ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 04 | April - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF DIAGNOSTIC PERFORMANCE OF SERUM AND BRONCHO-ALVEOLAR LAVAGE [BAL] FLUID GALACTOMANNAN ASSAY FOR DETECTION OF INVASIVE PULMONARY ASPERGILLOSIS [IPA]

Biochemistry

Susruta Sen	Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India
Sharmistha Choudhuri*	Department of Biochemistry, RG Kar Medical College & Hospital, Kolkata-700004, India*Corresponding Author
Sudip Roy	Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India
Niladri Sarkar	Department of Lab Services, BM Birla Heart Research Centre, Kolkata-700027, India
Atmaja Mukherjee	Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India
Rounak Ghosh	Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India
Saumya Chandra	Department of Lab Medicine, CK-Birla Hospitals-CMRI (The Calcutta Medical Research Institute) & BM Birla Heart Research Centre, Kolkata-700027, India
Soniya Karmakar	Department of Lab Services, BM Birla Heart Research Centre, Kolkata-700027, India

ABSTRACT

Introduction: Invasive pulmonary aspergillosis [IPA] is a common mycosis, afflicting immunocompromised individuals particularly hematological transplant patients. In recent times however particularly since COVID-19 pandemic, there have been increasing reports of concomitant occurrence of IPA with COVID-19 as well as influenza infections. Galactomannan (GM) is a polysaccharide component of the Aspergillus cell wall, released during hyphal growth. Currently, ELISA, employing a sandwich format using monoclonal antibodies targeting specific galactomannan epitopes and applicable to both serum and bronchoalveolar lavage (BAL) fluid, with BAL samples, coupled with the use of optical density index cutoffs (commonly ≥0.5 in serum and ≥1.0 in BAL) allows for a semi-quantitative diagnostic strategy for IPA. **Methods:** We conducted a prospective, analytical, comparative study in the Department of Laboratory Medicine of CK-Birla Hospitals, CMRI & BM Birla Heart Research Centre, Kolkata, from 1st January 2023 to 31st December 2025, following set inclusion & exclusion criteria. A total of 46 BAL fluid samples and 30 serum samples were finally selected for galactomannan [GM] assay by Dynamiker GM ELISA. Briefly, an OD of < 0.5 was considered as negative & ≥ 0.5 considered as positive with regard to serum while an OD of < 1.0 was considered as negative & ≥ 1.0 considered as positive for BAL fluid. For ease of analysis and representation, we designated a finite score of 20 to all positives [both serum and BAL fluid GM] and 10 to all the negatives [both serum and BAL fluid GM]. Concomitantly, serum and BAL fluid were used for assay of biomarkers namely C-reactive protein [CRP] and Procalcitonin [PCT], while cellular components namely total WBC count and neutrophil and eosinophil differential counts were also estimated both in blood as well as in the aspirated BAL fluid. The data was analyzed by GraphPad Prism (v.8.4.3) and MS Excel 2013, considering a p value of ≤ 0.05 to be statistically significant. **Results:** The percentages of Sensitivity, Specificity, Positive Predictive Value [PPV], Negative Predictive Value [NPV], Accuracy and Error rates were separately calculated for the 30 serum and 46 BAL fluid GM ELISA results. In brief, sensitivity, specificity of BAL fluid ELISA (75%), was found to be far more is more than that of serum; 75% vs 20% and 81.58% vs 80%, respectively. Similarly, Positive and Negative Predictive Values of BAL fluid ELISA (46.15% & 93.94%), were found to exceed the Positive and Negative Predictive Values of serum (16.67% & 83.33%). Moreover, the false positive, false negative and error rates were higher for serum (20%, 80% & 30%) as compared to BAL fluid GM ELISA (18.42%, 25% & 19.57%). The overall diagnostic accuracy for Bal fluid GM ELISA was higher as compared to serum GM ELISA [80.43% vis-à-vis 70%]. For assessing the concurrence of our selected biochemical and hematological biomarker levels with results of GM ELISA, we applied the Kruskal-Wallis test between the results of serum and BAL-fluid GM ELISA and selected biochemical biomarkers [serum CRP and serum PCT] and selected hematological parameters [TLC, percentages of neutrophil and eosinophil counts]. Kruskal-Wallis analysis showed a significant concurrence between serum GM ELISA negative as well as positive results and biochemical and hematological parameters [P < <0.0001] and also between BAL fluid GM ELISA negative as well as positive results and biochemical and hematological parameters [P < <0.0001]. **Conclusions:** Galactomannan antigen detection remains integral to IPA diagnosis. The BAL fluid GM ELISA showed better performance characteristics and hence can be a better diagnostic alternative to serum ELISA. Moreover, GM ELISA can strengthen the diagnosis of IPA when used in conjunction with selected biochemical and hematological markers with comparable extent of concurrence for both serum and BAL fluid results.

