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Feline sporotrichosis outcome and its impact in public health in Southern Brazil

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Poster session 3, September 23, 2022, 12:30 PM - 1:30 PM

Sporotrichosis due to *Sporothrix brasiliensis* is an emerging and neglected disease in Brazil. Domestic cats are susceptible to a severe presentation of this mycosis, carrying a high fungal load in their lesions. They frequently infect other animals and even humans by scratches and/or bites. Thus, the correct management and treatment of feline sporotrichosis are crucial aspects of the control of the disease in a population.

Objective: We aimed to evaluate the management and outcome of feline sporotrichosis cases in a hyperendemic city in southern Brazil (Rio Grande do Sul state).

Methods: Database from the Mycology Laboratory (LabMyco) of the Federal University of Rio Grande (FaMed–FURG) was consulted to gather data from all proven feline sporotrichosis cases (confirmed by mycological culture), between January 2019 and December 2021. It was included in this study in all cases in which the phone number of the cat owners was available. All of them were contacted and invited for an interview by quick and short questions regarding the management and the outcome of their cats with sporotrichosis. Disagreement to participate, and change/incorrect phone number contacted were used as exclusion criteria.

Results: During the 3-year period studied a total of 62 owners, from 165 felines diagnosed with sporotrichosis in the LabMyco, had a phone number available. A total of 35 owners were excluded, totalizing 27 participants in this study. More than half (51.8%; $n = 14$) reported returning only once to the veterinarian to clinical accomplishment, 48.1% ($n = 13$) of them do not use personal protective equipment to handle the infected animal, 44.4% ($n = 12$) highlighted the difficulty in daily administering drugs to the cat and only 18.5% ($n = 5$) affirmed to had isolated the infected animal during the treatment. Two animals (7.4%) with advanced signs of disseminate sporotrichosis died before starting treatment, and the others received itraconazole and/or potassium iodide as the drug of choice. Clinical cure was achieved in 40% of the cats treated (10/25), 28% (7/25) evolved to death, 16% (4/25) are still in treatment due to new lesions (recidive), and the other four animals were abandoned in the streets. In addition, zoonotic transmission occurred in three (11.1%) owners, which developed lymphocutaneous sporotrichosis after a scratch or bite by the infected cat.

Conclusion: Sporotrichosis in Southern Brazil is a public health threat, in view of this, our study shows the urgent necessity of government strategies and interventions that promote health education and implement a service to attend, and provide treatment accomplishment to feline sporotrichosis in view of control the current hyperendemic of this mycosis.

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The mechanism of action of antifungal activity of *Zanthoxylum armatum* fruit's oil against *Candida* cells does not involve ROS generation

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Objective: To explore the antifungal activity of *Zanthoxylum armatum* fruit's oil against different *Candida* species and its mechanism of action.

Methods: The *Z. armatum* fruit's oil activity was assessed against *C. albicans, C. krusei, C. glabrata, C. parapsilosis, C. tropicalis*, and *C. guilliermondii* through different drug susceptibility assays including, MIC, agar diffusion and spot assay. The mechanism of action was explored through sterol analysis, germ tube inhibition, epithelial cells adherence, and ROS generation.

Results: The oil from the fruits of *Z. armatum* was subjected to GC-MS analysis, and linalool (72%) was found as the major component. The drug susceptibility measured through different methods, including minimum inhibitory concentration (MIC), where end-point was 3% v/v for different species tested, and the same pattern was observed in agar diffusion and spot assay. The antifungal activity was found to be fungicidal in nature and the major reason appeared to be the reduction in ergosterol levels inside cells. It resulted in lowered germ tube formation, an important indicator in virulence of *C. albicans*. The oil reduced adherence of *Candida* cells to buccal epithelium significantly, which is the first step in invasion, biofilm formation, and damage to oral epithelial cells. Interestingly, unlike most antifungals, where reactive oxygen species generation mediated killing is involved, was not found significant in the present study.

Conclusions: The *Z. armatum* fruits oil exerts its antifungal activity by inhibiting ergosterol formation and reduced germ tube formation.

