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Changes in Candidemia during the COVID-19 Pandemic: Species Distribution, Antifungal Susceptibility, Initial Antifungal Usage, and Mortality Trends in Two Korean Tertiary Care Hospitals

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This study aimed to investigate changes in candidemia incidence, species distribution, antifungal susceptibility, initial antifungal use, and mortality trends in Korea before and during the COVID-19 pandemic. A retrospective analysis was conducted on candidemia cases from two tertiary care hospitals in Korea between 2017 and 2022. Data were compared between the pre-pandemic (2017-2019) and pandemic (2020-2022) periods. Statistical methods included incidence rate ratios (IRRs) and multivariate Cox regression to assess 30-day mortality risk factors. A total of 470 candidemia cases were identified, with 48.7% occurring pre-pandemic and 51.3% during the pandemic. While the overall incidence of candidemia remained similar across the two periods (IRR 1.15; p=0.13), the incidence in intensive care units (ICUs) significantly increased during the pandemic (IRR 1.50; p<0.01). The distribution of *Candida* species did not differ significantly between the two periods. Fluconazole non-susceptibility in *C. albicans* markedly decreased (10.0% vs. 0.9%, p<0.01), whereas *C. glabrata* exhibited a significant rise in caspofungin non-susceptibility during the pandemic (0% vs. 22.4%, p<0.01). Echinocandin use increased (21.8% vs. 34.4%; p<0.01), while fluconazole use declined (48.0% vs. 32.8%; p<0.01). Although the 30-day mortality rate was higher during the pandemic (60.2% vs. 57.2%), the difference was not statistically significant (p=0.57). The findings highlight the need for region-specific surveillance and tailored management strategies to improve candidemia outcomes, especially during healthcare disruptions like the COVID-19 pandemic.

Key Words: *Candidemia; COVID-19; Antifungal Susceptibility; Antifungal Agents*

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INTRODUCTION

The emergence of COVID-19 created an unprecedented public health crisis and introduced new healthcare challenges, including an increased risk of invasive fungal infections (IFI) such as COVID-19-associated pulmonary aspergillosis and candidemia.[1,2] Candidemia is one of the most common fungal infections among hospitalized patients in developed countries.[3] Similar to other opportunistic infections, the epidemiology of candidemia is influenced by patient-related predisposing factors, patterns of antibiotic or antifungal use, and healthcare environments, including infection control measures.[4] The COVID-19 pandemic led to increased admissions of geriatric and immunocompromised patients, widespread use of corticosteroids and immunomodulators, frequent central venous catheter placement, and prolonged ICU stays. Additionally, staff and equipment shortages and compromised infection control measures during outbreaks likely contri-

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buted to changes in the epidemiology of candidemia.[5] These factors have prompted researches into the evolving patterns of invasive Candida infections, with several studies reporting a rise in candidemia incidence and the emergence of resistance in certain species.[1,5-7] However, data on changes in candidemia epidemiology during COVID-19 in Korea are limited, with few studies addressing clinical outcomes.[8] Given that the epidemiology of candidemia can vary by region and healthcare setting, region-specific data are essential for accurate analysis and effective management.[9] Therefore, we conducted a study at two tertiary care hospitals in Korea to investigate the changes in species distribution, antifungal susceptibility, initial antifungal usage, and mortality trends of candidemia before and during the pandemic. This study aims to provide data to improve candidemia management and treatment strategies.

MATERIALS AND METHODS

1. Study design and population

We conducted a retrospective study for candidemia patients aged ≥18 years in two tertiary medical centers in Korea, Chonnam National University Hospital and Chonnam National University Hwasun Hospital containing 1,130 and 680 beds respectively, from January 2017 to December 2022. Only patients with their first episode of candidemia during study period were included. Study periods were divided into two parts: January 2017 to December 2019 (pre-pandemic) and January 2020 to December 2022 (COVID-19 pandemic). We investigated the change between two period in incidence, species distribution, antifungal susceptibility, initial antifungal usage and mortality trends. The Institutional Review Boards of both Chonnam National University Hospital and Chonnam National University Hwasun Hospital reviewed and approved the study protocol (CNUH-2024-170, CNUHH-2024-117). A waiver of consent was granted given the retrospective nature of the study.

