



Proceeding Paper

# Susceptibility Patterns of *Candida* spp. Collected from Intensive Care Units: A Prospective Study in 2020–2022 <sup>†</sup>

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<sup>†</sup> Presented at the 6th International Congress of CiiEM—Immediate and Future Challenges to Foster One Health, Almada, Portugal, 5–7 July 2023.

**Abstract:** The frequency of *Candida* spp. isolates as a cause of hospital infections has risen, and in vitro antifungal susceptibility testing (AST) plays an increasingly important role in guiding therapeutic decisions. This multicenter study aimed to determine AST pattern of *Candida* spp. isolates from Intensive Care Unit (ICU) patients. In total, 674 patients were enrolled, and axillar/inguinal swabs were collected at admission and during the ICU stay (5th and 8th day). In vitro AST was performed on 355 *Candida* spp. isolates, according to the concentration gradient Etest<sup>®</sup> strip technique. The overall susceptibility rates were 100%, 99.7%, 98.3%, and 97.7% for amphotericin B, voriconazole, anidulafungin, and fluconazole, respectively. The current study demonstrates that antifungal resistance remains infrequent among *Candida* spp. isolates in Portugal's ICUs.

**Keywords:** *Candida* spp.; ICUs; Fluconazole; Voriconazole; Amphotericin B; Anidulafungin; resistance



**Citation:** Nascimento, T.; Inácio, J.; Guerreiro, D.; Patrício, P.; Diaz, P.; Toscano, C.; Faria, I.; Barroso, H. Susceptibility Patterns of *Candida* spp. Collected from Intensive Care Units: A Prospective Study in 2020–2022. *Med. Sci. Forum* **2023**, *22*, 45. <https://doi.org/10.3390/msf2023022045>

Academic Editors: José Brito, Nuno Taveira and Ana I. Fernandes

Published: 25 August 2023



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## 1. Introduction

The frequency of *Candida* spp. isolates as a cause of hospital infections has risen in recent years, leading to high morbidity and mortality rates [1]. Studies have shown that *Candida* species are the second or the third most common cause of septicemia in Intensive Care Unit (ICU) patients [2], and *Candida* spp. colonization can be a predictor of candidemia among this cohort of patients [3]. Most often empirical antifungals are prescribed for candidemia, mainly based on locally and country-wide antifungal surveillance data, which differ for every geographic region [4]. Therefore, this study aimed to evaluate antifungal susceptibility pattern of *Candida* spp. colonization isolates from ICU patients.

## 2. Materials and Methods

In this multicenter prospective observational study, 675 patients in ICU were recruited from January 2020 through December 2022. Collection of axillar/inguinal swabs was made at admission and during the ICU stay (5th and 8th day). Patient data were obtained through a form containing epidemiological and clinical information. This investigation has been approved by the Institutional Ethical Board of all institutions enrolled. Isolates were identified by cultural, Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS), and molecular methods. In vitro antifungals susceptibility tests (AST) were performed for fluconazole, voriconazole, amphotericin B, and

anidulafungin, according to the concentration gradient Etest® strip technique, following the manufacturer's instructions. *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258 standard strains were used as quality controls. Results were interpreted based on the clinical breakpoints recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

### 3. Results

In total, 355 *Candida* species isolates were recovered from 988 samples. E-test determination was performed for the isolates, namely, *C. albicans* ( $n = 185$ ), the *C. parapsilosis* complex ( $n = 112$ ) (*C. parapsilosis sensu stricto* ( $n = 109$ ), *C. orthopsilosis* ( $n = 2$ ), and *C. metapsilosis* ( $n = 1$ )), *C. glabrata* ( $n = 36$ ), *C. tropicalis* ( $n = 15$ ), *C. lusitaniae* ( $n = 4$ ), and *C. guilliermondii* ( $n = 3$ ).

