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Distribution and antifungal resistance rate of yeast isolated from various samples

Erdal Özbek[1]*, Ayşe Batgi Azarkan[2], Hakan Temiz[1], Selahattin Atmaca[1]

1 Department of Medical Microbiology, Faculty of Medicine, Dicle University, Diyarbakir, TR
2 Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital Medical Microbiology, Diyarbakir, TR

*** Corresponding Author**: Erdal Özbek **E-mail:** erdalozbek@msn.com

ABSTRACT

Objective: Yeast causes hospital-acquired infections at increasing rates, which can cause serious mortality, especially in patients with a suppressed immune system. This study aimed to determine the species distribution and antifungal resistance rates of yeast isolated in a hospital.

Material and Methods: Isolated yeasts from clinical specimens of patients who received inpatient treatment in different clinics in our hospital between 1 December 2019 and 30 September 2020 were examined. In all of these isolates, species identification was made with an automated system in addition to classical methods. Additionally, the antifungal susceptibility of yeast against amphotericin B, flucytosine, Fluconazole, micafungin, caspofungin, and Voriconazole was investigated using an automated system.

Results: In the study, yeasts isolated from 183 clinical samples, including 64 vagen, 62 blood, 28 urine, 12 wounds, eight tracheal aspirates, five peritoneal fluids, three catheters and one cerebrospinal fluid (CSF) samples were included. Of these isolates, 93 were Candida albicans (50,82%), 40 were Candida parapsilosis (21,86%), 17 were Candida tropicalis (9,29%), eight were Candida glabrata (4,37%), eight were Stephanoascus ciferrii (4,37%), five were Candida lusitaniae (2,19%), four were Candida famata (2,19%), four were Cryptococcus laurentii (2,19%) and four were Candida krusei (2,19%). Antifungal susceptibility testing was performed in 103 of the isolates. The highest resistance was found against Fluconazole, with 16.8%, and the lowest resistance was against flucytosine, with 2.2%. Antifungal resistance rates of Fluconazole, Voriconazole, amphotericin B, flucytosine, caspofungin and micafungin were found as 16.8%, 8.2%, 6.1%, 2.2%, 2.9% and 6.8% respectively.

Conclusion: Due to the increasing frequency of fungal infections due to long-term hospitalization, it has been concluded that identifying the causative species and reporting the antifungal susceptibility status is important in monitoring the change in resistance rates and guiding the treatment.

Keywords: antifungal susceptibility, candida, candidemia

Research Article

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INTRODUCTION

Candidiasis is an infection which occurs on the skin and mucous membranes caused by the yeast-type opportunistic fungi Candida albicans and other species. Candidemia is especially common in intensive care unit patients and may present with a serious clinical picture that may result in mortality. The causative yeasts are usually found in the microbiota, but they are restricted from being transmitted by other microorganisms in the microbiota. Although candida infections are usually seen in the mouth and mucous membranes, they can also occur in moist and closed areas where the skin folds, such as armpits and under the breast. In addition, it can cause infections affecting many organs and systems, especially in immunosuppressed individuals with chronic diseases who need to be hospitalized for a long time. The clinical picture varies according to the site of infection (1, 2, 3, 4, 5).

Although candida infections are rare in healthy individuals, many facilitating factors may pose a risk for their occurrence. For any reason, the decrease in white blood cells in the blood, chemotherapy and/or radiotherapy, intensive use of antibiotics, diabetes, conditions requiring long-term hospitalization, and systemic steroid use are the main ones. Conditions in which the immune system is over-suppressed for any reason may predispose to the emergence of systemic and serious candida infections (1, 4, 6, 7).

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In the report titled "Antifungal resistance in candidas" published by the "Centers for Disease Control and Prevention" (CDC) in 2020, it was stated that antifungal resistance has increased in candida infections in recent years and treatment has become more difficult (8).

For example, it has been reported that fluconazole resistance was detected in 7% of candidas isolated from blood cultures (9). The report also states that resistance to echinocandins is also increasing. In particular, resistance to Fluconazole and echinocandins, albeit limited, has been reported in Candida glabrata for higher levels than in the past twenty years. Treatment options are limited in candida infections resistant to Fluconazole and echinocandins, and amphotericin B, which has high toxicity, is the first treatment option (10, 11). The report said the new species, called Candida auris, which is rare in most parts of the United States but has been identified as a growing threat, is worrisome because it is more resistant to antifungals than other species (6, 12, 13, 15).