KEYWORDS

Aspergillosis Galactomannan, Bal fluid, ELISA

INTRODUCTION

Aspergillus is a ubiquitous genus of filamentous fungi, particularly *A. fumigatus*, *A. flavus*, *A. terreus*, and *A. niger*. Invasive Pulmonary Aspergillosis (IPA), characterized by hyphal invasion of the lung parenchyma and vasculature and frequently leading to necrosis and potential dissemination, is a common worldwide affliction.[1] Global mortality rates usually range between 30–80%, especially in ICU settings. Classically, the risk of IPA is also higher in immune-compromised individuals particularly those with acute leukemia or undergoing hematopoietic stem-cell transplantation (HSCT), representing the highest risk groups.[2] Particularly, transplant recipients, inclusive of solid transplant recipients, are at very high risk of IPA. The risk is compounded by re-transplantation, renal dysfunction, corticosteroid use, CMV infection, prolonged ICU stays, and lung transplant recipients. [3,4] Global estimates have found approximately, 3,000,000 cases of chronic pulmonary aspergillosis.[5] In recent times however particularly since COVID-19 pandemic, there have been increasing reports of concomitant occurrence of IPA with COVID-19 as well as influenza infections. It is also worthwhile to note that IPA flourishes in hosts with defects in neutrophil-mediated immunity, whether quantitative (e.g., neutropenia) or qualitative (e.g., corticosteroid use, diabetes). In addition, structural lung damage from COPD, viral pneumonia, prolonged immunosuppression, and ICU interventions all make fungal growth conducive, thereby promoting of IPA.

The Enzyme Linked Immunosorbent Assay [ELISA] plays a significant role in the diagnosis of invasive fungal infections, particularly through the detection of galactomannan, a polysaccharide cell wall component released by actively growing Aspergillus species.

Galactomannan (GM) is a polysaccharide component of the Aspergillus cell wall, released during hyphal growth. Detection assays—typically enzyme immunoassays (EIAs) or lateral-flow assays (LFAs), identify circulating GM in bodily fluids such as serum, bronchoalveolar lavage (BAL) fluid, proximal airway samples, or cerebrospinal fluid (CSF). Galactomannan ELISA, employing a sandwich format using monoclonal antibodies, targets specific antigenic epitopes. The test can be applied to both serum and BAL fluid, with the latter generally offering higher sensitivity due to higher fungal load and reduced interference, unlike serum.[6] There are studies which have reported that BAL galactomannan ELISA can achieve sensitivities exceeding 85–90% and specificities above 90% in immunocompromised patients, including those with hematologic malignancies and stem cell transplants.[7]

The use of optical density index cutoffs (commonly ≥0.5 in serum and ≥1.0 in BAL) allows for a semi-quantitative diagnostic strategy for IPA.[8] Meta-analysis in hematological malignancy patients, and recipients of bone marrow transplantations have been shown to exhibit a sensitivity of ~35–78% and a specificity ~70–93% depending on cutoff. BAL fluid detection generally outperforms serum, with a pooled sensitivity ~0.80 and specificity ~0.95; using ODI cutoffs at 0.5 and 1.0, respectively, yielding a comparatively higher diagnostic accuracy.[9] Furthermore, coupling GM detection with PCR or β-d-glucan assay has been shown to improve sensitivity for serum samples to the tune of 0.81.[10]

However, concomitant use of β-lactam antibiotics (e.g., piperacillin–tazobactam), dietary galactomannan, or cross-reactivity with other fungal species, can contribute to false-positive results. Hence, serial testing simultaneously integrated with clinical and radiological findings are of paramount importance in enhancing diagnostic accuracy.[11] Presently, the GM assay is recommended for use by major guidelines namely the European Organisation for Research and Treatment of Cancer [EORTC] and the Mycoses Study Group Education and Research Consortium [MSGERC] as part of the diagnostic criteria for probable invasive aspergillosis. [12,13]

