

Antifungal Susceptibility of *Candida* Bloodstream Isolates collected during a 10-year period in Austria

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Objectiv

The aim of our study was to assess the current *status quo* of clinical *Candida* bloodstream isolates collected from several Austrian hospitals between 2007 and 2016 in high-throughput. We determined distributions and antifungal susceptibility patterns of various *Candida* species and examined whether there were trends in the development of resistance.

Methods

1360 clinical *Candida* isolates from blood cultures collected by six different Austrian centres were tested against fluconazole (FLZ), voriconazole (VOR), posaconazole (POS), itraconazole (ITR), isavuconazole (ISA), anidulafungin (ANI), caspofungin (CAS) and micafungin (MCA) according to the EUCAST method of broth microdilution using a robot-aided high-throughput protocol. A rigid quality control on each assay via growth curve assessment and inclusion of two reference strains was performed. Minimal inhibitory concentrations (MIC) were quantified according to EUCAST guideline E.DEF 7.3.1 and resistance was evaluated using clinical breakpoints provided by EUCAST.

Results

The species distribution was *C. albicans* (56%), *C. glabrata* (19%), *C. parapsilosis* (9%), *C. tropicalis* (5%) and *C. krusei* (3%) and is shown in Figure 1. Only a low number of other *Candida* species and fungi was detected. While the total number of isolates increased over time, species abundance and resistance rates remained constant. In general, the susceptibility to the tested antifungals were far above 90% and no increase in resistance has been observed during the last ten years (table 1). However, resistance to ANI was found in 8% of *C. albicans* and 6% of *C. glabrata*, 2% of *C. glabrata* were resistant to MCA. However, the MICs of these isolates were only one dilution above the respective breakpoints and may possibly not indicate resistance. Multiresistant isolates occurred rarely:

- *C. albicans*: 1% azole cross-resistance and 5% echinocandin cross-resistance
- *C. tropicalis*: 6% azole-cross resistance and 3% echinocandin-cross resistance
- *C. parapsilosis*: no cross-resistance

During the observation period no increase in azole or echinocandin resistance was observed. Figure 2 shows the distribution of resistance between 2007 and 2016 in Austria.

