Antifungal susceptibility profiles of common and rare clinical *Candida* species collected 2017-2021, New York

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Abstract

Background: Pathogenic yeasts cause serious healthcare-associated infections (HAIs). *Candida* spp. are the fourth most common cause of HAIs in US hospitals. Currently, three different classes of antifungal drugs are used to treat *Candida* infections. Antifungal susceptibility profiles and breakpoints for azoles and echinocandins are available for common *Candida* spp. However, the susceptibility breakpoints are not available for rare *Candida* spp. Similarly, the geographical variations in the antifungal susceptibility profiles of common and rare *Candida* spp. are less understood. Passive laboratory surveillance is an important tool to identify the prevalence of common and rare *Candida* and their resistance patterns. In this study, we report antifungal susceptibility profiles of 554 common and 336 rare *Candida* spp. submitted from 2017-2021.

Methods: All *Candida* isolates submitted to the Wadsworth Center Mycology Laboratory were identified to the species level by Matrix-Assisted Laser Desorption/Ionization - Time of Flight Mass Spectrometry (MALDI-TOF MS). Rare *Candida* spp. not identified by MALDI-TOF MS were confirmed by Sanger sequencing of the internal transcribed spacer (ITS) ribosomal genes. Antifungal susceptibility testing (AST) was done using CLSI microbroth dilution, E-test, and YeastOne methods.

Results: A total of 6,900 *Candida* isolates between 2017-2021 were analyzed. Of these, 336 isolates were rare *Candida* spp., and 1,200 isolates were common *Candida* spp. Antifungal susceptibility testing (AST) was performed on all 336 rare *Candida* isolates comprising sixteen species while AST was performed on 554 of 1,200 *Candida* isolates comprising seven common species. Of rare *Candida* spp., *C. fermentati* was the predominant species (19%) followed by *C. duobushaemulonii* (17%), *C. metapsilosis* (10%), *C. kefyr* (9%), *C. niverensis* (9%), *C. orthopsilosis* (8%), *C. haemulonii* (7%), *C. bracarensis* (6%) and rest (15%) were other species. *C. fermentati* showed modest resistance to azoles and rare resistance to echinocandins. All of the *C. haemulonii* and *C. duobushaemulonii* isolates were resistant to amphotericin B. Of ten *C. blankii*, eight were azole-resistant, and three were echinocandins-resistant. Of four *C. famata*, three were resistant to amphotericin B. Among the common *Candida* spp., *C. albicans* was the predominant species (49%) followed by *C. parapsilosis* (23%), *C. tropicalis* (12%) and rest (16%) were other species. Of common *Candida* spp., 13% of *C. albicans*, 9% of *C. parapsilosis*, and 8% of *C. tropicalis* were resistant to at least one of the azoles. Other common *Candida* spp. were susceptible to all antifungals tested in this study.

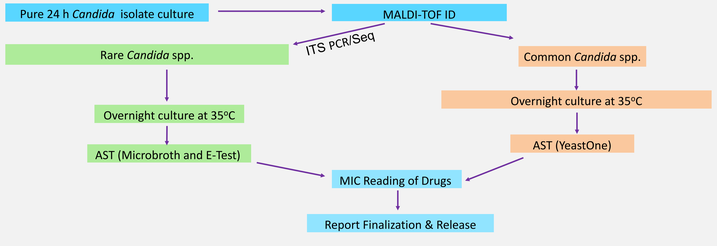
Conclusion: The antifungal susceptibility profile of common and rare *Candida* spp. were consistent with published studies from a global collection of yeasts. Azole resistance was notable in common and rare *Candida* spp. Amphotericin B and echinocandin resistance were limited to few rare *Candida* spp.

