Objective: Candida auris (C. auris) infections are associated with nosocomial transmission, intrahospital transmission, poor treatment outcomes, and higher mortality. Prompt detection, earlier initiation of therapy and effective surveillance can control C. auris in hospitals. We aimed to study epidemiology, risk factors, and therapeutic management of invasive infections caused by C. auris in patients with hepatobiliary disease.

Methods: Single-center, prospective study of patients with suspected invasive fungal infections between January 2017-December 2021 in the patients with hepatobiliary disease. Demographics, comorbidities, and laboratory variables were recorded. The patient's culture isolates were identified by VITEK 2 (BioMerieux, India) and antifungal susceptibility confirmed by broth microdilution in accordance with CLSI guidelines. The final outcomes considered were mortality within 2 months after discharge of the patient with the viable pathogen.

Results: Total of 109 isolates of C. auris from 73 patients, blood 23 (31.5%), abdominal fluids 29 (35.5%), urine 90 (47.6%), respiratory 3 (4.1%), liver abscess 2 (0.3%), pancreate ice abscess 1 (0.5%), and wound infections 31 (5.5%). Underlying disease was chronic liver disease 49 (60.8%), post transplant liver patients 15 (19.5%), acute liver failure 2 (1.3%), acute pancreatitis 1 (1.3%), and pancreatic neuroendocrine tumor 1 (1.3%). 18 (25%) patients were discharged, the mortality rate was 54 (74.6%). Risk factors were MELD 40 (5.55), Child C 0 (0.05) and CTP score above 2.12. Prior use of steroids (P = 0.02), neomycin (P = 0.03), prolonged hospital stay (P = 0.02), the use of broad-spectrum antibiotics >7 days (P = 0.05) were the risk factors significantly associated with the development of C. auris infections, and higher mortality. Co-morbidities, acute renal failure, diabetes, and hypertension were not significant in invasive fungal infections and invasive candidiasis.

Conclusions: Our study depicts the spectrum of invasive infections caused by C. auris, its prevalence, risk factors, and therapeutic options. The presence of risk factors, neomycin, neomycin, broad-spectrum antibiotic use, and a hospital stay >7 days should prompt toward escalating diagnostic measures for rapid identification of C. auris infection and therapy.

Active screening of patients with risk factors can also reduce mortality. The study results also help to guide empiric therapy with echinocandins as azoles and amphoteric B show high resistance in these isolates.

P429 Bloodstream detection for the diagnosis of disseminated histoplasmosis in people living with HIV/AIDS in Southern Brazil - a year of implementation

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Background: Disseminated histoplasmosis (DH) is an important opportunistic disease in HIV/AIDS patients. Objective: We aimed to report partial results of the implementation of the histoplasmosis antifungal therapy protocol as a routine test for the diagnosis of DH in people living with HIV/AIDS (PWHAs) admitted to a reference hospital in Southern Brazil.

Methods: The study was performed in a tertiary hospital, which is recognized as a regional reference center to 24 cities for the treatment of PWHAs. At this service, since the beginning of 2021, a new protocol for DH investigation was adopted, including the systematic execution of antigenic tests for histoplasmosis (Histoplasma GM Elisa, DEMET) at PWHs. We retrospectively evaluated data from all of those patients diagnosed with DH in the last 2 years, between March 2021 and March 2022. The study was approved by our university ethics committee (CEP/FURG/ NSP 23/2018).

Results: Within the 12 months prior, 245 patients from our hospital were investigated by Histoplasma GM Elisa through urine samples. A total of 19 were diagnosed with DH through this test, resulting in a prevalence of 7.9%. Interestingly, none of them were also investigated by antibody detection through immunodiffusion test (IMMY), being all negative in this serology. DH was associated to intravenous drug use in 21% of these patients (40/191), and concomitantly with Mycobacterium tuberculosis infection was detected in 37% (7/19). Half of the patients (10/19) were severe immunosuppressed (CD4 lymphocytes < 200 cells/µL), 21% (n = 4) had histories between 100 and 200 cells/µL, and 21% (n = 4) had >200 cells/µL. The majority of the patients (79%) in 14 had advanced signs of DH, showing pulmonary impairment, bone, renal, neurologic, and/or skin lesions and lymphadenopathy, suggesting late diagnosis, 14 (73.7%) of the patients had few signs of DH (suggesting proctitis), and two patients were diagnosed before the onset of the classical manifestation, with the strategy of use of GM Histoplasma Elisa as a screening tool. Although the antifungal treatment, five of them (26.3%) died.