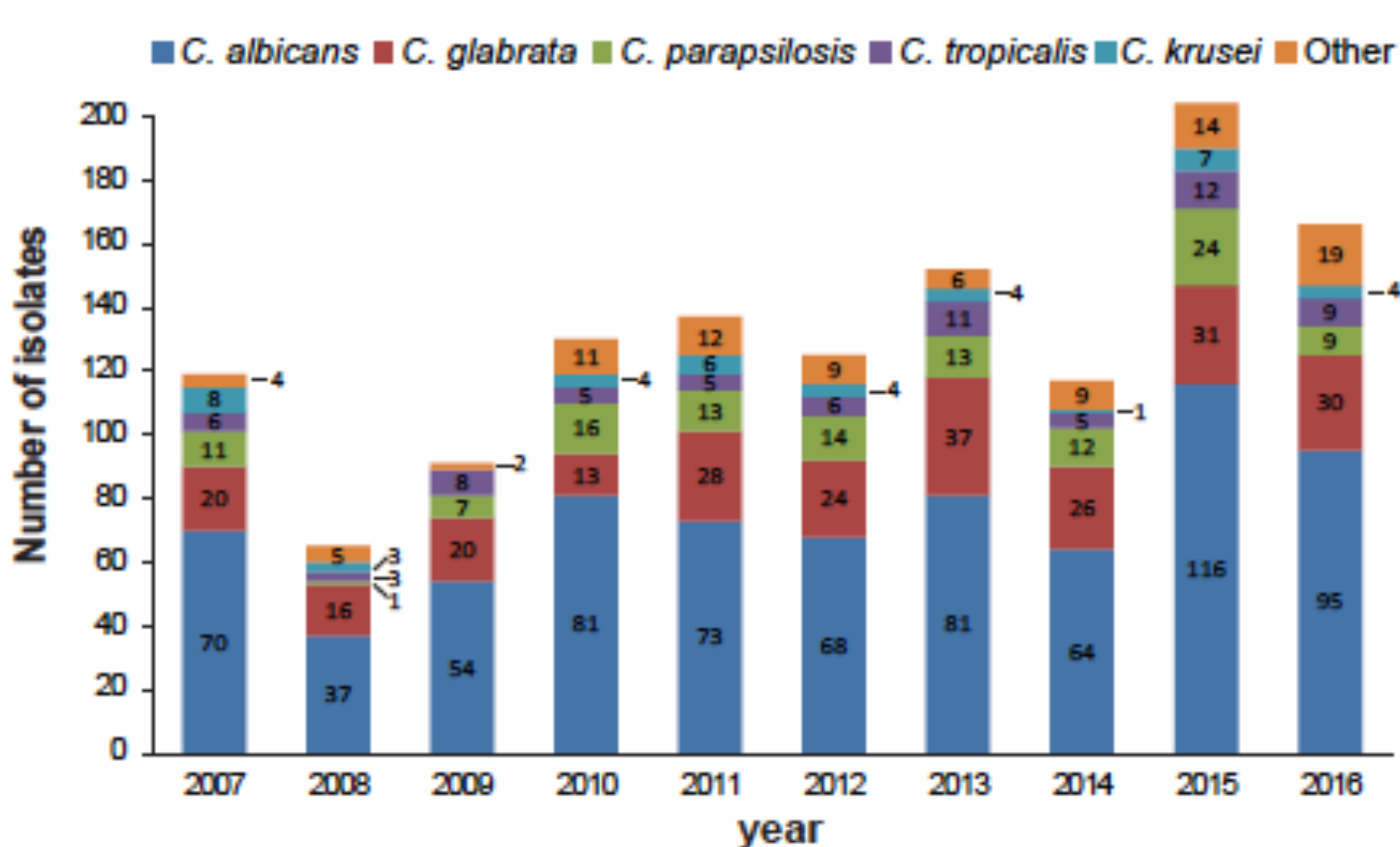


Figure 1: Species distribution 2007 - 2016

Conclusion

Over the last decade, the distribution of *Candida* species and the occurrence of antifungal resistance remained largely constant in Austria and did not show any emergence of individual species. Our obtained data showed results similar to that of other European countries. Though there has been a slightly higher rate of ANI-resistance in *C. albicans* and a significant higher rate of MIC resistant *C. glabrata* it seems that this is not of clinical significance as the observed MICs were only one dilution above the breakpoints. Further studies will have to address this issue. However, in general increases in antifungal resistance rates remained limited to individual years.

Candida species	MIC range (mg/L)	MIC ₅₀ (mg/L)	MIC ₉₀ (mg/L)	% isolates		
				S	SDD/I	R
C. albicans n=773						
FLZ	0.125-256	0.125	0.25	97	1	2
VOR	0.016-8	0.016	0.016	96	1	3
POS	0.016-32	0.016	0.064	95	-	5
ITR	0.008-16	0.016	0.064	93	-	7
ANI	0.008-16	0.008	0.032	92	-	8
MCA	0.008-16	0.016	0.032	84	-	16
C. glabrata n=256						
FLZ	0.125-256	8	64	-	87	13
VOR	0.016-8	0.5	2	-	-	-
POS	0.016-32	0.5	2	-	-	-
ITR	0.008-16	0.5	2	-	-	-
ANI	0.008-16	0.032	0.064	94	-	6
MCA	0.008-16	0.008	0.016	98	-	2
C. parapsilosis n=127						
FLZ	0.125-256	0.5	2	92	3	5
VOR	0.016-8	0.016	0.064	96	2	2
POS	0.016-32	0.064	0.125	81	-	19
ITR	0.008-16	0.064	0.125	93	-	7
ANI	0.008-16	2	4	-	100	0
MCA	0.008-16	1	2	-	100	0
C. tropicalis n=75						
FLZ	0.125-256	0.25	1	91	1	8
VOR	0.016-8	0.032	0.125	92	1	7
POS	0.016-32	0.032	0.125	84	-	16
ITR	0.008-16	0.032	0.125	91	5	4
ANI	0.008-16	0.032	0.064	92	-	8
MCA	0.008-16	0.032	0.064	-	-	-

Table 1: in vitro susceptibilities of the four most common *Candida* sp.

