Epidemiology and antifungal susceptibilities of clinically significant filamentous fungi from a tertiary hospital in Singapore from 2018 – 2021

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Background

- Filamentous fungi infections are associated with significant morbidity and mortality
- Data regarding antifungal resistance in Singapore is lacking
- We investigated the species distribution and susceptibility profiles of molds isolated from a tertiary hospital in Singapore

Methods

- Antifungal susceptibility results reported from 2018 to 2021 were retrospectively reviewed
- Unique isolates per patient were included
- Molds were identified primarily by morphology
- Molecular studies were used as an adjunct where required
- Susceptibility testing was performed via Sensititre YeastOne (ThermoFisher Scientific) and E-test (Liofilchem)

Results

- 125 isolates were analyzed (**Table 1**)
- The most common molds recovered were *Aspergillus*, *Fusarium* and *Mucorales*
  - *Aspergillus* and *Mucorales* frequently involved the respiratory tract and skin and soft tissue (SST) whereas *Fusarium* was isolated from SST and blood
- Amphotericin B had moderate activity against all molds (**Table 2**), with only 11 out of 88 isolates (12.5%) being non-wild type
- The echinocandins exhibited good activity against *Aspergillus* and other hyaline molds but not *Fusarium* and *Mucorales*
- The triazoles were most useful against *Aspergillus*, with posaconazole demonstrating the lowest geometric mean of 0.067
- *Fusarium* had high MICs when tested against the azoles
- Posaconazole was the azole of choice for *Mucorales*
- Six *Aspergillus* isolates (all *A. fumigatus*) were non-wild type when tested against voriconazole, with a MIC >1
  - Of these six isolates, three were also non-wild type for amphotericin B, with a MIC >2
  - One *Aspergillus fumigatus* complex isolate demonstrated resistance across all tested azoles and sequencing revealed Cyp51 mutations

Conclusions

- *Aspergillus* species is the most prevalent clinically significant mold in our hospital
- Although triazoles and echinocandins exhibit good activity, 13.33% of *Aspergillus* isolates were non-wild type for amphotericin B
- Given the detection of these non-wild type *Aspergillus* species, susceptibility testing may be indicated in seriously ill patients to aid clinicians in selecting antifungal therapy

References

- Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antifungal Susceptibility Testing of Filamentous Fungi. 2nd ed. CLSI guideline M61. Wayne, PA: CLSI, 2021.
- Berkow EL, Lockhart SR, Ostrosky-Zeichner L. Antifungal Susceptibility Testing: Current Approaches. Clin Microbiol Rev. 2020 Apr 29;33(3):e00069-19.

Group	Number (%) of isolates						
	Respiratory	SST	Blood	Ear	Eye	Other[f]	Total
Aspergillus spp.[a]	62 (49.6)	12 (9.6)	0 (0)	5 (4.0)	1 (0.8)	2 (1.6)	82
Fusarium spp.[b]	2 (1.6)	13 (10.4)	8 (6.4)	0 (0)	2 (1.6)	1 (0.8)	26
Mucorales isolates[c]	4 (3.2)	4 (3.2)	0 (0)	0 (0)	0 (0)	2 (1.6)	10
Scedosporium and *Lomentospora* spp.[d]	2 (1.6)	1 (0.8)	0 (0)	1 (0.8)	0 (0)	0 (0)	4
Other hyaline molds[e]	3 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3
Total	73 (58.4)	30 (24.0)	8 (6.4)	6 (4.8)	3 (2.4)	5 (4)	125

Table 1: Distribution of clinically significant molds by specimen site

[a] *A. fumigatus* (38), *A. flavus* (17), *A. niger* (17), *Aspergillus* spp. (4), *A. terreus* (2), *A. nidulans* (2), *A. sydowii* (1), *A. versicolor* (1)
[b] *F. solani* complex (7), *F. oxysporum* complex (1), *Fusarium spp.* (18)
[c] *R. microsporus* (2), *R. pusillus* (1), *R. oryzae* (1), *Rhizopus* spp. (1), *M. irregularis* (1), *Mucor* spp. (1), *L. hyalospora* (1), *L. corymbifera* (1), *Lichtheimia* spp. (1)
[d] *S. apiospermum* complex (2), *Scedosporium* spp. (1), *L. prolificans* (1)
[e] *Penicillium* spp. (2), *Tritirachium oryzae* (1)
[f] Includes three isolates from bone and two isolates from peritoneal fluid

Group	Descriptor	AMB	AND	MIF	CAS	FC	POS	VOR	ITC	FLU	ISA
Aspergillus spp.	N	82									29
	MIC range	0.5/8	≤0.015/0.12	≤0.008/0.12	≤0.008/2	1/≥64	≤0.008/1	0.03/>8	≤0.015/>16	16/>256	0.023/≥32
	$MIC_{50/90}$	2/4	≤0.015/0.03	0.015/0.057	0.015/0.03	32/64	0.06/0.12	0.5/2	0.12/0.25	192/256	0.19/0.38
	GeoM	2.19	0.018	0.016	0.017	22.06	0.067	0.67	0.12	155.47	0.19
Fusarium spp.	N	26									10
	MIC range	2/4	2/>8	0.5/>8	0.06/>8	32/>64	0.25/>8	0.5/>8	16/>16	4/>256	0.064/>32
	$MIC_{50/90}$	4/4	>8/>8	>8/>8	>8/>8	>64/>64	>8/>8	8/>8	>16/>16	>256/>256	32/>32
	GeoM	3.06	7.19	5.66	6.28	62.32	7	6.64	16	162.71	4.06
Mucorales isolates[c]	N	10									7
	MIC range	1/4	4/>8	8/>8	8/>8	64/>64	0.12/>8	8/>8	0.12/>16	128/>256	0.25/>32
	$MIC_{50/90}$	1.5/4	>8/>8	>8/>8	>8/>8	>64/>64	0.75/>8	>8/>8	>16/>16	>256/>256	2/>32
	GeoM	1.63	7.46	8	8	64	1.3	8	4.58	238.86	3.34
Scedosporium and *Lomentospora* spp.[d]	N	4									0
	MIC range	2/>8	0.5/8	0.06/1	0.03/8	64/>64	0.5/>8	0.5/>8	16/>16	4/>256	-
Other hyaline molds[e]	N	3									1
	MIC range	2/>8	<=0.015/>8	0.03/>8	<=0.008/>8	2/>64	0.25/1	0.5/>8	0.06/>16	1/>256	2/2

Table 2: Susceptibility of mold isolates to antifungal agents

AMB, amphotericin B; **AND**, anidulafungin; **MIF**, micafungin; **CAS**, caspofungin; **FC**, flucytosine; **POS**, posaconazole; **VOR**, voriconazole; **ITC**, itraconazole; **FLU**, fluconazole; **ISA**, isavuconazole.

N, number of isolates tested against the antifungal. **$MIC_{50/90}$**, minimum inhibitory concentration for 50% and 90% of isolates, respectively. Denotes minimum effective concentrations (MECs) for the echinocandins. **GeoM**, geometric mean. Values are reported in mcg/ml. $MIC_{50/90}$ and GeoM were not calculated for *Scedosporium*, *Lomentospora* and other hyaline molds due to the low number of isolates.