A 7-year review of *Candida* isolates and antifungal susceptibility testing from clinical specimens in Alberta, Canada

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Introduction

Manifestations of infection due to *Candida spp.* can range from local mucous membrane disease to widespread dissemination. Infections due to *Candida spp.* can result in significant morbidity and/or mortality. Although not all infections are necessarily invasive, they continue to pose challenges for definitive diagnosis and, at times, treatment.[1,2] Over time, epidemiological studies have documented an increase in azole resistance as well as shift of species causing infections – particularly those that are invasive.[3] The objective of this study was to describe the species distribution and susceptibility profiles of *Candida spp.* isolated from clinical specimens in Alberta, Canada over a 7-year period.

Materials & Methods

The Provincial Laboratory (ProvLab) for Public Health (Microbiology) in Alberta, Canada is a major microbiology reference testing centre. All *Candida spp.* isolated from clinical microbiology specimens from January 1, 2007 up until November 29, 2013 were tested against a standard panel of anti-fungal agents that included amphotericin B (AMB), 5-flucytosine (5-FC), itraconazole (ITRA), fluconazole (FLUC), voriconazole (VORI), posaconazole (POSA), caspofungin (CASP), and micafungin (MICA) using standardised broth microdilution methods (Clinical and Laboratory Standards Institute (CLSI) M27-S4). POSA and MICA were incorporated into the susceptibility panel in 2009 and 2010 respectively. Growth endpoints were measured at 24 hours of incubation and MIC values were determined as per CLSI methodology. Speciation of isolates was carried out using the API® Candida system (bioMérieux) or matrix assisted light desorption ionisation time-of-flight (MALDI-TOF) device (Vitek® MS, bioMérieux) (2012 and onward). Susceptibility profiles of the four most prevalent *Candida spp.* was summarised as an MIC distribution with determination of the MIC90. Determination of the percentage of non-susceptible isolates was calculated via comparison to the revised interpretive clinical breakpoints (CBPs; CLSI) and/or published epidemiological cut-off values (ECOFFs).

Results

Over the 7-year surveillance period, a total of 1834 isolates of *Candida spp.* were submitted for evaluation. Figure 1 displays the distribution of species isolated. The MIC distributions of the four most prevalent species are shown in Table 1 along with the MIC90 values and the percentage of isolates deemed non-susceptible (%NS). 97% of *C. glabrata* and 11% of *C. albicans* isolates had MIC90 values above the CBP for caspofungin, yet both populations were both normally distributed. 28% of *C. tropicalis* isolates displayed high MIC90s for voriconazole. 4% of *C. albicans* and 5% of *C. glabrata* had elevated MIC90s for fluconazole. All four species displayed low MIC90 values against CBP for micafungin. Amphotericin B continues to remain an agent with low MIC90s for all species evaluated.

Figure 1. Distribution of *Candida spp.*

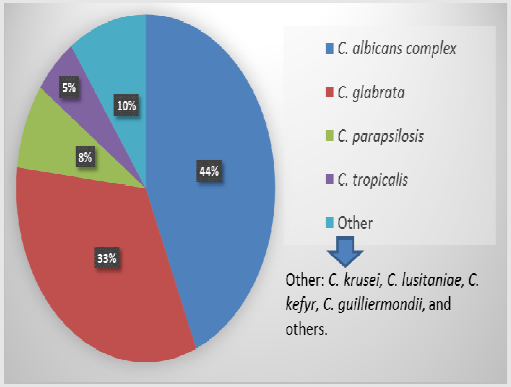

Table 1. MIC distribution and susceptibility of common *Candida* species.