Research shows that the widespread use of empirical anti fungi in the treatment of fungal infections has led to the emergence of resistant fungal isolates (8).

This situation increases the need for in vitro antifungal susceptibility tests for widespread and effective antifungal treatment, selection of drugs to be used in treatment according to test results, and monitoring of sensitivity test results and monitoring of resistance developments (1, 11, 12, 13, 14, 15, 16).

The aim of this study was to determine the distribution and antifungal resistance status of yeast isolated from various clinical samples in our hospital in 2020. Additionally, to investigate changes in resistance rates, it was compared with a similar study conducted in our province in 2009-2010.

MATERIAL and METHODs

Yeast obtained from clinical samples of patients who received inpatient treatment in different clinics in our hospital between December 1, 2019 and September 30, 2020 were included in the study. 183 species of yeast in total have been isolated. Antifungal susceptibility testing was conducted on isolates obtained from sterile samples as well as on isolates recovered from nonsterile samples that were considered to be clinically significant infectious agents.. Antifungal susceptibility tests were not applied for isolates found in repeat cultures of the same patient and isolates that were not considered to be infectious agents.

For species identification, a germ tube test was applied to yeast abstracted from the samples taken into the study, and the microscopic appearance of Egyptian flour Tween 80 agar was examined. In addition, type identification was made using the VITEK 2 Compact® (BioMérieux, France) system YST identification cards.The sensitivity of isolates to amphotericin B, flucytosine, Fluconazole, micafungin, caspofungin, and Voriconazole was investigated using AST-YST01 cards (BioMérieux, France) according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) antifungal agent breakpoint tables for the interpretation of MICs 2018 (version 9) (17).

The resistance rates determined in this study were compared to the resistance rates in a study conducted 12 years ago in our province, which included 55 isolates (18).

Statistical Method: The distribution and resistance rates of yeast traces were determined as percentages, and the data were analyzed using Statistical Package for the Social Science v.22.0 software (SPSS Inc., Chicago, USA) chi-square ($\chi 2$) test or Fisher's certainty test to compare the resistance rates with the previous study conducted in our province. The P value of <0.05 was considered significant.

Ethics: This study was conducted in accordance with the "World Medical Association (WMA) Declaration of Helsinki Ethical Principles in Medical Research".

RESULTs

In this study, yeasts isolated from 183 clinical samples, 64 of which were vagina, 62 of which were blood, 28 of which were urine, 12 of which were wounds, 8 of which were tracheal aspirate, 3 of which were catheters, 5 of which were peritoneal fluid and 1 of which was CSF, were examined. Of these isolates, 93 were Candida albicans (50.82%), 40 were Candida parapsilosis (21.86%), 17 were Candida tropicalis (9.29%), eight were Candida glabrata (4.37%), eight were Stephanoascus ciferrii (4.37%), five were Candida lusitaniae (2.73%), four were Candida famata (2.19%), four were Cryptococcus laurentii (2.19%), and one was Candida krusei (0.55%) (Table 1)..

Of these 183 isolates considered to be infectious agents, 103 were tested for antifungal susceptibility in the automated system. The isolates subjected to antifungal susceptibility testing showed the highest resistance to Fluconazole at 16.8%, while the lowest resistance was observed against flucytosine at 2.2%. The distribution of antifungal sensitivity for the candida isolates studied is shown in Table 2.

In the study conducted in our city in 2009-2010, when the antifungal sensitivities of candida isolates were examined, resistance was not detected in non-albicans candida isolates (24 isolates) against Fluconazole, while resistance was found in 3.2% in C. albicans isolates (31 isolates). In the same study, resistance to Voriconazole was not detected in C. albicans isolates, whereas resistance was found in non-albicans candida isolates at a rate of 4.2%. The researchers did not detect resistance to amphotericin B and flucytosine in any isolates (20). In this 2020 study, the fluconazole resistance among C. albicans (n=51) isolates was 7.8%, while non-albicans Candida isolates (n=52) showed a resistance of 26%. Voriconazole resistance was 13.7% among C. albicans isolates and 4.3% among non-albicans isolates. For amphotericin B, C. albicans isolates had a resistance rate of 7.9%, while non-albicans isolates had a rate of 4.3%. The study also detected a 4.8% resistance rate to flucytosine in C. albicans isolates, but no flucytosine resistance was found in non-albicans Candida isolates.

