

Original article

Seasonality and epidemiological trends in species distribution and antifungal susceptibility of *Candida* species isolated from various clinical specimens conducted during 2011–2022, Korea: a retrospective surveillance study

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Abstract

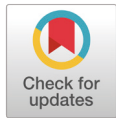
Background: As most *Candida* species cause opportunistic infections, it is helpful for patient care to determine species name of *Candida* spp. and their distribution in both sterile and non-sterile specimens. We aimed to investigate trends in the distribution of *Candida* species isolated from a hospital in Korea, along with their antifungal susceptibilities and seasonal variations.

Methods: This study was conducted at the Chung-Ang University Hospital and included 8,760 different clinical specimens from March 2011 to December 2022. Identification of the fungal species and its antifungal susceptibility testing were performed using VITEK 2 ID-YST system for six drugs: amphotericin B, caspofungin, fluconazole, voriconazole, micafungin, and flucytosine.

Results: The most common fungal species was *Candida albicans*. The *C. albicans* positivity rate gradually increased from 2012 to 2022. Since 2020, however, this trend reversed and the non-*albicans Candida* (NAC) superseded the count of *C. albicans*. Among the NAC, *C. glabrata* showed significant increase. When a weekly analysis was performed, *C. glabrata* was evenly distributed without any noticeable peak; however, the positive rate decreased from late December to early January across all years.

Conclusion: Monitoring of future trends should necessarily be continued. Our findings revealed that the positive rate for *Candida* was the lowest in the months of December and January of the studied years, which can be attributed to environmental factors. However, further research needs to be conducted.

Keywords: Antifungal agents, *Candida albicans*, Epidemiology, Opportunistic infections, Republic of Korea



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Introduction

Background

Globally, antimicrobial resistance is the leading cause of death due to microbial infections [1]. In 2015, the World Health Organization launched the Global Antimicrobial Resistance Surveillance and Use System (GLASS), which was the first global collaboration to monitor antimicrobial resistance [2]. GLASS presents epidemiological data to monitor the impact and degree of antimicrobial resistance in populations worldwide

[2]. In 2019, with an increasing number of fungal infections becoming resistant to antifungal drugs, a protocol was developed for collecting data on the early detection of *Candida* species [3]. However, compared to bacteria, accurate identification of *Candida* species and testing their antifungal resistance is a challenge because numerous microbiological laboratories worldwide lack the facility for these measurements [3]. In Korea, the Korea Centers for Disease Control and Prevention launched a system (Kor-GLASS) in 2017 to monitor antimicrobial resistance [4]. *Candida* is one of the most common causes of hospital-acquired infections [5]. According to the 2021 National Antimicrobial Resistant Microbial Survey annual report published by Kor-GLASS, surveillance of *Candida* began in the year 2020; among the *Candida* isolates from blood collected in 2021 from centers in nine regions, 360 were hospital-acquired infections, and 50 cases were community-acquired infections [5].

Regarding domestic research in Korea, several reports have been published focusing on surveillance of the antifungal susceptibility of *Candida* identified in sterile specimens, especially blood [6–8]. However, reports monitoring the distribution of *Candida* species and their antifungal drug susceptibility in various clinical samples—such as oral, skin, and urine as well as rare aseptically collected samples—exist in Korea [9–11]. As most *Candida* species cause opportunistic infections, it is helpful to analyze the distribution of *Candida* species detected in sterile specimens like blood, and in nonsterile specimens like the human mucous membranes, to identify the infectious species and conduct epidemiological investigations [11]. The distribution of *Candida* species in the studied specimens varied depending on the region, hospital, and the type of specimen [12].

Several studies have reported seasonal changes in the incidence of various infectious diseases [13]. Multiple factors, including temperature, humidity, school term, eating habits, and the environment preferred by microorganisms, are responsible for seasonal changes in infectious diseases. Therefore, studies conducted across different seasons may reveal various seasonal patterns in the growth of different types of microorganism, and may exhibit multiple growth peaks during the year [13]. However, few studies have investigated the seasonality of *Candida* epidemiology, and even these were limited to either one species of *Candida* or to a fixed age group of the study participants [14,15]. Moreover, no reports of *Candida* seasonality have been published in Asian countries.

