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Candida strains and resistance patterns identified in a tertiary hospital

Canan Demir

Department of Infectious Diseases, Bursa City Hospital, Bursa, Turkey

ABSTRACT

Objectives: *Candida* species are the most common fungal infectious agents. *Candida* species are important with their increasing frequency in hospital-acquired infectious agents. The issue of antibiotic resistance, which frequently encountered in bacterial agents, is unfortunately also valid in fungal infections. In the present study, we aimed to determine the resistance of *Candida* species in our hospital including 1350 patient beds, the materials and units of production, and their sensitivity to antifungal drugs, in particular fluconazole.

Methods: Yeast growths, colony morphology, germ tube formation and VITEK 2 Compact automated identification system detected in the samples evaluated in the central laboratory of our hospital between February 1, 2020 and December 31, 2020 were typed. Antifungal susceptibilities, especially fluconazole, caspofungin, and amphotericin B susceptibilities, were determined by an automated system.

Results: In total, 2446 within the *Candida* growing sample was determined as 49% *Candida albicans*, 26.9% *Candida parapsilosis*, %17.9 *Candida tropicalis*, *Candida glabrata* and *Candida krusei* were observed in 2.3%. Although the distribution of *Candida* species in other intensive care units and services was comparable to the general incidence, *C. albicans* was detected in 38%, *C. parapsilosis* 30% and *C. tropicalis* 27% in surgical intensive care units. Moreover, *C. tropicalis* was the dominant species in the neonatal intensive care unit (75%)

Conclusions: In the present study, *C. albicans* was the most common candida species, and *C. parapsilosis* was the second most frequently reproduced species. It has been suggested that resistance patterns differ between species and between wards, therefore species identification and susceptibility analysis are important, and these should be taken into account when starting empirical, preemptive and antifungal treatment.

Keywords: *Candida*, fungal infection, antifungal agents

Candida species are the most commonly cultivated fungal strains. They are natural flora elements of the gastrointestinal tract, skin and urogenital system in humans. They can be isolated from various clinical specimens, especially in hospitalized immunocompromised individuals, and cause many different infections focus. *Candida glabrata*, *Candida tropicalis Candida parapsilosis, Candida krusei*, most commonly *Candida albicans*, are found in human flora. *C. albicans* is major source for fungemia engendered by *candida*, and the mortality rate due to this candidemia is reported as 38-49% [1-5].

The circumstances such as body pH changes, immunosuppressive treatments, cancer precipitate an increase in the frequency of candida infections. *Candida* species shift their resistance and susceptibility to antifungal drugs. It is also stated that the frequency of *Candida* species diverges in various age and risk groups. For instance, while *C. parapsilosis* is spotted in 30% of candidemia cases in newborns, it is detected

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Address for correspondence: *Canan Demir, MD., Bursa City Hospital, Department of Infectious Diseases, Doğanköy Mah., 16110 Nilüfer, Bursa, Turkey. E-mail: drcanandemir@hotmail.com, Phone: +90 224 975 00 00*

in 10-15% of adults, and *C. glabrata* is more common in elderly and in patients with malignancy [6-8].

Although the number of *Candida* species exceeds 150, those isolated as pathogens in humans are 15. Although *C. albicans* is still the most frequently isolated species, it is observed that different species are gradually taking its place in different regions. Increased central catheter use and increased fluconazole prophylaxis are expressed as the main reasons for this. In recent years, while *C. albicans* infections have decreased gradually in continental United States and many European territories, it has been mentioned that the frequency of *C. parapsilosis* or *C. tropicalis* disorders is surging at other locations where they are replaced by *C. glabrata* infections [9-12].

It is obvious that the delay in initiating appropriate antifungal therapy is a factor that augments the mortality rate, particularly candidemia, and therefore, knowing the species and antimycotic susceptibilities of candida agents seems essential for choosing appropriate treatment, especially for empirical therapy. In the current era, when antifungal resistance has become a problem similar to antibiotic resistance, knowing the predominantly culture species in the region and the unit and their resistance has gained importance in rapid and effective treatment [6, 13, 14].

By the present investigation, the aim was to specify the sensitivity status of *Candida strains* and antifungal drugs extracted from cultures of clinical cases in different age groups from different clinics sent to microbiology laboratory in Bursa City Hospital.

METHODS

The replications detected from different materials in the central laboratory of Bursa City Hospital between 01.02.2020 and 31.12.2020 were included in the present study, identification was made with the VITEC 2 Compact (Biomerieux, France) system and identification was accomplished at species level. In addition, the susceptibility of these species to Fluconazole, Amphotericin B and Caspofungin was investigated. Germ tube test and microscopic appearance of *Candida* species in Corn Flour-Tween 80 Agar medium were explored.

The included subjects were the hospitalized patients with *Candida* growth in any of their samples. Exclusion criteria were as follows: *Candida* growths in the cultures of outpatients, growth in the culture without *Candida* typing or resistance patterning and growths of the same *Candida* species detected in repeat cultures of the same patient.

