Original Article

Epidemiology and Antifungal Susceptibility in Patients with Candidemia in a University Hospital, Thailand

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Background: Candidemia is the most common nosocomial invasive fungal infection that causes high mortality. Emergence of drug-resistant *Candida* is reported worldwide but there are few studies in Thailand.

Objective: To determine the epidemiology, antifungal susceptibility of *Candida*, and outcomes among adult patients with candidemia.

Materials and Methods: A prospective, observational study in adult patients with candidemia was conducted in 2015 at a university hospital. Demographic, microbiological, and outcome data were recorded.

Results: Fifty-two patients with candidemia were identified, of whom 76.9% had an underlying disease and 69.2% had risks for candidemia. Sixty-four percent of candidemia patients contracted non-*albicans Candida* and 36% had *Candida albicans*. *C. tropicalis* was the most common non-*albicans Candida* species isolated (35%), followed by *C. parapsilosis* (19%), and *C. glabrata* (10%). Fluconazole resistance was found in 12.5% of *C. albicans* and in 11.1% of *C. parapsilosis* isolates. Reduced fluconazole susceptibility or high-level fluconazole resistance was found in 68.7% of *C. tropicalis* isolates. All except *C. parapsilosis* had excellent susceptibility to echinocandins. Seventy-three percent (38/52) of patients received antifungal treatment, of whom, 78.9% received empiric fluconazole therapy, and 89.7% were started on antifungal treatment 24 hours after the isolation of *Candida*. The overall mortality rate was 51.9%.

Conclusion: Fluconazole-resistant *Candida* became more prevalent particularly in *C. tropicalis*, which was the predominant species among non-*albicans Candida* causing candidemia. Empiric treatment with either amphotericin B or echinocandins would be appropriate in high-risk patients with suspected candidemia.

Trial registration: Thai Clinical Trials Registry, TCTR20150605001

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Candida is an important cause of nosocomial fungal infection, ranking the fourth most commonly isolated pathogen in patients with nosocomial bloodstream infection[1]. Candidemia is associated with high mortality, long hospital stays, and high medical costs[2]. The incidence of candidemia has increased substantially in the last decade due to an increase in patient population at risk[3,4]. In critically-ill patients, the well-recognized risk factors for candidemia are abdominal surgery, neutropenia, *Candida* site colonization, indwelling central venous or urinary catheter, parenteral nutrition, and broad-spectrum antimicrobial agents[5,6]. While *Candida albicans* is still considered the most common species causing candidemia, increasing rates of candidemia have been reported worldwide as being caused by *Candida parapsilosis*, *Candida tropicalis*, *Candida krusei*, and *Candida glabrata*[7,8]. The reasons for the emergence of non-*albicans Candida* species are not completely understood. Some medical conditions may elevate the risk of developing candidemia due to these species, such as the association between

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(a) *C. parapsilosis* and receiving parenteral nutrition[9], (b) *C. tropicalis* and cancer or neutropenia[10], and (c) *C. krusei* and *C. glabrata* and having a history of exposure to azoles[11,12].

Knowledge of local *Candida* species epidemiology and antifungal susceptibilities affects the choice of antifungal therapy; however, in resource-limited countries, species identification of non-*albicans Candida* and antifungal susceptibility testing are not routinely performed. Physicians usually prefer empiric fluconazole for treatment of invasive *Candida* infection due to limited access to costly echinocandins and its being less toxic than amphotericin B. Although azoles have good activity against *C. albicans*, an emerging resistance to azoles in non-*albicans Candida* species has been increasingly reported, particularly, where fluconazole is routinely used for prophylaxis[13,14]. Delayed appropriate antifungal treatment is likely associated with a greater risk of hospital mortality[15]. Therefore, the availability of recent data on *Candida* species epidemiology and their antifungal susceptibilities is crucial for selecting the best antifungal therapy.

The epidemiology of candidemia may vary by country. In Thailand, there have been several epidemiological studies of candidemia. All but one of these studies lacked data on antifungal susceptibility[16-21], so the authors conducted a prospective, observational study to determine the epidemiology, antifungal susceptibilities, treatment, and outcomes among adult patients with candidemia.

Materials and Methods

The present study was conducted at Srinagarind Hospital, a tertiary, university hospital in northeastern Thailand. The study included in-patients over 15 years old with clinical sepsis and that had at least one blood culture that grew *Candida* species. The study was conducted between January 1, 2015 and December 31, 2015.