Conclusions: The systematic use of the test to detect a specific biomarker in urine samples has improved remarkably the diagnosis of DH in PWHAs in our hospital (19 cases in one year). In addition, since we could diagnose DH with positivity in five patients, we suspect that in regions where DH is hyperendemic, the GM Histoplasma Elisa could be used as a screening tool for all AIDS patients, similar to what is proposed in cryptococcal disease. More robust studies must be performed to verify this strategy, and its benefits to an early diagnosis, resulting in a better quality of life, better prognosis, and consequently reduction of the mortality rate.

P440 Genealogical protocol applied to the identification and production of new biomarkers with potential use for the diagnosis of histoplasmosis

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Objective: To identify and produce biomarkers with potential use for the specific diagnosis of H. capsulatum infection.

Methods: Here, we design a novel strategy to search and select new Candida genes for biomarkers that integrate the use of a computational analysis model that includes the application of bioinformatics tools such as OrthoMCL, BLASTp, TargetScan, and SignalP, applied on a local collection of proteome database obtained manually from Gasca-Fuentez-NCBR, and the analysis of published bioinformatic and bibliographic data sets, including a previous proteome database obtained from pathogen-year phase H. capsulatum culture filtrates, a Histoplasma yeast and mycelium transcriptional databases, and a yeast-pelicule database from Histoplasma-susceptible-positive patients.

For the screening of the Candida, an internal protocol for the production of recombinant proteins in prokaryotic and eukaryotic systems was applied. Obtaining polyclonal antibodies (PAb) specific for each biomarker was carried out by applying an immunization protocol for RABEs mice. Finally, the computational model was experimentally validated, evaluating the reactivity and specificity of PAb anti-Histoplasma with fungal culture extracts and samples from patients with histoplasmosis.

Results: The construction of expression vector for each candidate and the production of these genes were achieved using a standardized protocol for the production of recombinant proteins.
Polycystic adhesions (PA) anti-histoplasma were obtained and shown to be reactive against purified H. capsulatum- antigens. Finally, we confirmed the presence of these antigens in year culture extract of H. capsulatum and demonstrated the immunoreactivity of anti-Histoplasma PA with urine samples from patients previously diagnosed with histoplasmosis.

Conclusions: The generation of novel strategies that combine data analyses, computational tools, and transcriptomic and proteomic techniques could be very useful for the identification of new biomarker genes and the development of microfluidic diagnostic tests for important pathogens.

P461
Molecular identification, genotyping, and antifungal susceptibility of Trichophyton species isolated from clinical samples of patients at various parts of the Indian subcontinent

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Objectives: (1) To study mycological characteristics of strains belonging to Trichophyton and its related genera obtained from clinical samples of patients from India. (2) Molecular identification by intergenic spacer (IGS) region 1 sequencing of the rDNA locus. (3) Genotyping of the major causative agents, T. aureus, and its in vitro drug susceptibility testing.

Materials and Methods: A total of 35 clinical isolates of Trichophyton species were collected from NCMC (National Culture collection of pathogenic fungi) NGMER, Chandigarh along with different health institutions of India. These isolates were cultured on agar, blood, selenite, brain heart infusion broth, Sabouraud broth, and wound discharge over a period of 12 years (2006-2018). The isolates were molecularly characterized and genotyped using IGS-1 region sequencing. In vitro drug susceptibility testing of the isolates was performed against amphotericin B, fluconazole, itraconazole, and posaconazole according to the CLSI M27-A1 guidelines (CLSI 2018).

Results: Predominant underlying risk factors identified were presence of a insulin dependent, use of broad-spectrum antibiotics, presence of immunosuppressed conditions such as diabetes, hypothyroidism, and asthma. A total of 47.25% (n = 35) of the 75 isolates were identified as T. aureus, 6 were T. ketok (5%), and 2 were Catno Trichophyton dematiae (2.6%). Trichophyton aureus genotypes III (22, 41%) was the most common type, followed by genotypes IV (12, 22%), II (9, 15%), and VII (2, 4%). In addition to the 13 known species in Trichophyton, one novel genotype was identified. In this study, T. aureus isolates showed high MIC ranges against amphotericin B (0.04-4.0 µg/ml) and fluconazole (0.25-64 µg/ml). Relatively low MIC ranges were found in the case of voriconazole (0.05-5 µg/ml), Posaconazole (0.06-1.0 µg/ml), and itraconazole (0.06-1.0 µg/ml). Voriconazole appeared to be the most active drug in T. aureus isolates. The MIC for all the drugs were comparatively lower in the case of T. nr aureus strain.

