Occurrence of *Aspergillus* species in hospitalized patients and azole antifungal susceptibility profile

Cafarchia Claudia^{1*}, Aneke Chioma Inyang¹, Iatta Roberta¹,
Otranto Domenico¹

¹Dipartimento di Medicina Veterinaria, Università degli Studi "Aldo Moro", Bari, Italy;
*claudia.cafarchia@uniba.it

OBJECTIVES

Aspergillus spp. are ubiquitous filamentous fungi causing a variety of diseases depending on the host's immunocompetence. The pharmacological choice for the prophylaxis and therapy of *Aspergillus* spp. infections is the triazole drugs. Although cases of aspergillosis by azole resistant strains have been recently reported, data on the prevalence and drug resistance in isolates of *Aspergillus* spp. from southern Italy are scant. Therefore, the purpose of this study was to evaluate the occurrence of *Aspergillus* spp. and the *in vitro* susceptibility to azole of isolates from hospitalized patients as well as to monitor the azole resistance phenomenon in this geographical area.

A. fumigatus

A. niger

A. flavus

METHODS

A total of 567 patients admitted to Hematology (n=152), Cystic Fibrosis (n=169) and Intensive Care (n=246) units of Ospedale Policlinico Consorziale di Bari, Southern Italy, were sampled in the study. 3585 (three thousand five hundred and eighty five) samples were collected divided into pharyngeal swab (n=599), nasal swab (n= 638), expectorates (n=465), bronchial secretions (n=1650) and bronchoalveolar lavage (n=233). All the *Aspergillus* spp. were microscopically and molecularly identified by PCR and sequencing of partial calmodulin and β -tubulin genes. The minimum inhibitory concentrations (MICs) of azoles were determined by the broth microdilution method according to the CLSI M38-A2 protocol with itraconazole (ITZ), voriconazole (VOR) and posaconazole (POS) at concentrations of 0.016-32 μ g/ml and the isolates were considered resistant if they showed a MIC value above the breakpoints proposed (>2 μ g/ml for ITZ and VOR; >0.5 μ g/ml for POS) (Verweij *et al.*, 2009; Arendrup *et al.*, 2012). MIC range, MIC mean value (mMIC) and standard deviation (SD), MIC₅₀ and MIC₉₀ (i.e., MIC at which 50% and 90% of the strains were inhibited) were determined after 48 hours of incubation (CLSI, 2008).

RESULTS

A high prevalence of *Aspergillus* spp. was recorded amongst patients with cystic fibrosis (15.4%), followed by haematological patients (10.5%) and with lung disease admitted to Intensive Care unit (3.2%). The most frequently isolated species was *A. fumigatus* (4.6%), followed by *A. terreus* (1.4%), *A. flavus* (1.2%) and *A. tubingensis* (1.2%). The distribution of *Aspergillus* species varied according to the sources, being *A. tubingensis* (2.6%) *A. terreus* (3%) and *A. flavus* (0.8%) the second most frequently isolated species from haematological, cystic fibrosis and Intensive Care unit patients, respectively. The highest MIC ranges and MIC values (i.e., mMIC, MIC₅₀ and MIC₉₀) to ITZ and PSZ were recorded in *A. tubingensis* and *A. flavus*.

<i>Aspergillus</i> spp.	ITZ				VRZ				PSZ			
	MIC ranges	mMIC (SD)	MIC ₅₀	MIC ₉₀	MIC ranges	mMIC (SD)	MIC ₅₀	MIC ₉₀	MIC ranges	mMIC (SD)	MIC ₅₀	MIC ₉₀
<i>A. flavus</i> (7)	0.25-0.5	0.29 (0.09)	0.25	0.25	0.25-0.5	0.42 (0.12)	0.5	0.5	0.5	0.5 (0)	0.5	0.5
<i>A. fumigatus</i> (26)	0.25-0.5	0.38 (0.13)	0.5	0.25	0.25-0.5	0.28 (0.08)	0.25	0.25	0.125-0.5	0.27 (0.12)	0.25	0.25
<i>A. niger</i> (1)	0.25	0.25 (0)	0.25	0.25	0.25	0.25 (0)	0.5	0.5	0.25	0.25 (0)	0.5	0.5
<i>A. tubingensis</i> (7)	0.5-1	0.93 (0.19)	1	1	0.5-1	0.64 (0.24)	0.5	0.5	0.5	0.5	0.5	0.5
<i>A. awamori</i> (3)	0.25-0.5	0.42 (0.14)	0.5	0.25	0.125-0.5	0.29 (0.19)	0.25	0.125	0.06-0.5	0.27 (0.22)	0.25	0.06
<i>A. terreus</i> (8)	0.25-0.5	0.31 (0.01)	0.25	0.25	0.25-0.5	0.31 (0.01)	0.25	0.25	0.25-0.5	0.31 (0.01)	0.25	0.25

CONCLUSIONS

The results show that the highest occurrence rate in the clinical setting was recorded with *A. fumigatus*, followed by *A. terreus*, *A. flavus* and *A. tubingensis* depending on the type of patient. The azole susceptibility varied according to the species and *A. tubingensis* and *A. awamori* were the less susceptible ones. However, all the isolates were characterized by a high *in vitro* susceptibility to triazoles and the resistance phenomena are not, at present, a threat to public health in our geographical area.