The patient demographic, epidemiological and microbiological data were recorded. The information included patient age, gender, underlying co-morbid diseases, and risk factors (neutropenia, recent chemotherapy, prior prednisolone treatment, parenteral nutrition, recent abdominal surgery, previous antibiotic use, presence of an indwelling urinary catheter, endotracheal intubation, central venous catheterization, and presence of *Candida* colonization). The following other information were also recorded, admission ward at onset of candidemia, prior antifungal prophylaxis or treatment, acute physiology and chronic health evaluation II (APACHE II) score, and "Candida score" at the time of candidemia diagnosis.

The source of candidemia, type and duration of antifungal therapy, and mortality rate within 30 days after diagnosis of candidemia were also recorded. Neutropenia was defined as an absolute neutrophil count of less than 500 cells/mm^3 at the onset of candidemia.

Corticosteroid use was assumed to be a risk factor if the patient had received 20 mg/day or more of prednisolone for seven days or longer before the onset of candidemia. Other factors including previous therapy with antibiotic, recent chemotherapy, and previous abdominal surgery were considered as risks for candidemia if these events occurred within 30 days of the onset of candidemia. Parenteral nutrition, endotracheal intubation, urinary and central venous catheterization were considered risk factors if present for more than 48 hours prior to the onset of candidemia.

The severity of the illness was estimated, using the APACHE II score, the day the blood culture was positive. A "Candida score" was calculated based on the presence or absence of the following composite components, severe sepsis (2 points), surgery on admission (1 point), total parenteral nutrition (1 point), and *Candida* colonization (1 point). A "Candida score" of more than 2.5 points indicated an increased risk for developing candidemia[22].

The present study protocol was reviewed and approved by the Institutional Review Board of Khon Kaen University. All participants provided written informed consents.

A blood culture was performed using an automated blood culture system (BacT/ALERT VirtuO™, BioMérieux, France). Species identification was based on colony morphology on chromogenic agar, carbohydrate assimilation characteristics, or a Vitek Yeast Biochemical Card. All available isolates were tested for antifungal drug susceptibility using a Sensititre™ YeastOne YO10 colorimetric kit (TREK Diagnostic Systems, UK). Antifungal susceptibility was determined following the recommendation of the Clinical Laboratory Standards Institute (CLSI), 2017 and 2018[23,24].

Statistical analysis

Variables were expressed as medians and ranges for continuous variables, and as frequencies and percentages for categorical variables. Comparisons of categorical data between patients with candidemia

Table 1. Demographic characteristics of patients with candidemia

Characteristic	Total	Types of fungal isolation; n (%)		p-value
		C. albicans	Non-*C. albicans*	
No. of patients	52 (100)	19 (36.5)	33 (63.5)	
Age (years); median (range)	64.5 (16 to 93)	64 (23 to 87)	65 (16 to 93)	0.92
Sex: male	32 (61.5)	11 (57.9)	21 (63.6)	0.68
Admission ward at onset of candidemia				0.39
General ward	24 (46.2)	11 (57.9)	13 (39.4)	
Semi-intensive care unit	5 (9.6)	1 (5.3)	4 (12.1)	
Intensive care unit	23 (44.2)	7 (36.8)	16 (48.5)	
Underlying diseases	40 (76.9)	14 (73.7)	26 (78.8)	0.74
Solid malignancy	19 (36.5)	6 (31.6)	13 (39.4)	0.57
Diabetes mellitus	15 (28.8)	7 (36.8)	8 (24.2)	0.36
Chronic hemodialysis	8 (15.4)	3 (15.8)	5 (15.2)	1.00
Hematologic malignancy	6 (11.5)	2 (10.5)	4 (12.1)	1.00
Transplant	1 (1.9)	0 (0)	1 (3.0)	1.00
Associated risk factors	36 (69.2)	13 (68.4)	23 (69.7)	0.92
Steroid treatment	13 (25.0)	5 (26.3)	8 (24.2)	1.00
Indwelling Foley's catheter	25 (48.1)	7 (36.8)	18 (54.5)	0.22
Central venous catheterization	30 (57.7)	12 (63.2)	18 (54.5)	0.55
Parenteral nutrition	14 (26.9)	7 (36.8)	7 (21.2)	0.22
Recent abdominal surgery	12 (23.1)	5 (26.3)	7 (21.2)	0.74
Assisted ventilation	25 (48.1)	6 (31.6)	19 (57.6)	0.07
Neutropenia	4 (7.7)	1 (5.3)	3 (9.1)	1.00
Received chemotherapy	8 (15.4)	2 (10.5)	6 (18.2)	0.69
Candida colonization	12 (23.1)	6 (31.6)	6 (18.2)	0.32
Prior received antibiotics	50 (96.2)	19 (100)	31 (93.9)	0.53
Prior received fluconazole	4 (7.7)	2 (10.5)	2 (6.1)	0.62
Hospitalized time before developing candidemia (days); median (range)	23.5 (0 to 86)	16 (0 to 83)	28 (0 to 86)	0.93
Candida score (point); median (range)	2 (0 to 4)	3 (0 to 4)	2 (0 to 4)	0.11
APACHE score; median (range)	18.5 (2 to 38)	15 (8 to 38)	19 (2 to 33)	0.73
Cause of candidemia				
Catheter related	13 (25.0)	4 (21.1)	9 (27.3)	0.75
Primary, non-catheter related	29 (55.8)	10 (52.6)	19 (57.6)	0.96
Intraabdominal infection	10 (19.2)	5 (26.3)	5 (15.1)	0.54

