Diagnostic Microbiology and Infectious Disease 79 (2014) 205–208

Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

# Candidemia surveillance in Iowa: emergence of echinocandin resistance☆

Eiyu Matsumoto [a], Linda Boyken [b], Shailesh Tendolkar [b], Jennifer McDanel [b], Mariana Castanheira [c], Michael Pfaller [b,c], Daniel Diekema [a,b,*]

[a] Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, IA 52246
[b] Department of Pathology, University of Iowa Carver College of Medicine, Iowa City, IA 52246
[c] JMI Laboratories, North Liberty, IA

ARTICLE INFO

*Article history:*
Received 29 January 2014
Received in revised form 17 February 2014
Accepted 18 February 2014
Available online 1 March 2014

*Keywords:*
*Candida*
Bloodstream infection
Echinocandin
Antifungal resistance
Surveillance

ABSTRACT

We performed prospective surveillance for candidemia at 14 Iowa hospitals in 2011–2012. A total of 163 episodes were analyzed. *Candida albicans* (n = 69 [42%]) and *Candida glabrata* (n = 58 [36%]) were the most common species. Antifungal resistance was uncommon; 9% of *C. glabrata* were fluconazole resistant, and 5% (3 isolates) were intermediate or resistant to 1 or more of the echinocandins. Molecular analyses of the *fks*1 and *fks*2 hotspots of the *C. glabrata* revealed no mutations except in 2 of these 3 isolates (L628R and S629P in *fks*1). Compared with previous surveillance performed in 1998–2001, there was a decrease in proportion of candidemia due to *C. albicans* (58 to 42%) and an increased proportion due to *C. glabrata* (20 to 36%). Further emergence of echinocandin resistance among the increasingly common species *C. glabrata* would complicate the management of this life-threatening infection.

© 2014 Elsevier Inc. All rights reserved.

## 1. Introduction

*Candida* species are the third leading cause of bloodstream infections in US intensive care units (Hidron et al., 2008). Because candidemia is so common and so devastating, both prophylactic and therapeutic antifungal use has increased over the past 2 decades in the United States (Berrouane et al., 1999). Changes in antifungal use may be associated with changing epidemiology of candidemia. For example, the increase in azole use that occurred during the 1990s was associated with a shift in species distribution from a preponderance of *Candida albicans* to more frequent isolation of less azole-susceptible *Candida* species such as *Candida glabrata* (Trick et al., 2002). The more recent increase in echinocandin use has been associated with emergence of echinocandin-resistant *C. glabrata* (Alexander et al., 2013, Cleveland et al., 2012, Pfaller et al., 2012), resulting in concern for wider emergence of multiple-drug–resistant *C. glabrata* (Ostrosky-Zeichner, 2013).

Most of the published data on candidemia are from very large tertiary care centers, often located in urban areas. There is a relative paucity of data regarding candidemia in small- and medium-sized hospitals in rural areas. Many of these hospitals have limited capability to perform species identification (beyond *C. albicans*), and most do not perform on site antifungal susceptibility testing. Thus, there is a need to better describe the epidemiology of candidemia in regions that include representative samples of hospitals and to provide these centers with better local information with which to direct antifungal therapy.

Over 10 years ago, we performed statewide candidemia surveillance in Iowa (Diekema et al., 2002), establishing baseline data regarding the burden of candidemia in this rural Midwestern state. In this study, we repeated this surveillance. Our objectives were to monitor trends in species distribution and antifungal susceptibility of *Candida* species causing bloodstream infection in Iowa and to provide this information to participating institutions and practitioners to increase awareness of antifungal susceptibility patterns and help direct treatment approaches.

## 2. Methods

### 2.1. Surveillance

Fourteen Iowa hospital laboratories submitted consecutive unique patient blood culture isolates of *Candida* species. The hospitals ranged in size from 43 to 699 beds (median bed size, 277). All isolates were sent to the University of Iowa College of Medicine (Iowa City) for storage and further characterization by reference identification and susceptibility testing methods. In addition, a data form with demographic and epidemiologic information was submitted for each isolate. The de-identified form (with no protected health information included) included basic demographics, underlying illness and associated risk factor information, time and location of onset of signs and symptoms of infection, date of culture collection, patient

☆ This work was presented in part at IDWeek 2013 in San Francisco, CA, October 2–6, 2013.

* Corresponding author. Tel.: +319-356-7740; fax: +319-356-4916.
*E-mail address:* daniel-diekema@uiowa.edu (D. Diekema).

http://dx.doi.org/10.1016/j.diagmicrobio.2014.02.016
0732-8893/© 2014 Elsevier Inc. All rights reserved.