2. Data collection and definitions

Candidemia case were defined as a positive blood culture for Candida species identified during our study period. Demographic and clinical data were extracted from electronic medical records, including age, sex, existing comorbidities, predisposing medical conditions, the presence of intravascular devices, initial antifungal agents, and outcomes. Neutropenia was defined as an absolute neutrophil count <1,000/mm^3 within one week before the onset of bacteremia. Recent surgery was defined as any surgical procedure performed within 30 days prior to the onset of candidemia. History of chemotherapy included administration of cytotoxic drugs, targeted therapies, or immunotherapies within three months prior to the onset of candidemia. Corticosteroid use was defined as the administration of a systemic steroid at a dose equivalent to or greater than 20 mg/day of prednisone for a duration of 14 days or more within three months prior to the onset of candidemia. The 30-day mortality was defined as death from any cause within 30 days following the first recorded episode of candidemia.

3. Candida isolation, identification and susceptibility testing using automated systems

Blood cultures performed using BACTEC 9240 system (Becton Dickinson, Sparks, MD, USA) or BacT/ALERT system (bioMérieux). For the species identification, VITEK 2 system (bioMérieux, Hazelwood, MO, USA) and/or Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (Microflex MALDI, Biotyper Bruker Daltonics, Billerica, MA, USA or ASTA MicroIDSys, ASTA, South Korea or VITEK MS, BioMérieux, Marcy L'Étoile, France) were used. Antifungal susceptibility testing was performed using the VITEK 2 YST07 or YST08 cards. Antifungals used in the susceptibility test were fluconazole, voriconazole, caspofungin, micafungin. The results of antifungal susceptibility testing were interpreted according to Clinical and Laboratory Standards Institute (CLSI) document M60-Ed2.

4. Statistical analyses

The incidence rates were calculated as the number of candidemia episodes per 10,000 patient days (10,000 PD). Continuous variables were described using medians and interquartile ranges (IQRs), and were compared using the Student's t-tests or Kruskal-Wallis test, as appropriate depending on the appropriateness of data distribution and sample size. Categoric variables were analyzed using Fisher's exact test or the Chi-squared test. Multivariate analysis was employed, using the Cox proportional hazards regression model, to identify factors associated with 30-day mortality of candidemia. All statistical analyses were conducted using SPSS software, version 27.0 (IBM Corp.; Armonk, NY, USA). All significance tests were two-tailed, with a p-value ≤ 0.05 indicating statistical significance.

RESULTS

1. Incidence and species distribution of candidemia before and during the COVID-19 pandemic

A total of 470 patients with candidemia were identified between 2017 and 2022, with 229 cases (48.7%) occurring during the pre-pandemic period and 241 cases (51.3%) during the pandemic period. While the overall incidence of candidemia showed an increasing trend during the pandemic, the difference was not statistically significant (incidence rate ratio [IRR] 1.15, 95% confidence interval [CI] 0.96-1.38; p=0.13) (Table 1). Subgroup analysis by clinical settings revealed a statistically significant increase in incidence in intensive care unit (ICU) settings (IRR 1.50, 95% CI 1.14-1.99; p<0.01), whereas no significant change was observed in non-ICU settings. Species analysis demonstrated a significant increase in the incidence of *C. albicans* during the pandemic (IRR 1.38, 95% CI 1.05-1.81; p=0.02),

Table 1. Incidence rates of *Candida* species isolated from blood culture in ICU and non-ICU patients before (2017-2019) and during the COVID-19 pandemic (2020-2022)