caused by *C. albicans* and non-*C. albicans* species were performed using the chi-square or Fisher's exact test, while the Wilcoxon rank sum test was used for continuous data. A p-value of less than 0.05 was considered statistically significant. Factors related to overall mortality were evaluated using a univariate analysis with binary logistic regression. Multiple logistic regression analysis, using backward likelihood ratio selection, was used to determine the independent factors for overall mortality. All statistical analyses were done using IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY, USA).

Results

There were 52 cases of candidemia identified during the present study period, indicating an incidence of 14.3 cases per 10,000 hospital admissions. Among these, 33 patients (63.5%) were infected with non-*albicans Candida* and the remaining 19 (36.5%) were infected with *C. albicans*.

Patient demographics and the risk factors

associated with candidemia are shown in Table 1. The median age of the patients was 64.5 years (range, 16 to 93) and about two-thirds were male. Forty-six percent of the patients were admitted to the general ward and 44.2% to the intensive care unit. Seventy-seven percent of the patients had at least one underlying disease such as solid malignancy (36.5%), diabetes mellitus (28.8%), chronic hemodialysis (15.4%), hematologic malignancy (11.5%), and transplantation (1.9%). Seventy percent of the patients had at least one risk factor associated with candidemia such as central venous catheterization (57.7%), urinary catheterization (48.1%), assisted ventilation (48.1%), parenteral nutrition (26.9%), steroid treatment (25%), recent abdominal surgery (23.1%), *Candida* colonization (23.1%), recent chemotherapy (15.4%), and neutropenia (7.7%). The most common cause of candidemia was non-catheter-related (55.8%) followed by catheter-related candidemia (25%) and secondary infection from intra-abdominal infection (19.2%) (Table 1).

Of the 12 patients who had a recent abdominal surgery, all except one had bowel surgery. Ninety-six percent of the patients had a history of recent antibiotic use but only 7.7% had received fluconazole prior to developing candidemia. The median (range) length of hospital stays before developing candidemia was 23.5 (0 to 86) days. The median (range) "Candida score" and the APACHE II score were 2 (0 to 4) and 18.5 (2 to 38), respectively. Thirty-five percent of the patients had a "Candida score" over 2.5 points. There were neither demographic nor other risk factors for candidemia significantly different between those with *C. albicans* and non-*albicans Candida* infections (Table 1).

Candida species isolation and susceptibility testing results

The most common non-*albicans Candida* species isolated were *C. tropicalis* (35%), followed by *C. parapsilosis* (19%), and *C. glabrata* (10%). Antifungal susceptibility testing was performed on 46 isolates. Ninety-six percent of *Candida* isolates were susceptible to amphotericin B. All *C. albicans* isolates were susceptible to anidulafungin and caspofungin, 93.8% to micafungin, and 87.5% to fluconazole and voriconazole. All *C. tropicalis* isolates were susceptible to anidulafungin and micafungin, 93.8% to caspofungin, 31.2% to fluconazole, and 12.5% to voriconazole. All *C. parapsilosis* isolates were susceptible to voriconazole, 88.9% to fluconazole and caspofungin, and 77.8% to anidulafungin and micafungin. All *C. glabrata* isolates were susceptible to anidulafungin and micafungin, 80% to caspofungin, and all were susceptible dose-dependent to fluconazole (Table 2).