**Table 1**
Patient characteristics for 163 *Candida* bloodstream isolates.

| Variable | All *Candida* | CA, N = 69 | CGLA, N = 58 | CPRP, N = 13 | CTRO, N = 12 |
|---|---|---|---|---|---|
| Sex (N, % female) | 89 (55) | 36 (52) | 35 (60) | 4 (31) | 6 (50) |
| Age, median (range) in years | 56 (0–94) | 55 (0–93) | 60 (1–89) | 44 (29–73) | 60 (42–94) |
| LOS in days, median (range) | 9 (0–108) | 8 (0–53) | 10 (0–108) | 11 (2–33) | 7 (1–18) |
| LOS from + culture to discharge, median (range) | 5 (0–48) | 4 (0–48) | 7 (0–36) | 4 (0–21) | 3 (0–17) |
| Crude mortality, N (%) | 33 (20) | 16 (23) | 12 (21) | 0 (0) | 2 (17) |
| ICU stay, N (%) | 59 (36) | 23 (33) | 26 (45) | 0(0) | 6 (50) |
| Antifungal therapy, N (%)[a] | | | | | |
| Fluconazole | 87 (53) | 39 (57) | 36 (62) | 6 (46) | 5 (42) |
| Voriconazole | 4 (2) | 2 (3) | 1 (2) | 0 (0) | 1 (8) |
| Amphotericin B | 2 (1) | 1 (1) | 0 (0) | 0 (0) | 1 (1) |
| Caspofungin | 33 (20) | 12 (17) | 13 (22) | 2 (15) | 4 (33) |
| Micafungin | 27 (17) | 7 (10) | 17 (29) | 2 (15) | 0 (0) |

CA = *C. albicans*; CGLA = *C. glabrata*; CPRP = *C. parapsilosis*; CTRO = *C. tropicalis*.
[a] Percentage receiving the antifungal drug at any point during therapy.

outcome (in-hospital mortality), antifungal therapy given, and local laboratory findings (species ID and, if available, any susceptibility testing performed).

### 2.2. Organism identification

All *Candida* species blood culture isolates were subcultured onto potato dextrose agar not containing antibiotics (Remel, Lenexa, KS, USA) and BBL CHROMagar *Candida* medium (BD Diagnostics, Sparks, MD, USA) to ensure viability and purity. All *Candida* species identifications were performed using combinations of CHROMagar appearance, additional biochemical testing (e.g.. rapid trehalose for *C. glabrata*), Vitek YBC system (bioMerieux, St. Louis, MO, USA), appearance on cornmeal agar, and additional molecular identification methods as required. Isolates were stored as suspensions in sterile distilled water at ambient temperature prior to susceptibility testing, which was performed within 1 week of receipt of all isolates.

### 2.3. Susceptibility testing

Antifungal susceptibility testing was performed by the reference broth microdilution method exactly as described in the CLSI document M27-A3 (CLSI, 2007). Drugs tested included amphotericin B, fluconazole, voriconazole, itraconazole, posaconazole, caspofungin, micafungin, and anidulafungin. Newly approved CLSI breakpoints were applied for those drug-organism combinations for which CLSI breakpoints exist (Pfaller et al., 2010, 2012), and epidemiological cutoff values (ECVs) were used for drug-organism combinations, which do not have CLSI-approved breakpoints (Espinel-Ingroff et al., 2014). Quality control was performed by testing *Candida parapsilosis* ATCC 22091 and *Candida krusei* ATCC 6258.

### 2.4. Molecular characterization of echinocandin resistance

All *C. glabrata* isolates had sequencing of the FKS-encoding genes *fks*1 and *fks*2 for mutations associated with echinocandin resistance, as previously described (Castanheira et al., 2010).

## 3. Results

During the surveillance period from January 1, 2011, to September 15, 2012, a total of 163 unique *Candida* bloodstream infection isolates were submitted. The age range of patients with *Candida* bloodstream infection was from 2 months to 94 years (median, 56 years), and 55% were female. Fifty-nine (36%) patients were in the intensive care unit at the time of the candidemia, and overall crude mortality was 20%. Table 1 summarizes selected patient characteristics.