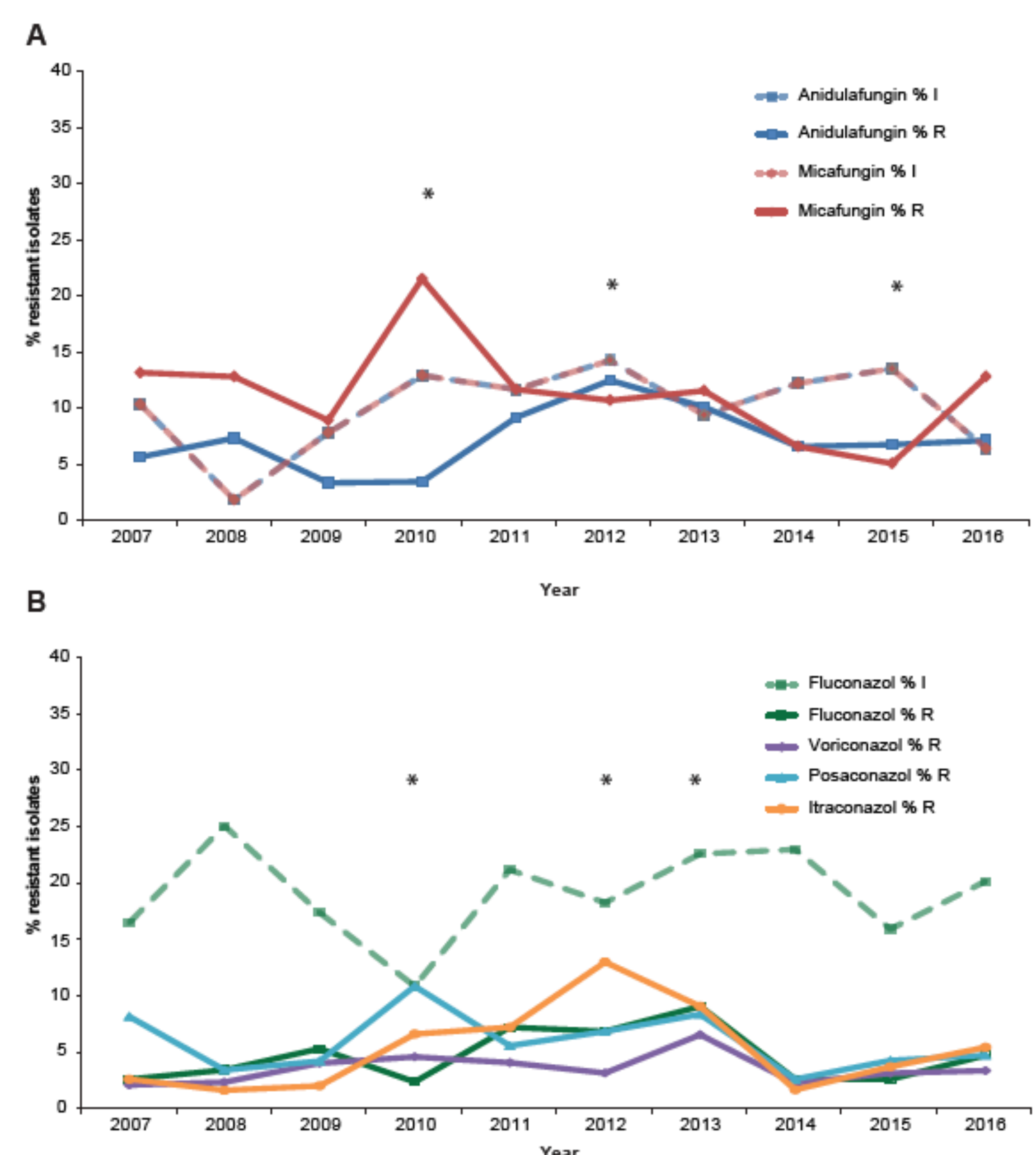


Figure 2: Development of antifungal resistance in different *Candida* species between 2007 and 2016