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Genomic epidemiology of antifungal-resistant *Candida auris* in Colombia

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Poster session 1, September 21, 2022, 12:30 PM - 1:30 PM

Introduction: *Candida auris* is a public health threat. Five major clades of *C. auris* have been identified (Clades I–V). In Colombia, *C. auris* infections were first reported in 2016 with ongoing transmission reported from multiple cities. Here, we describe *C. auris* genomic epidemiology in Colombia detailing cases from 2016–2021.

Methods: A total of 99 isolates from *C. auris* cases were collected between June 2016 to January 2021 in Colombia, representing 11 geographic locations. Species confirmation, antifungal susceptibility testing, and whole-genome sequencing (WGS) were performed. In all, 37 genomic sequences generated previously from isolates from *C. auris* cases in Colombia, Venezuela, Panama, Israel, and United States were also analyzed MycoSNP workflow was used to assess sequence quality, map reads to the reference, and identify single-nucleotide polymorphisms (SNPs). Pairwise distances and a neighbor-joining tree were generated. IQtree was used to generate a maximum-likelihood tree with bootstrap values.

Results: Phylogenetic analysis identified 1 493 SNP positions. Isolates from Colombia clustered to Clade IV and predominately grouped by country except for 16 fluconazole-resistant isolates from Bogota, Colombia that grouped with five isolates from Venezuela. In this cluster, 20 (95%) were resistant to fluconazole and 5 (24%) were resistant to fluconazole and the echinocandin micafungin. Remaining isolates from Bogota did not group in this cluster and were susceptible to fluconazole and micafungin.

A total of 98 isolates from Colombia clustered together. Within this Colombian cluster, there were two subgroups that had bootstrap support of 100% and were separated by 13 SNPs. The first subgroup was a cluster that contained 18 isolates from the north coast; 17 (94%) isolates were resistant to amphotericin B. A second subgroup consisted of 26 isolates from Cesar and Norte de Santander, and 22 (84%) isolates were resistant to fluconazole.

Conclusions: Based on the phylogenetic reconstruction, *C. auris* in Colombia continues to be of Clade IV. Amphotericin B-resistant isolates were predominately from the north coast, fluconazole-resistant isolates were from a wider geographic area in Colombia, and echinocandin-resistant isolates were from Bogota. Within the Colombian cluster comprising two subgroups, we observed high genetic relatedness between isolates from different geographic locations suggesting transmission among cities.

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The value of PCR-based azole resistance detection in invasive aspergillosis: A prospective multicenter study

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Poster session 1, September 21, 2022, 12:30 PM - 1:30 PM

Objectives: Prompt detection of azole-resistant *Aspergillus fumigatus* will result in the timely start of active treatment and may improve the survival of invasive aspergillosis (IA). The use of a multiplex polymerase chain reaction (PCR) targeting *Aspergillus* species and fumigatus DNA as well as the two most prevalent azole resistance- associated mutations (RAMs) in the cyp51A gen (TR34/L98H and TR46/Y121F/T289A) could shorten the time to detect azole-resistant IA.

Methods: In a prospective study in 12 Dutch and Belgian centers, we evaluated the clinical value of the multiplex AsperGenius®PCR in hematology patients with a pulmonary infiltrate undergoing bronchoalveolar lavage (BALf) sampling. The primary endpoint was antifungal treatment failure in the 6 weeks after antifungal treatment initiation in the patients in which azole-resistant IA was detected. Treatment failure was defined as death or a switch to an antifungal agent from another class after at least 5 days of first-line therapy. Patients with a mixed azole-susceptible/resistant infection were excluded from this analysis to ascertain that the infection was indeed caused by the resistant strain.