Introduction

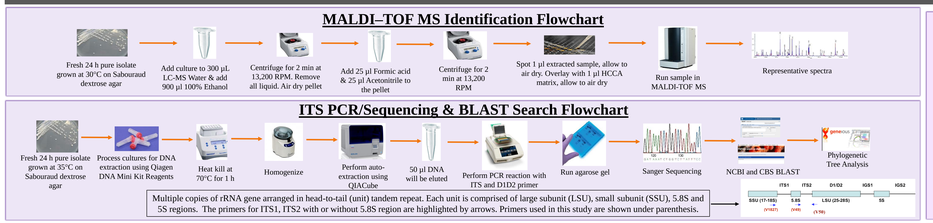
Candida spp. are the most common cause of fungal infections, leading to a range of life-threatening invasive diseases such as blood stream candidiasis to non-life-threatening mucocutaneous candidiasis such as genitourinary candidiasis, vulvovaginal candidiasis, and oropharyngeal candidiasis. Until recently, *C. albicans* was recognized as the commonest species causing most of the cases of candidiasis. However, in the last few decades, several studies reported that there has been a progressive shift from a predominance of *C. albicans* to non-*albicans Candida* spp. (NAC) such as *C. parapsilosis*, *C. tropicalis*, *C. glabrata* and *C. krusei.* Drug resistance are also increasing among *Candida* spp. Therefore, accurate identification and antifungal susceptibility profile are crucial for infection control and patient care.

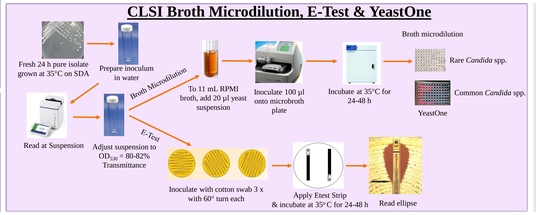
In the present study, *Candida* isolates received at the Wadsworth Center Mycology Laboratory were confirmed to species level by MALDI-TOF MS. The rare *Candida* were speciated by ITS PCR/Sequencing followed by BLAST search utilizing NCBI and CBS databases. A subset of common and all rare *Candida* spp. were subjected to antifungal susceptibility testing by broth microdilution, E-test and YeastOne methods. The MIC were interpreted based on CLSI breakpoints established for azoles and echinocandins for certain common *Candida* spp. The breakpoints for all rare *Candida* spp. are currently not available, and hence they were interpreted using surrogate breakpoints.

The flowchart describes *Candida* identification to species level followed by AST utilizing broth microdilution, E-test, and YeastOne methods.



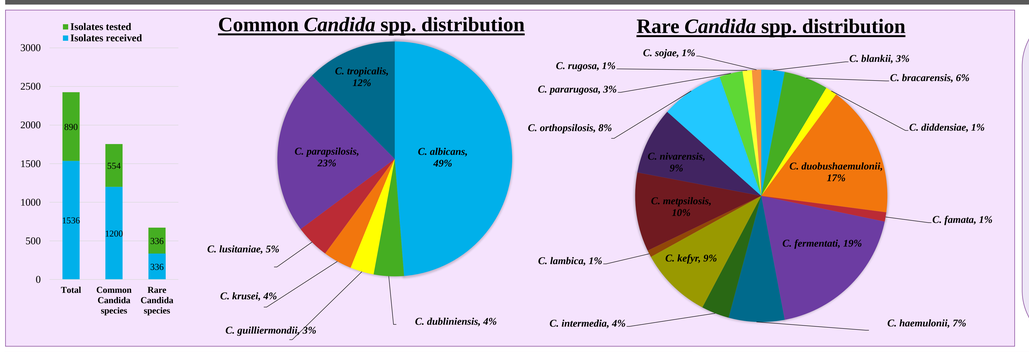
Methods

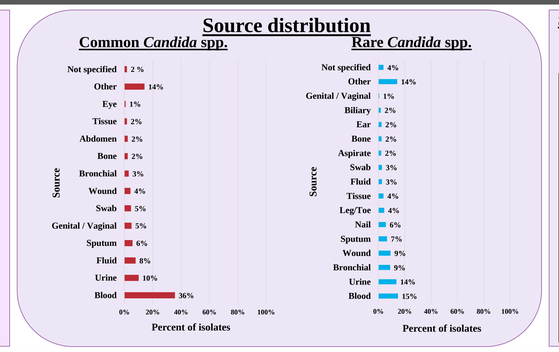




- Antifungal Susceptibility testing was performed using CLSI broth microdilution method for azoles and echinocandins and E-test method for Amphotericin B. All common *Candida* isolates were tested using YeastOne method. MICs were read at 50% growth inhibition for all drugs in broth microdilution and 100% growth inhibition on E-test for amphotericin B. MICs for all drugs on YeastOne was read based on color change from blue to pink.