The current study was undertaken to assess the diagnostic efficacy of galactomannan ELISA in both serum as well as BAL fluid in patients of clinically suspected IPA admitted into the intensive care unit [ICU] of our institute and whose BAL fluid and serum samples had been routinely sent for biochemical and hematological analyses, to determine which body fluid could yield a more accurate and reliable result, for clinching the diagnosis of IPA, keeping in mind the comparatively much more non-invasive nature of acquisition of serum vis-a-vis the more invasive method for acquisition of BAL fluid. Also the galactomannan ELISA results were compared with the results of selected biochemical and hematological biomarker levels to assess the ability of these biomarkers to supplement and support the diagnosis of IPA.

Materials and Methods:

Study variables: A retrospective, analytical, comparative study was conducted in the Department of Laboratory Medicine of CK-Birla Hospitals, CMRI & BM Birla Heart Research Centre, Kolkata, from 1st January 2023 to 31st December 2025, following set inclusion & exclusion criteria, using patients of clinically suspected invasive pulmonary aspergillosis [IPA], admitted into the ICU of our institute.

Case selection and sampling details: Briefly, 100 patients of clinically suspected invasive pulmonary aspergillosis [IPA], admitted into the ICU of our institute were initially screened for the the study from 1st January 2023 to 31st December 2025. Out of these 100, BAL fluid was obtained from 60 patients and serum was obtained from 37, while both BAL fluid and serum samples were available from the remaining three. Excluding those who were unwilling to participate and those less than 18 years of age, a total of 46 BAL fluid samples and 30 serum samples were finally selected for galactomannan [GM] assay by ELISA [Fig 1].

Ethical considerations: Since the entire study was conducted on samples of patients, coming to lab for routine investigations, hence ethical clearance was not required separately for the same.

Study parameter estimations: Around 2 mL serum obtained from 5 mL of blood drawn by venepuncture and 10 mL aspirated BAL fluid in sterile saline obtained by bronchoscopy, were collected using complete aseptic precautions. Serum was used for Galactomannan [GM] assay as well as for assay of biomarkers namely C-reactive protein [CRP] and Procalcitonin [PCT]. The same biomarkers were independently assayed in BAL fluid. Moreover, cellular components namely total WBC count and differential neutrophil and eosinophil counts were also estimated both in blood as well as in the aspirated BAL fluid.

Serum and BAL fluid Galactomannan [GM] Assay: Serum and BAL fluid GM were assayed using the Dynamiker GM ELISA is a sandwich enzyme immunoassay used for the qualitative or semi-quantitative detection of Aspergillus Galactomannan (GM) antigen in human serum or BAL fluid, with the help of monoclonal antibodies specific to Galactomannan. Determination of positivity for GM was based on optical density (OD) measured at 450 nm (with 620–650 nm as reference). Briefly, an OD of < 0.5 was considered as negative & ≥ 0.5 considered as positive with regard to serum GM. Likewise, an OD of < 1.0 was considered as negative & ≥ 1.0 considered as positive for BAL fluid GM. For ease of analysis and representation, we designated a finite score of 20 to all positives [both serum and BAL fluid GM] and 10 to all the negatives [both serum and BAL fluid GM].

Serum and BAL biochemical and hematological analyses: Among the biochemical markers analyzed were serum and BAL fluid CRP, analyzed by immunoturbidimetry and the serum and BAL fluid PCT analyzed by electro-chemiluminescence [ECLIA], on automated platforms, viz; the Roche COBAS c501 and Roche COBAS e601. The cellular components ie the total leucocyte count [TLC] and the differential percentages of neutrophils and eosinophils were quantified by Coulter principle & flow cytometric analysis using an automated platform viz; HORIBA ABX Pentra XL 80.

Statistical analyses: The data generated was analysed by Graph-Pad Prism v.8.4.3, using appropriate statistical tools. Normality of the sample distribution was tested by D'Agostino & Pearson omnibus normality test. For assessing the diagnostic accuracy of serum vis-à-vis BAL fluid GM ELISA, sensitivity, specificity, positive predictivity, negative predictivity, homogeneity and error rates were calculated and Receiver-Operating-Characteristic [ROC] curve was generated **[Fig 2]**. Additionally, to assess the extent of concurrence of selected biochemical and hematological biomarker levels with results of GM ELISA, Kruskal-Wallis Test was applied [since data was found to be non-parametric in distribution]. In all statistical analysis P value ≤0.05, was considered as statistically significant.