Incidence/ 10,000 PD	Total				ICU				Non-ICU			
	Pre-pandemic	Pan-demic	IRR (95% CI)	p	Pre-pandemic	Pan-demic	IRR (95% CI)	p	Pre-pandemic	Pan-demic	IRR (95% CI)	p
C. albicans	0.56	0.77	1.38 (1.05-1.81)	0.02	2.00	3.42	1.71 (1.12-2.63)	0.01	0.39	0.46	1.17 (0.82-1.68)	0.41
C. tropicalis	0.27	0.25	0.92 (0.60-1.43)	0.74	1.35	1.71	1.27 (0.73-2.21)	0.48	0.14	0.07	0.52 (0.25-1.11)	0.11
C. glabrata	0.25	0.33	1.31 (0.86-1.98)	0.21	0.82	1.27	1.54 (0.78-3.05)	0.23	0.18	0.22	1.18 (0.70-1.99)	0.6
C. parapsilosis complex	0.15	0.15	0.96 (0.54-1.71)	>0.9	0.35	0.51	1.44 (0.50-4.15)	0.6	0.13	0.10	0.81 (0.41-1.61)	0.6
M. guiliermondii	0.02	0.02	1 (0.21-4.79)	>0.9	0.00	0.06	-	-	0.02	0.01	0.73 (0.12-4.38)	>0.9
C. lusitaniae	0.02	0.02	1 (0.21-4.79)	>0.9	0.00	0.13	-	-	0.02	0.01	0.37 (0.04-3.52)	0.63
C. krusei	0.02	0.02	1 (0.21-4.79)	>0.9	0.18	0.13	0.72 (0.12-4.31)	>0.9	0.00	0.01	-	-
Other *Candida* species[a]	0.12	0.06	0.50 (0.23-1.10)	0.09	0.23	0.19	0.81 (0.18-3.62)	>0.9	0.10	0.04	0.44 (0.17-1.13)	0.09
Total	1.40	1.61	1.15 (0.96-1.38)	0.13	4.93	7.42	1.50 (1.14-1.99)	<0.01	0.99	0.93	0.94 (0.74-1.19)	0.63

ICU: intensive care unit, PD: patients-days, IRR: incidence rate ratio, CI: confidence interval. [a]Other *Candida* species included cases involving more than two *Candida* species identified concurrently (n=12), unspecified *Candida* species (n=2), *Wickerhamomyces anomalus* (formerly *C. pelliculosa*) (n=2), *Pichia jadinii* (formerly *C. utilis*) (n=2), *Yarrowia lipolytica* (formerly *C. robusta*) (n=2), *C. dubliniensis* (n=2), *Debaryomyces hansenii* (formerly *C. famata*) (n=1), *C. haemolunii* (n=1), *C. intermedia* (n=1), *C. auris* (n=1), *C. ciferrii* (n=1), *Kluyveromyces marxianus* (formerly *C. kefyr*) (n=1).

Table 2. Species distribution of *Candida* species isolated from blood culture in ICU and non-ICU patients before (2017-2019) and during the COVID-19 pandemic (2020-2022)

Species	Total, n (%)			ICU, n (%)			Non-ICU, n (%)		
	Pre-pandemic	Pandemic	p	Pre-pandemic	Pandemic	p	Pre-pandemic	Pandemic	p
C. albicans	91 (39.7)	115 (47.7)	0.09	34 (40.5)	54 (46.2)	0.47	57 (39.3)	61 (49.2)	0.11
C. tropicalis	44 (19.2)	37 (15.4)	0.27	23 (27.4)	27 (23.1)	0.51	21 (14.5)	10 (8.1)	0.13
C. glabrata	41 (17.2)	49 (20.3)	0.56	14 (16.7)	20 (17.1)	>0.9	27 (18.6)	29 (23.4)	0.37
C. parapsilosis complex	25 (10.9)	22 (9.1)		6 (7.1)	8 (6.8)	>0.9	19 (13.1)	14 (11.3)	0.71
M. guiliermondii	3 (1.3)	3 (1.2)	>0.9	0 (0)	1 (0.9)	>0.9	3 (2.1)	2 (1.6)	>0.9
C. lusitaniae	3 (1.3)	3 (1.2)	>0.9	0 (0)	2 (1.7)	0.51	3 (2.1)	1 (0.8)	0.63
C. krusei	3 (1.3)	3 (1.2)	>0.9	3 (3.6)	2 (1.7)	0.65	0 (0)	1 (0.8)	0.46
Other *Candida* species[a]	19 (8.3)	9 (3.7)	0.05	4 (4.8)	3 (2.6)	0.46	15 (10.3)	6 (4.8)	0.11
Total	229 (100)	241 (100)		84 (100)	117 (100)		145 (100)	124 (100)	

ICU: intensive care unit. [a]Other *Candida* species included cases involving more than two *Candida* species identified concurrently (n=12), unspecified *Candida* species (n=2), *Wickerhamomyces anomalus* (formerly *C. pelliculosa*) (n=2), *Pichia jadinii* (formerly *C. utilis*) (n=2), *Yarrowia lipolytica* (formerly *C. robusta*) (n=2), *C. dubliniensis* (n=2), *Debaryomyces hansenii* (formerly *C. famata*) (n=1), *C. haemolunii* (n=1), *C. intermedia* (n=1), *C. auris* (n=1), *C. ciferrii* (n=1), *Kluyveromyces marxianus* (formerly *C. kefyr*) (n=1).

driven primarily by cases in ICU settings (IRR 1.71, 95% CI 1.12-2.63; p=0.01).