The results of antifungal resistance rates for both periods are given in Table 3.

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Table 1: Genus/species and specimen species distribution in the yeasts included in the study (1, 2, 3).

	C. albicans Number (Percentage)	*C. parapisilosis* Number (Percentage)	*C. tropicalis* Number (Percentage)	*C. glabrata* Number (Percentage)	*C. famata* Number (Percentage)	*Cryptococcus laurentii* Number (Percentage)	*Stephanoascus cifferi* Number (Percentage)	*C. lusitaniae* Number (Percentage)	*C. krusei* Number (Percentage)	SUM Number (Percentage)
Vague	42 (45.16%)	12 (30.00%)	0 (0%)	8 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (50.00%)	64 (34.97%)
Jug	22 (23.66%)	18 (45.00%)	7 (41.18%)	0 (0%)	3 (75.00%)	3 (75.00%)	5 (62.50%)	2 (40.00%)	2 (50.00%)	62 (33.88%)
Urine	11 (11.83%)	6 (15.00%)	8 (47.06%)	0 (0%)	1 (25.00%)	0 (0%)	2 (25.00%)	0 (0%)	0 (0%)	28 (15.30%)
Wound	9 (9.68%)	1 (2.50%)	2 (11.76%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (6.58%)
Trakeal aspirated	6 (6.45%)	1 (2.50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (20.00%)	0 (0%)	8 (4.37%)
Catheter	2 (2.15%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (12.50%)	0 (0%)	0 (0%)	3 (1.64%)
Peritoneal fluid	0 (0%)	2 (5.00%)	0 (0%)	0 (0%)	0 (0%)	1 (25.00%)	0 (0%)	2 (40.00%)	0 (0%)	5 (2.73%)
FOREST	1 (1.08%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.55%)
All Examples	93 (50.82%)	40 (21.86%)	17 (9,29%)	8 (4.37%)	4 (2,19%)	4 (2.19%)	8 (4.37%)	5 (2.73%)	4 (2.19%)	183 (100%0)

1. In the 1st table, the percentage ratio of yeast fungi in the species columns according to the samples in which all species were isolated is given.
2. In the last row, the percentage ratio of the yeast fungus species among all isolated fungi is given.
3. In the last column, the number and distribution percentages of the sample types are given.

Table 2: Antifungal resistance status according to yeast species

		Antifungal Susceptibility Distribution by Candida Species* Antifungal Period																	
LON	**(n)**	**Fluconazole**			**Vorikonazol**			**Kaspofungin**			**Micafungin**			**Amphotericin B**			**Flusitozin**		
		S¹	**I²**	**R³**	**S¹**	**I²**	**R³**	**S¹**	**I²**	**R³**	**S¹**	**I²**	**R³**	**S¹**	**I²**	**R³**	**S¹**	**I²**	**R³**
***C. albicans*[4]**	**51**	42 82.4%	5 9.8%	4 7.8%	44 86.3%	0 %0	6 13.7%	48 94.1%	0 0%	3 5.9%	46 90.2%	0 0%	5 9.8%	47 92.1%	0 0%	4 7.9%	40 95.2%	0 0%	2 4.8%
Non albicans[5]	**52**	37 74%	0 0%	13 26%	42 89.4%	3 6.4%	2 4.3%	50 96.2%	0 0%	2 3.8%	48 92.3%	2 3.8%	2 3.8%	45 95.7%	0 0%	2 4.3%	48 97.9%	1 2%	0 %0
C. parapsilosis[6]	28	20 71.5%	0 0%	8 28.5%	25 89.3%	3 10.7%	0 0%	26 92.9%	0 0%	2 7.1%	24 85.7%	2 7.1%	2 7.1%	27 96.4%	0 0%	1 3.6%	24 100%	0 0%	0 %0
C. tropicalis	17	12 70.6%	0 0%	5 29.4%	15 88.2%	0 0%	2 11.8%	17 100%	0 0%	0 0%	17 100%	0 0%	0 0%	16 94.1%	0 0%	1 5.9%	17 100%	0 0%	0 0%
C. lusitaniae[7]	5	5 100%	0 0%	0 0%				5 100%	0 0%	0 0%	5 100%	0 0%	0 0%				5 100%	0 0%	0 0%
C. krusei[8]	2				2 100%	0 0%	0 0%	2 100%	0 0%	0 0%	2 100%	0 0%	0 0%	2 100%	0 0%	0 %0	1 50%	1 50%0	0 0%
SUM	**103**	**79 78.2%**	**5 4.9%**	**17 16.8%**	**86 88.7%**	**3 3.1%**	**8 8.2%**	**100 97.1%**	**0 0%**	**3 2.9%**	**94 91.3%**	**2 1.9%**	**7 6.8%**	**92 93.9%**	**0 0%**	**6 6.1%**	**88 97.8%**	**0 0%**	**2 2.2%**