Objectives

This study, conducted at the Chung-Ang University Hospital, investigated the distribution of fungal species and antifungal drug susceptibility in various clinical and sterile specimens to confirm the latest epidemiology of *Candida* and to obtain information for future *Candida* treatment in South Korea. We also analyzed seasonal variations in *Candida* by evaluating long-term data.

Methods

Study design

It is a retrospective surveillance study based on the laboratory records. It was described according

to the Microbiology Investigation Criteria for Reporting Objectively: a framework for the reporting and interpretation of clinical microbiology data available at: <https://bmcmicrobiology.biomedcentral.com/articles/10.1186/s12916-019-1301-1>.

Setting

This study was conducted at the Chung-Ang University Hospital and targeted 8,760 different clinical specimens, including both sterile and non-sterile specimens, from patients who visited the hospital over a period of 12 years from March 2011 to December 2022. Duplicate samples were excluded from the analyses. Sterile specimens included blood, ascites, pleural fluid, and amniotic fluid, while non-sterile specimens included respiratory specimens, urine, feces, vaginal discharge, abscess, pus, and catheter tips.

Laboratory work

Species were identified using the VITEK 2 ID-YST system (bioMérieux, Inc.) according to the manufacturer's instructions. Antifungal susceptibility testing was conducted using the VITEK AST-YS07 (bioMérieux, Inc.) card of the VITEK 2 ID-YST system for the following six drugs: amphotericin B, caspofungin, fluconazole, voriconazole, micafungin, and flucytosine until November, 2019. Antifungal susceptibility testing was conducted using a VITEK AST-YS08 card (bioMérieux, Inc.) of the VITEK 2 ID-YST system. The minimum inhibitory concentration (MIC) was determined according to the standards defined by the Clinical and Laboratory Standards Institute (CLSI), which are periodically updated.

Quality assurance

The Department of Laboratory Medicine at Chung-Ang University College of Medicine has been participated in the External Quality Assurance/Proficiency Testing Program of the Korean Association of External Quality Assessment Service and has been accredited by the Outstanding Laboratory Accreditation Program of the Laboratory Medicine Foundation/Korean Society for Laboratory Medicine.

Bias

Duplicate and sequential isolates from the same patient were not consistently done.

Statistical methods

Statistical analysis was performed using the chi-square test with MedCalc software v. 19.5.1 (MedCalc Software), and $p < 0.05$ was considered statistically significant. Weekly trend analysis was performed for 52 weeks over 11 years to determine *Candida* seasonality. The number of *Candida* species over the period of 52 weeks, calculated weekly, and the proportion of *Candida* species compared to all specimens requested for microbial identification at the Chung-Ang University Hospital were graphed for visual comparison.

Results

Antifungal susceptibilities

The antifungal drug susceptibility test results for the 8,760 *Candida* strains are summarized in Table 1. The most common *Candida* species was *C. albicans* (4,226 strains, 48.2%), followed by *C. tropicalis* (2,083 strains, 23.8%), *C. glabrata* (1,445 strains, 16.5%), and *C. parapsilosis* (554 strains, 6.3%). The MICs of amphotericin B, caspofungin, flucytosine, fluconazole, micafungin, and voriconazole for the 8,760 strains of *Candida* were distributed in the range of 0.25–16 µg/mL, 0.125–8 µg/mL, 1–64 µg/mL, 0.25–64 µg/mL, 0.06–8 µg/mL, and 0.125–8 µg/mL, respectively, with differences depending on the fungal species. *C. tropicalis* showed 100% sensitivity to amphotericin B; however, seven strains of *C. albicans* showed resistance, and one strain of *C. glabrata*, and four strains of *C. parapsilosis* showed intermediate resistance. *C. albicans*, *C. tropicalis*, and *C. parapsilosis* were 98.6%, 98.8%, and 97.8% sensitive to fluconazole, respectively. However, only 228 (15.8%) *C. glabrata* strains were sensitive to fluconazole, 779 (83.7%) strains showed intermediate resistance, and 8 strains (0.6%) showed resistance.