The study was approved by the University of Health Sciences, Bursa Yüksek Ihtisas Training and Research Hospital Clinical Research Ethics Committee (Date: 10.08.2022 and Decision No: 2011-KAEK-25 2022/08-04).

Statistical Analysis

Descriptive statistical methodologies were implemented to display the properties of the data collected for the study.

RESULTS

Over 2446 *Candida-growing* samples, *C. albicans* was detected in 1199 (49%), *C. parapsilosis* identified in 658 (26.9%), C. tropicalis in 438 (17.9%), *C. glabrata* and *C. krusei* were observed in 2.3% (Table 1). The most frequently isolated clinics in the hospital were followed as anesthesia intensive care, surgical intensive care, internal medicine intensive care and COVID-19 intensive care (21.8%, 21%, 16.2% and 16.1%; respectively) (Table 1).

Although the frequency of *Candida* strains in other critical treatment units and services was comparable to the general incidence, *C. albicans* was detected in 38%, *C. parapsilosis* 30% and *C. tropicalis* 27% in surgical intensive care units. Moreover, *C. tropicalis* was the dominant species within the infantile critical care facility (75%) (Table 1).

Of the 2446 isolated *Candida* strains, 64% were obtained from blood, 14% from urine, 12% from respiratory, 5% from peritoneum, 3% from wound and 2% from CSF samples (Table 2). Considering the antifungal resistance rates, fluconazole resistance was disclosed as 6% for *C. albicans*, 14.2% for *C. glabrata*, 66.6% for *C. krusei*, 53.5% for *C. parapsilosis*, 4.1% for *C. tropicalis* and total fluconazole resistance rate was 22% (Table 3).

Caspofungin resistance rate was 1.5% in *C. albicans*, 66.6% in *C. glabrata*, 3.1% in *C. parapsilosis*, 2.7% in *C. tropicalis*. No resistance was found against *C. krusei*. The total Caspofungin resistance ratio was

Table 1. The incidence of *Candida* strains in the clinics

	Anesthesia ICU	COVID Service	COVID ICU	Surgery service	Surgery ICU	Pediatric ICU	Internal medicine service	Internal medicine ICU	Infant ICU	n (%)
C. albicans	264 (49.5)	72 (83.7)	180 (45.6)	173 (61)	196 (38)	45 (60.1)	101 (70.6)	162 (41)	6 (25)	**1199 (49)**
C. dubliniensis	4	0	8 (2)	0	0	0	0	0	0	**12 (0.5)**
C. glabrata	3	4 (4.6)	23 (5.8)	4 (1.4)	13 (2.6)	0	3	7 (1.7)	0	**57 (2.3)**
C. guilliermondii	0	0	0	0	0	6 (8)	0	0	0	**6 (0.2)**
C. krusei	23 (5)	0	11 (2.8)	12 (4.2)	8 (1.5)	0	0	2 (.5)	0	**56 (2.3)**
C. lipolytica	0	0	8 (2)	0	0	0	0	0	0	**8 (0.3)**
C. lusitaniae	0	0	4 (1)	0	0	0	0	4 (1)	0	**8 (0.3)**
C. parapsilosis	150 (28)	10 (11)	100 (25)	52 (18)	158 (30)	23 (31.1)	15 (10.5)	150 (37.8)	0	**658 (26.9)**
C. pelliculosa	0	0	0	0	0	0	0	4 (1)	0	**4 (0.19)**
C. tropicalis	89 (17)	0	60 (15)	42 (14.9)	138 (27)	0	24 (16.7)	67 (17)	18 (75)	**438 (17.9)**
Total, n (%)	**533 (21.8)**	**86 (3.5)**	**394 (16.1)**	**283 (11.6)**	**513 (21)**	**74 (3)**	**143 (5.8)**	**396 (16.2)**	**24 (1)**	**2446**

ICU = intensive care unite

Table 2. Materials from which *Candida* samples were obtained

Location of sample taken	n	%
Blood	1564	64
Urine	342	14
Respiratory tract	294	12
Peritoneum	123	5
Wound	74	3
CSF	49	2
Total	2446	100

CSF = Cerebrospinal fluid

2.2% (Table 4).

Amphotericin resistance ratio was 4% for *C. albicans* and *C. tropicalis*, 3.1% for *C. parapsilosis*. No resistance was detected in *C. glabrata* and *C. krusei*. Total Amphotericin resistance percent was 3.4% (Table 5).

