P048

Antifungal susceptibility and mechanism of azole resistance in *Candida albicans* clinical isolates from oropharyngeal candidiasis patients in Iran

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Objectives: Oropharyngeal candidiasis (OPC) is the most frequent opportunistic fungal infection in head and neck cancer patients. This study was done to investigate the azole susceptibility of *Candida albicans* (*C. albicans*) from oropharyngeal candidiasis (OPC) patients and to determine the relationship between ERG11 gene mutations in these isolates and azole resistance.

Methods: A total of 324 clinical isolates of *Candida* species were collected. Identification of the oral clinical samples was determined by culturing on CHROMagar, carbohydrate assimilation and ITS sequencing methods. Azole susceptibility was tested *in vitro* in microdilution studies. The ERG11 genes of 42 isolates of *C. albicans* were amplified and sequenced.

Results: Of the 324 isolates collected, 44.75% (145 isolates) were *C. albicans*. ERG11 gene was sequenced in 42 isolates. In total, 14 missense mutations were detected in ERG11 genes from 42 isolates. Among them, A945C and T495A substitutions were most prevalent and were known to cause fluconazole resistance.

Conclusions: A total of 14 mutations in the ERG11 gene were identified in azole-resistant *C. albicans* isolates, which indicated a possible relation with the increase in resistance to azole drugs and the recurrence of oropharyngeal candidiasis. Finding more mutations and relevance requires studies with a higher number of samples.

P049

Candidemia: Isolate profiling and antifungal susceptibility testing experience from Jodhpur, Western India

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Objectives: The study was undertaken over a 9-month study period at a tertiary care and super specialty hospital situated in Jodhpur, Western Rajasthan, India, with the following objectives:

1. To determine the prevalence of Candidemia among all blood culture positives
2. Isolate profiling or speciation of *Candida* spp.
3. Antifungal susceptibility testing of the *Candida* isolates

Methods: Automated blood culture bottles (BD BACTEC 960) that flagged positive were taken up for gram staining. Those bottles which showed gram-positive budding yeast with or without pseudohyphae were selected as the study isolates for candidemia. All such bottles were subcultures on Sabouraud's dextrose agar and incubates aerobically at 37˚C for 2-5 days. Creamy, pasty, off-white colonies of *Candida* were further taken up for identification by germ tube testing, CHROM agar, and VITEK-MS.

Antifungal susceptibility testing was performed for all isolates by VITEK 2 against fluconazole, caspofungin, voriconazole, micafungin, flucytosine, and amphotericin B.

Results: During the study period May 1, 2021-January 31, 2022, the microbiology laboratory received a total of 10 841 automated blood culture bottles, of which, overall, 1051 flagged positive. Budding yeasts were seen in 92 bottles.

The prevalence of candidemia was found to be 1.49%. Budding yeasts made up 8.75% of all positive blood cultures.

Conventional and automated identification methods showed the non-*albicans Candida* made up the majority (85.87%) of isolates. *Candida tropicalis* (43.47%) was the most common species overall, followed by *C. parapsilosis* (17.37%), *C. albicans* (14.13%), *C. guilliermondi* (5.43%), *C. glabrata* (5.43%), and *C. auris* (4.34%). Two isolates each of *C. kruzei*, *C. utilis*, *C. rugosa*, and *Trichosporon* spp. were also obtained.

The antifungal susceptibility testing results for the commonest species *C. tropicalis* showed susceptibility of 90% against caspofungin and micafungin, 82% against fluconazole and voriconazole, 45% for flucytosine, and 47.5% against amphotericin B. *C. albicans* showed 100% susceptibility to fluconazole, and caspofungin, while *C. parapsilosis* showed a lower susceptibility percentage against all drugs in the panel. The two strains of *C. auris* were solely susceptible to caspofungin.

Demography of the patients showed a male preponderance (M:F ratio was 2:1). The mean age of patients was 44 years.

Conclusion: The prevalence of candidemia in Jodhpur, Western India was found to be 1.45%, a figure much less than that reported from most other tertiary care centers of the country. The commonest isolate was *C. tropicalis* (43.47%), same as that reported from most Indian studies. Our isolates were largely (>90%) susceptible to the drug of choice caspofungin, including the multidrug-resistant *C. auris* strains. The study findings reflect a low prevalence of candidemia, indicating adequate antibiotic and antifungal stewardship practices at Jodhpur.

P050

***Candida auris* and non- *auris* candidemia in adult patients in a tertiary care set-up, New Delhi, India**

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Objectives: The aim of this study was to determine the species distribution, compare Candida *auris* and non-*C. auris* candidemia risk factors and antifungal susceptibility pattern of candidemia cases in adult patients at a tertiary care hospital, New Delhi, India.

