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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/correct 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 have 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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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 predominantly grouped by country except for 16 fluconazole-resistant isolates from Bogotá, 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 Bogotá 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 predominantly from the north coast, fluconazole-resistant isolates were from a wider geographic area in Colombia, and echinocandin-resistant isolates were from Bogotá. 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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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 (BAL) 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 BAL 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 BAL 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.