*: Antibiograms were not performed for isolates defined as C. famata, Cryptococcus laurentii, Stephanoascus cifferi by the automated system.
1: Sensitive, 2: Medium sensitive, 3: Resistant,
In 4: 9 strains the automated system did not give an antibiogram result for flucytosine, in 5: 4 strains the automated system did not give an antibiogram result for flucytosine, in 5 strains for voriconazole, 5 strains of amphotericin B 2 strains were not evaluated because they were naturally resistant to fluconazole, in 6: 4 strains the automated system did not give an antibiogram result for flucytosine , 7: It is naturally resistant to amphotericin B. Antibiogram test for automated system Voriconazole has not worked, 8: Naturally resistant to Fluconazole.

Table 3: Comparison of resistance rates in isolates of 2020 and resistance rates of isolates of 2010-2011 (20).

Antifungal Rezistance (%)	*C. albicans*			Non-albicans			All		
	2009-2010	2020	p	2009-2010	2020	p	2009-2010	2020	p
Fluconazole	3.2	7.8	0.645	0	26	**<0.05**	1.8	16.8	**<0.05**
Vorikonazol	0	13.7	0.078	4.2	4.3	1,000	1.8	8.7	0.874
Amphotericin B	0	7.9	0.292	0	4.3	1,000	0	6.1	0.093
Flusitozin	0	4.8	0.524	0	0	-	0	2.2	0.543

DISCUSSION

Candida infections can manifest as cutaneous or mucosal infections, chronic mucocutaneous candidiasis, urinary tract candidiasis, candidemia, and diffuse candidiasis. The incidence of candidemia among inpatients varies considerably depending on the population studied. This variability has been observed at different rates in both European countries (19) and in our country. In the Aegean region, the rate of candidemia was reported as 5.6/10,000 between 2002-2006, in the Marmara region as 4.2/10,000 between 2004-2007, and in the Thrace region as 16.8/10,000 in 2008. The researchers attributed the regional incidence difference to factors such as problems in infection control measures, excess of the risky patient population, high sampling habits. When the incidence of the detected rates in patient groups is examined, it is seen that newborn, pediatric and adult intensive care units and cancer centers are in the front row (20, 21, 22).

Five species in particular (C. albicans, C. glabrata, C. krusei, C. parapsilosis and C. tropicalis) have been found to be responsible for 90% of infection in yeasts of the genus Candida, which has more than two hundred species. In this study, these five species were the most common species.

An important feature of the host defence against candidiasis is the barrier formed by the skin whose integrity is intact. The intensity of colonization in patients before the development of the causative agent of candidiasis plays an important role in the development of infection. Candidiasis typically affects long-term hospitalized patients, and the clinical picture of the infection is determined primarily by the state of the host defence. Although research shows that general facilitating factors such as suppression of the immune system for any reason play an important role, it cannot explain the occurrence of all infections.

Due to the importance of antifungal susceptibility tests in the treatment of fungal infections, both CLSI (Clinical and Laboratory Standards Institute) and the European Committee for Antimicrobial Testing and its affiliated Subcommittee for Antifungal Susceptibility Testing (EUCAST-AFST) have developed reliable, reproducible and standardized phenotypic methods for the detection of the minimum inhibitory concentration (MIC) of yeast (23).

Resistance to antifungal therapy in yeast infections may be related to individual factors. In addition, resistance may be acquired due to the inhibition of the antifungal mechanism of the active fungi, or the low level of the drug used for treatment. Candida isolates can develop resistance to antifungal drugs by reducing the accumulation of drugs into the cell, changing the density and structure of antifungal target proteins, or differentiating the sterol composition in the cell membrane.