RESULTS:

1. Segregation of GM ELISA results into true positives, true negatives, false positives and false negatives: The GM ELISA done in serum and BAL fluid yielded positive and negative results both. A true positive [TP] result was that result where GM ELISA and radiological finding were both positive for IPA. A false positive [FP], on the other hand, was such a result where though GM ELISA was positive, radiological finding was negative for IPA. Conversely, a false negative [FN] result was one where GM ELISA was negative but radiological evidence was positive for IPA. A true negative [TN] result was one where GM ELISA and radiological finding were both negative for IPA.

Going by these definitions we segregated the 30 serum GM ELISA results as 6 positives and 24 negatives along with TP [n=1], FP [n=5], FN [n=4] and TN [n=20]. Likewise for the 46 BAL fluid GM ELISA results, we obtained 13 positives and 33 negatives which were further segregated into TP [n=6], FP [n=7], FN [n=2] and TN [n=31].

2. Determination of percentages of Sensitivity, Specificity, Positive Predictive Value [PPV], Negative Predictive Value [NPV], Accuracy and Error and construction of ROC curve: The percentages of Sensitivity, Specificity, Positive Predictive Value [PPV], Negative Predictive Value [NPV], Accuracy and Error rates were separately calculated for the 30 serum and 46 BAL fluid GM ELISA results. Tables 1a & 1b summarises the same. In brief, sensitivity of BAL fluid ELISA (75%), was found to be far more is more than that of serum (20%). Likewise, specificity of BAL fluid ELISA (81.58%) was higher than that of serum (80%), although marginally. Similarly, Positive and Negative Predictive Values of BAL fluid ELISA (46.15% & 93.94%), were found to exceed the Positive and Negative Predictive Values of serum (16.67% & 83.33%). Moreover, the false positive, false negative and error rates were higher for serum (20%, 80% & 30%) as compared to BAL fluid GM ELISA (18.42%, 25% & 19.57%). The overall diagnostic accuracy for Bal fluid GM ELISA was higher as compared to serum GM ELISA [80.43% vis-à-vis 70%].

3. Concurrence of selected biochemical and hematological biomarker levels with results of GM ELISA: For assessing the concurrence of our selected biochemical and hematological biomarker levels with results of GM ELISA, we applied the Kruskal-Wallis test between the results of serum and BAL-fluid GM ELISA and selected biochemical biomarkers [serum CRP and serum PCT] and selected hematological parameters [TLC, percentages of neutrophil and eosinophil counts]. For statistical analysis purposes, we designated a score of 20 to all the positive results of serum and BAL fluid GM ELISA and a score of 10 to all the negatives. Kruskal-Wallis analysis showed a significant concurrence between serum GM ELISA negative as well as positive results and biochemical and hematological parameters [P < <0.0001; Fig 3a & Fig 3b] as well as between BAL fluid GM ELISA negative as well as positive results and biochemical and hematological parameters [P <0.0001; Fig 4a & 4b].

DISCUSSION:

Aspergillus is a saprophytic and ubiquitous mold, known to arise from varied sources namely soil, decomposing plant matter, plant and flowers, food, household dust or building materials. [14,15] Invasive pulmonary aspergillosis [IPA] is not an uncommon occurrence among immunocompromised individuals particularly, in hematopoietic transplant recipients as well as those with co-existing pulmonary pathologies namely cystic fibrosis [16,17]

Currently the galactomannan [GM] ELISA diagnostic strategy is gaining increasing popularity. This polysaccharide component of the fungal cell wall of Aspergillus, has been validated for detection in serum as well as in BAL fluid and CSF, and offers a higher vantage point over culture in terms of sensitivity.[7] Our current study performed in both serum and BAL fluid, yielded a starkly higher sensitivity of BAL fluid ELISA over its serum counterpart [75% vs 20%] as well as markedly lower false negative rate compared to serum [25% vs 80%]. The overall accuracy rate for BAL fluid GM ELISA was higher than that of serum [80.43% vs 70%] as was a markedly lower overall error rate [30% vs 19.57%].

