

Objectives: The Clinical and Laboratory Standards Institute (CLSI) Subcommittee on Antifungal Susceptibility Testing has newly introduced species-specific clinical breakpoints (CBPs) for fluconazole and voriconazole. When CBPs are absent, establishing wild-type (WT) MIC distributions and epidemiological cutoff values (ECVs) provides sensitive means for detecting emerging resistance. In the present study our aim is to determine WT *Candida* isolates that are susceptible and isolates possessing acquired resistance mutations by using these newly CLSI CBPs. Methods: *Candida* isolates (n = 140) obtained from blood cultures of invasive candidiasis patients from various intensive care units in Turkey between 2011-2012. Organisms were identified by conventional methods. Susceptibility testing was performed against fluconazole, itraconazole and voriconazole, by the 24-h CLSI BMD method. Rates of resistance to all agents were determined using the new CLSI CBPs and ECV criteria, as appropriate. Results: Of the 140 isolates included in the study, *Candida parapsilosis* (n=31), *Candida tropicalis* (n=26), *Candida glabrata* (n=21), *Candida albicans* (n=18), *Candida lusitanae* (n=16), *Candida krusei* (n=16), *Candida kefyr* (n=9), *Candida guilliermondii* (n=2), and were *Candida dubliniensis* (n=1). According to adjusted CLSI CBPs for fluconazole and *C. albicans*, *C. parapsilosis*, *C. tropicalis* (S, <=2 mcg/ml; SDD, 4 mcg/ml; R, >=8 mcg/ml), and *C. glabrata* (SDD, <=32 mcg/ml; R, >=64 mcg/ml) and for voriconazole and *C. albicans*, *C. parapsilosis*, *C. tropicalis* (S, <=0.12 mcg/ml; I, 0.25-0.5 mcg/ml; R, >=1 mcg/ml), and *C. krusei* (S, <=0.5 mcg/ml; I, 1 mcg/ml; R, >=2 mcg/ml) were found to be resistant. 3 of *C. albicans*, 1 of *C. parapsilosis*, 1 of *C. glabrata*, 2 of *C. albicans*, 2 of *C. tropicalis*, respectively. The ECVs of 0.5 mcg/ml for voriconazole and *C. glabrata* was used to differentiate WT (WT MIC <= ECV) from non-WT (MIC > ECV) strains. Six of *C. glabrata* were non-WT for voriconazole. Due to the lack of CBPs for the less common species, the ECVs for fluconazole, itraconazole and voriconazole, respectively were used for *C. lusitanae* (2 mcg/ml, 0.5 mcg/ml, 0.03 mcg/ml), *C. guilliermondii* (8 mcg/ml, 1 mcg/ml, 0.25 mcg/ml), *C. dubliniensis* (0.5 mcg/ml, 0.25 mcg/ml, 0.03 mcg/ml), and *C. kefyr* (1 mcg/ml and 0.015 mcg/ml) to categorize isolates of these species as WT and non-WT. Using the ECVs for fluconazole, 1 each of *C. lusitanae*, *C. dubliniensis* and *C. kefyr*; for voriconazole, 3 of *C. lusitanae* and 1 of *C. kefyr* were non-WT (Table 1). Conclusions: Overall, a total of five *Candida* species were determined to be resistant for fluconazole and four for voriconazole and among these species 1 each of *C. parapsilosis*, *C. tropicalis*, *C. glabrata*, *C. lusitanae*, *C. kefyr* and 3 of *C. albicans* were exhibited cross-resistance to at least two azoles.

Table 1. Epidemiological cutoff values and clinical breakpoints for fluconazole, itraconazole and voriconazole and nine species of *Candida* determined by 24-h CLSI broth microdilution methods^a (n=140).

Organism	Antifungal agent	ECV (mcg/ml)		CBP (mcg/ml)			
		WT	Non-WT	S	SDD	I	R
<i>Candida albicans</i> (n=18)	Fluconazole	13	5	14	1		3
	Itraconazole	9	9	9	7		2
	Voriconazole	12	6	13		3	2
<i>Candida parapsilosis</i> (n=31)	Fluconazole	29	2	29	1		1
	Itraconazole	30	1				
	Voriconazole	29	2	29		2	
<i>Candida glabrata</i> (n=21)	Fluconazole	20	1	20			1
	Itraconazole	19	2				
	Voriconazole	16	5				
<i>Candida tropicalis</i> (n=26)	Fluconazole	26		26			
	Itraconazole	25	1				
	Voriconazole	19	7	22		2	2
<i>Candida krusei</i> (n=16)	Fluconazole	16					
	Itraconazole	12	4				
	Voriconazole	16		16			
<i>Candida lusitanae</i> (n=16)	Fluconazole	15	1				
	Itraconazole	16					
	Voriconazole	13	3				
<i>Candida kefyr</i> (n=9)	Fluconazole	8	1				
	Voriconazole	8	1				
<i>Candida guilliermondii</i> (n=2)	Fluconazole	2					
	Itraconazole	2					
	Voriconazole	2					
<i>Candida dubliniensis</i> (n=1)	Fluconazole		1				
	Itraconazole	1					
	Voriconazole	1					

^aECV, Epidemiological cutoff values; CBP, Clinical breakpoints; WT, wild type; non-WT, non-wild type; S, Sensitive; SDD, Sensitive dose dependent; I, Intermediate; R, Resistance.