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Nosocomial candidemia: A threat beyond nosocomial bacterial infections in intensive care units

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Candida bloodstream infections (BSI) have become an increasing cause of BSI in intensive care units (ICUs). The increasing incidence of nosocomial infections and multidrug-resistant bacteria in ICUs prolong hospitalization and cause prolonged exposure to multiple broad-spectrum antibiotics and invasive procedures. As a result of these risk factors, candidemia becomes a major threat for ICU patients. Moreover, the cause of candidemia has shifted from *Candida albicans* to non-albicans species, which causes problems in therapy (1,2).

We conducted a retrospective chart review of ICU patients who had candidemia between 2003 and 2009. The aim was to assess the change in the incidence of candidemia over 7 years and to determine the distribution of *Candida* species, risk factors for candidemia, and mortality rates.

The study was carried out at the Erciyes University Hospital. We performed retrospective laboratory-based surveillance from January 2003 to December 2009 in 7 adult (>16 years) ICUs (general surgery, medical, anesthesiology, neurosurgery, pulmonary, coronary, and cardiovascular surgery ICU). The hospital had an automated blood culture system (BACTEC) and data were recorded in an electronic database. Patient chart reviews were performed in order to identify clinically relevant episodes and to determine the demographic and epidemiologic characteristics of patients. Nosocomial candidemia was defined according to the criteria outlined by the Centers for Disease and Control (3).

To calculate incidence rates, the numbers of patient-days were collected. Incidence rates were calculated as the number of nosocomial infection episodes per 1000 patient-days and candidemia episodes per 10,000 patient-days. Data were entered and analyzed using SPSS 15.0 (SPSS, Inc. Chicago, IL, USA). Categorical data were analyzed using chi-square or Fisher's exact tests, as appropriate, and continuous variables were compared using Student's t tests. P values <0.05 were accepted as statistically significant.

During the period 2003-2009, a total of 124 cases of candidemia were detected, for an overall incidence of 16.1 per 10,000 patient-days (Table 1). All patients had had a single episode. As shown in Table 2, the incidence rate of candidemia in ICUs ranged from 0.8 to 18 per 10,000 patient-days/year and increased during the 7 years. The high incidence was in the general surgery ICU (20.3/10,000 patient-days) and medical ICU (18.9/10,000 patient-days). Demographic and clinical characteristics of 124 candidemia episodes are shown in Table 1. The length of stay in the ICU and hospital was long and 98% of patients had had at least one nosocomial infection and

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Table 1. Clinical characteristics of 124 adult episodes of candidemia.

Variable	No. (%)
Incidence per 10,000 patient days	16.1
Distribution of cases in ICU	Incidence per 10,000 patient days
General surgery	20.3
Medical	18.9
Anesthesiology	11.9
Neurosurgery	4.4
Pulmonary	7.8
Coronary	4.5
Cardiovascular surgery	1.8
Age (years; mean ± SD)	60.43 ± 15.81
Male gender	55 (45)
Duration of hospitalization before candidemia (days; mean ± SD)	22.62 ± 16.45
Duration from admission in ICU before candidemia (days; mean ± SD)	19.78±17.01
Underlying disease	29 (23)
Diabetes mellitus	23 (19)
Coronary artery disease	23 (19)
Gastrointestinal bleeding	22 (18)
Chronic lung disease	21 (17)
Malignancy	16 (13)
Congestive heart failure	10 (8)
Chronic renal failure	10 (8)
Trauma	9 (7)
Cerebrovascular disease	4 (3)
Cirrhosis	2 (2)
Myasthenia gravis	1 (0.8)
Transplantation	26 (21)
Steroid therapy	121 (98)
Previous nosocomial infection	121 (98)
Previous antibiotic therapy	84 (69)
Bacteremia	116 (94)
Invasive procedures	113 (91)
Foley catheter	107 (86)
Central venous catheterization	61 (49)
Endotracheal tube	58 (47)
Tracheostomy	102 (82)
Drainage tube	75 (61)
Total parenteral nutrition	48
Operation	27
Gastrointestinal	83
Others	58
Previous antibiotic therapy	54
Carbapenems	36
Glycopeptide	36
Cephalosporin	29
Quinolone	29
Piperacillin/tazobactam	10
Ampicillin/sulbactam	6
Aminoglycoside	6
Tigecycline	1
Metronidazol	1
Clindamycin	1
Trimetoprim/sulfamethoxazole	
Penicillin	
Clarithromycin	

Table 2. Incidence and distribution of candidemia between 2003 and 2009 at Erciyes University Hospital intensive care units expressed in number and percentage of isolates.