However, the false positivity rate was comparable for both BAL fluid as well as serum GM ELISAs [18.42% and 20% respectively]. Such false positivity can arise due to cross-reactivity with other fungal species such as *Penicillium* or *Fusarium*, contamination of BAL samples with fluids like Plasmalyte, or even the use of certain antibiotics, particularly older formulations of piperacillin–tazobactam or amoxicillin–clavulanate, which may contain trace fungal polysaccharides. [18,19]

A certain percentage of false negative result implies the absence of galactomannan detection despite the presence of active IPA. This may occur in early stages of infection, in patients already on antifungal therapy (which reduces fungal burden), or in localized infections where galactomannan has not yet entered the bloodstream. In neutropenuc patients in particular, the propensity towards false negative results in GM ELISA has been observed in quite a few instances, but the cause remains as yet unknwn.[20] Another probable reason is encapsulation of the antigen making it difficult to detect the same in serum, in which cases genetic detection by polymerase chain reaction [PCR] remains the primary alternative viable option.[21,22] In our study, we segregated the false negatives and false positives using radiological detection as the segregator, with radiology positive but ELISA negatives being designated as false negatives and radiology negative but ELISA positives being grouped as false positives.

We also assessed the extent of concurrence of the GM ELISA results with CRP which is a common biomarker of acute inflammation and PCT which is a common biomarker elevated in sepsis. Since our samples belonged to patients undergoing treatment in the hospital ICU, it was deemed fit to gauge how reliably routine biochemical markers of inflammation and sepsis were in agreement with GM ELISA results. High level of both these biochemical markers are known to signify a more progressive form of IPA and a consequently poorer prognosis.[23] However, a contrasting picture of high CRP with low PCT may be well observed in IPA particularly with neutropenia; a common feature among immunocompromised individuals. Infact discerning such a biochemical picture is of prime importance in initiating anti-fungal therapy at the earliest.[24] We did observe such a trend in our serum as well as BAL fluid samples analysed for CRP and PCT. However overt neutropenia was not observed in our patients, a possible reason possibly being some overlaying bacterial infection having taken root simultaneously.

Overall, the GM ELISA results in both serum and BAL fluid showed significant concurrence with CRP and PCT results (assayed in both body fluids), as well as with total leucocyte count and also percentages of neutrophils and eosinophils [P<0.0001]. Infact the TLC and particularly neutrophil percentages have been shown to exhibit promise as surrogate end-points for outcome prediction and mortality. [25] In particular eosinophilia and associated elevated TLCs have been found to have a higher preponderance of cavity, consolidation, ground-glass opacity, and halo sign in IPA patients.[26] Since a proportionately higher number of our samples showed high TLC values and positivity for GM ELISA, particularly wrt BAL fluid, hence concomitant assay of these biomarkers in conjunction with GM ELISA was carried out keeping in mind their potential to act as definitive aids in designing as well as successfully executing therapeutic strategies in IPA.

CONCLUSIONS:

Currently, Galactomannan antigen detection remains integral to IPA diagnosis. In our present study, the BAL fluid GM ELISA showed better performance characteristics, overall and hence can be a better diagnostic alternative to serum ELISA. Moreover, GM ELISA can strengthen the diagnosis of IPA when used in conjunction with selected biochemical and hematological markers with comparable extent of concurrence for both serum and Bal fluid results. However, standardization of cutoffs, strategies to reduce false results, and integration with molecular assays are areas for further research. Notably, longitudinal studies examining GM kinetics in therapy response are underway. Future guidelines will likely integrate multistep diagnostics coupled with imaging strategies to improve early detection and clinical outcomes.

Tables

Table 1a: Performance characteristics of serum Galactomannan [GM] ELISA; performance parameters analyzed; sensitivity, specificity, false positive rate [FPR], false negative rate [FNR], positive predictive value [PPV], negative predictive value [NPR], accuracy rate and error rate

Performance parameters	Calculation formula applied	Rates [%]
Sensitivity [True positive]	TP/TP+FN	20
Specificity [True negative]	TN/TN+FP	80
False positive rate [FPR]	FP/FP+TN	20
False negative rate [FNR]	FN/FN+TP	80
Positive predictive value [PPV]	TP/TP+FP	16.67
Negative predictive value [NPV]	TN/TN+FN	83.33
Accuracy	TP+TN/ TP+TN+FP+FN	70
Error	1- Accuracy	30

