P086

Clinical outcome and *in vitro* antifungal susceptibility of clinical isolates of rhino-orbito-cerebral mycosis associated with post COVID 19 from North India

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Objectives: This study aimed primarily to determine the etiology, clinical features, and comorbidities of patients with rhino-orbito-cerebral mycosis. Secondly, antifungal susceptibility pattern of the isolates and lineage by ITS-sequencing was also studied.

Methods: The study was conducted from May to December 2021 on all suspected cases of rhino-orbito-cerebral mycosis in post-COVID-19 patients at a tertiary care center. Data pertaining to demographics, recent COVID-19 infection, clinical features, comorbidities, laboratory, radiological investigations, management, and outcomes were collected after obtaining informed consent from all patients. Staging of ROCM was done using the proposed code Mucor and diagnosis of COVID-19 was done on basis of real-time polymerase chain reaction (RT-PCR) test. KOH Mount examination, fungal culture, and histopathological examination was performed on samples collected endoscopically or post-debridement. Mucormycosis was proven based on fungal culture or specific histological features from biopsy specimens. *In vitro* susceptibility profiles for antifungal drugs as per CLSI microbroth dilution method (M38-A2) was studied by HiMIC^{TM} plate (HiMedia) for amphotericin B, voriconazole, posaconazole, itraconazole, and isavuconazole. MIC ranges and the drug concentrations required to inhibit 50% (MIC50) or 90% of isolates (MIC90) were determined. ITS Sequencing was also performed on representative isolates.

Results: A total of 70 patients were diagnosed with mucormycosis. Rhino-orbital and rhino-orbito-cerebral forms were observed in 35.7% of cases each. Diabetes mellitus (DM) was present in 95.7% patients while 78.5% of the patients were treated with corticosteroids in recent past, and 25.7% presented with active COVID-19 pneumonia. Most cases showed onset of symptoms of mucormycosis between 29 ± 17 days from diagnosis of COVID-19. On imaging, orbit was involved in 52.8% and cranial involvement is seen in 35.7% of patients. Diagnosis of mucormycosis was established on KOH direct microscopy 68.6%, culture 47.14%, histopathology 55.7%. Isolates obtained were *Rhizopus arrhizus* (42.4%), *Apophysomyces* variabilis (3.03%), and *Aspergillus* spp (69.7%) while mixed infection was seen in 42.4%. The MIC50 and MIC90 of amphotericin B for *R. arrhizus* strains were 0.25 and 4 μg/ml; and MIC50 and MIC90 results for itraconazole, posaconazole, and isavuconazole were 8 and 8, 2 and 2, and 2 and 8 μg/ml respectively. *Aspergillus* spp was susceptible to amphotericin B (38.8%), itraconazole (50%), voriconazole (50%), posaconazole (11.1%), and isavuconazole (44.4%). Overall treatment included intravenous amphotericin B along with functional endoscopic sinus surgery (FESS)/paranasal sinus (PNS) debridement in 68.2%, orbital exenteration in 4.2%, orbital decompression in 11.4% patients and partial maxillectomy in 22.8% cases. Intraorbital injection of amphotericin B was administered in 15.7%. At final follow-up, mortality was 19.7%. *In vitro* MICs showed that amphotericin B was the most active compound against most species.

Conclusion: High index of suspicion, early diagnosis, and appropriate management of mucormycosis can improve survival. Rational use of steroids and strict glycemic control in diabetic patients can prevent occurrence of mucormycosis. Use of standard methods for antifungal susceptibility testing to guide antifungal treatment may be clinically useful in cases of treatment failure.

P087

A clinicomycological study of dermatophyte infection including antifungal susceptibility testing in patients attending a tertiary care hospital in north-western state of rajasthan

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Objectives: Treatment-resistant ermatophytosis caused by *Trichophyton rubrum (T. rubrum)* or *Trichophyton mentagrophytes (T. mentagrophytes)/Trichophyton indotineae* have recently emerged as a global public health issue. This phenomenon is spreading, and is particularly important in endemic areas such as India. However, due to lack of focused studies on dermatophyte prevalence, there is paucity of such data from Rajasthan. Hence, for better understanding of the prevalence, antifungal susceptibility, and resistance pattern to enable best empiric treatment the present study was done.

Materials & Methods: A total of 100 patients attending Dermatology and Venereology outpatient department during the period of December 2019-October 2020 were enrolled under this prospective study. Samples were subjected to KOH, culture examination, and identified by standard techniques at the mycology section of department of microbiology. Antifungal susceptibility testing was performed by Microbroth dilution as per CLSI guidelines (M38-A2) with the following drug concentration ranges—amphotericin B 0.0313-16 μg/ml; flucytosine 0.125-64 μg/ml, ketoconazole 0.0313-16 μg/ml. Itraconazole and voriconazole 0.0078-4 μg/ml, fluconazole 0.0625-32 μg/ml, caspofungin 0.0313-16 μg/ml and terbinafine 0.0156-8 μg/ml.