	2003	2004	2005	2006	2007	2008	2009
Incidence density of NI*(n/1000 patient-days)	34.2	33.1	39.1	36.7	40.2	46.5	44.2
Total candidemia	1	2	9	27	35	31	19
Incidence of candidemia/10,000 patient-days	0.8	1.7	6.6	17	18	15	8.7
Candida species							
Not typed (n = 63)	1	2	3	12	23	18	5
C. albicans (n = 26)	0	0	2	6	4	6	8
C. parapsilosis (n = 27)	0	0	4	8	6	5	4
C. tropicalis (n = 5)	0	0	0	0	1	2	2
C. glabrata (n = 2)	0	0	0	1	1	0	0
C. kefyr (n = 1)	0	0	0	0	0	0	0

*Nosocomial infection

antibiotic usage before candidemia. Furthermore, 84 (69%) of these patients had had bacteremia before candidemia. All of the patients had had at least one invasive procedure, and urinary catheter and central venous catheter were the most prevalent procedures. Seventy-five (61%) patients had had an operation, and 64% of these patients had had a gastrointestinal operation. Total parenteral nutrition had been given in 82% of the patients. Most of the candidemia episodes were defined as primary (n = 114, 92%) and sources of candidemia episodes were catheter (n = 7), urinary (n = 6), wound (n = 3), and lung (n = 1). *C. albicans* (n = 26) and *C. parapsilosis* (n = 27) were the most prevalent species (Table 2). In the comparison of demographic characteristics, risk factors, and mortality for these 2 species, no statistically significant difference was identified. Except for 2 *C. glabrata* isolates, all *Candida* isolates were susceptible to all antifungals; fluconazole was used for the susceptible isolates and amphotericin B was used for the azole-resistant isolates. The crude mortality rate was 76%.

Candidemia is not only associated with high mortality, but also increases morbidity, length of hospitalization, and medical costs in hospitals and ICUs. The estimated incidence was 4.6 bloodstream infections per 10,000 admissions and 6%-11% of all bloodstream infections (1). In recent years candidemia incidence has been increasing, especially in ICUs, due to advances in medical technology, invasive procedures, and broad spectrum antibiotics due to multi-drug resistant bacteria. The incidence of candidemia increased during the 7-year period in our ICUs, and 98% of these patients had at least one nosocomial infection and antibiotic usage before candidemia. The high incidence of nosocomial infections and multi-drug resistant bacteria (4,5) predispose for candidemia in our ICUs. Furthermore, patients had had long hospital and ICU stays (22.62 ± 16.45 and 19.78 ± 17.01, respectively) before candidemia, probably due to these nosocomial infections. The long stay and exposure to invasive procedures and antibiotics impair the host defense mechanisms of the patients. Moreover, TPN solutions and attendant central venous catheters altered cutaneous and gastrointestinal barriers that predispose candida colonization and candidemia. Ninety-one percent of our patients had central venous access and 82% received TPN solutions. Prior surgery, especially gastrointestinal surgery, is another familiar risk factor for candidemia (1). Additionally, 61% of the patients had surgery and gastrointestinal surgery comprised 64% of this group. Moreover, most of our episodes were defined as primary, which may reflect gastrointestinal colonization.

Unfortunately, *Candida* species were not observed in 51% of the isolates in this study. However, *C. parapsilosis* was as prevalent as *C. albicans,* which

reflects the problems concerning infection control measures in our ICUs. *C. parapsilosis* has different epidemiologic features than other species, and can occur without prior colonization. Furthermore, this species is frequently transmitted horizontally via contaminated external sources, such as medical devices or fluids, the hands of healthcare workers, prosthetic devices, and catheters.

The mortality rate of candidemia is still high despite advances in drugs and range between 30% and 70% with 20%-50% attributable mortality. Moreover, crude mortality rates were excessively high (76%) in the present study. However, we did not use any severity index. The high mortality rates may reflect the severity of underlying diseases, rather than being the direct consequence of candidemia as mentioned in literature (1).

The study has some limitations: it is not a case-control study, colonization index was not evaluated, and some data about patients and isolates were absent. However, this study showed the threat beyond high nosocomial infection rates and multi-drug resistant bacteria. To control bacterial infections and other risk factors in ICUs and to identify patients at highest risk, using colonization index, for candidemia, and prophylactic antifungal therapy may be a suitable approach for preventing nosocomial candidemia.

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