TP= True positive; FP= False positive; TN=True negative; FN= False negative

Table 1b: Performance characteristics of broncho-alveolar lavage [BAL] Galactomannan [GM] ELISA; performance parameters analyzed; sensitivity, specificity, false positive rate [FPR], false negative rate [FNR], positive predictive value [PPV], negative predictive value [NPR], accuracy rate and error rate

Performance parameters	Calculation formula applied	Rates [%]
Sensitivity [True positive]	TP/TP+FN	75
Specificity [True negative]	TN/TN+FP	81.58
False positive rate [FPR]	FP/FP+TN	18.42
False negative rate [FNR]	FN/FN+TP	25
Positive predictive value [PPV]	TP/TP+FP	46.15
Negative predictive value [NPV]	TN/TN+FN	93.94
Accuracy	TP+TN/ TP+TN+FP+FN	80.43
Error	1- Accuracy	19.57

TP= True positive; FP= False positive; TN=True negative; FN= False negative

Table 1b: Performance characteristics of broncho-alveolar lavage [BAL] Galactomannan [GM] ELISA; performance parameters analyzed; sensitivity, specificity, false positive rate [FPR], false negative rate [FNR], positive predictive value [PPV], negative predictive value [NPR], accuracy rate and error rate

Performance parameters	Calculation formula applied	Rates [%]
Sensitivity [True positive]	TP/TP+FN	75
Specificity [True negative]	TN/TN+FP	81.58
False positive rate [FPR]	FP/FP+TN	18.42
False negative rate [FNR]	FN/FN+TP	25
Positive predictive value [PPV]	TP/TP+FP	46.15
Negative predictive value [NPV]	TN/TN+FN	93.94
Accuracy	TP+TN/ TP+TN+FP+FN	80.43
Error	1- Accuracy	19.57

TP= True positive; FP= False positive; TN=True negative; FN= False negative

Figures:

Fig 1: Segregation of recruited cases into sampling sub-groups; BAL fluid samples [n=46] and serum samples [n=30]

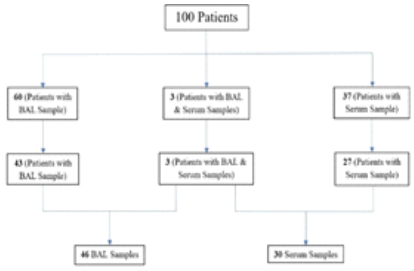


Fig 2: Receiver operating characteristic [ROC] curve, for ascertaining sensitivity and specificity of serum and broncho-alveolar lavage [BAL] fluid galactomannan [GM] ELISA results; True positive [sensitivity] of serum GM ELISA 0.2 [20%] and of BAL fluid GM ELISA 0.75 [75%]; False positive rate [FPR] of serum GM ELISA 0.20 [20%] and of BAL fluid GM ELISA 0.18 [18%]

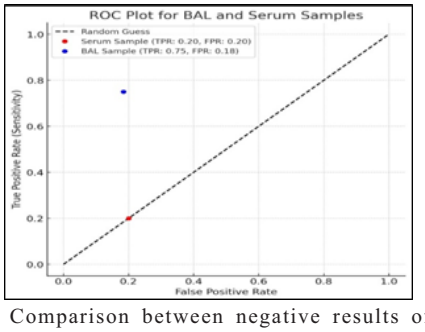


Fig 3A: Comparison between negative results of serum galactomannan [GM] ELISA and assorted serum biochemical & hematological parameters; Kruskal-Wallis test applied; concurrence between tested parameters highly significant [P <0.0001]

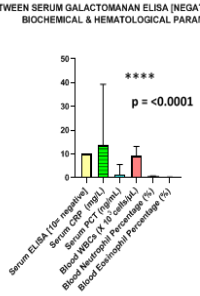


Fig 3B: Comparison between positive results of serum galactomannan [GM] ELISA and assorted serum biochemical & hematological parameters; Kruskal-Wallis test applied; concurrence between tested parameters highly significant [P <0.0001]

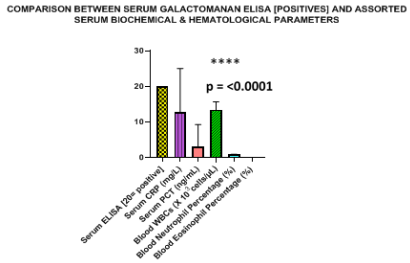


Fig 4A: Comparison between negative results of BAL fluid galactomannan [GM] ELISA and assorted serum biochemical & hematological parameters; Kruskal-Wallis test applied; concurrence between tested parameters highly significant [P <0.0001]

