Results: Comparable results were obtained using EUCAST and CLSI methods. Resistance (MIC > 4 μg/mL) to terbinafine and fluconazole was observed in 100% of isolates, both CAR and CAS. On the contrary, a statistically significant difference in terbinafine, echinocandins, disporzole, propozole, and fluconazole MICs between CAR strains and CAS strains was observed with higher geometric means (GM) in CAS (4.9-9.3 μg/mL) than in CAR (0.7-2.7 μg/mL). Propozole showed the lowest GMs: 0.6 and 0.25 μg/mL in CAS and CAS strains, respectively. A significant difference of the GMs for all the DMIs tested, except propozole, was observed between the isolates harboring an F219L or a F219I mutation (GM ranging 0.16-4.6 μg/mL) and those with other CYPA11 mutations (GM ranging 0.4-4.6 μg/mL). In the CAS showing high DMI MICs, the absence of CYPA11 mutations was confirmed, while a synonymous mutation P199F, was identified in CAS1B. No mutations in HMG1 were found.

In the induction test, the prolonged exposure to DMIs showed an induced phenotypic resistance of 100% (13/13 isolates) for terbinafine, of 72.7% (9/13) for fluconazole and of 91.1% (12/13) for propozole. Molecular analyses to understand if the phenotypic resistance corresponds to induced mutations in CYPA11, CAS1B, and HMG1 genes is in progress.

Conclusion: Preliminary results confirm cross-resistance between clinical azoles and DMIs, with MIC differences between CAR and CAS and between strains with different mutations in the CYPA11 gene. Furthermore, the ability of DMIs to induce resistance in vitro was highlighted.

P076

Study of magnitude and risk factors in patients with candidiasis at a tertiary care hospital with speciation and antifungal susceptibility of pathogenic Candida isolates.

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

Objective: Non-cosal candidiasis is associated with a mortality rate of over 60% while the attributable mortality rate is 49%. The present study was to determine the magnitude and risk factors in patients with candidiasis at a tertiary care hospital with speciation and antifungal susceptibility of pathogenic Candida isolates.

Methods: The present study was a prospective, cross-sectional, observational study, conducted at a tertiary care hospital for a period of 1 year at approximately 100 patients with a total of 190 cases of all azoopathies, admitted to hospital for ≥48 h and diagnosed as proven Candida with isolation of Candida species from at least two blood culture samples or from a clinically significant single blood culture sample. A thorough history and clinical characteristics of each patient was noted. Blood was collected and processed as per standard protocol. Pathogenic Candida species were identified and their antifungal susceptibility testing was performed by disk diffusion method as per the standard method. The antifungal disks used were fluconazole (25 μg), itraconazole (10 μg), voriconazole (1 μg), and amphotericin B (10 μg). Results were analyzed statistically using SPSS version 20.

Results: Candida species were isolated on the plates in 24/190 (12.7%) of clinically suspected cases of candidiasis. Candida species isolated were non-albicans Candida (NAC) species, mainly C. glabrata 112/48 (68.7%) followed by C. parapsilosis 24/53 (33.35%), and C. tropicalis 52/42 (20.83%). Candida glabrata was isolated as the pathogen, predominantly in patients of age group 50-60 years (10/14, 71.4%). Majority of Candida species were isolated from patients who had prolonged ICU stay. Among 24 patients of proven candidiasis, 2 (8.3%) patients were from NICU, 10 (41.6%) from PICU, and 13 (52.5%) from MICU. Other important risk factors observed in the present study were, recent major abdominal surgery, malignancy, and mechanical ventilation, each accounting for 25/42 (59.5%) cases. The resistance pattern of isolates of Candida species to antifungals showed that C. glabrata showed 100% resistance to fluconazole, 63.4% to itraconazole, and 45.4% to voriconazole. C. tropicalis showed 80% resistance to fluconazole, 65% to itraconazole, and 40% to voriconazole. Candida parapsilosis showed 87.5% resistance to fluconazole, 42.5% to itraconazole, and 57.5% to voriconazole. All three isolates showed Candida pathogenic Candida spp. showed 100% susceptibility to amphotericin B. Mortality observed in present study was 72/25 (28.7%). A total of 57 patients were from ICU.