Table 1. Antifungal susceptibilities of 8,760 *Candida* isolates from clinical specimens determined using the VITEK AST-YS07,08 card (continued)

Species	No. of isolates	Antifungal agent	MIC (µg/mL) range	% of MICs by category		
				S	I/SDD	R
<i>C. albicans</i>	4,226	Amphotericin B	≤ 0.25-8	99.8	0.0	0.2
		Caspofungin	≤ 0.125-0.5	100.0	0.0	0.0
		Flucytosine	≤ 1-≥ 64	94.7	0.1	5.2
		Fluconazole	≤ 0.25-≥ 64	98.6	1.4	0.2
		Micafungin	≤ 0.06-0.25	100.0	0.0	0.0
		Voriconazole	≤ 0.125-≥ 8	99.1	0.1	0.8
<i>C. tropicalis</i>	2,083	Amphotericin B	≤ 0.25-1	100.0	0.0	0.0
		Caspofungin	≤ 0.125-≥ 8	99.6	0.0	0.4
		Flucytosine	≤ 1-≥ 64	99.9	0.0	0.1
		Fluconazole	≤ 0.5-≥ 64	98.8	0.5	0.8
		Micafungin	≤ 0.06-2	99.6	0.1	0.4
		Voriconazole	≤ 0.125-4	99.3	0.0	0.6
<i>C. glabrata</i>	1,445	Amphotericin B	≤ 0.25-2	99.9	0.1	0.0
		Caspofungin	≤ 0.125-4	42.3	43.2	14.6
		Flucytosine	≤ 1-≥ 64	99.6	0.0	0.4
		Fluconazole	≤ 0.5-≥ 64	15.8	83.7	0.6
		Micafungin	≤ 0.06-0.5	99.8	0.0	0.2
		Voriconazole	≤ 0.125-≥ 8	-	-	-
<i>C. parapsilosis</i>	554	Amphotericin B	≤ 0.25-2	99.3	0.7	0.0
		Caspofungin	0.125-2	100.0	0.0	0.0
		Flucytosine	≤ 1	100.0	0.0	0.0
		Fluconazole	≤ 0.5-≥ 64	97.8	1.1	1.3
		Micafungin	≤ 0.06-2	100.0	0.0	0.0
		Voriconazole	≤ 0.125-≥ 8	99.1	0.4	0.5
<i>C. utilis</i>	92	Amphotericin B	≤ 0.25-≥ 16	98.9	0.0	1.1
		Caspofungin	≤ 0.125-0.25	100.0	0.0	0.0
		Flucytosine	≤ 1	100.0	0.0	0.0
		Fluconazole	≤ 0.5-32	98.9	1.1	0.0
		Micafungin	≤ 0.06-0.125	100.0	0.0	0.0
		Voriconazole	≤ 0.125-0.5	100.0	0.0	0.0

Table 1. Antifungal susceptibilities of 8,760 *Candida* isolates from clinical specimens determined using the VITEK AST-YS07,08 card

