribute independently to a fatality outcome. Statistical analysis failed to confirm an association between central catheter placement and mortality. This finding may be explained by the fact that 97.8% of the patients studied had a central catheter, making the group of patients without central catheter too small for comparison.

In summary, species distribution of *Candida* BSI at the PRMC was found to differ from the one published in literature. *C. parapsilopsis* was the most common species encountered, in contrast to *C. albicans* at other similar settings. This finding may be accounted for by the frequent use of central venous catheters (97.8% of the evaluated cases) and recent reports of changing *Candida* epidemiology in Latin America.

The mortality of patients with candidemia and the prevention of this infection seem to be greatly influenced by knowledge of local epidemiology and risk factors. Further investigation studies regarding aseptic techniques, care of inserted medical

devices, removal of unnecessary catheters, and avoidance of unnecessary antibiotic administration should be designed to determine if these factors could be contributing to the rate of candidemia at our institution. *Candida* species susceptibility testing, which was not being performed on a regular basis at the PRMC at the moment of this investigation, is currently available. A prospective investigation should be designed to integrate susceptibility testing to our study and to confirm the role of fluconazole as first line agent.

Resumen

Las especies de *Candida* constituyen la cuarta causa de infecciones del torrente sanguíneo aisladas por hemocultivo, siendo *Candida albicans* la especie más común. Este estudio evaluó la distribución de las especies de *Candida* aisladas en cultivos de sangre en un Centro Médico de cuidado terciario. Los factores asociados y el desenlace final de los pacientes con candidemia en el Centro Médico de Puerto Rico fueron evaluados. Se revisó la información del laboratorio de microbiología desde mayo del 2005 hasta abril del 2006. Los cultivos de sangre reportados positivos para alguna especie de *Candida* fueron identificados y los expedientes médicos de estos pacientes fueron revisados. Se reportaron un total de doscientos cuatro cultivos de sangre positivos para especies de *Candida* los cuales correspondían a ochenta y dos pacientes: tres de los cuales presentaron 2 episodios de candidemia con diferentes especies de *Candida* aisladas. El setenta y dos por ciento (61/85) de las candidemias fueron secundarias a especies de *Candida* no-albicans, siendo *C. parapsilosis* la especie más comúnmente aislada con un total de cuarenta y nueve por ciento (42/85). Sesenta y cinco expedientes fueron evaluados, de los cuales revisamos cuarenta y cinco casos. Los factores de riesgo predominantes eran: haber recibido antibióticos de amplio espectro, 95.6% (43/45); catéteres venosos centrales, 97.8% (44/45); tubo endotraqueal para ventilación mecánica, 64.4% (29/45); y catéteres urinarios, 73.3% (33/45). El índice de mortalidad entre los casos revisados fue de 48.9% (22/45).

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