Treatment and clinical outcomes

Seventy-three percent of the patients received antifungal treatment, of whom 78.9% received fluconazole and 21.1% received amphotericin B deoxycholate as an empirical antifungal therapy. The median time (range) to starting empiric antifungal treatment after *Candida* was isolated from the blood culture was 54.5 (7.5 to 100.2) hours.

Six of the patients with candidemia had a change in their antifungal treatment regimen during treatment where three were changed from amphotericin B to fluconazole, two from fluconazole to echinocandin (based on susceptibility testing results), and one was changed from fluconazole to amphotericin B (because the patient had neutropenia and developed clinical deterioration). The median duration (range) of antifungal therapy was 14 (2 to 41) days. Of the 30 cases having central venous catheterization, 46.7% had the catheter removed.

The overall mortality rate was 51.9%. There was no significant difference (p=0.10) in the overall mortality between patients with *C. albicans* candidemia (36.8%) and non-*albicans Candida* candidemia (60.6%) (Table 3). Overall mortality was not statistically different (p=0.44) between patients who received antifungal treatment (47.4%) and no antifungal treatment (64.3%). Of the 38 patients that received antifungal treatment, three received empiric antifungal therapy within 24 hours of having a positive blood culture for *Candida* and two died. Thirty-five patients received antifungal treatment after 24 hours of a positive blood culture for *Candida* and 16 (45.7%) died.

The factors associated with overall mortality on univariate analysis are shown in Table 4. Factors significantly associated with overall mortality were having (a) a high APACHE II score (odds ratio [OR] 1.19; 95% confidence interval [CI] 1.08 to 1.31), and (b) a central venous catheter (OR 9.33; 95% CI 1.51 to 57.65). In multivariate analysis, the APACHE II score was the only independent factor associated with overall mortality after adjusting for gender, age, group of *Candida* species, type of candidemia, time interval between positive blood culture for *Candida* and empiric antifungal treatment, and type of antifungal agent received (OR 1.18; 95% CI 1.05 to 1.32).

Table 2. Susceptibility pattern of *Candida* species

Candida species/drug	Susceptibility pattern; n (%)			
	Susceptible	SDD	Intermediate	Resistant
C. albicans (n=16)				
Amphotericin B	15 (93.8)	-	-	1 (6.2)
Fluconazole	14 (87.5)	0 (0.0)	-	2 (12.5)
Voriconazole	14 (87.5)	-	0 (0.0)	2 (12.5)
Anidulafungin	16 (100)	-	0 (0.0)	0 (0.0)
Caspofungin	16 (100)	-	0 (0.0)	0 (0.0)
Micafungin	15 (93.8)	-	0 (0.0)	1 (6.2)
C. tropicalis (n=16)				
Amphotericin B	16 (100)	-	-	0 (0.0)
Fluconazole	5 (31.2)	4 (25.0)	-	7 (43.7)
Voriconazole	2 (12.5)	-	7 (43.7)	7 (43.7)
Anidulafungin	16 (100)	-	0 (0.0)	0 (0.0)
Caspofungin	15 (93.8)	-	1 (6.2)	0 (0.0)
Micafungin	16 (100)	-	0 (0.0)	0 (0.0)
C. parapsilosis (n=9)				
Amphotericin B	8 (88.9)	-	-	1 (11.1)
Fluconazole	8 (88.9)	0 (0.0)	-	1 (11.1)
Voriconazole	9 (100)	-	0 (0.0)	0 (0.0)
Anidulafungin	7 (77.8)	-	2 (22.2)	0 (0.0)
Caspofungin	8 (88.9)	-	0 (0.0)	1 (11.1)
Micafungin	7 (77.8)	-	2 (22.2)	0 (0.0)
C. glabrata (n=5)				
Amphotericin B	5 (100)	-	-	0 (0.0)
Fluconazole	-	5 (100)	-	0 (0.0)
Anidulafungin	5 (100)	-	0 (0.0)	0 (0.0)
Caspofungin	4 (80.0)	-	1 (20.0)	0 (0.0)
Micafungin	5 (100)	-	0 (0.0)	0 (0.0)