Results: Of 323 patients enrolled, sufficient BALf for PCR testing remained in 299. Probable fungal disease was diagnosed in 95 (34%), *Aspergillus* cultured in 24 (8%), *Aspergillus* DNA detected in 118 (39%), and *A. fumigatus* DNA in 88 (29%) patients. The resistance PCR was conclusive in 54/88 (61%) and RAMs were detected in 8 (15%), Table 1. All 8 had probable IA but 2 had a mixed infection and were excluded. In the 6 remaining patients, treatment failure was observed in one. Compared with the GM negative patients and despite antifungal therapy, a positive GM test was associated with a 13% higher 6-week overall mortality ($P = .01$), Table 2. Surprisingly, the 6-week mortality in the 65 patients who had a positive *Aspergillus* PCR but a negative GM and culture was not increased compared to those with a negative PCR (PCR + 14% vs. PCR- 16% mortality, $P = .68$).

Conclusions: In patients with an underlying hematological disease and a pulmonary infiltrate, the detection of *Aspergillus* DNA by PCR on BALf was not associated with increased mortality. The exact place of the *Aspergillus* PCR in the EORTC-MSGERC invasive fungal infection criteria is therefore uncertain. In 15% of the patients in whom *A. fumigatus* DNA was present, azole RAMs were detected by PCR. In only 1/6 probable cases of IA with RAMs detected, antifungal treatment failure was observed. Basing the choice of antifungal therapy on the result of a cyp51a resistance PCR may help to reduce the impact of azole resistance on mortality.

BAL GM (OD) Number of patients (n) [a]	<0.5 217	0.5–0.99 32	≥1 72
Aspergenius Performed (n)	201	30	67
PCR ***Aspergillus*** species positive (n)	55 (27%)	16 (53%)	47 (70%)
PCR ***Aspergillus*** species negative (n)	146 (73%)	14 (47%)	20 (30%)
PCR ***A. fumigatus*** positive (n)	39 (19%)	12 (40%)	37 (55%)
PCR ***A. fumigatus*** negative (n)[c]	162 (81%)	18 (60%)	30 (45%)
PCR ***A. terreus*** positive (n)	1 (0.5%)	0 (0%)	2 (3%)
TR_{34}/L98H PCR successful (n) [b] TR_{46}/Y121F/T289A PCR successful (n) [b]	18 (46%) 19 (49%)	6 (50%) 5 (42%)	33 (89%) 33 (89%)
TR_{34}/L98H and TR_{46}/Y121F/T289A both WT	15	4	29
TR_{34}/L98H and TR_{46}/Y121F/T289A both not successful (n)	13	3	3
TR_{34}/L98H WT and TR_{46}/Y121F/T289A not successful (n)	1	2	0
TR_{34}/L98H not successful and TR_{46}/Y121F/T289A (n)	2	1	0
TR_{34}/L98H Resistant and TR_{46}/Y121F/T289A WT (n)	1	0	3 (2[c])
TR_{34}/L98H WT and TR_{46}/Y121F/T289A Resistant (n)	1	0	1
Culture positive for ***Aspergillus*** (n)	7	1	16
Culture positive for ***A. fumigatus*** (n)	5	0	16
Culture positive for ***A. niger*** (n)	1	0	0
Culture positive for ***A. terreus*** (n)	1	0	0
Culture positive for ***A. flavus*** (n)	0	1	0

Table 1. Microbiology results including BAL GM, AsperGenius PCR and culture.

Abbreviations: A.=Aspergillus; BAL=brochoalveolar lavage; GM=Galactomannan; OD=optical density; PCR=polymerase chain reaction; WT=wild type.[a] BALf volume is occasionally too small to perform all tests in all patients. In total BAL PCR was performed in 299 patients, however in one patient, GM was not available, therefore total amount of patients in this table is 298. [b]The number of patients in the GM subgroup for whom *A. fumigatus* PCR was positive, was used as denominator (39, 12 and 37 respectively for GM<0.5, GM 0.5-0.99 and GM≥1.0). [c] There were 2 patients in which DNA of wildtype *A. fumigatus* and the TR_{34}/98H mutation was detected simultaneously.

	GM positive (N=75)	GM or culture or PCR positive (N=147)	GM and culture negative but *Aspergillus* species PCR positive (N = 65)	GM, culture and *Aspergillus* species PCR negative (N = 157)
Antifungal therapy started around BAL (-5, +14 days) (n/N)	71/75 (95%)	129/147 (88%)	52/65 (80%)	103/157 (66%)
Median duration of antifungal treatment (days and IQR)	28 (12–78)	28 (11 – 85)	26 (11 – 131)	18 (7 – 63)
6-week mortality (n/N)	21/74 (28%)	21%	9/65 (14%)	25/156 (16%)

Table 2. Outcome of patients according to the mycological test that was positive.