During the pre-pandemic period, *C. albicans* was the most prevalent species (n=91, 39.7%), followed by *C. tropicalis* (n= 44, 19.2%), *C. glabrata* (n=41, 17.9%), and the *C. parapsilosis* complex (n=25, 10.9%) (Table 2). During the pandemic period, *C. albicans* remained the most common species (n=115, 47.7%), with *C. glabrata* became the second most prevalent (n=49, 20.3%), followed by *C. tropicalis* (n=37, 15.4%) and *C. parapsilosis* complex (n=22, 9.1%). Subgroup analysis by clinical setting demonstrated consistent trends in the ICU across both periods. The most common species were *C. albicans* (40.5%, 46.2%), *C. tropicalis* (27.4%, 23.2%), *C. glabrata* (16.7%, 17.1%), and *C. parapsilosis* (7.1%, 6.8%), in that order. In non-ICU settings, the distribution differed between the two periods. During the pre-pandemic period, *C. albicans* (39.3%) was followed by *C. glabrata* (18.6%), *C. tropicalis* (14.6%), and *C. parapsilosis* (13.1%). During the pandemic period, *C. albicans* (49.2%) was followed by *C. glabrata* (23.4%), *C. parapsilosis* (11.3%), and *C. tropicalis* (8.1%). These differences in species distribution between the pre-pandemic and pandemic periods were not statistically significant.

2. Changes in antifungal susceptibility patterns before and during the COVID-19 pandemic

Information on in vitro antifungal susceptibility was available for a subset of isolates 373/470 (79.4%) for fluco-

nazole, 323/470 (68.7%) for voriconazole, and 422/470 (89.8%) for both caspofungin and micafungin. The antifungal susceptibility test results for the four most common *Candida* species are summarized in Table 3.

When comparing fluconazole susceptibility between the pre-pandemic and pandemic periods, a statistically significant reduction in non-susceptibility was observed for *C. albicans* during the pandemic period (10.0% vs. 0.9%, p< 0.01). Conversely, *C. glabrata* exhibited a statistically significant increase in non-susceptibility to caspofungin during the pandemic period compared to the prepandemic period (0% vs. 22.4%, p<0.01). No statistically significant differences were observed for micafungin or voriconazole susceptibility between the two periods.

3. Changes of initial antifungal regimens and 30-day mortality in the pre-pandemic and pandemic periods

Overall, 72% of patients received systemic antifungal treatment, with no significant difference observed between the pre-pandemic and pandemic periods. Table 4 summarized the pattern of initial antifungal regimen use. Fluconazole (40.2%) and micafungin (24.0%) were the two most commonly used initial antifungals. However, the rate of fluconazole uses as the initial antifungals significantly decreased from 48.0% in pre-pandemic period to 32.8% in pandemic period (p<0.01). Conversely, the use of micafungin significantly increased from 14.8% during the pre-pandemic period to 32.8% during the pandemic period (p< 0.01). The 30-day mortality rate was higher during the pandemic period compared to the pre-pandemic period (57.2% vs. 60.2%), but this difference was not statistically significant (p=0.57).

4. Risk factors of 30-mortality in patients with candidemia

Univariate analysis identified that chronic renal disease, hemodialysis, chronic lung disease, neutropenia, parenteral nutritional support, corticosteroid use, mechanical ventilation, indwelling urinary catheter, and central venous catheter were significantly associated with 30-day mortality (Table 5). In contrast, recent surgery, *C. parapsilosis* infection, and the choice of fluconazole as the initial antifungals were associated with improved outcome.

Multivariate logistic regression analysis revealed that parenteral nutritional support (OR 2.25, 95% CI 1.30-3.90; p<0.01) and mechanical ventilation (OR 2.18, 95% CI 1.34-3.54; p<0.01) were independent risk factors for 30-day mortality. In contrast, recent surgery (OR 0.37, 95% CI 0.21-0.65; p<0.01), *C. parapsilosis* infection (OR 0.45, 95% CI 0.22-0.92; p=0.03), and initial treatment with fluconazole (OR 0.39, 95% CI 0.25-0.59; p<0.01) were independently associated with reduced 30-day mortality.

