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How frequent are infrequent *Candida* species causing candidaemia? Proportion of cases, antifungal susceptibility, and biofilm formation

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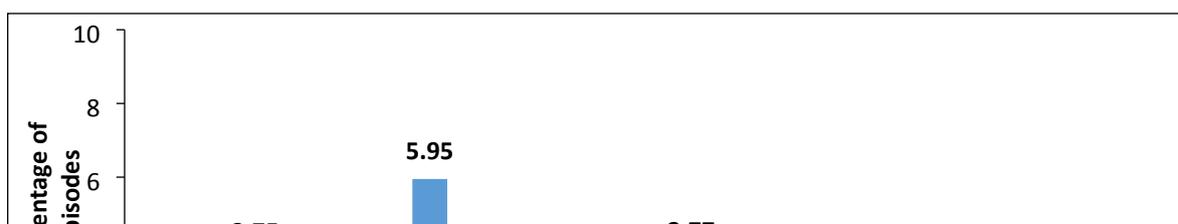
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Background: We studied the frequency, molecular identification, antifungal susceptibility, and capacity to form biofilm of uncommon *Candida* spp. isolates causing candidemia

Material/methods: We selected the incident isolates of uncommon *Candida* species (non-*C. albicans*, non-*C. parapsilosis* complex, non-*C. glabrata* complex, non-*C. tropicalis*, and non-*C. krusei*) causing candidemia in patients admitted to Gregorio Marañón Hospital, Madrid, Spain (January 2007 to November 2016). Isolates were molecularly identified and their antifungal susceptibility – EUCAST – to amphotericin B (AmB), fluconazole (FLU), posaconazole (POS), voriconazole (VRC), micafungin (MYC), anidulafungin (AND), and caspofungin (CAS) was assessed and compared to that of a set of 54 blood cultured *C. albicans* isolates. According to their biofilm biomass production isolates were classified as low, moderate, or high biofilm-forming.

Results: We found 18 episodes of candidemia caused by uncommon *Candida* species concerning 2.5% of all the episodes of candidemia recorded in the institution. The proportion of episodes per year ranged between 0% and 6% and no a clear trend over time in the isolation of these species was found.



The species found were *C. guilliermondii* complex n=8 (*C. guilliermondii* sensu stricto n=6, *C. fermentati* n=2), *C. lusitaniae* n=5, *C. kefyr* n=2, *C. inconspicua* n=1, *C. pelliculosa* n=1, and *Kodamaea ohmeri* n=1. The overall antifungal susceptibility of the uncommon *Candida* spp. was significantly lower than that showed by the *C. albicans* isolates (AmB 0.36 mg/L; FLU 0.21 mg/L; VRC 0.02 mg/L; POS 0.02 mg/L; MYC 0.02 mg/L; CAS 0.07 mg/L; AND 0.02 mg/L).

	<i>C. guilliermondii</i> complex		<i>C. lusitaniae</i>		Other <i>Candida</i> spp.		Overall	
	GM	Range	GM	Range	GM	Range	GM	Range
AmB	0.55	(0.25 - 1)	0.75	(0.125 - 2)	0.5	(0.062 - 2)	0.58	(0.062 - 2)
FLU	4	(2 - 16)	1.14	(0.125 - 16)	2	(0.25 - 8)	2.33	(0.125 - 16)
VRC	0.17	(0.062 - 2)	0.04	(≤0.015 - 0.25)	0.03	(≤0.015 - 0.062)	0.07	(≤0.015 - 2)
POS	0.17	(0.031 - 1)	0.05	(≤0.015 - 0.25)	0.06	(≤0.015 - 0.25)	0.09	(≤0.015 - 1)
MYC	0.45	(0.125 - 4)	0.08	(0.062 - 0.125)	0.05	(≤0.015 - 0.5)	0.15	(≤0.015 - 4)
CAS	0.42	(0.25 - 2)	0.38	(0.25 - 0.5)	0.12	(≤0.015 - ≥8)	0.29	(≤0.015 - ≥8)
AND	1	(0.5 - 2)	0.12	(0.062 - 0.25)	0.05	(≤0.015 - 0.5)	0.24	(≤0.015 - 2)

The rate of fluconazole resistance to according to the non-species-related EUCAST breakpoints was 27.7% being higher for *C. guilliermondii* complex (2/8) and *C. lusitaniae* (2/5). The isolates were low biofilm forming (n=12) or moderate biofilm forming (n=6).

Conclusions: Uncommon *Candida* species caused 2.5% of the episodes of candidemia and a stable trend in their isolation was found. Resistance to fluconazole was high and isolates showed a low or moderate capacity to form biofilms.