Materials and Methods: *Candida* species identification was performed by phenotypic methods, VITEK (Biomerieux, France), and DNA sequencing (PGIMER, Chandigarh). The antifungal susceptibility was performed by broth microdilution method as per CLSI M27-A4 guidelines 2017.

Results: Out of 1274 blood samples, 70 samples (5.5%) yielded the growth of *Candida* species. There was a predominance of NAC spp. over *C. albicans* in candidemia patients. *C. auris* (12.85%, 9/70) and non-*auris* candidemia (87.14%, 61/70) was isolated in this study. In non-*auris* candidemia, *C. tropicalis* (28.57%, 20/70) was the predominant *Candida* species followed by *C. parapsilosis* (22.85%, 16/70), *C. glabrata* (14.28%, 10/70). Rare species among NAC spp. included *C. mesorugosa*, *C. lusitaniae*, *C. krusei* and *C. haemulonii* were isolated. The most common predisposing factor for *C. auris* and non-*auris* candidemia was urinary catheter (72.85%, 51/70) followed by an increased period of hospitalization (42.85%, 30/70), diabetes mellitus (21.5%, 15/70), etc. The significantly associated risk factor associated with *C. auris* was diabetes mellitus ($P = .02$). The overall resistance was 22.57% to all antifungal drugs. The multidrug resistance (MDR) was noted in 5.71% of isolates.

Conclusions: Early identification of risk factors, *Candida* speciation, and timely management are crucial for the outcome of candidemia cases. Non-*albicans* species were predominant over *C. albicans* depicting the change in the epidemiology and emergence of MDR *Candida* spp. like *C. auris*, *C. glabrata*, *C. mesorugosa*, *C. lusitaniae,* and *Pichia kudriavzevii* (*C. krusei*). This warrants routine antifungal susceptibility testing (AFST) and close monitoring. The knowledge of local epidemiological profiles of *Candida* spp., accurate species identification, and their antifungal susceptibility is crucial for overall patient management.

P051

A case of recalcitrant sporotrichosis by infection of *Sporothrix* globosa

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Objectives: Sporotrichosis is the leading subcutaneous mycosis caused by the *Sporothrix* (*S.*) *schenckii* complex. *S. globosa* is the causative organism of fixed sporotrichosis in Korea. The preferred regimen of cutaneous sporotrichosis is itraconazole for 3-6 months, however, there were few studies for recalcitrant sporotrichosis.

Methods: In 2018, we performed a histological examination of a patient who suffered sporotrichosis for 3 years and cultured part of the specimen. Despite various regimens for years, improvement and exacerbation were repeated, so we took another skin biopsy and cultured it in 2021. Isolates from the 2018 and 2021 lesions were identified as *S. globosa* by ribosomal DNA ITS sequencing (GenBank accession number: MH499862 and MH499863). The *in vitro* antifungal sensitivity tests were performed by broth microdilution method according to CLSI M38-A2 guidelines or Sensititre YeastOne® manufacturer's instructions. They were incubated at 30°C in a non-CO2 incubator for 7 days.

Results: In 2018, histologically, we observed chronic inflammatory granuloma comprising lymphocytes, histiocytes, and giant cells, and several spores with periodic acid-Schiff (PAS) staining. Microscopic findings and ITS sequences of rRNA gene were identical with S. globosa. The antifungal susceptibility profile in 2018 revealed sensitive to terbinafine (0.125 μg/ml), and moderate to high MIC values for amphotericin B (2 μg/ml), itraconazole (>16 μg/ml), voriconazole (>16 μg/ml), and echinocandins (>16 μg/ml). Treatment with terbinafine, itraconazole, or amphotericin B, the skin lesions were partially improved, but were not cured. In 2021, we took another skin biopsy and culture specimen. Histopathological and mycological examination results were the same as before. The antifungal susceptibility profile revealed sensitive to itraconazole (0.5/ml), and high MIC for others. Clinically, skin lesions were not improved with the use of itraconazole 200 mg/d. Itraconazole 400 mg/d with local heating induced moderate improvement. There was no evidence of immune deficiency.

Conclusion: We experienced recalcitrant sporotrichosis that did not respond to itraconazole and terbinafine, and the sensitivity of antifungal was changed. In this case, the combination treatment including local heating, saturated KI may be considered, and frequent antifungal susceptibility tests are needed.

P053

Invasive Mucormycosis (Zygomycosis) -Pre-Covid Era and Covid Era: a retrospective study at a tertiary care centre, chennai

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Objectives:

- To compare the prevalence and clinical presentation of Mucormycosis in pre-COVID era (January 2017-December 2019) and COVID era (January 2020-till date).
- To compare the AFST pattern of the zygomycetes causing Mucormycosis in pre-COVID era and COVID era.

