6-15-2009

Epidemiology and outcomes of candidemia in 2019 patients: data from the prospective antifungal therapy alliance registry.

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MAJOR ARTICLE

Epidemiology and Outcomes of Candidemia in 2019 Patients: Data from the Prospective Antifungal Therapy Alliance Registry

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Background. Candidemia remains a major cause of morbidity and mortality in the health care setting, and the epidemiology of *Candida* infection is changing.

Methods. Clinical data from patients with candidemia were extracted from the Prospective Antifungal Therapy (PATH) Alliance database, a comprehensive registry that collects information regarding invasive fungal infections. A total of 2019 patients, enrolled from 1 July 2004 through 5 March 2008, were identified. Data regarding the candidemia episode were analyzed, including the specific fungal species and patient survival at 12 weeks after diagnosis.

Results. The incidence of candidemia caused by non–*Candida albicans Candida* species (54.4%) was higher than the incidence of candidemia caused by *C. albicans* (45.6%). The overall, crude 12-week mortality rate was 35.2%. Patients with *Candida parapsilosis* candidemia had the lowest mortality rate (23.7%; $P < .001$) and were less likely to be neutropenic (5.1%; $P < .001$) and to receive corticosteroids (33.5%; $P < .001$) or other immunosuppressive drugs (7.9%; $P = .002$), compared with patients infected with other *Candida* species. *Candida krusei* candidemia was most commonly associated with prior use of antifungal agents (70.6%; $P < .001$), hematologic malignancy (52.9%; $P < .001$) or stem cell transplantation (17.7%; $P < .001$), neutropenia (45.1%; $P < .001$), and corticosteroid treatment (60.8%; $P < .001$). Patients with *C. krusei* candidemia had the highest crude 12-week mortality in this series (52.9%; $P < .001$). Fluconazole was the most commonly administered antimicrobial, followed by the echinocandins, and amphotericin B products were infrequently administered.

Conclusions. The epidemiology and choice of therapy for candidemia are rapidly changing. Additional study is warranted to differentiate host factors and differences in virulence among *Candida* species and to determine the best therapeutic regimen.

Candidemia is a major cause of morbidity and mortality in the health care setting. However, the incidence of candidemia is increasing with greater complexity of surgical procedures, patient populations at higher risk of infection, and changes in patient demographic characteristics. Prolongation of survival among critically ill patients, especially in the intensive care unit setting, has lead to increased use of invasive procedures, intravenous catheters, and intravenous hyperalimentation, all of which are risk factors for candidemia [1–3]. Recently, the introduction of additional antifungal agents has led to new strategies for empirical and prophylactic therapies. An increasing number of candidial infections are now caused by non–*Candida albicans Candida* species [4–10].

Candidemia remains associated with high crude and attributable mortality rates and with increased costs of

Received 23 October 2008; accepted 7 February 2009; electronically published 14 May 2009.

Presented in part: 45th Annual Meeting of the Infectious Diseases Society of America, San Diego, CA, 4–7 October 2007; and 46th Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Diseases Society of America, Washington, DC, 25–28 October 2008.

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Clinical Infectious Diseases 2009; 48:1695–703

1058-4838/2009/4812-0011$15.00
DOI: 10.1086/599039

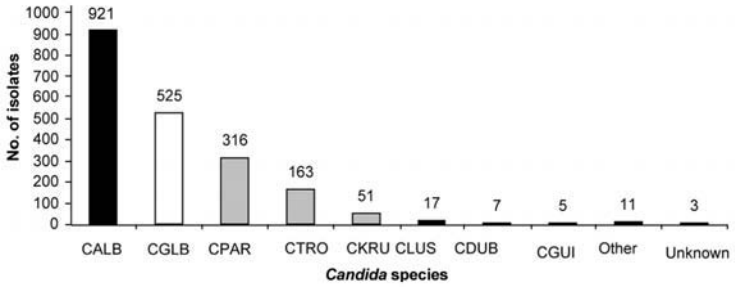

Figure 1. Distribution of isolated *Candida* species. CALB, *Candida albicans;* CDUB, *Candida dubliniensis;* CGLB, *Candida glabrata;* CGUI, *Candida guillermondii;* CKRU, *Candida krusei;* CLUS, *Candida lusitaniae;* CPAR, *Candida parapsilosis;* CTRO, *Candida tropicalis.*

care and duration of hospitalization. Attributable mortality has been reported to range from 5% to 71%, and crude mortality rates have been reported to be as high as 81% [11–23]. Inappropriate therapy or delays in initiation of therapy have also been linked to increased mortality [24, 25]. This study was performed to evaluate contemporary epidemiology and outcomes of candidemia in multiple North American centers.

