Antifungal resistance in Spain: epidemiological survey in 10 hospitals (FILPOP2 STUDY)


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Background: Antifungal resistance has emerged in the last years representing a possible public health threat. Resistance in *A. fumigatus* has been linked to mutations in *cyp*51A gene being some of them related with azole exposure in the environment. A previous study performed in Spain (FILPOP) showed no *A. fumigatus* strains with secondary resistance to azoles. The aim of this work was to reevaluate the epidemiology of antifungal resistance and to assess secondary resistance in *A. fumigatus* strains in Spain.

Material/methods: 500 Plates with 2 mg/L of itraconazole were sent to 10 participating hospitals. All clinical samples submitted to the Microbiology lab service for molds testing were subcultured in a classical media and an itraconazole-supplemented media. Positive samples were sent to the Mycology Reference Laboratory (MRL). Antifungal susceptibility testing was performed at the MRL following EUCAST methodology. Molecular identification was carried out by means of sequencing the informative targets. *cyp*51A gene was sequenced in those *A. fumigatus* showing resistance to azoles.

Results: 506 isolates were isolated from 10 Spanish hospitals. Seven were yeasts and five did not grow and were not further analyzed. A total of 494 strains were included in the study, 156 of them grew in itraconazole media. *Aspergillus* was the most frequent genera isolated with 80.2% followed by *Scedosporium* (7.9%), *Penicillium* (4.5%), *Fusarium* (2.8%) and the order Mucorales (3.6%). Resistance to antifungals was found in *Fusarium* spp., *Scedosporium* spp. (including *Lomentospora prolificans*), Mucorales and cryptic species of *Aspergillus*. In addition, three strains of *A. fumigatus* senso stricto were resistant to azoles, two of them harbored TR$_{34}$/L98H mechanism of resistance and the third one had no mutations in *cyp*51A.

Conclusions: Antifungal resistance is emerging in Spain. Resistance to azoles is present in *Aspergillus* but also in other emerging moulds such as *Scedosporium* and *Fusarium*. We also found *A. fumigatus* strains resistant to azoles with no mutations in *cyp*51A.