Results: Among 100 clinical samples tested, culture positivity was found to be 63%, including *dermatophytes* (76.1%), non-*dermatophytes* molds (19.04%), and yeasts (~ 4%). Among *dermatophytes*, *T. mentagrophyte* was the predominant isolate (33.3%) followed by T. rubrum (29.1%). Most common clinical type was tinea cruris (53%) followed by tinea corporis (23%). Itraconazole and voriconazole were found to be most effective at MIC range of 0.0078-4 μg/ml for *T. mentagrophyte* and at 0.0078-1 μg/ml for *T. rubrum*, mostly corroborating with clinical outcome. Itraconazole resistance was highest (57%) in *T. rubrum*, whereas terbinafine resistance (>0.2 μg/ml) was seen in ~ 31-37% of these two major species.

Conclusion: It is important for clinicians to emphasize upon microbiological diagnosis of dermatophytosis as these infections have many mimics, highlighting the need of confirmation by culture. High prevalence of terbinafine resistance in both *T. mentagrophyte* and *T. rubrum* and itraconazole resistance in T. rubrum is of concern and highlights the need to routinely perform antifungal drug susceptibility testing as a necessary adjunct to treatment and for surveillance.

P088

Molecular identification and antifungal susceptibility of pathogenic yeasts from the China Antifungal Resistance Surveillance Trial (CARST-fungi) Study

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Objectives: Invasive fungal diseases (IFDs) caused by yeast species have considerable morbidity and mortality, especially in immunocompromised hosts, and those with antifungal resistance represent a major clinical challenge. In order to have a comprehensive understanding of the characteristics of epidemiology and antifungal susceptibilities in clinical yeasts, the China Antifungal Resistance Surveillance Trial (CARST-fungi) study, a prospective national surveillance program for IFDs in mainland China, was conducted.

Methods: The CARST-fungi study encompassed nine 'rank-A tertiary' hospitals distributed throughout different cities in China in the year 2019-2020. All yeast isolates recovered from various clinical samples were subcultured and identified by sequencing of the internal transcribed spacer (ITS), 28S ribosomal subunit (D1/D2), and the intergenic spacer (IGS, for *Trichosporon* spp. and *Cryptococcus* spp.). Antifungal susceptibilities of fluconazole (FLC), itraconazole (ITC), voriconazole (VRC), posaconazole (POS), caspofungin (CAS), anidulafungin (ANF), micafungin (MCF), and amphotericin B (AMB) against the yeast isolates were performed according to the Clinical and Laboratory Standards Institute (CLSI) M27-A4 broth microdilution method.

Results: A total of 269 nonduplicate yeast isolates from 261 patients were collected. About half of the yeast isolates (127, 47.9%) were recovered from blood, followed by ascetic fluid (46, 17.4%). *C. albicans* remained the most prevalent (120, 44.6%), followed by *C. parapsilosis* complex (50, 18.5%), *C. tropicalis* (40, 14.9%), and *C. glabrata* (36, 13.4%). Among *C. albicans*, 5 (4.2%), 11 (9.2%), 6 (5%), 10 (8.4%) isolates were resistant/non-wide-type (NWT) to FLC, ITC, VRC, and POS, respectively, and 9 (7.5%) isolates were cross-resistant to triazoles. As for *C. parapsilosis* complex, only 1 (2.4%) isolate of *C. parapsilosis sensu stricto* was cross-resistant to FLC and POS, while all the 9 C. metapsilosis isolates were wide-type (WT) to triazoles. However, only 45% (18/40) *C. tropicalis* were susceptible/WT to triazoles, and 12 (30%), 3 (7.5%), 8 (20%), 19 (47.5%) isolates were resistant/NWT to FLC, ITC, VRC, and POS, respectively, and 8 (20%) isolates were cross-resistant to triazoles. Among *C. glabrata*, 2 (5.6%) isolates were resistant to FLC and the remaining 34 isolates were susceptible-dose dependent (SDD), 20 (55.6%), and 8 (22.2%) isolates were resistant/NWT to VRC and POS, respectively, and 4 (10.3%) isolates were cross-resistant to triazoles. One isolate of *Meyerozyma guilliermondii* was NWT to POS. Except for 3 isolates of *C. tropicalis* exhibiting intermediate to CAS and ANF, and 2 isolates of *C. glabrata* were cross-resistant to CAS, MCF, ANF, which were also NWT to POS and defined as multidrug-resistant, other isolates of common *Candida* species were all susceptible to echinocandins. All yeast isolates tested in this study were WT to AMB (MICs $\leq$ 2 μg/ml). For less common species, 1 isolate of *Rhodotorula mucilaginosa* exhibited high MICs to echinocandins and FLC, and 1 isolate of *Trichosporon asahii* showed high MICs to all the antifungals tested except AMB.

Conclusion: Among 269 yeast isolates from the CARST-fungi study, *C. albicans* remain the most predominant, followed by *C. parapsilosis* complex, *C. tropicalis*, and *C. glabrata*. Triazole-resistance is notable among *C. tropicalis* and *C. glabrata*. Multidrug-resistant isolates of *C. glabrata* and less common yeast have been emerging.