TABLE 3. Antifungal susceptibilities of the four most common *Candida* species isolated from blood culture before (2017-2019) and during the COVID-19 pandemic (2020-2022)

Antifungal agent/ species	Total				Pre-pandemic				Pandemic				
	No	% R	% SDD/I	% NS	No	% R	% SDD/I	% NS	No	% R	% SDD/I	% NS	p*
Fluconazole													
C. albicans	205	4 (2.0)	6 (2.9)	10 (4.9)	90	4 (4.4)	5 (5.6)	9 (10.0)	115	0	1 (0.9)	1 (0.9)	<0.01
C. tropicalis	80	3 (3.8)	1 (1.3)	4 (5.0)	44	2 (4.5)	0	2 (4.5)	36	1 (2.8)	1 (2.8)	2 (5.6)	>0.9
C. glabrata	42	0	42 (100)	42 (100)	37	0	37 (100)	37 (100)	5	0	5 (100)	5 (100)	-
C. parapsilosis complex	46	2 (4.3)	0	2 (4.3)	24	1 (4.2)	0	1 (4.2)	22	1 (4.5)	0	1 (4.5)	>0.9
Total	373	9	49	58 (15.5)	195	7 (3.6)	42 (21.5)	49 (25.1)	178	2 (1.1)	7 (3.9)	9 (5.1)	<0.01
Voriconazole													
C. albicans	201	2 (1.0)	0	2 (1.0)	90	1 (1.1)	0	1 (1.1)	111	1 (0.9)	0	1 (0.9)	>0.9
C. tropicalis	80	1 (1.3)	1 (1.3)	2 (2.5)	44	1 (2.3)	0	1 (2.3)	36	0	1 (2.8)	1 (2.8)	>0.9
C. parapsilosis complex	42	1 (2.4)	1 (2.4)	2 (4.8)	24	1 (4.2)	0	1 (4.2)	18	0	1 (5.6)	1 (5.6)	>0.9
Total	323	4 (1.2)	2 (0.6)	6 (1.9)	158	3 (1.9)	0	3 (1.9)	165	1	2	3 (1.8)	>0.9
Caspofungin													
C. albicans	206	0	1 (0.5)	1 (0.5)	91	0	0	0	115	0	1 (0.9)	1 (0.9)	>0.9
C. tropicalis	80	1 (1.3)	0	1 (1.3)	44	0	0	0	36	1 (2.8)	0	1 (2.8)	0.45
C. glabrata	90	2 (2.2)	9 (10.0)	11 (12.2)	41	0	0	0	49	2 (4.1)	9 (18.4)	11 (22.4)	<0.01
C. parapsilosis complex	46	1 (2.2)	0	1 (2.2)	24	0	0	0	22	1 (4.5)	0	1 (4.5)	0.48
Total	422	4 (0.9)	10 (2.4)	14 (3.3)	200	0	0	0	222	4 (1.8)	10 (4.5)	14 (6.3)	<0.01
Micafungin													
C. albicans	206	0	1 (0.5)	1 (0.5)	91	0	0	0	115	0	1 (0.9)	1 (0.9)	<0.01
C. tropicalis	80	1	0	1 (1.3)	44	0	0	0	36	1 (2.8)	0	1 (2.8)	0.45
C. glabrata	90	0	0	0 (0)	41	0	0	0	49	0	0	0	-
C. parapsilosis complex	46	1 (2.2)	0	1 (2.2)	24	0	0	0	22	1 (4.5)	0	1	0.48
Total	422	2	1	3 (0.7)	200	0	0	0	222	2 (0.9)	1 (0.5)	3 (1.4)	0.25

R: resistant, I: intermediate, SDD: susceptible-dose-dependent, NS: non-susceptible. *p represents the comparison of non-susceptible (NS) percentages between pre-pandemic and pandemic.