Conclusions: Trichophyton aureus remains the most common otologyst of Trichophyton in India and presents a challenge for both diagnosis and treatment. With increasing drug resistance, therapeutic options are limited, and antifungal regimens with triazole especially triazole appear to be the best. Accurate timely identification, removal of underlying immunosuppressive venue lines, and triazole-based treatment along with control of underlying conditions were associated with favorable outcomes. Identification of the novel genotypes has epidemiological implications and requires further work up.

P462
Bacterial and fungal infection in COVID-19 diagnosed cases in a tertiary care ICU setting in the wake of second wave in Kolkata, India

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Prolonged mechanical ventilation support was associated with the development of nosocomial candidaemia and bacteremia. Parallel to the developments in the field of diagnosis and treatment, an increase in the incidence of fungal infections and the number of patients who are in the risk group for the development of opportunistic fungal infections have been observed in recent years. Among the hospitalized patients, those at risk or in terms of fungal infections are immune compromised ICU patients. The care of Candida infections amongst critical care patients is very important and may prove severe mortality if not diagnosed, treated, and handled effectively, and promptly.

P463
Altered expression of fungal CoRf, human glucose-regulated protein 78 (GRP78), and predicted miRNA in macrophages and model diabetic mice infected with Rhizopus oryzae

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Rhizopus oryzae is one of the most common causes of mucormycosis. Among the virulence factors of the Mucorales, CoRf protein has recently been identified, which causes the invasion of R. oryzae into endothelial cells. In this study, we aimed to examine the reaction between GRP78 and its level of human cell and different groups of mice and CoRf at the surface of R. oryzae. We evaluated the relative expression of GRP78 and CoRf genes and changes in the expression of some miRNA that target the human GRP78 gene.

Methods: In this study, the relative changes in gene expression were studied. In three groups (1) Macrophages derived from human monocytes: monocytes from the blood of healthy donors were isolated using Ficoll and in RPMI 1640 medium containing PCA 10% and with penicillin-streptomycin after 2 weeks were differentiated into macrophages. Two groups were investigated, including control and infected with R. oryzae hyphae, for 6 and 16 hours after infection. (2) Histological dissection mucormycosis model: Seven groups of male BALB/c mice were examined in control, infected, and treated groups with Liposomal amphotericin B. (3) Human mucormycosis model: In this study, two samples of patients with braincerebral mucormycosis with diabetes mellitus treated and untreated with liposomal amphotericin B were examined. Total RNA extraction and qDNA synthesis were performed from the studied samples. The relative expression changes of the target genes and miRNA were evaluated using real-time PCR carried out using TaqMan-based detection methods.

Results: Microarray-derived macrophages had a steady pattern in relative changes in gene expression. An increase in expression of two genes, GRP78 and GRP78, was observed in the samples, and all miRNA targeted by the GRP78 gene included lncRNA-16-5p; hsa-miR-535-5p and hsa-miR-95-5p showed a decreasing pattern. In the mice mucormycosis model, relative gene expression changes were observed, and miRNA-511-5p showed increased expression deviation in all groups. The clinical sample of diabetic patients with braincerebral mucormycosis also had a common pattern of GRP78 and CoRf increased expression gene. The has-miR-16-5p has-miR-535-5p have increased expression, while has-miR-95-5p decreased expression.

Conclusion. After validation, these miRNA can be used as valuable markers in mucormycosis diagnosis and treatment processes.

P464
Detection of causative agents of infectious keratitis in patients from western rajasthan

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Objectives: To determine the spectrum of causative agents, the related risk factors, and their association in patients of infectious keratitis.

Materials and Methods: An observational study was conducted over a period of 1 year from August 2018 to January 2020, which included 100 patients attending the Ophthalmology OPD with features of keratitis. Ophthalmological examination was followed by corneal scrapings' collection, which were subjected to culture, microscopy, and molecular diagnostic tools. Bacterial isolates were identified by conventional methods and MicroScan Walkaway system while the fungal isolates were identified conventionally. Pan-fungal primers were used to detect fungal elements directly from the sample.

Results: Out of 100, 41 cases were positives by culture, of which 12 (29.29%) held fungus and 29 (68.29%) had bacterial keratitis. Paenaurum spp. accounted for 33.3% of fungal and Panfilomaras aurmonorae accounted for 55.5% of the bacterial isolates. Fungal natural was detected in 45% using gas fungal primers. Cases were maximally recorded during July-October. Traumatic history was present in 78%, patients caused by vegetative matter (44%). A male predominance (87%) was also observed. Four patients underwent enucleation in spite of rigorous management.

Conclusion: Poorer prognosis emphasizes the need for faster diagnosis, which can detect the causative agents from the clinical specimen itself, reinforcing the concept of clinical instamgents.