Most *Candida* species exhibited susceptibility to antifungals. Amphotericin B, voriconazole, and anidulafungin were the drugs for which all *Candida* species showed more susceptibility, which were, respectively, 100%, 99.7%, and 97.5%. The overall rate of resistance to fluconazole was 2.3%. For fluconazole, NAC isolates were more resistant (1.4%) than *C. albicans* (0.8%). The rates of susceptibility to fluconazole were 96.8, 95.5, and 100% in *C. albicans*, *C. parapsilosis*, and *C. tropicalis*, respectively. For the other triazole tested, voriconazole, resistance was only observed for *C. albicans* (1.6%) isolates, but 3.2% (6/185) and 2.7% (3/112) of *C. albicans* and *C. parapsilosis*, respectively, presented MICs within the intermediate category. Resistance to drugs within the same class was detected, with two strains of *C. albicans* and one strain of *C. parapsilosis* showing resistance to the two azoles tested. Resistance to anidulafungin was observed for three species: *C. tropicalis* (6.7%), *C. albicans* (3.8%), and *C. parapsilosis* (2.7%).

### 4. Discussion

The current study demonstrates the prevalence and antifungal susceptibility pattern of *Candida* species in Portugal's ICUs. Within this cohort, antifungal resistance is infrequent among *Candida* isolates. Similarly to published data, in our isolates, azole resistance was noted in *C. albicans*, *C. parapsilosis*, and *C. glabrata*, whereas echinocandin resistance was noted in *C. albicans*, *C. parapsilosis*, and *C. tropicalis* [5–8].

The overall rates of resistance were 2.3 and 0.3% for fluconazole and voriconazole, respectively, which were in line with previous reports, particularly from other European countries [2]. Studies on antifungal susceptibility profiles in Portugal are not recent and used small samples, making it impossible to draw conclusions about antifungal resistance [9,10]. Still, despite the differences in practical details and origin of the isolates, Faria-Ramos et al. [10] reported higher resistance rates: 5 and 12% for fluconazole and voriconazole, respectively.

In this study, three *Candida* spp. exhibited resistance to anidulafungin, namely, *C. tropicalis* (6.7%, 1/15), *C. albicans* (1.6%, 3/185), and *C. parapsilosis* (0.9%, 1/112). *C. glabrata* and other *Candida* spp. did not show any resistance to anidulafungin. These results were in line with the resistance values reported in the literature [6,11,12].

In conclusion, these observations emphasized the importance of knowing the local epidemiology and resistance patterns for *Candida* spp. within institutions to guide therapeutic decisions.

**Author Contributions:** Conceptualization, T.N. and H.B.; methodology, T.N., H.B., D.G., I.F., P.D., C.T. and P.P.; investigation, T.N., H.B., D.G., I.F. and C.T.; writing—original draft preparation, T.N.; writing—review and editing, T.N., H.B. and J.I.; supervision, H.B. and J.I.; project administration, H.B.; funding acquisition, H.B. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by Egas Moniz Cooperativa de Ensino Superior, CRL, grant number EI 19/01.

**Institutional Review Board Statement:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethical Committee of the Prof. Doutor Fernando Fonseca Hospital on 13/11/2019 (54/2019) and by the Ethical Committee of the Beatriz Ângelo Hospital on 21/07/2021 (3655/2021).

