Objective: This study was done to assess the role of Bronchoalveolar lavage fluid (BALF) galactomannan (GM) in the diagnosis of invasive pulmonary aspergillosis (IPA) in non-neutropenic patients and to determine the optimal cut-off value of BALF GM for diagnosing IPA in non-neutropenic hosts.

Methods: We conducted a cross-sectional observational study on 96 non-neutropenic patients of age > 18 years with suspected pulmonary infections of fungal etiology. A detailed history of predisposing conditions was obtained and routine laboratory investigations with chest computed tomography were performed. Fiberoptic bronchoscopy under local anesthesia and sedation was done using a video bronchoscope. Bronchoalveolar lavage was done from the segment or lobe of interest instilling 40-100 ml of saline withdrawn under low pressure and the sample was tested for a battery of investigations, fungal KOH smears, fungal culture, GM by Pimarilla Aspergillus enzyme immunoassay, and others required for diagnosis. A protected brush specimen and transbronchial lung biopsy were done whenever feasible. The yield from the BALF GM assay was compared with diagnosis based on definitions given by EORTC/MSG excluding host factors. Patients were classified into three groups namely non-IPA, probable IPA, and proven IPA. For statistical analysis, probable and proven IPA were taken as one group i.e., the IPA group. Mann Whitney run and Chi square test along with Fisher’s exact test were performed for inter-group comparison between quantitative and qualitative variables respectively. The receiver operator characteristic curve was used to establish a cut-off point of BALF GM and Serum GM for predicting IPA. Sensitivity, specificity, PPV, and NPV were calculated. The McNemar test was used for the comparison of sensitivity and specificity. Intraclass kappa agreement was used to find the strength of agreement of BALF GM, BALF culture, and BALF DM.

Results: Out of 96, 1 was diagnosed with proven IPA, 58 were probable IPA cases and 38 were non-IPA cases. Chronic kidney disease (CKD) as a risk factor was more common in IPA cases compared to non-IPA cases (25.7% vs. 8.2%, P-value <0.05). Chest CT showed cavity in a significant number of IPA patients compared to non-IPA cases (69% vs. 29.5%, P-value <0.005). BALF direct microscopy, cultures, and serum GM had sensitivities <60% but specificities close to 93%. BALF GM showed promising results with a sensitivity of 88.5% and specificity of 87.7% at cut-off value of 0.8.

See Figures below.

Conditions: Our study highlights the magnitude of IPA in non-neutropenic hosts with unconventional risk factors like CKD, diabetes, and the need for increased vigilance for diagnosis of IPA in each patient. We suggest a lower cut-off value of BALF GM against 1 as in EORTC/MSG criteria and consider CKD as one of the risk factors for IPA.
Sciensano, the Belgian federal scientific centre for public and animal health, houses the BCCM/IHEM Fungi Collection which contains more than 15,000 strains belonging to over 1,000 different species. The collection is managed according to ISO 9001 standards.

Its purpose is to make fungal strains available for academics, clinicians, industry, and education.

Fungal pathogens are not as often encountered as bacteria in the clinical laboratory. Additionally, laboratories may not have the knowledge or logistics for the long-term preservation of fungal isolates. Without an array of fungal strains with confirmed identity, it is complicated to implement new protocols and equipment when these need to be validated for the identification of fungi.

To short-cut this problem and support laboratories in identifying clinical fungi in routine activities, BCCM/IHEM has developed two validation panels for the identification of fungi via MALDI-TOF mass spectrometry: there is a validation panel with yeasts and a validation panel with filamentous fungi. The selection of strains is based on species that are routinely encountered in a clinical laboratory, and also contains rare, but emerging fungal pathogens, like Trichophyton interdigitale and Candida aeris. The identity and purity of the strains in these panels have been verified according to ISO 17025 accredited protocols. This allows the laboratory to evaluate, in a short turn the extraction protocol, the MALDI-TOF machine, and the database of reference mass spectra.