METHODS

The patient population for this study was extracted from the Prospective Antifungal Therapy (PATH) Alliance database. The PATH Alliance is a comprehensive multicenter, prospective, observational registry that collects detailed clinical data on patients with invasive fungal infections (IFIs), with special emphasis on fungal epidemiology, diagnosis, treatment, and associated patient outcomes [26, 27].

This study is based on data for the 2019 patients (pediatric and adult) enrolled from 1 July 2004 through 5 March 2008 from 23 North American centers who received a diagnosis of proven candidemia. Detailed information with regard to candidemia episodes were analyzed, including underlying patient characteristics, the specific fungal pathogen and species, antifungal therapy, and survival.

A diagnosis of candidemia was made on the basis of $\geq$1 blood cultures growing *Candida* species and the presence of relevant clinical signs and symptoms, as enumerated in the guidelines of the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group [28]. Only the first episode of candidemia was reported for patients with recurrent or subsequent episodes of infection. Patients whose cultures grew >1 documented species of *Candida* were excluded from analysis. Some of these patients are described elsewhere [26].

Fisher's exact test or χ^2 test, as appropriate, was used for testing associations between categorical patient characteristics and *Candida* species. Analysis of variance was used for testing the difference in mean values across *Candida* species. Survival distribution function was estimated using the Kaplan-Meier product-limit method; nonparametric (log-rank and Wilcoxon) tests were used to compare the survival functions among the different *Candida* species. Patients were considered to be lost to follow-up if they were discharged home or transferred to another institution prior to the 12-week assessment date and no additional information was available.

RESULTS

Among the 4010 patients with completed case reports of IFIs, 2019 patients (50.3%) with proven candidemia caused by a single species were identified by the PATH Alliance registry. The distribution of isolated *Candida* species is shown in figure 1. *C. albicans* was commonly identified (45.6%); however, collectively, non–*C. albicans Candida* species were more frequently isolated from blood cultures (54.4%). The majority of the other species identified included *Candida glabrata* (26.0%), *Candida parapsilosis* (15.7%), *Candida tropicalis* (8.1%), and *Candida krusei* (2.5%).

The mean age of patients was 53.5 years (range, 0–96.4 years), and 53.7% were male. Most of the patients were white (62.6%), followed by black (21.7%). Of note, 43.0% of the patients had received antifungal agents as prophylaxis or empirical therapy within 30 days prior to their diagnosis of candidemia. A comparison of patient characteristics across isolated *Candida* species is presented in table 1. Statistically significant differences were found in the distribution of *Candida* species with regard to age ($P < .001$), sex ($P = .002$), prior antifungal therapy ($P < .001$), presence of hematologic malignancy ($P < .001$), hematopoietic stem cell ($P < .001$) or solid organ transplantation ($P = .009$), neonatal intensive care unit stay ($P = .009$), surgery ($P = .04$), requirement of total parenteral nutrition ($P = .04$), mechanical ventilation ($P = .04$), use of central catheters (peripherally inserted, $P = .05$; tunneled, $P = .01$; nontunneled, $P = .03$), presence of neutropenia ($P < .001$), use of corticosteroids ($P < .001$) or other immunosuppressive agents ($P = .002$), and presence of concomitant bacterial infections ($P = .04$).

Table 1. Patient baseline characteristics, by isolated *Candida* species.