TABLE 4. The patterns of initial antifungal uses and mortality in pre-pandemic (2017-2019) and pandemic (2020-2022) period

Initial antifungal regimens	Total (n=470) n (%)	Pre-pandemic (n=229) n (%)	Pandemic (n=241) n (%)	p
Fluconazole	189 (40.2)	110 (48.0)	79 (32.8)	<0.01
Micafungin	113 (24.0)	34 (14.8)	79 (32.8)	<0.01
Caspofungin	15 (3.2)	11 (4.8)	4 (1.7)	0.07
Amphotericin B or liposomal amphotericin	12 (2.6)	5 (2.2)	7 (2.9)	0.77
Anidulafungin	5 (1.1)	5 (2.2)	0 (0)	0.03
Voriconazole	4 (0.9)	1 (0.4)	3 (1.2)	0.62
No antifungal treatment	132 (28.1)	63 (27.5)	69 (28.6)	0.84
Initial antifungal regimens category				<0.01
Echinocandin	133 (28.3)	50 (21.8)	83 (34.4)	
Non-echinocandin	337 (71.7)	179 (78.2)	158 (65.6)	
30-day mortality	276 (58.7)	131 (57.2)	145 (60.2)	0.57

TABLE 5. Risk factors associated with the 30-day mortality in patients with candidemia during 2017-2022

	Survivors (n=194) n (%)	Death (n=276) n (%)	p	Adjusted OR (95% CI)	p
Age, median (IQR)	72 (60.8-79.0)	73 (63.0-80.8)	0.16	1.01 (1.00-10.3)	0.14
Sex, male	121 (62.4)	136 (59.1)	0.5		
Comorbidities					
Chronic renal disease	24 (12.4)	68 (24.6)	<0.01	1.62 (0.81-3.24)	0.17
Hemodialysis	15 (7.7)	48 (17.4)	<0.01	1.82 (0.78-4.24)	0.16
Chronic lung disease	56 (28.9)	112 (40.6)	0.01	1.13 (0.72-1.78)	0.6
Predisposing conditions					
Neutropenia	6 (3.1)	24 (8.7)	0.02	1.82 (0.64-5.11)	0.26
Recent surgery	46 (23.7)	36 (13.0)	<0.01	0.37 (0.21-0.65)	<0.01
Parenteral nutrition	143 (73.7)	245 (88.8)	<0.01	2.25 (1.30-3.90)	<0.01
Corticosteroid use	14 (7.7)	48 (17.4)	<0.01	1.74 (0.86-3.51)	0.14
Chemotherapy	33 (17.0)	64 (23.2)	0.11		
Mechanical ventilator	48 (24.7)	143 (51.8)	<0.01	2.18 (1.34-3.54)	<0.01
Indwelling urinary catheter	135 (69.9)	232 (84.1)	<0.01	1.41 (0.83-2.39)	0.21
Central venous catheter	122 (62.9)	212 (76.8)	<0.01	1.40 (0.85-2.32)	0.19
Species					
C. albicans	85 (43.8)	121 (43.8)	>0.9		
C. tropicalis	27 (13.9)	51 (19.6)	0.14		
C. glabrata	35 (18.0)	55 (19.9)	0.64		
C. parapsilosis	29 (14.9)	18 (6.5)	<0.01	0.45 (0.22-0.92)	0.03
Others	13 (6.7)	15 (5.4)	0.56		
Initial antifungal regimen					
Fluconazole	107 (55.2)	82 (29.7)	<0.01	0.39 (0.25-0.59)	<0.01
Echioncandin	59 (30.4)	74 (26.8)	0.41		

IQR: interquartile range, OR: odds ratio, CI: confidence interval.

DISCUSSION

An increase in candidemia incidence during the COVID-19 pandemic has been observed in various regions, with the degree of increase varying by geographic location.[1,6,7,10] A recent study in Korea reported a 1.2-fold rise in overall incidence, consistent with the findings of our study.[8] However, greater increases were documented in other regions, including Spain, Greece, and Brazil, where incidences rose by 1.9-fold, 1.9-6.5-fold, and 4.8-fold, respectively.[1,6,7,10] The higher incidence of candidemia among COVID-19 patients compared to non-COVID-19 patients can be attributed to multiple factors, including immune dysregulation (e.g., lymphopenia and impaired T-cell function), corticosteroid and immunomodulator use (e.g., IL-6 inhibitors and Janus kinase inhibitors), prolonged ICU stays, invasive devices, and mechanical ventilation required due to respiratory failure or other complications.[11] Interestingly, several studies also reported increased candidemia incidence among non-COVID-19 patients during the pandemic.[1,6] This could be explained by hospital responses to the COVID-19 surge, such as canceling non-urgent procedures and discharging

patients with less severe conditions early, leaving a higher proportion of severely ill patients hospitalized. Additionally, challenges like staff and equipment shortages may have compromised infection control practices, further contributing to this trend. These observations highlight the importance of close monitoring of infectious diseases, particularly opportunistic infections like candidemia, during significant healthcare disruptions.