Species	No. of isolates	Antifungal agent	MIC ($\mu\text{g/mL}$) range	% of MICs by category		
				S	I/SDD	R
<i>C. famata</i>	73	Amphotericin B	≤ 0.25 -1	100.0	0.0	0.0
		Caspofungin	≤ 0.25 -1	100.0	0.0	0.0
		Flucytosine	≤ 1	100.0	0.0	0.0
		Fluconazole	≤ 1 -32	98.6	1.4	0.0
		Micafungin	≤ 0.06 -0.125	100.0	0.0	0.0
		Voriconazole	≤ 0.125 -0.25	100.0	0.0	0.0
<i>C. krusei</i> ^a	73	Amphotericin B	≤ 0.25 -2	90.8	9.2	0.0
		Caspofungin	≤ 0.125 -0.5	84.7	15.3	0.0
		Flucytosine	2-16	4.1	4.1	91.8
		Fluconazole	2- ≥ 64	0.0	0.0	100.0
		Micafungin	≤ 0.06 -0.25	100.0	0.0	0.0
		Voriconazole	≤ 0.125 -0.25	100.0	0.0	0.0
<i>C. lusitaniae</i>	64	Amphotericin B	≤ 0.25 -1	100.0	0.0	0.0
		Caspofungin	≤ 0.25 -0.5	100.0	0.0	0.0
		Flucytosine	≤ 1	100.0	0.0	0.0
		Fluconazole	≤ 0.5 -8	100.0	0.0	0.0
		Micafungin	≤ 0.06 -0.5	100.0	0.0	0.0
		Voriconazole	≤ 0.125	100.0	0.0	0.0
Others ^b	150	Amphotericin B	≤ 0.25 - ≥ 16	91.6	1.4	7.0
		Caspofungin	≤ 0.125 - ≥ 8	91.0	5.4	3.6
		Flucytosine	≤ 1 - ≥ 64	96.2	3.0	0.8
		Fluconazole	≤ 0.5 - ≥ 64	74.6	6.6	19.4
		Micafungin	≤ 0.06 - ≥ 8	97.9	1.0	1.0
		Voriconazole	≤ 0.125 -4	91.8	7.4	0.8
Total	8,760					

Abbreviations: MIC, minimum inhibitory concentration; S, susceptible; SDD, susceptible dose-dependent; I, intermediate; R, resistant.

^a*C. krusei* was resistant to fluconazole, irrespective of its MIC.

^bOthers include *C. haemulonii*, *C. orthopsiiosis*, *C. guilliermondii*, *C. kefyr*; *C. auris*, *C. ciferrii*, *C. norvegensis*, *C. lipolytica*, and *C. inconspicua*.

Species distribution

Table 2 summarizes and compares the species distribution of *Candida* isolates in non-sterile and sterile specimens. Very rare samples and cases, where the sample type was not recorded, were excluded. A total of 1,351 *Candida* strains were isolated from sterile specimens, including blood, ascites, pleural fluid, and cerebrospinal fluid. The most commonly isolated fungal species from the total sterile body fluid specimens were *C. albicans* (673 strains, 49.8%), and *C. glabrata* (240 strains, 17.8%), followed by *C. tropicalis* (230 strains, 17.0%), *C. parapsiiosis* (131 strains, 9.7%), and *C. krusei* (22 strains, 1.6%).

A total of 7,324 *Candida* strains were isolated from non-sterile specimens, including respiratory samples, urine, stool, and vaginal discharge; most of the commonly isolated strains were from urine samples (6,320 strains, 86.3%), followed by respiratory samples (338 strains, 4.6%). *C. albicans* was the most common species isolated from non-sterile specimens (3,483 strains, 47.6%), followed by *C. tropicalis* (1,823 strains, 24.9%), *C. glabrata* (1,187 strains, 16.2%), and *C. parapsiiosis* (419 strains, 5.7%).

Table 2. Species distribution of *Candida* isolates from sterile and nonsterile clinical specimens

Species	Pus/Wound										Non-sterile Total	Blood	Ascitic fluid	Pleural fluid	^b Other sterile fluid	Sterile Total	Sterile vs. Non-sterile p-value
	Respiratory	Ear discharge	Eye discharge	Other pus/wound	Urine	Stool	Tissue	Vaginal discharge	Cath tip								
<i>C. albicans</i>	194	10	3	87	2,967	1		165	56	3,483	461	19	15	178	673	0.2725	
<i>C. tropicalis</i>	117	4		36	1,632			9	25	1,823	154	8	12	56	230	<0.0001 ^a	
<i>C. glabrata</i>	4	1		13	1,131		2	23	13	1,187	206	12	6	16	240	0.2272	
<i>C. parapsilosis</i>	2	108	4	19	271		1		14	419	123		1	7	131	<0.0001 ^a	
<i>C. utilis</i>		1		1	85			1		88	4				4	0.0026 ^a	
<i>C. famata</i>	3	7			135			2		147	9	1	1		11	0.0021 ^a	
<i>C. krusei</i>	11			2	31			3		47	4	1	12	5	22	0.0001 ^a	
<i>C. lusitanae</i>	6				44				1	51	8			4	12	0.4218	
<i>C. haemulonii</i>		31	1						3	35	0				0	-	
<i>C. orthopsilosis</i>		3			9				1	13	11				11	0.0002 ^a	
<i>C. guilliermondii</i>		2			11				1	14	15	1			16	<0.0001 ^a	
<i>C. kefyr</i>										0	1				1	-	
<i>C. auris</i>		8							1	9	0				0	-	
<i>C. ciferrii</i>		3			1					4	0				0	-	
<i>C. norvegensis</i>					2					2	0				0	-	
<i>C. lipolytica</i>					1					1	0				0	-	
<i>C. inconspicua</i>	1									1	0				0	-	
Total	338	178	8	158	6,320	1	3	203	115	7,324	996	42	47	266	1,351		