SDD=susceptible dose dependent

Table 3. Management and outcome of treatment of 52 patients with candidemia

	Total	Types of fungal isolation; n (%)		p-value
		C. albicans	Non-*C. albicans*	
No. of patients	52 (100)	19 (36.5)	33 (63.5)	
Received antifungal treatment	38 (73.1)	16 (84.2)	22 (66.7)	0.17
Type of empiric antifungal agents				1.00
Amphotericin B	8/38 (21.1)	3 (18.8)	5 (22.7)	
Fluconazole	30/38 (78.9)	13 (81.3)	17 (77.3)	
Time to starting empirical antifungal treatment (hours); median (range)	54.5 (7.5 to 100.2)	51.7 (7.5 to 100.2)	58.0 (21.1 to 99.5)	0.36
Duration of antifungal treatment (days); median (range)	14 (2 to 41)	15.5 (3 to 41)	13 (2 to 25)	0.14
CVC removal	14/30 (46.7)	4/12 (33.3)	10/18 (55.6)	0.28
Overall mortality	27 (51.9)	7 (36.8)	20 (60.6)	0.10

CVC=central venous catheter

Table 4. Factors associated with mortality in patients with candidemia by univariate analysis

Factors	Unadjusted mortality rate		
	OR	95% CI	p-value
Female	1.22	0.40 to 3.75	0.73
Age	1.01	0.98 to 1.05	0.48
Non-*albicans Candida*	1	-	-
C. albicans	0.38	0.12 to 1.22	0.10
APACHE II score	1.19	1.08 to 1.31	0.001
Received antifungal treatment	1	-	-
Not received antifungal treatment	2.00	0.56 to 7.09	0.28
Received empirical antifungal treatment after 24 hours of positive blood culture	1	-	-
Received empirical antifungal treatment within 24 hours of positive blood culture	2.38	0.20 to 28.67	0.50
Primary candidemia	1	-	-
Secondary candidemia	1.82	0.45 to 7.39	0.41
Removed vascular catheter	1	-	-
Retained vascular catheter	9.33	1.51 to 57.65	0.02
Amphotericin B treatment	1	-	-
Fluconazole	0.46	0.09 to 2.28	0.34

OR=odds ratio; CI=confidence interval

Discussion

The incidence of nosocomial candidemia has been high and has increased in some countries[4,25]. In USA, Zilberberg et al[25] reported that the incidence of candidemia rose by 49%, from 2.8 to 4.2 cases per 10,000 hospitalizations between 2000 and 2005. Hii et al[4] observed an increase trend in incidence of healthcare-associated candidemia in Taiwan from 7.6 per 10,000 discharges between 2001 and 2003 to 11.4 per 10,000 discharges between 2009 and 2012. In Thailand, the incidence of candidemia has ranged between 7.2 and 14.1 cases per 10,000 hospitalizations[18,19]. The present study revealed a high incidence of candidemia (14.3 per 10,000 hospitalizations) at the authors' hospital and the rate was similar to a previous report[18] referencing data collected between 1999 and 2003 (14.1 per 10,000 hospitalizations). The difference in the incidence rate and trend in nosocomial candidemia vis-à-vis location may be due to differences in the population studied (high or low risk for candidemia, healthcare practices awareness, antifungal prophylaxis, and early empiric treatment), and mode of data collection (active or passive surveillance system). In the authors' setting, as a tertiary referral hospital, many factors contribute to a persistently high incidence of candidemia, including a large proportion of patients at high risk of candidemia, non-implementation of antifungal prophylaxis, and lack of physician awareness of candidemia in high-risk patients.

In western counties, data from the ARTEMIS DISK Global Antifungal Surveillance Study show that between 1997 and 2007 *C. albicans* was the most prevalent species (61% to 73%) among invasive *Candida* isolates, followed by *C. glabrata* (10% to 12%), *C. tropicalis* (5% to 8%), and *C. parapsilosis* (4% to 7%)[26]. In Asian countries, the species distribution of *Candida* causing invasive candidiasis was different. Data from the laboratory-based surveillance of patients with candidemia between 2010 and 2011 reveal that non-*albicans Candida* was a more common cause of candidemia than *C. albicans* (59% versus 41%, respectively)[27]. Among non-*albicans Candida* isolates, *C. tropicalis* (25.4%) was the most frequently isolated, followed by *C. glabrata* (13.9%), and *C. parapsilosis* (12.1%)[27]. In the present study and a previous study in the authors' hospital[18], non-*albicans Candida* remains the more common cause of candidemia over *C. albicans*, but the most common non-*albicans Candida* species changed from *C. parapsilosis* to *C. tropicalis* and the incidence of *C. glabrata* increased. Other epidemiological studies on candidemia in Thailand also reported the predominance of non-*albicans Candida* species causing candidemia over *C. albicans*[16,17,19-21]. Among non-*albicans Candida*

species, *C. tropicalis*, and *C. parapsilosis* were the two most common isolates[16,17,19-20] except for a report from a university hospital in Bangkok where *C. glabrata* ranked the second most common isolated[21]. This difference could be due to the underlying or associated conditions of the major patient populations, and the frequent use of fluconazole prophylaxis at each hospital[9-12].