The rise of antifungal-resistant *Candida* species globally remains a significant concern, although resistance rates vary by region, hospital, and ICU setting.[9] A study conducted in Korea across 11 hospitals during 2017-2018 reported azole resistance rates of 0.3% for *C. albicans*, 1.3% for *C. tropicalis*, 6.3% for *C. glabrata*, and 3.6% for *C. parapsilosis*.[12] Similarly, data from the Korean Global Antimicrobial Resistance Surveillance System (KorGLASS) for 2020-2021 revealed stable resistance rates: 0% for *C. albicans*, 2.2% for *C. tropicalis*, 5.3% for *C. glabrata*, and 5.6% for *C. parapsilosis*.[13] In our study, fluconazole resistance during the pre-pandemic period (2017-2019) was higher for *C. albicans* (4.4%) and *C. tropicalis* (4.5%) compared to prior reports. However, during the pandemic, resistance decreased to 0% and 2.8%, respectively. This trend aligns with findings by Won et al.[8], who also reported a reduction in fluconazole resistance during the pandemic period. Variations in resistance rates between studies may reflect differences in hospital settings and patient populations.

Echinocandin resistance was rarely reported in earlier studies, and in our study, echinocandin resistance remained rare during the pre-pandemic period.[12] However, isolates with reduced susceptibility, including intermediate susceptibility to caspofungin, significantly increased during the pandemic. Whether this reflects a gradual global trend toward increasing echinocandin resistance or is specifically related to the pandemic requires further investigation.[14]

When comparing initial antifungal use between the pre-pandemic and pandemic periods, the proportion of cases treated with fluconazole decreased, while the use of echinocandins increased. The increasing use of echinocandins has been observed since the introduction of national health insurance coverage for critically ill patients with invasive candidiasis in Korea in 2014 and aligns with the 2016 IDSA guidelines recommending echinocandins as first-line therapy.[15,16] Whether the observed increase in echinocandin use during the pandemic represents a continuation of this trend or a pandemic-specific phenomenon warrants further investigation.

Several studies have reported higher mortality rates among COVID-19 patients with candidemia compared to non-COVID-19 patients.[5,17,18] Additionally, some studies observed increased mortality rates among both COVID-19 and non-COVID-19 patients with candidemia during the pandemic.[6,7] In contrast, other studies found no significant difference in candidemia mortality between COVID-19 and non-COVID-19 patients, suggesting that any observed differences were likely due to variations in the severity of underlying conditions rather than COVID-19 itself.[19,20] In our study, although there was a slight increase in mortality during the pandemic, it did not reach statistical significance. This finding supports the perspective that factors other than COVID-19 status, such as patient comorbidities and the severity of underlying conditions, might play a more critical role in determining candidemia outcomes.

This study has several limitations. First, its retrospective design, conducted in two tertiary care hospitals in Korea, may introduce bias in data collection and interpretation and limit the generalizability of the findings to other regions or healthcare settings. Second, antifungal susceptibility testing was not performed for all isolates, which could have influenced the accuracy of resistance trend analysis. Finally, we were unable to calculate the candidemia incidence separately for COVID-19 and non-COVID-19 patients, as accurately determining COVID-19 patient-days was not feasible due to nosocomial transmission of COVID-19 during the pandemic. However, among candidemia cases reported during the pandemic, 14.5% in ICU settings and 6.5% in non-ICU settings were associated with COVID-19, suggesting that this study provides valuable insights into the direct and indirect impacts of the COVID-19 pandemic on candidemia epidemiology.

In conclusion, our findings underscore the need for continued vigilance, region-specific data collection, and tailored management strategies to improve outcomes for patients with candidemia, particularly during healthcare disruptions like the COVID-19 pandemic.

CONFLICT OF INTEREST STATEMENT

None declared.

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