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Antifungal Susceptibility of *Candida* Blood Culture Isolates from Canadian Hospitals: Results of the CANWARD 2007 and 2010 study

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ABSTRACT

Background: CANWARD is an ongoing national surveillance study that assesses pathogens causing infections in patients attending Canadian hospitals, as well as determines the prevalence of antimicrobial resistance in these isolates. In this study, antifungal susceptibility of *Candida* blood culture isolates was analyzed. **Methods**: Study isolates were obtained as part of the larger, ongoing CANWARD initiative. *Candida* species from bloodstream infections were collected from 12 participating medical centres during the 2007 and 2010 study periods. Antifungal susceptibility testing and interpretation were performed as per CLSI M27-S4 broth microdilution method and the new provisional species-specific breakpoints (BP) for triazoles and echinocandins. Data is presented only for species with ≥10 isolates collected. **Results**: In total, 170 and 134 candidemia isolates from 2007 and 2010, respectively, were collected. *C. albicans* (CALB) was the predominant species, followed by *C. glabrata* (CGLA) and *C. parapsilosis* (CPARA). MICs and susceptibility rates (%S) are shown below. Notably, *C. glabrata* resistance rates to caspofungin (Cas) and voriconazole (Vor) using provisional BP of ≤0.125 and ≤0.5, respectively, were 64% and 11% in 2007 and 59% and 20% in 2010. **Conclusions**: Canadian surveillance of antifungal resistance in invasive *Candida* infections will be an important long-term objective of the CANWARD program. The validation of revised, species-specific interpretive breakpoints should facilitate more accurate detection of changing resistance patterns.

BACKGROUND

The Canadian Ward Surveillance Study (CANWARD) is an established and ongoing program that monitors epidemiology of antimicrobial resistant pathogens in Canadian tertiary care hospitals.

In 2007 and 2010, candidemia surveillance was included as a specific CANWARD objective. [1]

The distribution of *Candida* species causing candidemia and their antifungal susceptibility distribution is presented here.

MATERIALS & METHODS

Tertiary care medical centres representing 8 of 10 Canadian provinces submitted candidemia isolates from patients attending hospital clinics, emergency rooms, medical/surgical wards, and intensive care units.

Susceptibility testing was performed using CLSI M27-S3 broth microdilution guidelines.[2] *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258 served as quality control strains. MIC endpoints were determined visually.

CLSI breakpoints and/or provisional epidemiologic cut-off values (ECV) for 5-flucytosine, itraconazole, fluconazole, voriconazole, and caspofungin were applied as follows: ≤ 4, ≤ 0.125, ≤2, ≤0.125, and ≤ 0.25 for *C. albicans*; ≤ 4, ≤ 0.125, ≤32, ≤0.5, and ≤ 0.125 for *C. glabrata*; ≤ 4, ≤ 0.125, ≤2, ≤0.125, and ≤ 2.0 for *C. parapsilosis.*

CONCLUSIONS

The CANWARD program has generated important baseline data for monitoring antifungal resistance in *Candida.*

Significant proportions of *C. glabrata* were found to cluster around the new CLSI provisional ECVs for caspofungin.

Despite not having performed mutational analyses on these isolates, it is likely that the challenges of caspofungin visual endpoint interpretation contributed to large number of *C. glabrata* MICs above the ECV.

Longterm surveillance and application of new ECVs will be critical to guide informed empiric management of candidemia and other severe *Candida* infections.

RESULTS

There were 304 candidemia isolates collected overall; 133 (44%) from British Columbia/Alberta, 35 (12%) from Manitoba and Saskatchewan, 58 (19%) from Ontario, 55 (18%) from Quebec, and 23 (8%) from New Brunswick and Nova Scotia.

In order of predominance, 173 *C. albicans* (57%) were recovered, followed by 75 *C. glabrata* (25%), 28 *C. parapsilosis* (9%), 14 *C. tropicalis* (5%), and <5 isolates each for *C. dublinensis*, *C. krusei*, *C. lipolytica*, and *C. lusitaniae*.

Susceptibility data is shown in **Table 1.**

Caspofungin resistance for *C. albicans* was 5% in 2010 with an MIC_{50} of 0.03 and MIC range ≤0.015 to 2.0 mg/L; In 2007, the MIC_{50} was 0.12 mg/L, MIC range of 0.06 to 0.25 mg/L.

Caspofungin MICs greater than the ECV of 0.125 mg/L was observed in more than half of *C. glabrata* isolates in both study periods. In 2007, MICs ranged from 0.03 to 1.0 mg/L; of the 36 isolates tested, 13 and 16 had an MIC of 0.12 mg/L and 0.25 mg/L, respectively. In 2010, the MIC range was 0.12 to 2.0 mg/L; of the 39 isolates tested, 13 and 19 had an MIC of 0.12 mg/L and 0.25 mg/L, respectively.

Voriconazole MICs for *C. glabrata* greater than the ECV of 0.5 mg/L was recorded for 11% (4 of 36) and 20% (8 of 39) of isolates in 2007 and 2010, respectively.

Molecular resistance testing of isolates with elevated echinocandin or azole MICs was not performed for this study.

Table 1. Antifungal susceptibility of *Candida* species isolated from blood in 2007 and 2010

Year/ Organism		MIC_{90} (mg/L)						% Susceptible					
	N	AmB	5FC	Itra	Flu	Vor	Cas	AmB	5FC	Itra	Flu	Vor	Cas
2007													
C. albicans	99	2	1	0.06	0.25	0.015	0.25	-	99	99	99	99	100
C. glabrata	36	2	≤0.06	2	32	1	0.5	-	100	8	92*	89	36
C. parapsilosis	18	2	0.12	0.25	2	0.06	2	-	100	78	94	94	89
2010													
C. albicans	74	1	1	0.12	0.5	0.06	0.25	-	100	96	99	99	95
C. glabrata	39	1	0.12	1	16	1	0.5	-	100	5	100*	80	41
C. parapsilosis	10	1	0.25	0.25	8	0.25	1	-	100	80	80	80	100

AmB, amphotericin B; 5FC, 5-flucytosine; Itra, itraconazole; Flu, fluconazole; Vor, voriconazole; Cas, caspofungin; -, no breakpoint; *, susceptible dose-dependent

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