Epidemiology: risk factor analysis and management of invasive Candida auris infections in tertiary care hematology center in India

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Poster session 3, September 25, 2022, 12:30 PM - 1:30 PM

Objectives: Candida auris (C. auris) infections are associated with multidrug-resistant, interhospital 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 hematological diseases.

Methods: Single-center, prospective study of patients with suspected invasive fungal infections between January 2017-December 2021 in the patients with hematopoietic diseases. Demographics, comorbidities, and laboratory variables were recorded. The positive isolate cultures were identified by VITEK 2 (bioMérieux, India) and amphotericin sensitivity confirmed by Broth microdilution in accordance with CLSI guidelines. The final outcomes considered were mortality within a month after discharge of the patient with positive cultures.

Results: Total of 109 isolates of C. auris from 73 patients, blood 25 (31.3%), abdominal fluids 29 (35.5%), urine 90 (47.6%), respiratory 7 (8.6%), liver abscess 2 (2.5%), pancreateic abscess 1 (1.5%), and wound infections 31 (35.5%). Underlying disease was chronic leukemia in 49 (49.5%), post transplant peritonitis patients 15, (23.2%) post liver transplant patients, 15 (23.2%) post kidney transplant patients, 13 (19.1%) post bone marrow transplant patients, 6 (8.8%) gastroenterological, and 7 (9.6%) other associated conditions. The most common species was C. auris isolate with an ID score above 92. Prior use of amphotericin (P = 0.02), neutropenia (P = 0.03), prolonged hospital stay (P = 0.29), the use of broad-spectrum antibiotics (>7 days) (P = 0.2) were the risk factors significantly associated with the development of C. auris infections, and higher mortality. Concomitant, acute renal failure, diabetes, and hepatitis infection were not significant risk factors for transplant mortality. The antifungal resistance: flucocano 48.42%, voriconazole 14.01%, daravancin 9.84%, and amphotericin B 28% with no resistance to caspofungin and micafungin.

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, neutropenia, neutropenia, broad-spectrum antibiotics use, and a hospital stay of >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 empirical therapy with schiconozal as azoles and amphotericin B show high resistance in these isolates.

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Diagnostic utility of serum beta D glucan test to prescribe antifungal treatment and its effect on patient’s outcome: a study from a tertiary care center in Western India

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Poster session 3, September 23, 2022, 12:10 PM - 1:30 PM

Serum Beta D glucan has 75%-80% sensitivity and 90% specificity to make a diagnosis of invasive candidiasis. Objectives: This study was undertaken to understand real-world diagnostic utility of Beta D-Glucan (BDG) on antifungal prophylaxis patterns associated patient outcomes.

Methods: Study design: Retrospective cohort study

Study Population: All consecutive patients who underwent BDG (flashtest assay) testing with culture (positive or negative) results in the intensive care unit (ICU) setting between January 1, 2021 to December 31, 2021 at a tertiary care center in western India.

Statistical Methods: We assessed the difference in continuous variables across compared groups using the independent samples t-test and binary logistic regression for categorical variables. We summarize the study results as odds ratios and 95% confidence intervals. All P-values are 2-sided and set at 5% for all comparisons. All data analysis were performed using IBM SPSS v28.

Results: A total of 4481 patients were admitted in the ICU, of which 198 patients underwent BDG testing. Of the 198, 113 tested positive and 45 negative and formed the denominator for the study. Patients with intermediate BDG (24.12%) were excluded from the analysis. The mean (SD) age for the study cohort was 57.5 (14.7) years with 30.8% females. All the patients were receiving broad-spectrum antibiotics at the time of BDG collection. A total of 24 study patients had a positive blood culture (25 bacterial isolates and 1 Candida pancreatidis). The groups, positive and negative test results for BDG, were comparable for routine ultrasound (P = 0.737), tawasepraspsion (P = 0.270), laboratory of surgery (P = 791) central line placement (P = 0.403), liver disease (P = 0.144), CRP (P = 0.434), COVID-19 pulmonary (P = 2.338), WBC count (P = 0.373), CRP (P = 0.768), and serum procalcitonin (P = 0.784). Patients with invasive heart disease (BIDP) (P = 0.013) and acute kidney injury requiring hemodialysis (AKDPI) (P = 0.017) were significantly higher in the positive test group. Test negative group patients received early BDG testing, mean (SD) time of 3.13 (3.77) days as compared to 4.58 days (6.98) P = 0.004. Most non-test-positive patients received antifungal therapy (P = 0.001), while 20.4% didn’t receive antifungals. Caspofungin (23.9%), fluconazol (18.4%), anidulafungin (7.5%), voriconazole (4.5%), and combination antifungals were used in 10.9% of study patients. Logistic regression model showed no difference in mortality between the two groups (P = 0.415) with higher Odds of mortality at non-positive patients (1.071,95% CI 0.705-2.409). Treatment with caspofungin was associated with higher Odds of mortality (3.897, 95% CI 1.324-9.239, P = 0.032) as compared with fluconazol. Similar trend was observed with anidulafungin (OR: 4.069 99% CI 1.022-15.886, P = 0.042) as compared to fluconazol. This significance remained for caspofungin (OR 3.407 (1.242-10.311) P = 0.017) while anidulafungin (OR: 3.754 (0.943-15.602) P = 0.06) didn’t show significance with the multivariate model.

Conclusions: Probable invasive candidiasis as diagnosed with positive BDG test don’t increase the risk of mortality. Patients treated with fluconazol were associated with better survival as compared with caspofungins.

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

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Poster session 3, September 23, 2022, 12:30 PM - 1:30 PM

Objectives: 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 bioinformatic tools such as OrthoMCL, BLASTp, TargetP, and SignalP, applied on a local collection of proteome database obtained manually from GenBank-NCBI, and the analysis of proteomic databases, bioinformatical and experimental data sets, including a new proteome dataset obtained from pathogenic yeast-phase H. capsulatum culture filtrates, a Histoplasma yeast and mycelial transcriptomes database, and a rice-proteome database from Histoplasma-pathogenesis-positive patients.

For the identification 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 using a capture-competition immunoprecipitation for ELIZAs mix.

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: Determination of the expression of each biomarker was identified. Subsequently, the expression of expression for each Candida and the production of these genes were achieved using a standardized protocol for the production of recombinant proteins.