Abbreviations: BAL=bronchoalveolar lavage; IQR=interquartile range; PCR=polymerase chain reaction

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Bee health and the antifungal activity of honey

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Objectives: Various components have been identified which contribute to the antimicrobial properties of honey, many of which are secreted by bees into the honey as it is being processed. Here we investigate the relationship between bee and hive health and the antifungal properties of honey.

Methods:Samples of honey were collected from hives that were either healthy or experiencing some kind of distress as assessed by beekeepers. Healthy hives displayed strong population numbers and good brood patterns while distressed hives exhibited warning signs such as low population numbers, patchy brood patterns, evidence of chalkbrood fungal disease, or small hive beetle infestation. Honey samples were tested for antifungal activity against yeast and mold species via broth microdilution, tested for hydrogen peroxide levels via colorimetric assay, and spread on agar plates to assess the abundance and diversity of microbes present in the raw honey.

Results:Honey samples were effective against the yeast *Cryptococcus deuterogattii* and the dermatophyte mold *Trichophyton interdigitale* but ineffective against the yeast *Candida dubliniensis* and the mold *Aspergillus flavus*. The hydrogen peroxide levels of the honeys were variable and did not always align with activity. Less microbes in number and abundance were present on agar plates grown from healthy hive honey compared to distressed hive honey.

Conclusion: These results indicate that bee health may play a role in contributing to the antifungal properties of honey and that promoting strong and healthy hives is beneficial.

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Monitoring antifungal resistance in a global collection of *Candida* spp. surveillance isolates, including *C. auris*—analysis of resistance in antifungals (ARIA) 2020 study

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Objectives: Analysis of resistance in antifungals (ARIA) is a recent longitudinal global surveillance initiative collecting yeast and fungal isolates from hospitals worldwide designed to determine susceptibility profiles and monitor the resistance trends among antifungal agents. ARIA reports the susceptibility patterns of data concerning echinocandins, second-generation triazoles, and fluconazole against clinical *Candida* spp., and filamentous fungal isolates from worldwide sources.

Methods: *Candida* spp. isolates ($n = 662$) were collected from hospitals worldwide during 2020 from 13 different sites—Argentina ($n = 1$), Australia ($n = 2$), Germany ($n = 1$), India ($n = 2$), Italy ($n = 1$), Panama ($n = 1$), Spain ($n = 1$), Turkey ($n = 1$), United Kingdom ($n = 1$), and United States ($n = 2$). These isolates were shipped to a central laboratory at IHMA Europe, Switzerland, and re-identified by MALDI-TOF or molecular methods. The MICs were performed by broth microdilution method in line with CLSI susceptibility testing standards—CLSI M27-A4 and M38-A2—methodologies and percentage susceptibility (%S) were calculated. Antifungals tested were amphotericin B (AMB), anidulafungin (ANID), fluconazole (FLU), isavuconazole (ISA), caspofungin (CASP), micafungin (MIC), posaconazole (POS), and voriconazole (VOR).

Results:

Table 1: Summary MIC and susceptibility data of *Candida* spp. isolates for all countries combined

Conclusions: The data from the ARIA 2020 study indicate that overall antifungal resistance is low among the *Candida* spp. isolates except for *C. glabrata* and *C. krusei* where resistance to one or more antifungal agents was observed. However, there was no significant difference in susceptibility pattern was observed when susceptibility data of *C. glabrata* and *C. krusei* from different continents were compared. The emergence of resistance was evident among *C. auris* isolates as they have shown reduced susceptibility to azoles in this study.

Antifungal resistance surveillance and investigation into resistance mechanisms are of paramount importance. The ongoing ARIA surveillance study will provide resources to monitor antifungal resistance trends, provide key information to caregivers and provide essential information with respect to the development of novel antifungal agents.