Characteristic	All (*n* = 2019)	*Candida albicans* (*n* = 921)	*Candida glabrata* (*n* = 525)	*Candida parapsilosis* (*n* = 316)	*Candida tropicalis* (*n* = 163)	*Candida krusei* (*n* = 51)	Other[a] (*n* = 43)	*P*
	Candida species							
Age, mean years (range)	53.5 (0–96.4)	51.9 (0–96.4)	58.7 (0.8–95.8)	50.1 (0–95.0)	53.8 (1.3–87.6)	49.7 (6.1–84.9)	50.9 (0–79.1)	<.001
Male sex	1084 (53.7)	502 (54.5)	251 (47.8)	173 (54.8)	105 (64.4)	24 (47.1)	29 (67.0)	.002
Ethnicity								
White	1264 (62.6)	571 (62.0)	342 (65.1)	193 (61.1)	93 (57.1)	32 (62.8)	33 (76.7)	.17
Black	439 (21.7)	200 (21.7)	115 (21.9)	69 (21.8)	41 (25.2)	6 (11.8)	8 (18.6)	.50
Hispanic	65 (3.2)	25 (2.7)	15 (2.9)	14 (4.4)	8 (4.9)	3 (5.9)	0 (0)	.26
Asian	24 (1.2)	10 (1.1)	5 (1.0)	4 (1.3)	3 (1.8)	1 (2.0)	1 (2.3)	.89
Other or unknown	227 (11.2)	115 (12.5)	48 (9.1)	36 (11.4)	18 (11.0)	9 (17.7)	1 (2.3)	.10
Prior antifungal therapy	869 (43.0)	358 (38.9)	272 (51.8)	119 (37.7)	68 (41.7)	36 (70.6)	16 (37.2)	<.001
Patient category[b]								
General medicine	1339 (66.3)	620 (67.3)	356 (67.8)	210 (66.5)	100 (61.4)	26 (51.0)	27 (62.8)	.14
Hematologic malignancy	197 (9.8)	54 (5.9)	51 (9.7)	23 (7.3)	34 (20.9)	27 (52.9)	8 (18.6)	<.001
Stem cell transplantation	58 (2.9)	13 (1.4)	19 (3.6)	9 (2.9)	5 (3.1)	9 (17.7)	3 (7.0)	<.001
HIV infection and/or AIDS	41 (2.0)	18 (2.0)	12 (2.3)	4 (1.3)	3 (1.8)	2 (3.9)	2 (4.7)	.61
Neonatal ICU stay	26 (1.3)	18 (2.0)	0 (0)	7 (2.2)	0 (0)	0 (0)	1 (2.3)	.009
Solid organ transplantation	166 (8.2)	65 (7.1)	64 (12.2)	20 (6.3)	10 (6.1)	3 (5.9)	4 (9.3)	.009
Solid tumor	351 (17.4)	167 (18.1)	94 (17.9)	45 (14.2)	26 (16.0)	9 (17.7)	10 (23.3)	.56
Surgical (nontransplantation)	662 (32.8)	317 (34.4)	159 (30.3)	117 (37.0)	48 (29.5)	9 (17.7)	12 (27.9)	.04
Organ function[b]								
Dialysis dependent	350 (17.3)	165 (17.9)	92 (17.5)	40 (12.7)	29 (17.8)	13 (25.5)	11 (25.6)	.09
Diabetes mellitus	705 (34.9)	314 (34.1)	198 (37.7)	107 (33.9)	60 (36.8)	11 (21.6)	15 (34.9)	.26
Total parenteral nutrition	751 (37.2)	349 (37.9)	197 (37.5)	131 (41.5)	50 (30.7)	11 (21.6)	13 (30.2)	.04
Mechanical ventilation	722 (35.8)	364 (39.5)	175 (33.3)	101 (32.0)	56 (34.4)	14 (27.5)	12 (27.9)	.04
Acute cardiac support	45 (2.2)	23 (2.5)	8 (1.5)	10 (3.2)	3 (1.8)	1 (2.0)	0 (0)	.57
Ventricular shunt	34 (1.7)	17 (1.9)	7 (1.3)	9 (2.9)	1 (0.6)	0 (0)	0 (0)	.32
Intravenous CC								
Peripherally inserted CC	714 (35.4)	317 (34.4)	175 (33.3)	136 (43.0)	57 (35.0)	18 (35.3)	11 (25.6)	.05
Tunneled CC	374 (18.5)	157 (17.0)	90 (17.1)	65 (20.6)	31 (19.0)	16 (31.4)	15 (34.9)	.01
Nontunneled CC	653 (32.3)	313 (34.0)	184 (35.0)	77 (24.4)	49 (30.1)	16 (31.4)	14 (32.6)	.03
Immune function[b]								
ANC <500 cells/mm^3	148 (7.3)	47 (5.1)	30 (5.7)	16 (5.1)	24 (14.7)	23 (45.1)	8 (18.6)	<.001
Corticosteroid therapy	828 (41.0)	369 (40.1)	225 (42.9)	106 (33.5)	71 (43.6)	31 (60.8)	26 (60.5)	<.001
Immunosuppressive therapy	208 (10.3)	78 (8.5)	77 (14.7)	25 (7.9)	15 (9.2)	5 (9.8)	8 (18.6)	.002
Concomitant infection[b]								
Cytomegalovirus	27 (1.3)	12 (1.3)	11 (2.1)	3 (1.0)	1 (0.6)	0 (0)	0 (0)	.47
Bacterial infection	1080 (53.5)	492 (53.4)	282 (53.7)	176 (55.7)	93 (57.1)	16 (31.4)	21 (48.8)	.04