DISCUSSION

Candida species are the most frequently isolated species among fungal species. They are the elements of natural flora in the gastrointestinal tract, skin and urogenital system within humans. They can be isolated from miscellaneous clinical archetypes, especially

Table 3. **Flucanazole sensitivity rates**

Fluconazole sensitivity	Sensitive (n)	Resistant n (%)	Total
Candida albicans	187	12 (6)	199
Candida glabrata	17	3 (15)	20
Candida krusei	4	8 (66.6)	12
Candida parapsilos	124	68 (53.5)	192
Candida tropicalis	69	3 (4.1)	72
	401	**94 (19)**	**495**

Table 4. **Caspofungin sensitivity rates**

Caspofungin sensitivity	Sensitive (n)	Resistant n (%)	Total
Candida albicans	**196**	**3 (1.5)**	**199**
Candida glabrata	**6**	**2 (25)**	**8**
Candida krusei	**5**	**0**	**5**
Candida parapsilos	**125**	**4 (3.1)**	**129**
Candida tropicalis	**71**	**2 (2.7)**	**73**
	405	**9 (2.2)**	**414**

Table 5. **Amphotericin B sensitivity rates**

Amphotericin B sensitivity	Sensitive (n)	Resistant n (%)	Total
Candida albicans	192	8 (4%)	200
Candida glabrata	17	0	17
Candida krusei	12	0	12
Candida parapsilos	125	4 (3.1%)	129
Candida tropicalis	72	3 (4%)	75
	418	**15 (3.4%)**	**433**

from hospitalized immunocompromised individuals, along with cause many different infections focus[1-3]. *Candida* genus yeasts, which constitute approximately 96% of opportunistic mycoses, are amid the most prevalent underlying factors of serious infective disorders such as candidemia as well as superficial mycoses [3, 6, 9].

In the last few years, there has been a significant increase in the frequency of candidemia in patients of intensive care units is reported, in cancer patients and in neutropenic cases. *Candida* species are responsible for 8-15% of infections within circulatory system and progresses with a mortality rate of 38% [8].

In a study conducted in Taiwan, 36-fold increase was detected in the rate of candidemia, from 1981 to 2000 [15]. The most consistently cultivated strain is *C. albicans*, while the ratio of *C. albicans* varies between 50-85% in the studies [16, 17]. Compatible with previous studies, in the present investigation, the most frequent candida species determined has been *C. albicans* (49%).

The strains out of *C. albicans* such as *C. tropicalis*, *C. krusei*, *C. glabrata* and *C. parapsilosis*, which are known to respond more difficult to antifungal treatment, are increasing day by day. As a matter of fact, in the current study 51% of the isolated species were non-albicans *Candida* [18].

Species identification is crucial for empirical treat-

ment, where nowadays *Candida* infections are increasing rapidly. Adiloglu *et al*. [19] reported *C. glabrata* as 13% and *C. tropicalis* and *C. parapsilosis* as 3% in their studies. Gultekin *et al*. [20] determined the species distribution as 23% *C. parapsilosis*, 14% *C. tropicalis*, and 12% *C. glabrata*. In our study, *C. parapsilosis* was detected in 26.9%, *C. tropicalis* in 17.9%, *C. glabrata* and *C. krusei* in 2.3% of the specimens. Consistent with other studies, *C. parapsilosis*, *C. glabrata* and *C. tropicalis* were found to be the most repeatedly segregated non-albicans candida strains [16, 17, 21].

By this study, in which the data of our center were evaluated, *C. albicans* was the most often *Candida* species, and *C. parapsilosis* was the second most prevalent *Candida* species and these results suggested that it should be taken into account when initiating antifungal therapy. Considering the increase in *Candida* infections and the relative increase in the rate of non-albicans species resistant to antifungals and since empirical treatment should be started as soon as possible, the incidence of the subjects in our hospital, the clinics they are isolated from, and the resistance patterns are of vital importance in initiating appropriate empirical treatment.

Zer *et al*. [22] found that fluconazole resistance was 23% in *C. albicans* strains. Fluconazole resistance was found to be lower (6%) in our study. However, fluconazole resistance was quite high in *C. parapsilosis* and *C. krusei* (53.5% and 66.6%; respectively). Resistance development in *C. albicans* strains against amphotericin B is quite low [19, 23]. In our study, amphotericin B resistance was less than 5% for all *Candida* species.

Caspofungin resistance was found as high as 25% in *C. glabrata*, while it was low (< 5%) in *C. albicans* and other strains. The resistance for Amphotericin B and Caspofungin were low (< 5%) in *C. parapsilosis* and *C. tropicalis* strains that we isolated most frequently after *C. albicans*. However, *C. parapsilosis* showed significant fluconazole resistance (53.5%), while *C. tropicalis* had resistance less than 5%.

CONCLUSION

The widespread use of antibiotics and antifungals causes detection of fungal infections and antifungal resistant strains more frequently. The fact that *Candida* species and their antifungal susceptibility differ in different clinics regionally and even within the hospital is of great importance because of the necessity to initiate accurate empirical antifungal treatment until the species and the sensitivity are determined, in cases of urgency.

Authors' Contribution

Study Conception:CD; Study Design: CD; Supervision: CD; Funding: CD; Materials: CD; Data Collection and/or Processing: CD; Statistical Analysis and/or Data Interpretation: CD; Literature Review: CD; Manuscript Preparation: CD and Critical Review: CD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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