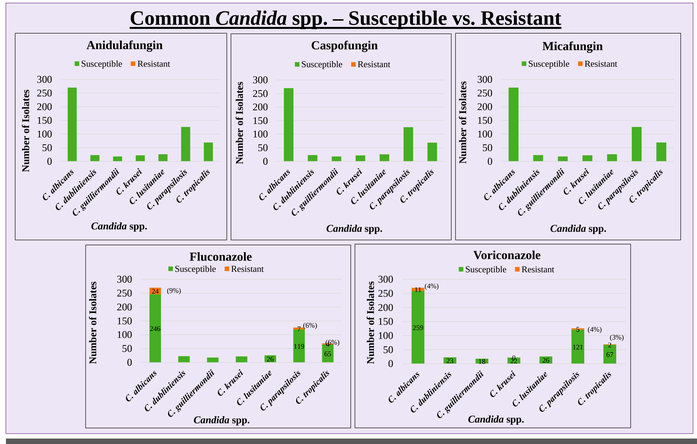
Results

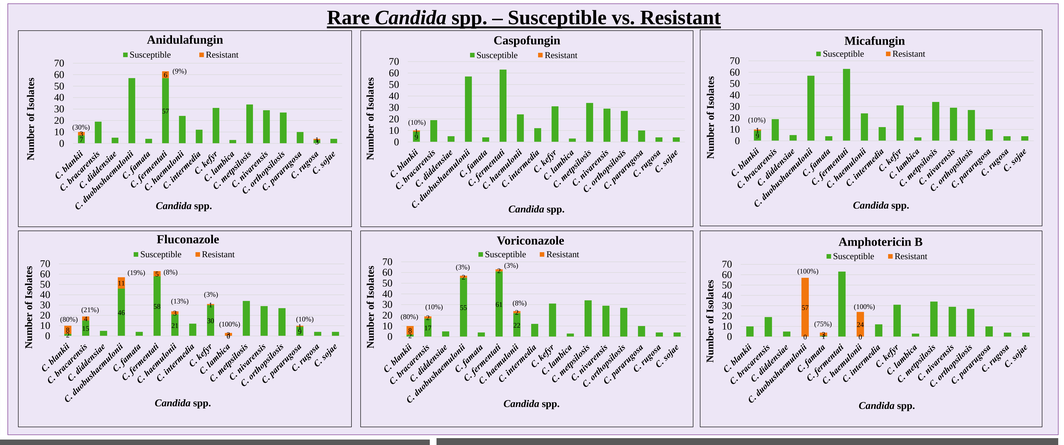




Surrogate MIC breakpoints followed in this study for rare *Candida* spp.

Antifungal Drugs	MIC breakpoints (mg/ml)
Anidulafungin	≥ 2
Caspofungin	≥ 2
Micafungin	≥ 2
Voriconazole	≥ 2
Fluconazole	≥ 32
Amphotericin B	≥ 2





Conclusions

- Among common *Candida* spp., *C. albicans* was the predominant spp. (49%), followed by *C. parapsilosis* (23%), *C. tropicalis* (12%), and rest (16%). Nearly 13% *C. albicans* and 9% *C. parapsilosis* were resistant to at least one of the azoles. None of the common *Candida* spp. were resistant to echinocandins. Of common *Candida* spp., 36% were isolated from blood, 10% from urine and 8% from other body fluids.
- Among rare *Candida* spp., *C. fermentati* was the predominant species (19%) followed by *C. duobushaemulonii* (17%), *C. metapsilosis* (10%), *C. kefyr* (9%), *C. nivarensis* (9%), *C. orthopsilosis* (8%), *C. haemulonii* (7%). *C. fermentati* exhibited modest resistance to azoles and rare resistance to echinocandins. All of the *C. duobushaemulonii* and *C. haemulonii* showed resistance against amphotericin B. About 80% of *C. blankii* isolates were resistant against azoles, and 10% were resistant against echinocandins. Of rare *Candida* isolates, 15% were recovered from blood, 14% from urine, 10% from wound and 9% from bronchial wash.
- These results highlight the importance of *Candida* identification to species level and antifungal susceptibility profile for infection control and patient care.

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