^ap < 0.05.

^bOther sterile fluids included bile, amniotic fluid, intraocular (vitreous and aqueous) fluid, homovac drainage, and percutaneous transhepatic biliary drainage.

Overall, *C. albicans* was the most commonly identified species in almost all samples, except pus. The most common non-*albicans Candida* species isolated from respiratory specimens was *C. tropicalis* whereas those isolated from urine and pus specimens were *C. tropicalis* and *C. parapsilosis*, respectively. In vaginal discharge, *C. albicans* was the most common species identified, followed by *C. glabrata*. *Candida* was the most common species with 996 strains isolated from blood, (73.7%), pleural fluid (3.5%), and ascitic fluid (3.1%).

Annual analysis

To conduct the annual analysis, we used data from January 2012 to December 2022. During this period, in total, 697,410 samples were requested for microbial culture tests at the Department of Laboratory Medicine, Chung-Ang University Hospital, of which 8,533 (1.2%) tested positive for *Candida*. The *Candida* positivity rate gradually increased from 2012 (465 of 55,448 positive cases, 0.84 %) to 2022 (1,164 of 65,685 positive cases, 1.77%). In 2020, 1,282 positive cases out of 59,669 culture tests requested (2.15%) showed the highest positivity rate (Table 3).

Approximately 91% of the non-*albicans Candida* (NAC) comprised three species: *C. tropicalis*, *C. glabrata*, and *C. parapsilosis*. Although no change was observed in the occurrence of *C. tropicalis*, the most dominant fungus, *C. glabrata* demonstrated a significant increase in abundance from 2020 (Fig. 1). From 2012 to 2019, *C. glabrata* accounted for 13.9% of *Candida* cases (697 of 2,995 positive cases); however, the proportion increased from 2020 to 2022, accounting for 20% of *Candida* cases (708 of 3,538 positive cases).

Table 3. Yearly comparison analysis showing the epidemiological trend of *Candida* infection between 2012 and 2022

<i>Candida</i> infection	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2012-2022
<i>Candida</i> spp.	465(0.84)	401(0.66)	414(0.67)	615(0.95)	794(1.20)	550(0.94)	802(1.13)	954(1.36)	1,282(2.15)	1,092(1.71)	1,164(1.77)	8,533(1.22)
% refers to the number of positive <i>Candida</i> cases relative to the total number of culture tests requested.												
<i>Candida albicans</i>	216(46.45)	216(53.87)	207(50.00)	267(43.71)	403(50.76)	243(44.18)	387(48.25)	519(54.40)	577(45.01)	503(46.06)	540(46.39)	4,078(47.79)
NAC	249(53.55)	185(46.13)	207(50.00)	348(56.59)	391(49.24)	307(55.82)	415(51.75)	435(45.60)	705(54.99)	589(53.94)	624(53.61)	4,455(52.21)
<i>C.tropicalis</i>	41(8.82)	61(15.21)	94(22.71)	139(22.60)	198(24.94)	191(34.73)	244(30.42)	207(21.70)	294(22.93)	251(22.99)	248(21.31)	1,968(23.06)
<i>C.glabrata</i>	94(20.22)	34(8.48)	34(8.21)	135(21.95)	118(14.86)	66(12.00)	73(9.10)	143(14.99)	272(21.22)	210(19.23)	226(19.42)	1,405(16.47)
<i>C.parapsilosis</i>	23(4.95)	23(5.74)	21(5.07)	44(7.15)	38(4.79)	17(3.09)	69(8.60)	45(4.72)	88(6.86)	74(6.78)	99(8.51)	541(6.34)
% means the number of <i>Candida</i> positive cases relative to the total number of <i>Candida</i> spp. positive cases.												
Total	55,448	60,344	61,735	64,943	66,428	58,371	71,027	69,998	59,669	63,762	65,685	697,410