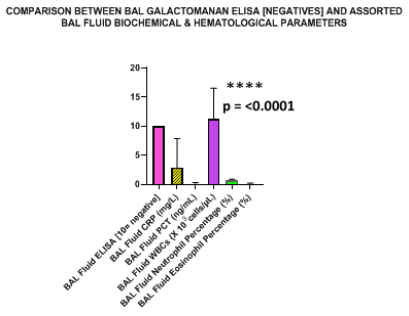
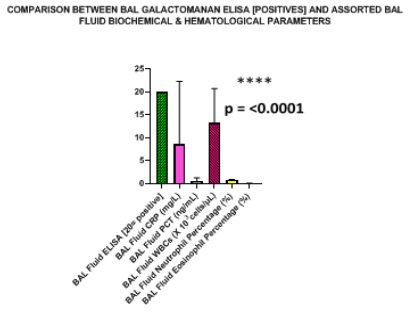


Fig 4B: Comparison between positive results of BAL fluid galactomannan [GM] ELISA and assorted serum biochemical & hematological parameters; Kruskal-Wallis test applied; concurrence between tested parameters highly significant [P <0.0001]



REFERENCES:

1. Ledoux MP.; Herbrecht R. Invasive Pulmonary Aspergillosis. J. Fungi 2023, 9, 131
2. Jantunen E; Ruutu P; Niskanen L; Volin L; Parkkali T; Koukila-Kähkölä P; Ruutu T. Incidence and risk factors for invasive fungal infections in allogeneic BMT recipients. Bone Marrow Transplant. 1997, 19, 801–808
3. Palmieri F, Koutsokera A, Bernasconi E, Junier P, von Garnier C and Ubags N (2022) Recent Advances in Fungal Infections: From Lung Ecology to Therapeutic Strategies With a Focus on Aspergillus spp. Front. Med. 9:832510. doi: 10.3389/fmed.2022.832510
4. Kousha M, Tadi R, Soubani AO. Pulmonary aspergillosis: a clinical review. Eur Respir Rev. (2011) 20:156–74
5. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases—estimate precision. J Fungi (Basel). (2017)3:57. doi: 10.3390/jof3040057
6. Ji Y, Liu DH, Xu LP, Liu KY, Huang XJ. The value of serum galactomannan detection for diagnosis of invasive aspergillosis in hematopoietic stem cell transplant recipients. Zhonghua Xue Ye Xue Za Zhi. 2007 Feb;28(2):83-6
7. Li C; Sun L; Liu, Y; Zhou H; Chen J; She M; Wang Y. Diagnostic value of bronchoalveolar lavage fluid galactomannan assay for invasive pulmonary aspergillosis in adults: A meta-analysis. J. Clin. Pharm. Ther. 2022, 47, 1913–1922
8. Marchetti O, Lamoth F, Mikulska M, Viscoli C, Verweij P, Bretagne S; European Conference on Infections in Leukemia (ECIL) Laboratory Working Groups. ECIL recommendations for the use of biological markers for the diagnosis of invasive fungal diseases in leukemic patients and hematopoietic SCT recipients. Bone Marrow Transplant. 2012 Jun;47(6): 846-54
9. Pfeiffer, C.D.; Fine, J.P.; Safdar, N. Diagnosis of invasive aspergillosis using a galactomannan assay: A meta-analysis. Clin. Infect. Dis. 2006, 42: 1417–1427
10. Dichtl K; Forster J; Ormanns S; Horns H; Suerbaum S; Seybold U; Wagener J. Comparison of beta-D-glucan and galactomannan in serum for detection of invasive aspergillosis: Retrospective analysis with focus on early diagnosis. J. Fungi. Basel 2020, 6, 253
11. Bassetti M, Giacobbe DR, Grecchi C, Rebuffi C, Zuccaro V, Scudeller L; FUNDICU Investigators. Performance of existing definitions and tests for the diagnosis of invasive aspergillosis in critically ill, adult patients: a systematic review with qualitative evidence synthesis. J Infect 2020; 81:131–46