NOTE. Data are no. (%) of patients, unless otherwise indicated. ANC, absolute neutrophil count; CC, central catheter; HIV, human immunodeficiency virus; ICU, intensive care unit.

[a] Other species includes *Candida lusitaniae* (17 cases), *Candida guillermondii* (5), *Candida dubliniensis* (7), other (11), and unknown *Candida* species (3).

[b] Patient category, organ function, immunologic risk factors, and concomitant infections were not mutually exclusive (patients could have >1 characteristic within a category).

The 316 patients with *C. parapsilosis* candidemia were least likely to have risk factors including nontunneled central catheter (24.4%), neutropenia (5.1%), or corticosteroid (33.5%) or other immunosuppressive therapies (7.9%); they were most likely to have had recent surgery (37.0%) or a peripherally inserted central venous catheter (43.0%). *C. krusei* candidemia (51 cases) was most commonly associated with younger age (mean age, 49.7 years), female sex (52.9%), prior use of antifungal agents (70.6%), hematologic malignancy (52.9%), stem cell transplantation (17.7%), neutropenia (45.1%), or corticosteroid therapy (60.8%), and patients with *C. krusei* candidemia were less likely to require total parenteral nutrition (21.6%) or mechanical ventilation (27.5%) or to have a concomitant bacterial infection (31.4%). The 525 patients with *C. glabrata* candidemia were more likely to be older (mean age, 58.7 years) or to have undergone solid organ transplantation (12.2%). Patients with *C. albicans* candidemia were the least likely to have a hematologic malignancy (5.9%) and/or to have undergone stem cell transplantation (1.4%). Although rarely encountered, candidemia due to the rarest *Candida* species (e.g., *Candida dubliniensis* and *Candida lusitaniae*) was more likely to occur in male patients (67.0%) or in patients who had tunneled central venous catheters (34.9%) or used immunosuppressive agents (18.6%).

Among the 2019 patients with candidemia, another 179 fungal infections due to *Candida* species were identified at sites other than blood, including the abdomen (95 cases [53.1%]), lungs (17 [9.5%]), skin and soft tissue (14 [7.8%]), eyes (9

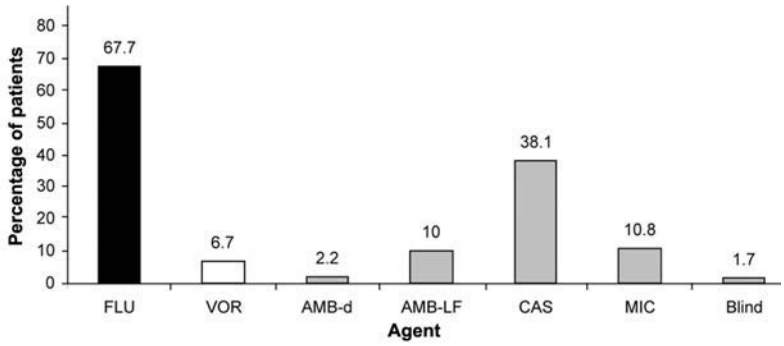

Figure 2. Administered antifungal agents; some patients received >1 agent. AMB-LF, any lipid formulation of amphotericin B; AMB-d, amphotericin B deoxycholate; CAS, caspofungin; FLU, fluconazole; MIC, micafungin; VOR, voriconazole.