P089

Candidemia: prevalence, species characterization ,and the antibiotic susceptibility profile from a tertiary care hospital in north india

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Objectives: The aim of this study was to characterize the *Candida* spp. isolated from blood cultures and determine the antifungal susceptibility pattern of the *Candida* species prevalent in a tertiary care hospital in North India.

Methods: This retrospective study was conducted in Department of Microbiology of a tertiary care hospital in North India from April 2020 to March 2022. All blood cultures received in the department during this period were included in the study. *Candida* species isolated were identified and antifungal susceptibility testing was performed by VITEK as per standard protocol, The susceptibility pattern of 50 isolates was also performed by the broth microdilution method as per Clinical and Laboratory Standards Institute guidelines (CLSI) and the results were compared with VITEK results.

Results: Out of 21 804 blood cultures received during this period, 177 grew *Candida* species. Therefore, the overall prevalence of *Candida* species was 0.81% in our study. The incidence of bloodstream infection caused by non-*albicans Candida* species (80%) was higher than *C. albicans* (20%). Among NAC species, *C. tropicalis* (45%) was the most common, followed by C. pelliculosa (15%).

Candidemia was predominantly observed in ICU patients. Resistance was seen in 14.1% isolates to voriconazole and fluconazole, 4.2% to flucytosine and 3.9% to caspofungin and amphotericin-B. No resistance was seen to micafungin. A total of 15% of the isolates were resistant to more than one drug.

Conclusion: There was a predominance of non-*albicans Candida* over *C. albicans*. Maximum resistance was seen to voriconazole followed by fluconazole. Continuous surveillance is necessary to follow trends and monitor changes in epidemiological and resistance patterns in different geographical regions, especially in critically ill patients.

P090

Biofilm forming capabilities in multi-drug resistant *Candida* species with special emphasis on *Candida auris* isolated from intensive care unit patients

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Objective:

1) Biofilm forming capabilities of isolates obtained from intensive care unit (ICU) patients
2) To study the trend of antifungal susceptibility of *Candida* isolates using MIC method by VITEK-2

Methods: This is a hospital-based prospective study in which *Candida* isolates from urine, blood, and BAL fluid of ICU patients from March 2021 to February 2022 were included. Conventional identification methods were performed for all isolates, speciation was done by MALDI-TOF. Biofilm formation by microtiter plate method and anti-fungal susceptibility was performed by VITEK-2.

Results: In the present study, out of 360 positive fungal isolates, 20% *Candida* isolates (72) were obtained from the ICU patients. *Candida tropicalis* (45.2%) was the most common fungal isolate among all non-*albicans Candida* spp followed by *C. parapsilosis*, and *C. auris*. The biofilm formation was tested by microtiter plate method on *Candida* isolates. *Candida auris* showed strong biofilm formation tendency (28.5%). In this study, 16.6% of *Candida* isolates had resistance against fluconazole out of which 6 isolates were multiresistant to other antifungal. Use of automated machines helped in early identification of these species 24-48 h less than the conventional methods.

Conclusion: Parallel increase in number of non-*albicans Candida* beside *C. albicans* could be because of patients on prolonged antimicrobial therapy, immunosuppressive drugs, varied comorbidities and species selection in the presence of certain antifungals, given the higher level of resistance expressed by NAC. Biofilm production a probable cause for increasing antifungal resistance and therapeutic failure. NAC species are emerging as potential threats to cause infection and posing a therapeutic challenge. Early empirical antifungal therapy and further research to improve diagnostic, prevention, and therapeutic strategies are necessary to reduce the considerable morbidity and mortality.

P092

Otilonium bromide is a potent antifungal agent against fluconazole- and flucytosine-resistant *Cryptococcus neoformans* strains

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Objectives: *Cryptococcus neoformans* is a worldwide threat causing global pulmonary and systemic infections in humans. However, only three drugs are available for the treatment of cryptococcosis: fluconazole, amphotericin B, and flucytosine. Drug repurposing, the process of using a drug for an indication different from the initial indication, is an emerging approach in the discovery of new antifungal drugs. We've set out to identify repurposable drugs for cryptococosis.

Methods: We screened the United States FDA-approved drugs for antifungal activity against *C. albicans* lab strain SC5314. We tested the antifungal profile against major human fungal pathogens including *C. neoformans*. In order to uncover the mechanism of action against *C. neoformans*, lab strain H99 was used to evolve drug resistant adaptors. Next-generation sequencing technology was used to investigate the genome change of drug resistant adaptors. SNP calling was also performed to identify possible mutations causing drug resistance.

Results: Here we found that otilonium bromide (OTB), which is extensively used to treat patients affected by the irritable bowel syndrome, had broad-spectrum antifungal activity. OTB was active against fluconaozle-resistant and flucotysine-resistant *C. neoformans* strains. Furthermore, we found resistance to OTB was mostly due to duplication of chromosome 6. Further work will be on the identification of the Candidate gene on chromosome 6 which is required OTB resistance.

Conclusion: This study highlights the potential application of OTB as a new antifungal drug against *C. neoformans* strains susceptible or resistant to commonly used antifungal drugs.

P093

A novel GAL4-like transcriptional regulator modulate the azoles sensitivity of *Exophiala dermatitidis*

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