12. Siopi M, Karakatsanis S, Roumpakis C, Korantanis K, Sambatakou H, Sipsas NV, Tsirigotis P, Pagoni M, Meletiadis J. A Prospective Multicenter Cohort Surveillance Study of Invasive Aspergillosis in Patients with Hematologic Malignancies in Greece: Impact of the Revised EORTC/MSGERC 2020 Criteria. J Fungi (Basel). 2021 Jan 5;7(1):27: 1-11
13. Bassetti M, Azoulay E, Kullberg BJ, Ruhnke M, Shoham S, Vazquez J, Giacobbe DR, Calandra T, EORTC/MSGERC Definitions of Invasive Fungal Diseases: Summary of Activities of the Intensive Care Unit Working Group, Clin Inf Dis Suppl; 2021 Mar 72; 2(15): S121–S127
14. Hajjeh RA; Warnock DW. Counterpoint: Invasive aspergillosis and the environment–rethinking our approach to prevention. Clin. Infect Dis. 2001, 33: 1549–1552
15. Ledoux MP; Guffroy B; Nivoix Y; Simand C; Herbrecht R. Invasive pulmonary aspergillosis. Semin. Respir. Crit. Care Med.2020, 41, 80-98
16. Cornely OA.; Maertens J; Bresnik, M; Ebrahimi R; Ullmann AJ; Bouza E; Heussel CP; Lortholary O Rieger C; Boehme A; et al. Liposomal amphotericin B as initial therapy for invasive mold infection: A randomized trial comparing a high-loading dose regimen with standard dosing (AmBiLoad trial). Clin. Infect. Dis. 2007, 44, 1289–1297
17. Herbrecht R; Denning DW; Patterson TF; Bennett JE; Greene RE; Oestmann JW; Kern WV.; Marr KA; Ribaud P; Lortholary O; et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N. Engl. J. Med. 2002, 347, 408–415.
18. Garg P; Suyal S; Deepak Desh; Hembrom S; Chauhan AK; Kaur N; Malhotra S. Evaluating the causes associated with false positive Galactomannan assay in suspected cases of respiratory fungal infections. J Family Med and Primary Care; Feb 2025; 14(2): p 736-742
19. Hage CA, Reynolds JM, Durkin M, Wheat LJ, Knox KS. Plasmalyte as a cause of false-positive results for Aspergillus galactomannan in bronchoalveolar lavage fluid. J Clin Microbiol. 2007 Feb;45(2):676-7
20. Verweij PE, Weemaes CM, Curfs JH, Bretagne S, Meis JF. Failure to detect circulating Aspergillus markers in a patient with chronic granulomatous disease and invasive aspergillosis. J Clin Microbiol. 2000 Oct;38(10):3900-1
21. Bretagne S, Costa JM, Bart-Delabesse E, Dhédin N, Rieux C, Cordonnier C. Comparison of serum galactomannan antigen detection and competitive polymerase chain reaction for diagnosing invasive aspergillosis. Clin Infect Dis. 1998 Jun;26(6):1407-12
22. Maertens J, Verhaegen J, Demuynck H, Brock P, Verhoef G, Vandenberghe P, Van Eldere J, Verbist L, Boogaerts M. Autopsy-controlled prospective evaluation of serial screening for circulating galactomannan by a sandwich enzyme-linked immunosorbent assay for hematological patients at risk for invasive aspergillosis. J Clin Microbiol. 1999;37: 3223–3228
23. Badiee P, Ghasemi F, Jafarian H. Role of biomarkers in the diagnosis of invasive aspergillosis in immunocompromised patients. Ann Clin Microbiol Antimicrob. 2022 Nov 1;21(1):44
24. Marková M, Brodská H, Malíčková K, Válková V, Cetkovský P, Kolář M, Haluzík M; Substantially elevated C-reactive protein (CRP), together with low levels of procalcitonin (PCT), contributes to diagnosis of fungal infection in immunocompromised patients; Supp Care Can; 2013; 1-11
25. Wu TC-W, Lin CC, Chen Y-H, Keng L-T, Chang L-Y, Chen J-Y, Lee M-R, Wang J-Y, Ho C-C, Shih J-Y. Validation of serum galactomannan antigen assay for invasive pulmonary aspergillosis mortality outcome prediction. Microbiol Spectr. 2025 Oct 27;13(12): 1-11
26. Kang Y, Li Q, Ma W, Xu C, Jia W, Wang P. Epidemiological characteristics of patients with invasive pulmonary aspergillosis infected with Aspergillus fumigatus from a tertiary hospital in Ningxia, China. Sci Rep. 2025 Apr 15;15(1):1-8