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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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Objective: This study was designed to understand real-world diagnostic utility of S. Beta D Glucan (BDG) on antifungal prescription patterns associated patient outcomes.

Methods: Study design: Retrospective cohort study
Study Population: All consecutive patients who underwent BDG (fasting sample) testing with positives (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 analyses were performed using IBM SPSS 24.

Results: A total of 4881 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 38.8% 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% bacteraemia and 1 Candida panprotease). The groups, positive and negative test results for BDG, were comparable for ventilator use (P = 0.77), vasopressor prescription (P = 0.70), history of surgery (P = 0.78) central line placement (P = 0.40), liver disease (P = 0.14), CRP (P = 0.54), COVID-19 pneumonia (P = 0.23), WBC count (P = 0.17), CRP (P = 0.76), and serum procalcitonin (P = 0.74). Patients with ischemic heart disease (IHBD) (P = 0.015) and acute kidney injury requiring hemodialysis (AKIDR) (P = 0.017) were significantly higher in the positive test group. Test negative group patients received early BDG testing, mean (SD) stay of 3.13 (3.77) days as compared to 5.60 (9.09) days. More test positive patients received antifungal therapy (P = 0.001), while 20.4% didn’t receive antifungals. Caspofungin (23.9%), fluconazole (18.4%), amphotericin B (7.5%), voriconazole (6.5%), and combination antifungal were used in 10.9% of study patients. Logistic regression model showed no difference in mortality between the two groups (P = 0.41) with higher Odds of mortality at test positive patients (1.137, 95% CI 0.705-2.499). Treatment with caspofungin was associated with higher Odds of mortality (4.897, 95% CI 1.022-24.898, P = 0.017) as compared to fluconazole. Similar trend was observed with amphotericin (OR: 4.899 95% CI 1.012-15.888, P = 0.042) as compared to caspofungin. This significance remained for caspofungin (OR: 4.407 95% CI 1.220-14.911, P = 0.017) while amphotericin (OR: 3.514 (95% CI 1.046-11.032) P = 0.016) did not show significance with the multivariable model.

Conclusion: Probable invasive candidiasis as diagnosed with positive BDG test doesn’t increase the risk of mortality. Patients treated with fluconazole were associated with better survival as compared with caspofungin.

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Genomic 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, Tarred, and SignalP, applied on a local collection of proteome database obtained manually from Fundamental NCBI, and the analysis of proteome publications, bibliographical and experimental data sets, including a new proteome database obtained from pathogenic yeast phase H. capsulatum culture filtrates, a Histoplasma yeast and mycelial transcriptional database, and a urine-proteome database from Histoplasma-susceptible-positive patients.

For the selection 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 adapting a classical immunization protocol for RBLs mice.

Finally, the computational model was experimentally validated, evaluating the reaction and specificity of PAb anti-Histoplasma with fungus culture extracts and samples from patients with histoplasmoses.

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.