Conclusion: Non-albicans Candida (NAC) species, mainly C. glabrata, C. parapsilosis and C. tropicalis were the causative agent of candidiasis, seen to predominantly affect ≥50 year age group. Infections caused by Candida species remain a significant problem in ICU. An increase in resistance to azoles in a challenge to its empirical and prophylactic use. This necessitates the usage of antifungal, only on the basis of antifungal susceptibility patterns of the pathogenic isolates.

P079

Cross-resistance to clinical and agricultural azoles among Aspergillus fumigatus strains isolated from humans and in environment in Italy

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Objective: In Italy, a prevalence of 16.5% of resistance to clinical azoles was observed among Aspergillus fumigatus isolates from an agricultural environment. The spread ofazole resistance is attributed to the widespread use of 14o-demethylazole inhibitors (DMIs).

The aims of the present study were to investigate: the DMI resistance in Italian A. fumigatus strains of clinical and environmental origin, both susceptible and resistant to clinical azoles, the molecular mechanism of resistance in strains susceptible to clinical azoles but resistant to at least one of the tested DMIs; the in vitro DMI resistance induced by prolonged exposure to DMIs in isolates clinical and environmental strains, and the molecular mechanisms of resistance.

Methods: A total of 54 A. fumigatus strains were selected: 23 susceptible to clinical azoles (CAS) and 31 resistant (CAR) with and without mutations in the CYPA11 gene (TRAK1050, E219L, G486R, S491R, D492P, M226H, or P447S/Y-N724K/E215F/R427K). Antifungal susceptibility testing was performed for 8 DMIs (terbinafine, echinocandins, disporzole, flusilazole, fluconazole, voriconazole, itraconazole, and propozole) using broth microdilution method according to EUCAST and CLSI methods. Mutations in CYPA11, CAS1B, and HMG1 genes were investigated in CAS with the use of 8 DMIs values. The in vitro DMI resistance was performed using the 8 DMIs on 11.4 clinical and 5 environmental A. fumigatus susceptible both to clinical azoles and DMIs. A comparison of 106 conidia was conducted on glucose-yeast extracts agar plates containing different DMIs at different concentrations and incubated at 37°C for 72 h for six repeated passages.

Results: Comparable results were obtained using EUCAST and CLSI methods. Resistance (MIC > 4 μg/mL) to terbinafine and fluconazole was observed in 100% of isolates, both CAS and CAR. On the contrary, a statistically significant difference in terbinafine, echinocandins, disporzole, propozole, and fluconazole MICs between CAR strains and CAS strains was observed with higher geometric means (GM) in CAS (4.9-9.3 μg/mL) than in CAR (0.7-2.7 μg/mL). Propozole showed the lowest GMs: 0.6 and 0.25 μg/mL in CAS and CAS strains, respectively. A significant difference of the GMs for all the DMIs tested, except propozole, was observed between the isolates harboring an F219L or a F219I mutation (GM ranging 0.16-4.6 μg/mL) and those with other CYPA11 mutations (GM ranging 0.4-4.6 μg/mL). In the CAS showing high DMI MICs, the absence of CYPA11 mutations was confirmed, while a synonymous mutation P199F, was identified in CAS1B. No mutations in HMG1 were found.

In the induction test, the prolonged exposure to DMIs showed an induced phenotypic resistance of 100% (13/13 isolates) for terbinafine, of 72.7% (9/13) for fluconazole and of 91.1% (12/13) for propozole. Molecular analyses to understand if the phenotypic resistance corresponds to induced mutations in CYPA11, CAS1B, and HMG1 genes is in progress.

Conclusion: Preliminary results confirm cross-resistance between clinical azoles and DMIs, with MIC differences between CAR and CAS and between strains with different mutations in the CYPA11 gene. Furthermore, the ability of DMIs to induce resistance in vitro was highlighted.