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Study of epidemiology, risk factors and antifungal sensitivity pattern of fungal pneumonia in critically ill cirrhotics

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Objectives: Liver cirrhosis causes immune dysregulation and increased susceptibility to fungal infections. We studied the epidemiology and risk factors, and compared the rapid diagnostic methods and biomarkers for fungal pneumonia in critically ill cirrhotics.

Methods: Single-center, prospective cohort study of 100 critically ill cirrhotics with fungal pneumonia between January to September 2021. Comparative analysis was done for culture, realtime PCR and biomarkers, bronchoalveolar lavage and serum Galactomannan, and serum procalcitonin measured on days 1, 3, and 7. The final outcome considered was mortality within 1 month after diagnosis or discharge.

Results: *Aspergillus flavus* was the most common species (70/100,70%). Risk factors were, neutropenia (*P* .03), steroids prior to ICU admission (*P* .02), prolonged hospitalizations >21 days (*P* .05), and culture positivity was 80%. The culture was not inferior to realtime PCR for the diagnosis of fungal pneumonia. BAL Galactomannan was an early prognostic marker with a median rise above > 3.5 index value. The Median PCT level was higher from day 1in the fungal pneumonia non-survivor group (3.29 vs. 0.8 ng/ml) with higher 30-day mortality (72%). Higher PCT was associated with bacterial co-infection (48%), antibiotic (74%), antifungal therapy, and renal failure and mortality.

Conclusion: Fungal pneumonia complicates cirrhotics with neutropenia, prolonged hospitalization, and steroids as risk factors. *Aspergillus flavus* predominate in consensus with Asian epidemiology. Culture methods are reliable and a combination of molecular tests with BAL Galactomannan is useful for rapid diagnosis. Serum PCT is raised in patients with fungal pneumonia and is associated with higher mortality. In our study the baseline PCT at admission to ICU was higher in the non-survivor group, and levels on D3 and D7 were persistently higher. High serum procalcitonin level is an independent prognostic biomarker of mortality risk in fungal pneumonia.

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Aspergillus fumigatus **sensitization among the patients with chronic obstructive pulmonary disease (COPD)— a cross sectional study**

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Objectives: Allergic bronchopulmonary aspergillosis (ABPA) caused by hypersensitivity to A. *fumigatus* complicates the course of asthma. Fungal sensitization due to A. *fumigatus* among asthmatic patients and their progression to ABPA is well studied. Similar data on *Aspergillus* sensitization among patients with COPD and their progression are still not well established. The objective of this study was to evaluate the Total serum IgE (TIgE) and *A. fumigatus* specific IgE (Af sp IgE) levels among patients with COPD.

Method: A total of 100 stable patients with COPD above 40 years of age from the Department of Pulmonary Medicine were included. TIgE and Af sp IgE levels were detected using VIDAS total IgE assay and M3 ImmunoCap with Phadia 100 respectively. The subjects were grouped into three (TIgE <500 IU/l, 500-1000 IU/l, and >1000 IU/l) based on the TIgE values. They were also categorized based on Af sp IgE levels as sensitization likely (AS ≥0.35 kUA/l), sensitization indeterminate (AI 0.1-0.35 kUA/l), and sensitization unlikely (AU ≤0.1 kUA/l). This categorization was based on the kit manufacturer's guidelines that sensitization is unlikely with specific IgE <0.1 kUA/l and the proposed ISHAM ABPA working group criteria of >0.35 kUA/l for diagnosis of sensitization. A comparison of Asf sp IgE with TIgE was done using the Fischer exact test.

Result: Among 100 patients, the prevalence of elevated TIgE [>150 IU/l (kit cutoff)] and *Aspergillus* sensitization [Af Sp IgE >0.35kUA/l (ISHAM cutoff)] was 47% and 6%, respectively. A total of 5% of subjects satisfied the criteria for serological ABPA. The results of the comparison of Asf sp IgE with total IgE using the Fischer exact test are given in Table 1.

AS category: TIgE was >1000 IU/l in 5 (83.3%) of the 6 subjects. One (16.7%) had between 500-1000 IU/l. None of them had TIgE <500IU/l. *Aspergillus* sensitization was higher in 3/5 subjects with TIgE >1000 IU/ml (Asf sp IgE values of 2.55KUA/l, 12KUA/l, 14KUA/l, 0.38KUA/l, and 0.45KUA/l) compared with the one subject with TIgE <1000IU/l (Asf sp IgE of 0.73KUA/l). The clinical characteristics of subjects in the AS category is given in Table 2.

AI category: A total of 7 (50%) of the 14 subjects had the TIgE value >1000 IU/l, 5 (35.7%) had the TIgE between 500-1000 IU/l, and 2 subjects had the TIgE <500 IU/l.

AU category: In all, 1 (1.25%) had the TIgE value >1000 IU/l, 5 (6.25%) had the TIgE between 500-1000 IU/l. TIgE was <500 IU/l in 74 (92.5%) subjects.

Conclusion: The study results suggest the co-existence of COPD and *Aspergillus* sensitization/ABPA. Patients in the AI group (Af sp IgE level 0.1-0.35 kUA/l) must be evaluated and monitored to prevent the progression of the disease. Studies involving a larger patient population are warranted.

Table 1.Comparison of A.fumigatus specific IgE and Total IgE

Total IgE (IU/L)	Af Sp IgE (KUA/L)			*p* value
	<0.1 (AU) (n=80)	0.1 – 0.35 (AI) (n=14)	>=0.35 (AS) (n=6)	
<500 (n=76)	74 (92.5%)	2 (14.2%)	0	.00
500 – 1000 (n=11)	5 (6.25%)	5 (35.7%)	1 (16.66%)	
>1000 (n=13)	1 (1.25%)	7 (50%)	5 (83.3%)	

Table 2.Clinical profile of subjects in the *Aspergillus* Sensitisation likely (AS) category

Clinical characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender	M	M	M	F	M	M
Age (years)	70	70	61	60	45	57
H/O inhaled steroids	No	Yes	No	Yes	Yes	No
No of exacerbations	≤ 1	≤ 1	>1	≤ 1	≤ 1	≤ 1
Asf sp IgE (kUA/L)	.38	.45	.73	2.55	12	14
T IgE (IU/L)	>1000	>1000	680.23	>1000	>1000	>1000
FEV1%	S	S	VS	S	VS	VS
Chest x-ray	H	H	H + B	H	H + B	H
Culture (isolate)	-ve	-ve	-ve	-ve	+ve (A.fum)	+ve(A.flav)

S – severe, VS – Very severe, H – Hyperinflation, B – Bronchiectasis, H+B – Both hyperinflation and bronchiectasis, A.fum – A.fumigatus, A.flav – A.flavus