The aim of this study was to investigate whether there has been a difference in antifungal resistance compared to the past. To accomplish this, resistance rates were compared to those found in 2009-2010 in our province. In the earlier study, 3.2% resistance was found against Fluconazole, one of the antifungals tested in both studies, while resistance to Voriconazole, amphotericin B, and flucytosine was not detected. Resistance to Fluconazole was found at a rate of 4.2% in non-albicans Candida species. In contrast, the antifungal resistance rates in this study showed 7.8% resistance to Fluconazole, 13.7% to Voriconazole, 7.9% to amphotericin B, and 4.8% to flucytosine in C. albicans isolates. Non-albicans Candida isolates had resistance rates of 26% against Fluconazole, 4.3% against Voriconazole and amphotericin B, and no resistance to flucytosine was detected. When the statistical analysis of these results was examined, a statistically significant difference was found in terms of fluconazole resistance ($p<0.05$), and it was seen that the difference was due to non albicans candida's. Although there was no significant difference in statistical evaluation in terms of other antifungals, the increase in resistance rates in C. albicans strains for Voriconazole and in both C. albicans and nonalbicans candida strains for amphotericin B was considered to be noteworthy.

Since there is more than 10 years between the studies, it is inevitable that there will be differences in terms of evaluation criteria. In addition, in the first study, the CBD values of antifungals were not given.Therefore, the results could be compared qualitatively in terms of being "resilient or sensitive". Although this situation reduces the value of the statistical results obtained in the comparison, it is thought that it will constitute an important data on the increase in antifungal resistance.

The resistance rate of caspofungine C. albicans and non-albicans candida isolates from the antifungals in this study, which were not in the first study, was 5.9% and 3.8%, respectively, and 9.8% and 3.8% for micafungine.

When examining the antifungal sensitivity results obtained by Çalışkan et al. (24) with the VITEK 2 automated system in 2013, it was found that they did not detect resistance to Voriconazole, flucytosine, Fluconazole, or amphotericin B in any of the C. glabrata, C. parapsilosis, C. tropicalis, or C. albicans isolates they obtained. However, in the same study, they found that one of the C. guillermondi isolates was resistant to both Fluconazole and amphotericin B. Researchers have suggested that the increased use of prophylactic antifungals, especially in intensive care units, leads to the emergence of isolates resistant to or moderately sensitive to antifungals.

Etiz et al. (25) evaluated the antifungal susceptibility of 280 Candida isolates obtained from blood cultures between 2013 and 2014 using two different CLSI criteria. They found that three out of 77 C. albicans isolates were resistant to amphotericin B according to the criteria in CLSI M27-S3 document. Additionally, according to the CLSI M27-S4 document criteria, 16 isolates were resistant to caspofungin, three isolates were resistant to Voriconazole, and one isolate was resistant to Fluconazole. In non-albicans candida isolates, according to CLSI M27-S4, they found the highest resistance to Fluconazole in C. parapsilosis isolates (17 of 95 isolates were resistant, 17.9%); they also found resistance to capsofungin in five of 45 C. tropicalis isolates and eight of 27 C. glabrata isolates.

In their paper published in 2020, Beder et al. investigated the sensitivity tests against antifungals with the VITEK 2 automated system similar to this study (26). The researchers reported evaluating the antifungal results according to the threshold values set for antifungal agents in the Clinical Laboratory Standards Institute (CLSI) guidelines. Stating that they detected candida isolates most frequently from intensive care units (64.9%), the researchers stated that significant changes occurred in the resistance status of antifungals used in treatment in recent years. They reported that determining and periodically presenting antifungal resistance rates in candida isolates would contribute to empirical treatment planning. The researchers reported that they detected 242 candida isolates from blood cultures over a five-year period (2014-2018), while C. albicans ranked C. parapsilosis isolates in second place, they reported that they isolated C. parapsilosis from intensive care units most often. They suggested that this could be linked to the fact that this species is heavily present in the hand microbiota and that it can easily pass from the hands to medical instruments thanks to its adhesion-effective biofilm release properties.

When examining the antifungal sensitivity results of the researchers, they found that the lowest resistance for C. albicans isolates was 1% for flucytosine, while the highest resistance was 9% for Fluconazole. For C. parapsilosis isolates, they found 5.4% resistance to Fluconazole, amphotericin B, and Voriconazole in 1%, while C. tropicalis and C. glabrata isolates did not show any resistance to antifungal agents.