In the past, the susceptibility of *Candida* was generally predictable if the species of the isolate was known (*C. albicans*, *C. tropicalis*, and *C. parapsilosis*), which were generally susceptible to azole antifungal drugs, whereas *C. glabrata* and *C. krusei* were more resistant to azoles[28]. Over the last decade, resistance to fluconazole has been reported in the USA, Europe, and South America (*C. albicans* 2% to 17%, *C. parapsilosis* 2% to 68%, and *C. tropicalis* 4% to 50%), as the magnitude of resistance varies by region[29-31]. A recent study in the Asia-Pacific region[32] showed a significant proportion of reduced or high-level fluconazole-resistant *C. tropicalis* (24.3%) and to a lesser extent, *C. parapsilosis* (6.8%). *C. albicans* still had high susceptibilities to fluconazole (99.7%). The present study revealed a large proportion of reduced fluconazole susceptibility or fluconazole-resistant *C. tropicalis* (68.7%), and an alarming proportion of fluconazole-resistant *C. albicans* (12.5%) and *C. parapsilosis* (11.1%). Echinocandins remained the active drug for most *Candida* species except for *C. parapsilosis*. These findings suggest that the problem of resistance varies across countries even within the same region. Monitoring local data is needed to support appropriate treatment. Empiric fluconazole treatment in patients suspected of candidemia should be avoided. Notwithstanding, when needed, either amphotericin B or echinocandin are a better choice in the present setting.

Candidemia is associated with high mortality (up to 36% to 59%) despite antifungal treatment[14,16-21]. The overall mortality in the present study was also high. The independent factors associated with mortality in patients with candidemia were a high APACHE II score, intensive care unit admission, neutropenia, septic shock, on mechanical ventilation, presence of central venous catheter, and inappropriate antifungal therapy[17,18,20,21]. In the current study, the only independent predictive risk factor related to mortality was a high APACHE II score. Although most patients received antifungal treatment, a delay in the initiation of antifungal therapy was mostly observed, reflecting a lack of physician awareness regarding *Candida* as a cause of in-hospital sepsis in patients at high risk for contracting candidemia.

The present study had some limitations. Some of the patients died soon after enrolling in the study, so some of the clinical data were incomplete. The authors were thus unable to assess the reason for the presence of a large proportion of *C. tropicalis* resistance to fluconazole in the authors' setting. The present study was conducted at a single referral hospital in Thailand, so the results may not be generalizable to other hospital settings. Finally, the small number of patients limit the power to detect a significant difference with respect to the prognostic factors.

Conclusion

Candidemia is associated with high mortality. non-*albicans Candida* was a more common cause of candidemia than *C. albicans*. Fluconazole-resistant *C. tropicalis* has become more prevalent and the incidence of *C. glabrata* increased. Empiric treatment with either amphotericin B or echinocandin would be appropriate in patients with suspected candidemia, especially for severe cases. Monitoring anti-fungal susceptibility data is essential for improving patient management and outcomes.

What is already known in this topic?

Epidemiology and antifungal susceptibility of *Candida* causing candidemia has changed over time and varies by region. In Asian countries, non-*albicans Candida* is a more prevalent cause of candidemia than *C. albicans*. Among non-*albicans Candida* isolates, *C. tropicalis* is the most frequently isolated, followed by *C. glabrata*, and *C. parapsilosis*. *C. albicans* has high susceptibilities to fluconazole but a significant proportion of reduced or high-level fluconazole-resistant *C. tropicalis* and to a lesser extent, *C. parapsilosis* is observed.

What this study adds?

A large proportion of reduced fluconazole susceptibility or fluconazole-resistant *C. tropicalis*, and an alarming proportion of fluconazole-resistant *C. albicans* and *C. parapsilosis* were observed. Empiric treatment with either amphotericin B or echinocandin, not fluconazole, would be appropriate in patients with suspected candidemia, especially for severe cases.

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Conflicts of interest

The authors declare no conflict of interest.

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