Methods: This is a retrospective, hospital-based descriptive study. This study included patients admitted during the pre-COVID and COVID era at a tertiary care center, Chennai. The cases were categorized into two: (1) possible mucormycosis cases which included direct microscopy [Potassium hydroxide (KOH) and histopathological examination] positives and (2) confirmed cases which included direct microscopy and culture positives. Direct microscopic examinations like KOH wet mount and histopathological examination (H and E stain and special stains) were performed. Samples were cultured on Sabourauds dextrose agar and identification was done by analyzing the microscopic morphology using lactophenol cotton blue mount. AFST was performed for culture positive isolates with amphotericin B, itraconazole, posaconazole, voriconazole and isavuconazole by microbroth dilution method according to CLSI M38-A2.

Results: During the Pre-COVID era, out of the 365 samples received in the laboratory, 35 were possible mucormycosis cases. Only 17 were confirmed cases, out of which 16 grew *Rhizopus oryzae* and 1 grew *Apophysomyces elegans*. During the COVID era, among 886 samples received in the laboratory, 143 were possible mucormycosis cases, and 31 were confirmed cases that grew *Rhizopus oryzae* (26), *Rhizomucor pusillus* (2), *Mucor* sp (2), and *Basidiobolus ranarum* (1). Though the risk factors were common during the pre-COVID and COVID era, additional risk factors like steroid therapy (19.2%), and COVID infection (28.7%) were seen during the COVID era. Though clinical presentations were common during both pre-COVID and COVID era, additional complications like epistaxis (0.57%), orbital cellulitis (32.7%), and loss of smell (8.04%) were seen during COVID era. The prevalence of complications was more during COVID era compared to pre-COVID era. Treatment received during the pre-COVID era was only amphotericin B, whereas during the COVID era majority of the patients received posaconazole (74.5%) followed by liposomal amphotericin B (25.5%). The antifungal susceptibility test showed the following mean minimum inhibitory concentration (MIC) values: amphotericin B (1.8 μg/ml), itraconazole (3.6 μg/ml), posaconazole (0.31 μg/ml), and voriconazole (1.61 μg/ml) during the pre-COVID era while the mean MIC values during the COVID era had the following variations: amphotericin B (0.97 μg/mL), itraconazole (13.6 μg/ml), Posaconazole (13.4 μg/ml), voriconazole (14.5 μg/ml), and isavuconazole (1.10 μg/ml).

Conclusion: High incidence of Mucormycosis during the COVID-19 era may be related to common risk factors of COVID and mucormycosis. Though most of the risk factors and clinical presentations were similar during the pre-COVID and COVID era, serious complications like loss of vision and the percentage of complications were more during COVID era which may be attributed to the increased invasiveness of Zygomycetes during COVID infection. The high mean MIC value of amphotericin B during pre-COVID era and higher mean MIC value of posaconazole during COVID era may be contributed to the higher usage of these antifungals. Usage of the antifungal agents is the main contributor toward the resistance. Newer azole like isavuconazole which had a low mean MIC in our study, can be considered as a good therapeutic option for the future management of resistant infections. Hence timely management of the patients with an appropriate antifungal agent by performing AFST will help in the reduction of resistance in the future.

P054

Two effects of curcumin to *Candida albicans*

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Objectives: *Candida albicans* is a pathogenic yeast that causes candidiasis in immunocompromised patients. The overuse of antifungal drugs has led to the development of resistance to such drugs by this fungus, which is a major challenge in antifungal chemotherapy. The utilization of natural products is a significant trial for the development of new antifungals. Curcumin, one such natural product, has been widely studied as a drug candidate and is reported to exhibit antifungal activity against *C. albicans*. Although studies of the mechanism of curcumin against human cancer cells have shown that it inhibits heat shock protein 90 (Hsp90), little is known about its molecular function against *C. albicans*. In this work, we investigated the relationship between curcumin and Hsp90 of *C. albicans*.

Methods: For the molecular genetical analyses of *C. albicans* Hsp90, a doxycycline-mediated HSP90 strain and a HSP90-overexpressing strain of this fungus were constructed. The effect of curcumin on the gene expression of HSF1, AHR1, HOG1, and CDR1 as well as HSP90 was analyzed. Moreover, the stress responses to high temperature and osmotic pressure and the drug efflux of these strains were investigated.

Results: Curcumin reduced the transcription of HSP90 at the post-transcriptional level and it was suggested to lead to the decrease in Hsp90. This phenomenon resulted in the downregulation of HOG1 and CDR1. In addition, we confirmed curcumin also inhibited Cdr1 efflux activity in *C. albicans*.

Conclusion: Curcumin was suggested to influence not only HSP90 expression but also Cdr1 activity in *C. albicans*.