

Eleven-year retrospective survey of candidaemia in a university hospital in southwestern Greece

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Abstract

The aim of this study was to investigate the isolation and distribution rate of *Candida* spp. in blood cultures and evaluate antifungal susceptibility during an 11-year period (1998–2008) at a tertiary-care hospital. The causative species were as follows: *Candida albicans*, 163 strains (64%); *Candida parapsilosis*, 35 strains (13.7%); *Candida glabrata*, 25 strains (9.8%); *Candida tropicalis*, 19 strains (7.4%); and other *Candida* spp., 13 strains (5.1%). Candidaemia is predominantly caused by *C. albicans*. *C. parapsilosis* is the most common non-*albicans* *Candida* isolated in neonatal intensive-care units. All *Candida* isolates remain susceptible to amphotericin B, whereas the highest degree of resistance was observed for azoles.

Keywords: Antifungals, *Candida albicans*, candidaemia, epidemiology, non-*albicans* *Candida*

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Bloodstream infections (BSIs) are major causes of morbidity and mortality in developed countries. Recent studies in the USA have classified these infections as the eighth leading cause of infant death and the tenth leading cause (3.4%) of overall death. The incidence of *Candida* BSIs has doubled

during the past two decades [1], and *Candida* has become the fourth most frequent pathogen, accounting for 8% of cases of hospital-acquired sepsis [2]. Although *Candida albicans* remains the most prevalent yeast causing candidaemia, an increase in the number of cases caused by non-*albicans* species has been also reported [3]. Risk factors for candidaemia include prolonged stay in intensive-care units (ICUs), increased use of broad-spectrum antibiotics, treatment with corticosteroid and antineoplastic agents, use of central venous or other catheters, receipt of parenteral nutrition, abdominal surgery, solid organ or bone marrow transplantation, and the presence of haematological malignancy.

An 11-year surveillance of candidaemia cases was carried out in the University Hospital of Patras in southwestern Greece. This is a 750-bed hospital with about 100 000 ambulatory visits and 52 000 admissions per year. It offers a number of special services providing organ transplantation (kidney), haematology/oncology (including stem cell transplantation), infectious diseases, neurosurgery and intensive-care (neonatal, paediatric, and general adult) facilities. Clinics belong to four main departments: medical wards (internal medicine, cardiology, nephrology, neurology, haematology/oncology, and transplantation centre), surgical wards (general surgery units, orthopaedics, obstetrics, neurosurgery, and urology), an adult ICU, and a neonatal ICU. Determination of candidaemia cases, relative prevalence and species distribution, as well as susceptibility testing, was performed. An episode of candidaemia was defined as one or more positive blood cultures for *Candida* spp. isolated from patients with clinical signs of infection, according to the European Organization for Research and Treatment of Cancer [4]. Subsequent positive cultures from the same patient were defined as a new episode only if there was an interval of at least 12 weeks between the two episodes.

Candida isolation from blood cultures was performed with BactAlert 3D (Organon Teknika, Lyon, France). All isolates were identified using the germ-tube test and API32C system (Bio-Merieux, Lyon, France). Antifungal susceptibility was determined by Etest (AB Biodisk, Solna, Sweden) on RPMI–2% glucose agar, and MICs of amphotericin B, 5-fluorocytosine, ketoconazole, itraconazole, fluconazole, voriconazole, posaconazole and caspofungin were evaluated according to the manufacturer's instructions. Resistance to 5-fluorocytosine was defined as MIC ≥ 32 mg/L, resistance to fluconazole as MIC ≥ 64 mg/L, resistance to itraconazole as MIC ≥ 1 mg/L, and resistance to voriconazole as MIC ≥ 4 mg/L, whereas the MIC cut-off value for determination of resistance to caspofungin was 2 mg/L, as proposed by Etest Interpretive Criteria and in accordance with CLSI guidelines as described in M27-

A2 (no interpretive breakpoints for caspofungin are included) [5,6]. The MIC cut-off value for susceptibility to amphotericin B was 1 mg/L [5,7]. Isolates with MICs \leq 1 mg/L were considered to be susceptible to posaconazole [8] whereas strains with MICs \geq 1 mg/L were considered to be resistant to ketoconazole.