[5.0%]), heart (7 [3.9%]), tracheobronchial tree (7 [3.9%]), skeleton (3 [1.7%]), central nervous system (2 [1.1%]), and other sites (25 [14.0%]). *C. albicans* was identified in 88 cases (49.2%); non–*C. albicans Candida* species collectively were more often isolated (91 cases [50.8%]). A small number of patients had a concomitant IFI other than *Candida* infection, including IFI due to *Aspergillus* species (11 patients), the Zygomycetes (1), endemic fungi (1), other molds (1), and other yeasts (5).

Administered antifungal agents are shown in figure 2. Fluconazole was most frequently used (67.7%), followed by caspofungin (38.1%). Micafungin was the third most frequently administered agent in this series (10.8%), followed by the lipid formulations of amphotericin B (10.0%) and voriconazole (6.7%). Amphotericin B deoxycholate was the agent that was least frequently administered (2.2%). A small minority of patients had received sequential or combination therapies (3.4%). Administered antifungal agents, stratified by *Candida* species, are shown in table 2. Fluconazole was most commonly used for cases of *C. albicans* candidemia (77.5%), and patients with *C. krusei* candidemia were the most likely to receive therapy with voriconazole (19.6%) or amphotericin B lipid formulations (27.4%). Echinocandins (caspofungin and micafungin) were used for the majority of patients with *C. glabrata* (66.3%) and *C. krusei* (74.5%) candidemia. A total of 138 patients (43.7%) with *C. parapsilosis* received an echinocandin.

Patient outcomes at 12 weeks and survival, stratified by *Candida* species, are reported in table 3 and figure 3, respectively. The overall, crude 12-week mortality rate was 35.2% (711 of 2019 patients died; 604 patients were lost to follow-up). *C. parapsilosis* candidemia was associated with the lowest 12-week mortality rate (23.7%). In contrast, patients with *C. krusei* can-

Table 2. Antifungal therapy administered, by different *Candida* species.

	Candida species, no. (%) of treated cases						
Antifungal agent	All (n = 2019)	*Candida albicans* (n = 921)	*Candida glabrata* (n = 525)	*Candida parapsilosis* (n = 316)	*Candida tropicalis* (n = 163)	*Candida krusei* (n = 51)	Other[a] (n = 43)
FLU	1366 (67.7)	714 (77.5)	273 (52.0)	233 (73.7)	98 (60.1)	16 (31.4)	32 (74.4)
VOR	136 (6.7)	45 (4.9)	44 (8.4)	21 (6.6)	12 (7.4)	10 (19.6)	4 (9.3)
AMB-D	44 (2.2)	23 (2.5)	6 (1.1)	9 (2.9)	2 (1.2)	2 (3.9)	2 (4.7)
ABCD	6 (0.3)	3 (0.3)	2 (0.4)	0 (0)	0 (0)	1 (2.0)	0 (0)
ABLC	86 (4.2)	33 (3.6)	12 (2.3)	25 (7.9)	10 (6.1)	4 (7.8)	2 (4.6)
L-AMB	110 (5.5)	38 (4.1)	24 (4.6)	27 (8.5)	7 (4.3)	9 (17.6)	5 (11.6)
LF-AMB	202 (10.0)	74 (8.0)	38 (7.2)	52 (16.4)	17 (10.4)	14 (27.4)	7 (16.3)
CAS	769 (38.1)	272 (29.5)	262 (49.9)	111 (35.1)	79 (48.5)	29 (56.9)	16 (37.2)
MIC	219 (10.9)	74 (8.0)	86 (16.4)	27 (8.5)	17 (10.4)	9 (17.7)	6 (14.0)
Blind[b]	34 (1.7)	18 (2.0)	7 (1.3)	4 (1.3)	2 (1.2)	3 (5.9)	0 (0)
Combination therapy[c]	68 (3.4)	…	…	…	…	…	…

NOTE. One patient received itraconazole or posaconazole, 3 patients received anidulafungin, and 6 patients received 5-fluorocytosine. ABCD, amphotericin (AMB) colloid dispersion; ABLC, AMB lipid complex; AMB-D, AMB deoxycholate; FLU, fluconazole; L-AMB, liposomal AMB; LF-AMB, any lipid formulation of AMB; CAS, caspofungin; MIC, micafungin; VOR, voriconazole.

[a] Other species includes *Candida lusitaniae* (17 cases), *Candida guillermondii* (5), *Candida dubliniensis* (7), other (11), and unknown *Candida* species (3).

