# ANTIFUNGAL SUSCEPTIBILITY OF ENVIRONMENTAL *VERSUS* CLINICAL STRAINS OF *Aspergillus flavus* ISOLATED IN ARGENTINA

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**Introduction:** Invasive Aspergilosis (IA) is rare in immunocompetent people but contributes to significant morbidity and mortality in immunosuppressed patients. Approximately 80% of IA is caused by *Aspergillus fumigatus*, followed by *Aspergillus flavus* (15-20% of cases). After azoles were introduced to treat *A. fumigatus* infections, reports of resistance started to emerge. Minimal inhibitory concentrations (MICs) remain the most valuable laboratory tool available to predict resistance and to select the best alternative for antifungal treatment. Recently, cyp51A mutations typical for environmental azole resistance acquisition (for example, TR34/L98H) have been described in *A. fumigatus*. These mutations can also be found in isolates recovered from patients. Many studies determining the susceptibility patterns of clinical strains of *Aspergillus* spp. are available, but very few have evaluated the susceptibility patterns of environmental strains, especially of Aspergillus non-fumigatus strains, such as *A. flavus*.

**Aims:** To determine the susceptibility profiles of environmental strains of *A. flavus* to amphotericin B (AMB), itraconazole (ITC), voriconazole (VRC) and posaconazole (PSC) and to compare them with the susceptibility profiles of clinical strains.

**Methods:**

34 *A. flavus* isolates → MIC determination → PCR + SEQUENCING OF CYP51C

- 18 from chickpea and soy seeds
- 16 from cystic fibrosis patients

- CLSI M38-A2 Protocol

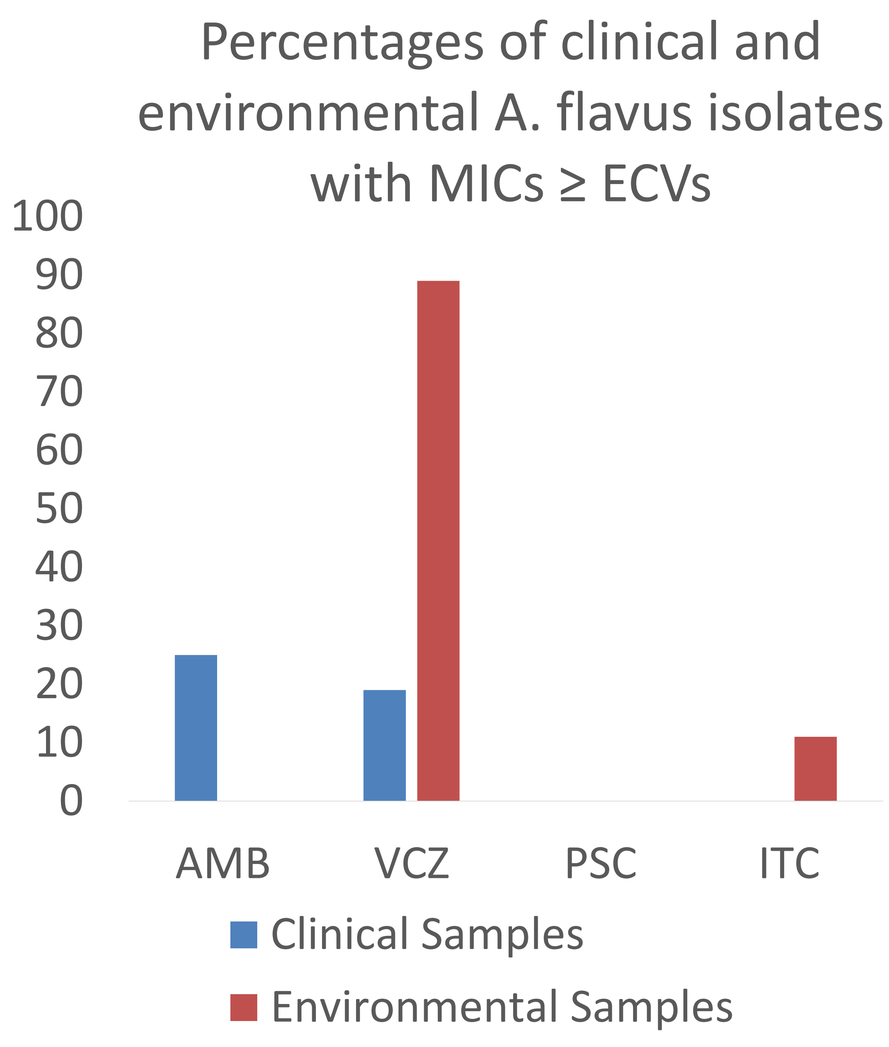
- *Aspergillus flavus* ≥ ECV

**Results:**

Amongst the environmental isolates, 89% of them (n=16) showed high MICs values for VCZ (≥2 ug/ml), while 11% of them (n=2) showed high MICs values for ITC (≥2 ug/ml). Amongst the clinical isolates, only 19% (n=3) displayed high MICs values for VCZ and 25% (n=4) for AMB (≥4 ug/ml). Cyp51C was bidirectional sequenced and point mutations were studied.

**Table 1 - MIC frequencies of *Aspergillus flavus* of Clinical and Environmental Samples**

| AMB (ug/ml) | 0,015 | 0,03 | 0,06 | 0,125 | 0,25 | 0,5 | 1 | 2 | 4 | 8 | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clinical | | | | | | 2 | 7 | 3 | | 4 | 16 | 25% |
| Environmental | | | | | | 1 | 9 | 8 | | | 18 | 0% |
| **VCZ (ug/ml)** | **0,015** | **0,03** | **0,06** | **0,125** | **0,25** | **0,5** | **1** | **2** | **4** | **8** | **Total** | **%** |
| Clinical | | | | | | 8 | 5 | 3 | | | 16 | 19% |
| Environmental | | | | | | | 2 | 11 | 4 | 1 | 18 | 89% |
| **PSC (ug/ml)** | **0,015** | **0,03** | **0,06** | **0,125** | **0,25** | **0,5** | **1** | **2** | **4** | **8** | **Total** | **%** |
| Clinical | 2 | 1 | 1 | 2 | 7 | 3 | | | | | 16 | 0% |
| Environmental | | | | 1 | 11 | 6 | | | | | 18 | 0% |
| **ITC (ug/ml)** | **0,015** | **0,03** | **0,06** | **0,125** | **0,25** | **0,5** | **1** | **2** | **4** | **8** | **Total** | **%** |
| Clinical | 3 | | | 1 | 5 | 7 | | | | | 16 | 0% |
| Environmental | | | | | 2 | 8 | 6 | 1 | | 1 | 18 | 11% |




**Conclusion:** To the best of our knowledge, this is the first report of antifungal screening of environmental strains of *A. flavus* in Argentina. Noteworthy, environmental strains of *A. flavus* high MICs values to VCZ in comparison to clinical strains. Susceptibility differences among environmental *A. flavus* isolates might explain native resistance to certain antifungals. In conclusion, our study demonstrates that azole resistance with an environmental signature is present in environments and patients from Argentina.