At the clinical laboratory of the microbiology department, 151 399 blood cultures were processed. Among 13 417 positive blood cultures accounting for 7811 BSI cases, 438 were positive for *Candida* spp., reflecting 255 candidaemia cases. No patient had more than one episode of candidaemia during hospitalization. An increasing frequency of *Candida* BSI during the study period was observed, varying from 1.33% (eight cases) of all BSIs or 0.068% of all blood cultures in 1998, to 4.4% (47 cases) or 0.472% respectively in 2008. *C. albicans* was the leading cause (163 cases; 64%), followed by *Candida parapsilosis* (35 cases; 13.7%). *Candida glabrata* was isolated from 25 cases (9.8%) and *Candida tropicalis* from 19 cases (7.4%). Other *Candida* species were isolated in 13 cases of candidaemia (5.1%). Relative frequencies were 1.56% (four cases) for *Candida guilliermondii*, 1.17% (three cases) for *Candida humicola*, 0.78% (two cases each) for *Candida lipolytica* and *Candida lucaniae*, and 0.4% (one case each) for *Candida krusei* and *Candida stellatoidea*. During the study period, a trend to *Candida* non-*albicans* spp. was observed between 2000 and 2003 (Fig. 1).

One hundred and six (106) candidaemia cases (41.6%) originated in medical wards, 61 cases (23.92%) in surgical wards, 61 cases (23.92%) in the neonatal ICU, and 27 cases (10.6%) in the adult ICU. *C. albicans* was the most frequent isolate in all departments, ranging from 58.5% in medical wards to 77.7% in the adult ICU. *C. parapsilosis* had a high incidence in the neonatal ICU (26.3%). *C. glabrata* was the most common non-*albicans* *Candida* species in the adult ICU (11.1%), and *C. tropicalis* was the most common in surgical wards (11.5%). Other *Candida* spp. had a relatively high incidence in medical wards (9.4%) (Table 1).

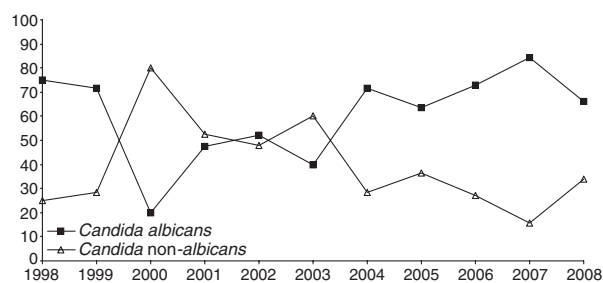


FIG. 1. *Candida albicans* vs. non-*albicans* *Candida* distribution (%) during the study period.

TABLE 1. Species and department distribution of *Candida* bloodstream isolates

Species	Medical wards, no. (%)	Surgical wards, no. (%)	ICU, no. (%)	Neonatal ICU, no. (%)
<i>Candida albicans</i>	62 (58.5)	42 (68.85)	21 (77.78)	38 (62.3)
<i>Candida parapsilosis</i>	13 (12.26)	5 (8.2)	1 (3.7)	16 (26.2)
<i>Candida glabrata</i>	12 (11.3)	5 (8.2)	3 (11.1)	5 (8.2)
<i>Candida tropicalis</i>	9 (8.5)	7 (11.4)	2 (7.4)	1 (1.6)
<i>Candida</i> spp.	10 (9.4)	2 (3.2)	0 (0)	1 (1.6)

ICU, intensive-care unit.

All strains were susceptible to amphotericin B. The highest resistance rates were observed for azoles, especially itraconazole, fluconazole, and ketoconazole. *C. glabrata* and *C. tropicalis* demonstrated the highest rates of resistance to azoles.

Although posaconazole is a relatively new azole that was first used in our setting in 2007, five of eight *C. glabrata* strains (62.5%) were found to be resistant (Table 2). In terms of antifungal consumption in our hospital, amphotericin B is considered to be the first-choice agent, and caspofungin is used as an alternative. Regarding azoles, fluconazole and, more recently, voriconazole and posaconazole are first-choice antifungal agents.

C. albicans represented more than half of all isolates, a finding that is in accordance with most European studies [9–11], in contrast to the USA [12] and Asia [13,14], where non-*albicans* *Candida* spp. account for more than half of candidaemia cases.

C. albicans predominated in all departments. *C. parapsilosis* had a high incidence in the neonatal ICU, which is a consistent finding in many studies [1,15–17] and may be attributed to the use of central venous catheters [18] and parenteral alimentation in premature infants. In the adult ICU, *C. glabrata* (11.1%) was the most common non-*albicans* *Candida* sp., a finding that is in accordance with other studies [17,19]. In medical wards, a relatively high incidence of not only *C. parapsilosis*, *C. tropicalis* and *C. glabrata* but also of other uncommon *Candida* spp. was observed as compared with other departments, and was associated with a relatively low incidence of *C. albicans* (58.5%). This is probably because haematology patients were included in this study, and it is well known that in such patients the prevalence of non-*albicans* *Candida* is relatively high [1,17,20]. In agreement with other studies, the high incidence of *C. tropicalis* in surgical wards (11.5%) may be attributed to underlying diseases of hospitalized patients [21]. Although *C. krusei* has emerged as a quite common species in other settings

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