Values are presented as n (%) or n.

In 2019, of the 954 positive cases for *Candida*, *C. albicans* and NAC accounted for 54.4 % (519 cases) and 45.6 % (435 cases), respectively. *C. albicans* was identified significantly more frequently ($p < 0.05$). In 2020, this trend was reversed and significantly more NACs were identified. This trend is expected to continue after the year 2020. Abbreviation: NAC, non-*albicans Candida*.

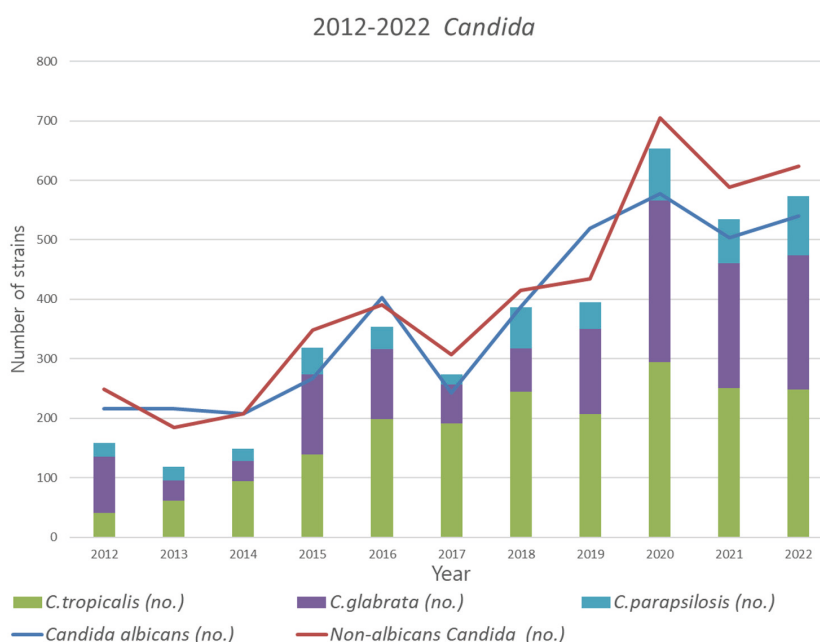


Fig. 1. Yearly analysis showing the number of *Candida*, including *C. albicans*, NAC, particularly *C. tropicalis*, *C. glabrata*, and *C. parapsilosis*, the three most predominant species of NAC. The *Candida* positivity rate gradually increased from 2012 (465 positive cases out of 55,448, 0.84%) to 2022 (1,164 positive cases out of 65,685 cases, 1.77%). *C. albicans* and NAC showed the same pattern. NAC, non-*albicans Candida*.

Weekly analysis

A weekly analysis performed for 52 weeks over 11 years revealed that the *Candida* positivity rate was the highest at week 44 (October 29 to November 4), followed by week 34 (August 20 to August 26) at 1.52%. It was lowest in week 1 at 0.91% (January 1 to January 7), followed by week 2 at 0.98% (January 8 to January 14), week 22 at 0.98%, and week 52 at 0.99%. Fig. 2 shows the number of *Candida* positive cases per week and with respect to the ratio of the total number of samples received. Overall, it was evenly distributed without a noticeable peak; however, the positivity rate was generally low across all years from late December to early January.