*C. albicans* (n = 69 [42%]) and *C. glabrata* (n = 58 [36%]) were the most common species causing candidemia during the study period. Differences in patient characteristics by the 4 major species are

**Table 2**
Antifungal susceptibility test results.

| Candida species | Antifungal | MICs in μg/mL | | % by category | | |
|---|---|---|---|---|---|---|
| | Agent | MIC range | MIC 50/90 | S | S-DD/I | R |
| All Candida N = 163 | Amphotericin | 0.25–2 | 1/2 | 100 | – | 0 |
| | Fluconazole | 0.12–128 | 0.25/4 | 63 | 33 | 4 |
| | Itraconazole | 0.007 to >8 | 0.06/1 | 98 | – | 2 |
| | Posaconazole | 0.007–2 | 0.06/1 | 96 | – | 4 |
| | Voriconazole | 0.007–4 | 0.015/0.12 | 96 | – | 4 |
| | Anidulafungin | 0.007–4 | 0.015/0.25 | 98 | 1 | <1 |
| | Caspofungin | 0.007–8 | 0.06/0.5 | 99 | 0 | <1 |
| | Micafungin | 0.007–8 | 0.03/0.25 | 95 | 4 | 1 |
| *C. albicans* N = 69 | Amphotericin | 0.5–2 | 1/1 | 100 | – | 0 |
| | Fluconazole | 0.12–1 | 0.12/0.25 | 100 | 0 | 0 |
| | Itraconazole | 0.007–0.12 | 0.06/0.06 | 100 | 0 | 0 |
| | Posaconazole | 0.007–0.06 | 0.03/0.06 | 100 | – | 0 |
| | Voriconazole | 0.007–0.06 | 0.007/0.007 | 100 | 0 | 0 |
| | Anidulafungin | 0.007–0.03 | 0.007/0.015 | 100 | 0 | 0 |
| | Caspofungin | 0.007–0.12 | 0.03/0.06 | 100 | 0 | 0 |
| | Micafungin | 0.007–0.06 | 0.03/0.03 | 100 | 0 | 0 |
| *C. glabrata* N = 58 | Amphotericin | 0.5–2 | 1/2 | 100 | – | 0 |
| | Fluconazole | 0.5–128 | 4/32 | 0 | 91 | 9 |
| | Itraconazole | 0.06 to >8 | 1/1 | 95 | – | 5 |
| | Posaconazole | 0.12–2 | 0.5/2 | 90 | – | 10 |
| | Voriconazole | 0.015–4 | 0.12/0.5 | 90 | – | 10 |
| | Anidulafungin | 0.015–2 | 0.03/0.06 | 98 | 0 | 2[a] |
| | Caspofungin | 0.015–8 | 0.06/0.12 | 98 | 0 | 2[a] |
| | Micafungin | 0.007–2 | 0.03/0.06 | 95 | 3[a] | 2[a] |
| *C. parapsilosis* N = 13 | Amphotericin | 0.5–1 | 1/1 | 100 | – | 0 |
| | Fluconazole | 0.12–1 | 0.5/0.5 | 100 | 0 | 0 |
| | Itraconazole | 0.03–0.25 | 0.12/0.25 | 100 | – | 0 |
| | Posaconazole | 0.03–0.06 | 0.06/0.06 | 100 | – | 0 |
| | Voriconazole | 0.007–0.03 | 0.007–0.015 | 100 | 0 | 0 |
| | Anidulafungin | 1–4 | 1/4 | 85 | 15 | 0 |
| | Caspofungin | 0.5–2 | 0.5/1 | 100 | 0 | 0 |
| | Micafungin | 1–8 | 2/4 | 62 | 31 | 8 |
| *C. tropicalis* N = 12 | Amphotericin | 1–2 | 1/2 | 100 | – | 0 |
| | Fluconazole | 0.12–1 | 0.25/1 | 100 | 0 | 0 |
| | Itraconazole | 0.03–0.5 | 0.06/0.25 | 100 | – | 0 |
| | Posaconazole | 0.015–0.25 | 0.06/0.06 | 92 | – | 8 |
| | Voriconazole | 0.007–0.12 | 0.015/0.06 | 100 | 0 | 0 |
| | Anidulafungin | 0.007–0.03 | 0.007/0.015 | 100 | 0 | 0 |
| | Caspofungin | 0.015–0.12 | 0.03/0.06 | 100 | 0 | 0 |
| | Micafungin | 0.015–0.06 | 0.03/0.06 | 100 | 0 | 0 |

MIC = Minimum inhibitory concentration as defined by CLSI; S = susceptible; S-DD/I = susceptible dose-dependent or intermediate; R = resistant; – = ECVs were used for this species-drug combination; thus, no S-DD/I category exists. For these combinations, S = wild type, R = non–wild type.
[a] One isolate resistant to all 3 echinocandins had S629P mutation in *fks*1; 1 isolate intermediate to micafungin had L628R mutation in *fks*1.

Download English Version:

https://daneshyari.com/en/article/6115834

Download Persian Version:

https://daneshyari.com/article/6115834

Daneshyari.com