In a study conducted at Bozok University Research and Application Hospital in 2017 to determine the species distribution and antifungal susceptibility rates of candida's isolated from various clinical samples, 42 clinical specimens isolated from candida species between October 2014 and January 2016 were evaluated retrospectively (16). Commercial VITEK 2 Compact® (Biomerieux, France) yeast identification system was used with germ tube test to identify isolates, and antifungal susceptibility of isolates was determined using VITEK 2 AST YS02 test cards containing fluconazole, voriconazole, caspofungine, micafungin, amphotericin B and flucytosine antifungals. A total of 42 species of Candida were isolated from various clinical specimens. While C. albicans was the most frequently isolated species with 66.7%, non-albicans species were detected in 33.3%. The researchers identified the isolated yeast species as C. glabrata (11.9%), Candida kefyr (7.1%), C. tropicalis (4.8%), C. famata (2.4%), C. krusei (2.4%), C. lusitaniae (2.4%) and C. spherica (2.4%). Antifungal resistance rates of all isolates respectively; Fluconazole 14%, flucytosine 3%, Voriconazole 6%, amphotericin-B 5%, caspofungine 6%, micafungine 3%. While the fluconazole resistance rate in C. albicans isolates was 11%; They did not detect resistance to existing antifungals in C. kefyr, C. lusitaniae, and C. tropicalis species.

Er et al. (27) identified 84 (48%) of the 175 Candida strains isolated in their 2021 study in Izmir as C. parapsilosis and 57 (32.6%) as C. albicans. The study found that the highest resistance rates were 54.8% for Fluconazole in C. parapsilosis strains and 15.8% for itraconazole in C. albicans strains. The researchers made the comments of antifungal susceptibility according to EUCAST criteria. It is noteworthy that C. parapsillosis was the most frequently isolated strain in Candida strains isolated from the blood cultures of the patients in the study and that the species showed high fluconazole resistance.

When the distribution of isolates was examined, it was found that blood and urine samples were in the first two places in both studies when vagen samples that were not included in the first study were excluded. In terms of isolated species, C. albicans and C. parapsillosis constituted the majority of isolates. In 2021, resistance to Fluconazole was 3.2% and in Voriconazole, amphotericin B, and flucytosine no isolates were found, while in the same year, resistance to Voriconazole, amphotericin B, and flucytosine was found at 13.7%, 7.9%, and 4.8%, respectively. In non-albicans candida isolates, resistance to Fluconazole, amphotericin B and flucytosine was not detected in the period 2009-2010, while resistance to 26% against Fluconazole, 4.3% resistance to Voriconazole and amphotericin was detected in 2020, and no resistance to flucytosine was detected. According to these results, resistance rates were increased in both C. albicans and non-albicans candida isolates. The exception to this is that the rate of resistance to flucytosine in non-albicans candida strains is not detected in both periods. However, when the results of this study were examined, it was seen that the automated system could not conclude the flucytosine susceptibility study in 9 of 51 C. albicans strains and in three of the 52 C. non-albicans isolates.

Limitations of the research:

1. Further identification of Cryptococcus laurentii and Stephanoascus ciferrii, which may be misidentified by automated systems, has not been made.
2. The other study comparing the rates of antifungal resistance with this study used guidelines from the same period in which it was conducted.
3. The automated system failed to provide results for a susceptibility study to flucytosine for 9 C. albicans isolates and three non-albicans Candida isolates.

CONCLUSION

Despite the above limitations, the distribution and antifungal susceptibility rates of yeast species isolated from different clinical specimens were found similar to the literature. However, when comparing the antifungal susceptibility data in this study with the previous study conducted in our province, it was found that the antifungal resistance rates in all isolates against the tested antifungals were 1.8%, 1.8%,

0%, and 0%, respectively, for Fluconazole, Voriconazole, amphotericin B, and flucytosine in 2009-2010. In contrast, the data from 2020 showed resistance rates of 16.8%, 8.2%, 6.1%, and 2.2%, respectively. With these data, it was observed that there was an increase in antifungal resistance rates compared to the past. Due to the increasing frequency of fungal infections due to long-term hospitalization, it was concluded that the identification of causative agents and reporting of antifungal susceptibility states are important in guiding treatment and observing the change in resistance rates.

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Author Contributions: EÖ, ABA, HT, SA: Project design, literature review, Data collection and analyzes. **SÖ:** Manuscript preparation and revisions.

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. Written consent was obtained from each patient to use their hospital data.

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