[b] Blinded therapy as part of a clinical trial.

[c] Some patients received ⩾1 antifungal agents as combination and/or sequential therapy.

Table 3. Twelve-week outcome, by isolated *Candida* species.

Status at 12 weeks after diagnosis of IFI	*Candida* species, no. (%) of patients						
	All (n = 2019)	*Candida albicans* (n = 921)	*Candida glabrata* (n = 525)	*Candida parapsilosis* (n = 316)	*Candida tropicalis* (n = 163)	*Candida krusei* (n = 51)	Other[a] (n = 43)
Alive	704 (34.9)	306 (33.2)	189 (36.0)	124 (39.2)	50 (30.7)	17 (33.3)	18 (41.9)
Dead	711 (35.2)	328 (35.6)	200 (38.1)	75 (23.7)	67 (41.1)	27 (52.9)	14 (32.6)
Unknown	604 (29.9)	287 (31.2)	136 (25.9)	117 (37.0)	46 (28.2)	7 (13.7)	11 (25.6)

NOTE. $P < .001$, by log-rank test.

[a] Other species included *Candida lusitaniae* (17 cases), *Candida guillermondii* (5), *C. dubliniensis* (7), other (11), and unknown *Candida* species (3).

didemia had the highest mortality rate (52.9%) in this cohort. A statistically significant difference in the 12-week survival distributions by *Candida* species ($P < .001$) was found (figure 3). Survival patterns among patients with candidemia due to *C. albicans, C. glabrata, C. tropicalis,* and other *Candida* species were similar. A statistically significant difference in the 12-week survival distributions ($P < .001$) was found based on age (83.2% for 0 to <19 years of age, 68.7% for 19–65 years of age, and 52.7% for >65 years of age) (figure 4). When analyzed by *Candida* species and age group, a similar pattern was seen with *C. albicans* ($P < .001$), *C. glabrata* ($P < .002$), and *C. parapsilosis* ($P < .007$). No statistically significant differences were observed with *C. tropicalis, C. krusei,* or other *Candida* species. No statistically significant difference in the 12-week survival distributions was found when analyzed by ethnicity (data not shown).

DISCUSSION

A cohort of 2019 patients with candidemia was identified and analyzed from the PATH Alliance registry, a prospective database of IFIs at major North American medical centers. To our knowledge, this is the largest cohort of patients with candidemia, with contemporary patients enrolled from July 2004 through March 2008. Other large series of patients with candidemia were from earlier periods, enrolled from 1991 through 2000 (1137 episodes of candidemia) [29] and from February 1995 through November 1997 (1447 adults and 144 children with candidemia) [8]. We observed a predominance of non–*C. albicans Candida* species (54.4%); *C. albicans* was the most frequently isolated species (45.6%). We report an overall, 12-week crude mortality rate of 35.2% among patients who experienced a single episode of candidemia, with the lowest mortality observed among patients with *C. parapsilosis* candidemia and the highest among patients with *C. krusei* candidemia.

Candidemia has been identified among the most common etiologic agents of bloodstream infections. It ranked seventh in a nationwide survey of 17 hospitals in Switzerland [29] and fourth in the Surveillance and Control of Pathogens of Epidemiologic Importance (SCOPE) surveillance study of bloodstream infections in hospitalized patients in the United States

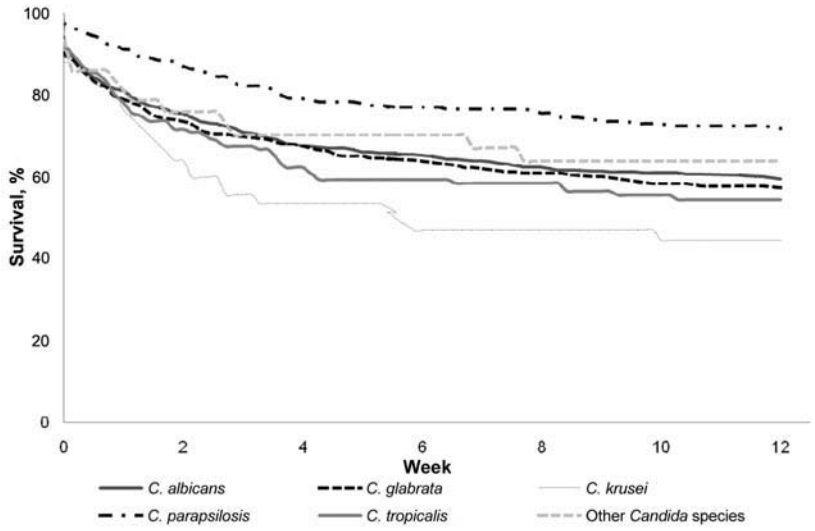

Figure 3. Survival among patients with candidemia at 12 weeks, by *Candida* species *(Candida albicans, Candida glabrata, Candida krusei, Candida parapsilosis,* and *Candida tropicalis).*

