Antifungal Susceptibility of Respiratory *Aspergillus* Isolates from Canadian Hospitals: Results of the CANWARD 2012 Study

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BACKGROUND

The Canadian Ward Surveillance Study (CANWARD) is an established and ongoing program that monitors epidemiology of antimicrobial resistant pathogens in tertiary care hospitals.

Invasive pulmonary disease and other serious respiratory infections caused by *Aspergillus* are a growing concern in managing immunocompromised and critically ill patients.

Aspergillus resistance to antifungals is largely undefined because culture isolation is poor and in vitro susceptibility testing is not routinely offered by clinical laboratories.

However, resistance is increasingly being reported and has been linked to clinical failures in *A. fumigatus*.

Antifungal clinical breakpoints have not been established for *Aspergillus* primarily due to insufficient clinical outcome data.

Epidemiologic cut-off values (ECOFFs), which categorize strains as wild-type (WT) and non-WT, are antifungal MIC thresholds for common *Aspergillus* species designed to aid the detection of acquired resistance mechanisms.

In collaboration with the national CANWARD network, we collected clinical isolates of *Aspergillus* species and characterized the antifungal MIC distributions.

Here we present the findings from the first year of this ongoing surveillance initiative.

REFERENCES

1. CLSI M38-A2. 2008. Broth microdilution testing for moulds.

2. Espinel-Ingroff et al. JCM. 2010; 48: 3251.

3. Pfaller et al. DMID. 2010;67: 56.

This work is supported by a grant from Astellas Pharma.

We thank all CANWARD participating sites and investigators.

METHODS

During the 2012 study period, 10 tertiary care medical centres representing 8 provinces submitted *Aspergillus* isolates from patients attending hospital clinics, emergency rooms, medical/surgical wards, and intensive care units.

Susceptibility testing to amphotericin B (AMB), itraconazole (ITRA), posaconazole (POSA), voriconazole (VORI) and caspofungin (CASP) was performed using CLSI M38-A2 broth microdilution standards.

Growth endpoints were measured at 24 h of incubation: minimum inhibitory concentration (MIC) for AMB and azoles; minimum effective concentration (MEC) for CASP.

ECOFFs values and are listed in **Table 1**.

RESULTS

A total of 587 isolates were collected, of which 563 were respiratory tract specimens included for this analysis. *A. fumigatus*, *A. flavus,* and *A. niger* represented 74.3%. 7.6%, and 9.8%, respectively. The majority of isolates were cultured from sputum (61.6%) and bronchoscopy (28.2%) specimens in Medicine (51.2%), Clinic (35.0%), and ICU (8.8%) patients. The average number of isolates submitted per site was 56 (range, 11 to 162).

The full distribution of species, ward locations, and participating regions are shown in **Figures 1, 2, and 3**.

The MIC/MEC data for the most common species exhibited normal distribution, as shown in **Table 1**.

Only three isolates of *A. fumigatus* had non-WT VORI MICs (2 to 16 mg/L) and three others had non-WT CASP MECs of 1 to 2 mg/L.

There were 11 *A. flavus* isolates that displayed non-WT MICs to VORI (2 to 4 mg/L), 6 of which had POSA non-WT MICs of 0.5 mg/L. Three other *A. flavus* showed non-WT MECs of 0.5 mg/L to CASP.

FIGURES

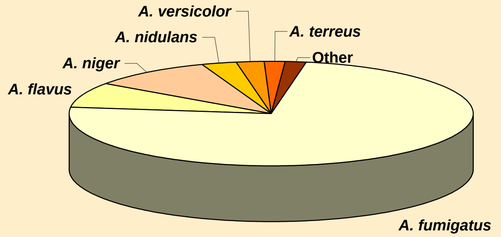

Figure 1. *Aspergillus* species distribution of respiratory isolates.

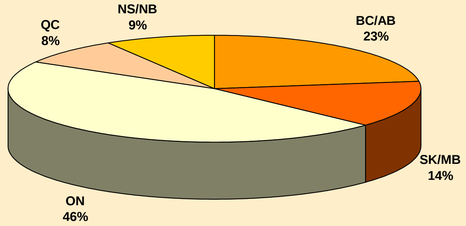

Figure 2. Provincial distribution of *Aspergillus* surveillance isolates.

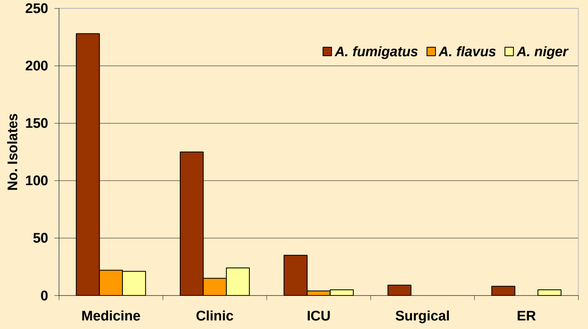

Figure 3. Distribution of common species in hospital ward locations.

TABLES

Agent	Species	Total Isolate	Mode (mg/L)	MIC/MEC$_{90}$ (mg/L)	Geometric Mean (mg/L)	ECOFF (mg/L)	>ECOFF (% non-WT)
AMB	*A. fumigatus*	418	0.25	1	0.328	≤2	0.0
	A. flavus	43	0.5	1	0.330	≤2	0.0
	A. niger	55	0.12	0.25	0.130	≤2	0.0
ITRA	*A. fumigatus*	418	0.5	0.5	0.432	≤1	0.0
	A. flavus	43	0.5	1	0.436	≤1	0.0
	A. niger	55	0.5	1	0.526	≤1	1.7
POSA	*A. fumigatus*	418	0.12	0.25	0.198	≤0.5	0.0
	A. flavus	43	0.25	0.5	0.178	≤0.25	13.3
	A. niger	55	0.12	0.25	0.140	≤0.5	0.0
VORI	*A. fumigatus*	418	0.5	1	0.486	≤1	0.7
	A. flavus	43	1	2	1.033	≤1	24.4
	A. niger	55	0.5	1	0.619	≤2	0.0
CASP	*A. fumigatus*	418	0.25	0.5	0.215	≤0.5	0.7
	A. flavus	43	0.12	0.25	0.174	≤0.25	6.7
	A. niger	55	0.12	0.25	0.117	≤0.25	1.7

CONCLUSIONS

The CANWARD 2012 program has generated important data characterizing hospital epidemiology and antifungal susceptibility distributions for common *Aspergillus* species.

The clinical correlation of *Aspergillus* susceptibility testing is not known but ECOFFs have been defined to facilitate the detection of microbiological resistance.

WT isolates of *A. fumigatus* were most prevalent in this study and evidence of non-WT isolates of other species was very limited. Molecular analysis of non-WT isolates is underway.

These results provide a baseline for monitoring temporal changes as national *Aspergillus* surveillance continues.