Agent	Species	Total	Range	Mode	MIC90	Geo. Mean	CBP/ECOFF	%NS
AMB	*C. albicans*	800	0.06 – 2	0.5	1	0.498	2	0
	C. glabrata	611	0.125 – 2	0.5	1	0.634	2	0
	C. parapsilosis	144	0.125 – 2	1	1	0.719	2	0
	C. tropicalis	99	0.25 - 2	0.5	1	0.74	2	0
5-FC	*C. albicans*	800	0.06 – 4	0.125	1	0.212	0.5	15.3
	C. glabrata	611	0.06 - >64	0.06	0.125	0.072	0.5	2.1
	C. parapsilosis	144	0.06 - >64	0.06	0.25	0.112	0.5	2.1
	C. tropicalis	99	0.06 - 0.5	0.09	0.25	0.128	0.5	0
ITRA	*C. albicans*	800	0.015 - >64	0.06	0.125	0.065	0.125	8.9
	C. glabrata	611	0.03 - 16	0.5	1	0.558	2	1.47
	C. parapsilosis	144	0.015 – 1	0.06	0.25	0.08	0.5	0.69
	C. tropicalis	99	0.015 - 64	0.06	0.25	0.105	0.5	2.0
POSA	*C. albicans*	597	0.015 - >64	0.03	0.06	0.038	0.06	7.5
	C. glabrata	478	0.015 - 16	0.5	1	0.447	2	1.88
	C. parapsilosis	114	0.015 - 0.5	0.03	0.125	0.046	0.25	0.88
	C. tropicalis	70	0.015 - 4	0.06	0.25	0.056	-	-
FLUC	*C. albicans*	800	0.06 - >64	0.25	1	0.338	2	4.3
	C. glabrata	611	1 - >64	4	16	6.96	≤32	5.4
	C. parapsilosis	144	0.125 - 16	0.5	1	0.574	2	4.16
	C. tropicalis	99	0.125 - 64	0.25	4	0.757	2	13.1
VORI	*C. albicans*	800	0.015 - >64	0.015	0.06	0.027	0.12	4.3
	C. glabrata	611	0.015 - 16	0.25	1	0.314	2	2.13
	C. parapsilosis	144	0.015 – 1	0.015	0.06	0.029	0.12	4.86
	C. tropicalis	99	0.015 - 8	0.06	0.25	0.081	0.12	28.3
CASP	*C. albicans*	800	0.007 - 2	0.25	0.5	0.098	0.25	(10.9)
	C. glabrata	611	0.007 - 8	0.5	1	0.409	≤0.12	(96.9)
	C. parapsilosis	144	0.03 - 4	0.75	1	0.598	2	0.69
	C. tropicalis	99	0.007 - 2	0.25	0.5	0.167	2	0
MICA	*C. albicans*	483	0.007 - 0.125	0.015	0.015	0.011	0.25	0
	C. glabrata	385	0.007 - 4	0.015	0.03	0.015	≤0.06	2.60
	C. parapsilosis	95	0.015 - 2	0.25	1	0.404	2	0
	C. tropicalis	55	0.007 - 0.25	0.015	0.03	0.019	2	0

References

1. *Clin Infect Dis* 2013; 56: 1724.
2. *Can J Infect Dis Med Microbiol* 2014; 25:17.
3. *Leuk Lymphoma* 2013; 54:1479.
4. *Antimicrob Agents Chemother* 2013; 57:5836.
5. *Clin Microbiol Infect* 2013; doi: 10.1111/1469-0691.12440.

Conclusions

Seven-year surveillance indicates that the activity of available antifungals remains excellent against common species of *Candida.* Species-specific MIC populations were normally distributed with no indication of temporal changes. The reported caspofungin resistance to *C. albicans* and *C. glabrata* is invalid and attributed to clinical breakpoints that are too low for our MIC distributions, which is consistent with recent reports[4]. Micafungin remains largely susceptible against all four prevalent species. The high azole resistance reported for *C. tropicalis* is largely related to MIC values one dilution above the cut-off.[5] This study highlights the importance for continued surveillance of antifungal susceptibility amongst *Candida spp.* and studies to define how this testing applies to clinical management of candidiasis.