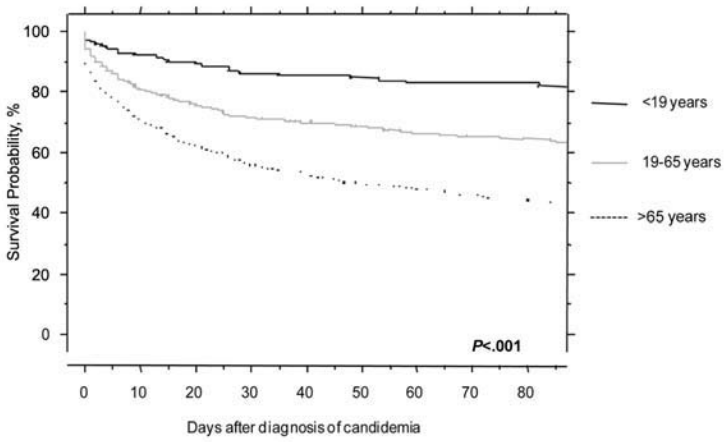

Figure 4. Survival among patients with candidemia at 12 weeks, by age group

[30]. *C. albicans* has traditionally been the predominant *Candida* species isolated, followed by *C. glabrata* and other non–*C. albicans Candida* species, in both pediatric and adult patient populations [8, 29, 30]. In a worldwide surveillance program (1997–2003) that included 134,715 consecutive clinical isolates of *Candida* species from 127 medical centers in 39 countries, a trend toward a decrease in *C. albicans* and an increase in *C. tropicalis* and *C. parapsilosis* was noted [31]. In addition, species distribution differences have been reported throughout the world. For example, *C. albicans* and *C. glabrata* were most frequently identified in series from Denmark and the United States, although South America had lower rates of these species [31].

In this study population from the PATH Alliance, non–*C. albicans Candida* species were more frequently isolated than was *C. albicans* (54.4% vs. 45.6%). Patients with *C. glabrata* and *C. krusei* candidemia were the most likely to have received prior antifungal therapy. This likely reflects, in part, selective pressure because of the extensive use of prophylactic fluconazole in susceptible hosts [32, 33]. In addition, severe immunosuppression or illness, prematurity, exposure to broad-spectrum antibiotics, and older age may contribute to the increased incidence of candidemia caused by non–*C. albicans Candida* species, especially *C. glabrata, C. krusei, C. parapsilosis,* and *C. tropicalis* [34–41]. We observed an association between neutropenia and the use of corticosteroids and *C. krusei* candidemia, consistent with the underlying medical conditions of these patients, including hematologic malignancy and stem cell transplantation, and the associated prior use of azole prophylaxis. Patients with *C. krusei* candidemia were younger and did not generally have such additional risk factors as parenteral nutrition, mechanical ventilation, and concomitant bacterial infections. Older age and receipt of a solid organ transplant were associated with *C. glabrata* candidemia. Our observations suggest that the changing patient population and practices involved in their care may contribute to the continual shift in the epidemiology of *Candida* species.

In the present study, the azole antifungals were the most frequently administered antifungal agents, followed by the echinocandins. Combination therapy remains an uncommon practice in the treatment of candidemia. Overall, amphotericin B products were infrequently administered, especially amphotericin B deoxycholate, which was used for <3% of patients. The relatively recent introduction of echinocandins and azoles will necessitate re-evaluation of clinical outcomes of therapy for candidemia over time. The differences observed in the use of antifungal agents based on the different *Candida* species may, in part, be explained by the variations in their susceptibility profiles (when available), empirical therapy based on existing treatment guidelines [10], or differences in clinical practice, including prophylactic programs, among the participating centers. As outlined in the recently revised guidelines for the treatment of candidemia by the Infectious Diseases Society of America, treatment should be adjusted on the basis of the *Candida* species isolated (42).