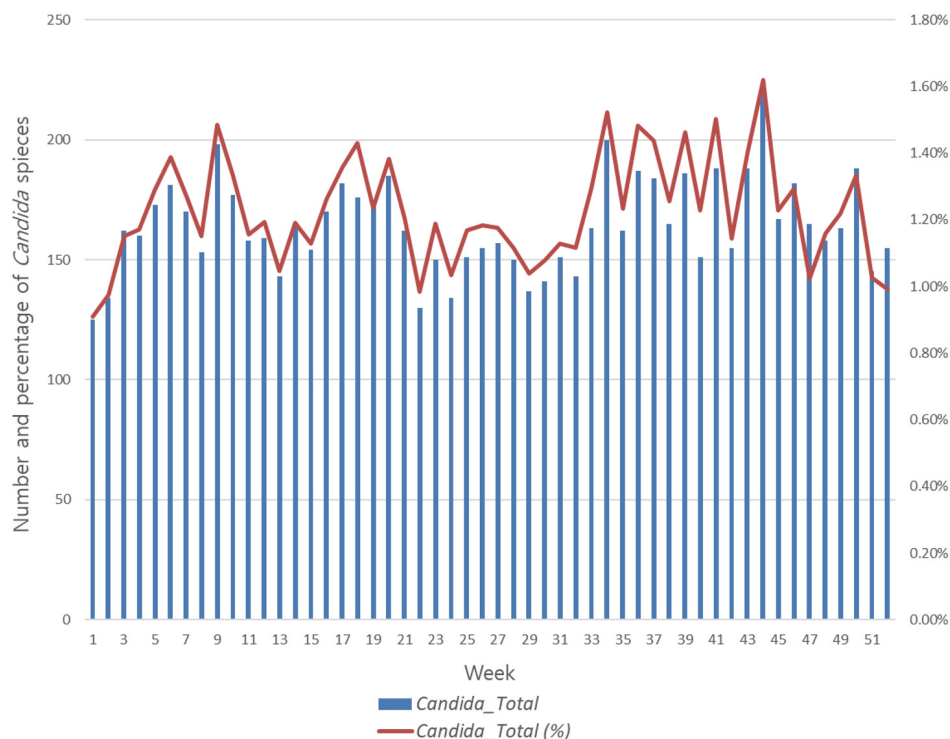


Fig. 2. Weekly comparison analysis showing the epidemiological trend of *Candida* infection between 2012 and 2022.

Discussion

Interpretation and comparison with previous studies

Fungal species with intrinsic resistance to antifungal drugs are well known; thus, major antifungal drug resistance information can be obtained by determining the distribution of fungal species [8]. Therefore, to appropriately treat fungal infections, periodic investigations of the distribution of the fungal species, isolated from clinical specimens in hospitals of relevant regions, and their antifungal drug resistance is necessary [8]. Among fungi, yeast is frequently isolated from clinical specimens that rapidly proliferate and form colonies similar to bacteria; thus, a standardized test for antifungal drug susceptibility has been developed and implemented in several laboratories [16]. In this study, the VITEK AST-YST07 and YST08 (bioMérieux, Inc.) of the VITEK 2 ID-YST system, an automated equipment that performs antifungal drug susceptibility testing,

were used. Antifungal susceptibility testing using the VITEK 2 ID-YST system has been reported to possess a remarkably high agreement rate with the CLSI M27 method, a standardized test with good reproducibility [17,18]. The broth microdilution method, which is the reference method for the antifungal susceptibility testing, relies on visual MIC determination. The VITEK 2 ID-YST system uses spectrophotometry to determine the MIC endpoint, which eliminates subjectivity [17]. However, the VITEK 2 ID-YST system also minimizes the effects of trailing growth, compromising the performance of systems that rely on visual MIC determination [18].

Although antifungal susceptibility testing for yeast is not yet recommended as a routine test, the gradual increase in the incidence of severe infections caused by yeast, especially *Candida* spp., necessitates an increase for in vitro antifungal drug susceptibility testing [9]. In addition, in the United States, candidemia has gradually increased over the past 20 years, accounting for approximately 9% of nosocomial bloodstream infections and is the fourth most commonly isolated causative agent in the blood [19]. Candidemia or invasive *Candida* bloodstream infections are major causes of increased morbidity and mortality in patients [20]. Among fungi, > 90% of bloodstream infections are caused by *Candida* [21]. In Korea, *C. albicans* is the most common and clinically important cause of bloodstream infections, but NAC, including *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*, are also commonly identified in the order listed, and together they comprise the five most causative fungi of candidemia [22].

