

Low rate of cryptic species and antifungal resistance in *Candida* isolates causing candidemia in Madrid

eP234

L.J Marcos-Zambrano^{1,2}, P. Escribano^{1,2,3}, E. Bouza^{1,2,3,4}, J. Guinea^{1,2,3,4}

¹Clinical Microbiology and Infectious Diseases Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain. ²Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain. ³CIBER Enfermedades Respiratorias-CIBERES (CB06/06/0058), Madrid, Spain. ⁴Medicine Department, School of Medicine, Universidad Complutense de Madrid

INTRODUCTION

Knowledge of the epidemiology of the species causing fungaemia is clinically relevant, particularly when starting empiric antifungal treatment, since antifungal susceptibility patterns are species-specific.

Reports on trends in the rate of antifungal resistance in isolates causing fungaemia are scarce, and the few studies performed were based only on the CLSI M27-A3 method.

We aimed to assess the epidemiology of fungaemia in a large tertiary institution located in Madrid, Spain, over a 7-year period after identifying isolates at molecular level and performed antifungal susceptibility testing

Epidemiology of species causing fungaemia. *C. albicans* was the main cause of fungaemia (46.2%), followed by *C. parapsilosis* complex (28%), *C. glabrata* (9.8%), *C. tropicalis* (8%), *Candida* spp. (1.6%), and other non-*Candida* yeasts (3%) (Figure 1).

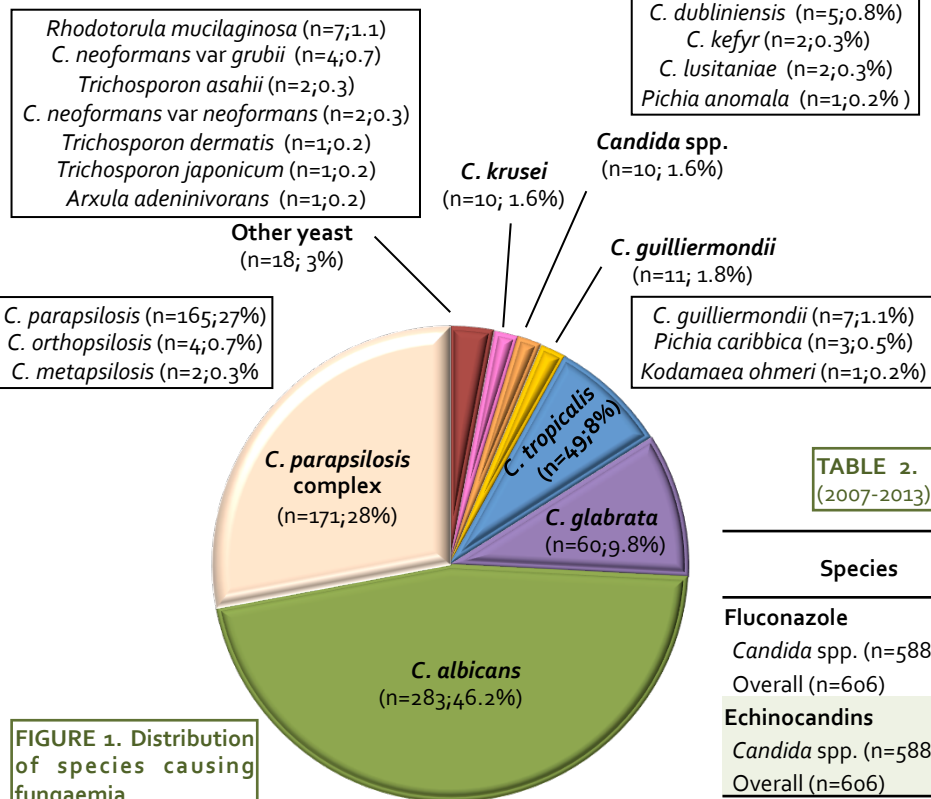


FIGURE 1. Distribution of species causing fungaemia.

METHODS

- 612 isolates**
 - All episodes of fungemia of patients (n=543) admitted to Gregorio Marañón Hospital (Madrid) from Jan 2007 to Dec 2013
- Molecular Identification**
 - Amplification and sequencing of the ITS1-5.8S-ITS2 region
- Antifungal Susceptibility Testing**
 - EUCAST EDef 7.2
 - In those species without CBP we used ECOFFs (<http://www.eucast.org>).
- Sequencing of *fks* genes in candid-resistant strains**
 - Isolates with MICs for candins greater than the CBP or ECOFFs

RESULTS

Antifungal susceptibility testing. All isolates were susceptible to amphotericin B. Overall resistance was 5.1% for fluconazole, 3.9% for micafungin, and 3.3% for anidulafungin (Table 1).

The rate of fluconazole resistance for *Candida* ranged from 0% (2009) to 6.3% (2010), although it has remained stable at around 4% since 2011 (Table 2).

The echinocandin resistance rate was low, and only 7 *Candida* strains showed phenotypic resistance to anidulafungin and/or micafungin (*C. albicans* [n=4], *C. tropicalis* [n=2], and *C. krusei* [n=1]) but only 1 *C. tropicalis* strain harbored a point mutation (R647G) in the HS1 region of the *fks1* gene.

TABLE 1. Percentage of resistance to the antifungal agents studied for the different *Candida* species.

Species	% of intermediate/resistant or N-WT isolates					
	AmB (R)	FLU (I/R)	VRC (R)	POS (R)	MYC (I/R)	AND (I/R)
<i>C. albicans</i>	0	0/0.7	0.7	0.7	0/1.4	0/0.4
<i>C. parapsilosis</i> complex	0	0/0	0	0	100/0	100/0
<i>C. glabrata</i>	0	91.2/8.8	5.3	7	0/0	0/0
<i>C. tropicalis</i>	0	0/0	0	0	0/4.4	0/2.2
<i>C. krusei</i>	0	0/100	0	0	0/10	0/10
<i>C. guilliermondii</i>	NA	72.7/27.3	36.4	63.6	100/0	100/0
<i>Candida</i> spp.	NA	0/10	NA	NA	NA	NA
Other yeasts	NA	0/55.6	NA	NA	0/94.4	0/94.4

N-WT, non wild-type. R, Resistant. I, intermediate. NA, not applicable.

TABLE 2. Trend in resistance during the study period (2007-2013).

Species	% of antifungal resistance						
	2007	2008	2009	2010	2011	2012	2013
Fluconazole							
<i>Candida</i> spp. (n=588)	3.3	1.3	0	6.3	4.7	4.1	3.4
Overall (n=606)	4.1	3.4	0	8.3	5.8	8.9	3.3
Echinocandins							
<i>Candida</i> spp. (n=588)	1.6	1.1	0	1.1	1.2	2.7	0
Overall (n=606)	4.1	1.1	4.1	3.1	3.5	8.9	3.3

CONCLUSIONS

- ✓ Molecular identification allowed us to show that the number of episodes of fungaemia caused by cryptic species was low.
- ✓ The rate of resistance to fluconazole and echinocandins in yeast isolates causing fungaemia was low and does not show signs of increasing.