Retrospective cohort studies involving patients with candidemia and varying underlying diseases have revealed worldwide crude and attributable mortality rates of 30%–81% and 5%–71%, respectively [11–22]. In our series, patients with candidemia had a crude 12-week mortality rate of 35.2%. Survival appears to be improved, compared with that in many older studies. The identification of candidemia as one of the leading causes of bloodstream infections [30] and greater knowledge of major risk factors for candidemia [21] have likely led to higher clinical suspicion, prompt initiation of diagnostic testing, and pre-emptive or empirical treatment with new, effective, and well-tolerated antifungal agents. In this series, the use of nonculture diagnostic methods was rarely a factor in the ini-

tiation of antifungal therapy (<1%). Thus, improved outcomes could not be attributed to these diagnostic tools.

The highest and lowest crude mortality rates reported in the SCOPE surveillance study [30] were for *C. krusei* and *C. parapsilosis* candidemia. Similarly, candidemia due to *C. krusei* was associated with the highest mortality rate observed in this series (52.9%). This can be explained, in part, by underlying immune deficits in the patient populations most frequently affected by these species, including patients with hematologic malignancies and stem cell transplant recipients. Our findings suggest that patients with *C. parapsilosis* candidemia have the lowest mortality rate (23.7%); this finding is consistent with the results of prior studies [20, 30, 43]. These patients were less likely to be neutropenic or to be receiving corticosteroids and other immunosuppressive agents; this is consistent with the mechanism by which *C. parapsilosis* causes infection, in association with contaminated infusates and catheters. As was reported in a separate analysis [44], we observed similar mortality rates for *C. albicans* and *C. glabrata* candidemia in this study. Our findings, based on a large number of patients, strongly suggest that there may not be significant differences in survival associated with infection due to the 2 most common *Candida* species. Additional prospective or case-control studies are needed to delineate differences between other specific *Candida* species.

Limitations of the present study include differences in clinical practices across different centers, limited follow-up data, the inability to clearly distinguish between prophylactic and empirical therapy or sequential and concomitant antifungal therapy, and the collection of data from only institutions in North America. Despite these limitations, the data collected by the PATH Alliance registry include a very large number of patients with IFIs with a broad spectrum of underlying conditions. This database will likely prove to be a significant asset in the understanding of IFIs, including candidemia [45]. Differences in the outcomes and presentations of IFIs will be addressed by the PATH Alliance with large cohort studies and case-control studies to provide more information on optimal approaches to candidemia and other IFIs.

PROSPECTIVE ANTIFUNGAL THERAPY (PATH) ALLIANCE

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Acknowledgments

We thank Astellas Pharma US, for their generous support; Axiom Real-Time Metrics (Axiom), for their expertise in registry management; and the many dedicated coordinators at each site.

Financial support. Astellas Pharma US.

Potential conflicts of interest. D.H. has received recent research funding from Astellas; has served as a consultant or advisor and has been a member of the speaker's bureau for Pfizer and Astellas; and has received speaking honoraria from Roche. D.N. has received research support from Astellas. E.A. has been a consultant and a member of the speaker's bureau for Astellas, Pfizer, Gilead, Merck, and Schering-Plough. J.F. has received educational/research grant support from Astellas; has received consulting fees from Merck, Biogen-IDEC, Hoffman LaRoche, Astellas, and Primera; and has been a member of the speaker's bureau for Astellas and Roche. W.S. is a member of the speaker's bureau for Pfizer, Astellas, and Enzon and has received consulting fees from Astellas and Schering-Plough. A.O. is a member of the speaker's bureau for Pfizer. M.P. has been a consultant and a member of the speaker's bureau for Pfizer, Astellas, Merck, and Schering-Plough. K.M. has been a consultant or a member of advisory boards for Astellas, Merck, Pfizer, and Schering Plough. C.H.C. has served as a statistical consultant to Pharmacia, Pfizer, and Eli Lilly; has served as a marketing analytics consultant to Roche; and has served as a statistical

consultant via third parties to Astellas, Topigen, and AstraZeneca. K.W. provided work on a contract basis for Astellas Pharma (US and Canada), through her previous employment at Axiom Real-Time Metrics.

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