Although differences in the proportion of each *Candida* species exist among countries, similar trends in the increased use of antifungal drugs have been observed worldwide [23]. Comparing the epidemiology of *Candida* in Korea between 2001 and 2007 with reference to previously published reports [12], *C. albicans* accounted for 70%–93% of the total *Candida* spp. in the early 2000s, which significantly decreased to 44%–54%, according to our data from 2012 to 2022.

After 2020, the NAC increased significantly, reversing the trend of *C. albicans*. *C. tropicalis*, *C. glabrata*, and *C. parapsilosis* are the three representative species of the NAC. *C. glabrata* exhibited the most significant increase. More than 97% of strains of *C. albicans*, *C. tropicalis*, and *C. parapsilosis* were susceptible to fluconazole, whereas 84% of strains of *C. glabrata* were non-susceptible. The antifungal susceptibility of *Candida* isolates showed similar patterns between the early 2000s and the period of this study (2011–2022) [12]. However, the proportion of fluconazole-non-susceptible strains among *C. glabrata* significantly increased (5%–84%).

Thus, this finding is important for healthcare-related infections because *C. glabrata* is closely associated with antifungal drug resistance. Globally and in Korea, an increasing trend of *C. glabrata* has been observed [24], and a study showing similar results was published, although the timing of the study was different and only blood samples were used [25]. Therefore, continuous observation of future trends and antifungal drug resistance in *Candida*, especially *C. glabrata* is required.

There have been few reports on the seasonality of *Candida*. A report on the seasonality of invasive *Candida* infection in preterm low-birth-weight newborns revealed that infants were significantly more likely to be diagnosed with *Candida* infection between September and February [14]. The report attributed this observation to environmental factors, such as overcrowding. Another report investigating seasonal variation in vaginal *Candida* infection rates in Belgium [15] revealed that during summer, there was a 11% increase in

the rate of vaginal presence of *Candida*. They observed a relationship between the frequency of *C. albicans* vaginitis and mean monthly temperature in the country, although this trend was not significant. Our results showed that the positivity rate of *Candida* was lowest in December and January, presumably influenced by environmental factors (e.g., temperature and humidity); however, this requires further research.

Limitations

Some studies have shown that commercial microbial identification systems are unable to accurately identify *C. auris* [26]. In this study, two *C. auris* isolates were misidentified as *C. albicans* (confidence value 86.0) and *C. haemulonii* (confidence value 99.9) using VITEK 2 ID-YST system [26]. Therefore, it is necessary to confirm the *Candida* species identified as *C. auris* using additional tests. However, in this study, the statistical results were reported based on the results obtained using the VITEK 2 ID-YST system and additional tests were not performed. In addition, the clinical breakpoints for the antifungal drug susceptibility testing were revised during the course of this study; however, we did not provide a description or interpretation of these revisions. Data analysis was conducted based on the antifungal susceptibility results at the time the specimen was tested.

Conclusion

This study is significant because it is based on long-term data and includes all clinical samples. Based on the results obtained, if we can prospectively predict the prevalence of *Candida*, the use of prophylactic antifungal drugs in high-risk patients can reduce disease morbidity and severity. Although there are a few reports on the seasonality of *Candida*, there is no consistent conclusion, and as there has been no research in Asian countries, the observation of the seasonality of *Candida* in this study — low positive rate in December and January — is significant.

Ethics statement

It is a retrospective surveillance study that includes only laboratory data with no clinical information; therefore, the obtainment of informed consent is not required.

Conflict of interest

Mi-Kyung Lee has been an ethics editor of the *Annals of Clinical Microbiology* since January 2024. However, she was not involved in the review process of this article. No other potential conflict of interest relevant to this article were reported.

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Data availability

The datasets generated during the current study are available from the corresponding author upon request.

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