**Informed Consent Statement:** Written informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Poissy, J.; Rouzé, A.; Cornu, M.; Nseir, S.; Sendid, B. The Changing Landscape of Invasive Fungal Infections in ICUs: A Need for Risk Stratification to Better Target Antifungal Drugs and the Threat of Resistance. *J. Fungi* **2022**, *8*, 946. [[CrossRef](#)] [[PubMed](#)]
2. Bassetti, M.; Giacobbè, D.R.; Vena, A.; Trucchi, C.; Ansaldi, F.; Antonelli, M.; Adamkova, V.; Alicino, C.; Almyroudi, M.P.; Atchade, E.; et al. Incidence and outcome of invasive candidiasis in intensive care units (ICUs) in Europe: Results of the EUCANDICU project. *Crit. Care* **2019**, *23*, 219. [[CrossRef](#)] [[PubMed](#)]
3. Alenazy, H.; Alghamdi, A.; Pinto, R.; Daneman, N. *Candida* colonization as a predictor of invasive candidiasis in non-neutropenic ICU patients with sepsis: A systematic review and meta-analysis. *Int. J. Infect. Dis.* **2021**, *102*, 357–362. [[CrossRef](#)] [[PubMed](#)]
4. Galia, L.; Pezzani, M.D.; Compri, M.; Callegari, A.; Rajendran, N.B.; Carrara, E.; Tacconelli, E. The Combacte Magnet Epi-Net Network. Surveillance of Antifungal Resistance in Candidemia Fails to Inform Antifungal Stewardship in European Countries. *J. Fungi* **2022**, *8*, 249. [[CrossRef](#)] [[PubMed](#)]
5. Castanheira, M.; Deshpande, L.M.; Messer, S.A.; Rhomberg, P.R.; Pfaller, M.A. Analysis of global antifungal surveillance results reveals predominance of Erg11 Y132F alteration among azole-resistant *Candida parapsilosis* and *Candida tropicalis* and country-specific isolate dissemination. *Int. J. Antimicrob. Agents* **2020**, *55*, 105799. [[CrossRef](#)] [[PubMed](#)]
6. Vannini, M.; Emery, S.; Lieutier-Colas, F.; Legueult, K.; Mondain, V.; Retur, N.; Gastaud, L.; Pomares, C.; Hasseine, L. Epidemiology of candidemia in NICE area, France: A five-year study of antifungal susceptibility and mortality. *J. Med. Mycol.* **2022**, *32*, 101210. [[CrossRef](#)] [[PubMed](#)]
7. Rogers, T.R.; Verweij, P.E.; Castanheira, M.; Dannaoui, E.; White, P.L.; Arendrup, M.C.; Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST). Molecular mechanisms of acquired antifungal drug resistance in principal fungal pathogens and EUCAST guidance for their laboratory detection and clinical implications. *J. Antimicrob. Chemother.* **2022**, *77*, 2053–2073. [[CrossRef](#)] [[PubMed](#)]
8. Dabas, Y.; Xess, I.; Pandey, M.; Ahmed, J.; Sachdev, J.; Iram, A.; Singh, G.; Mahapatra, M.; Seth, R.; Bakhshi, S.; et al. Epidemiology and Antifungal Susceptibility Patterns of Invasive Fungal Infections (IFIs) in India: A Prospective Observational Study. *J. Fungi* **2021**, *8*, 33. [[CrossRef](#)] [[PubMed](#)]
9. Costa-de-Oliveira, S.; Pina-Vaz, C.; Mendonça, D.; Gonçalves Rodrigues, A. A first Portuguese epidemiological survey of fungaemia in a university hospital. *Eur. J. Clin. Microbiol. Infect. Dis.* **2008**, *27*, 365–374. [[CrossRef](#)] [[PubMed](#)]
10. Faria-Ramos, I.; Neves-Maia, J.; Ricardo, E.; Santos-Antunes, J.; Silva, A.T.; Costa-de-Oliveira, S.; Cantón, E.; Rodrigues, A.G.; Pina-Vaz, C. Species distribution and in vitro antifungal susceptibility profiles of yeast isolates from invasive infections during a Portuguese multicenter survey. *Eur. J. Clin. Microbiol. Infect. Dis.* **2014**, *33*, 2241–2247. [[CrossRef](#)] [[PubMed](#)]
11. Lindberg, E.; Hammarström, H.; Ataollahy, N.; Kondori, N. Species distribution and antifungal drug susceptibilities of yeasts isolated from the blood samples of patients with candidemia. *Sci. Rep.* **2019**, *9*, 3838. [[CrossRef](#)] [[PubMed](#)]
12. Díaz-García, J.; Gómez, A.; Machado, M.; Alcalá, L.; Reigadas, E.; Sánchez-Carrillo, C.; Pérez-Ayala, A.; Gómez-García De La Pedrosa, E.; González-Romo, F.; Cuétara, M.S.; et al. Blood and intra-abdominal *Candida* spp. from a multicentre study conducted in Madrid using EUCAST: Emergence of fluconazole resistance in *Candida parapsilosis*, low echinocandin resistance and absence of *Candida auris*. *J. Antimicrob. Chemother.* **2022**, *77*, 3102–3109. [[CrossRef](#)] [[PubMed](#)]

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