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Aspergillus spp infection in immunocompromised and non-neutropenic patients in Infection Intensive Care: a retrospective observational study

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Introduction

- Although Aspergillus spp infection (AI) is more prevalent in immunocompromised patients (IP), it is becoming more frequent in patients admitted to Intensive Care Unit (ICU) and not part of the traditional risk groups. (1,2,3)
- The diagnostic criteria that define AI, are still controversial.
- This study aims to investigate the demographic, clinical, microbiological features and outcome associated with a diagnosis of IA in IP compared to non-neutropenic patients (N-NP) admitted to a single-center ICU over a 3-year period.

Study Design

- We conducted a retrospective observational study of patients with a microbiological diagnosis of IA admitted to ICU of National Institute for Infectious Diseases Lazzaro Spallanzani (INMI) from January 2021 to December 2023.

Methods

- All consecutive adult (>18 years) ICU patients with a positive Real Time Polymerase Chain Reaction (PCR) assay result for Aspergillus spp were eligible for inclusion.
- Data were collected from electronic medical records and included demographics (sex, age), the immunocompromising condition, the clinical characteristic (comorbidities, SARS-CoV-2 co-infection, tracheostomy, year of diagnosis of IA) and outcome (length of stay and mortality within 28 days) and other microbiology results (Galactomannan [GALAG], 1-3 Beta-D-glucan [BDGLU] and culture).
- Continuous variables were expressed as median and interquartile range (IQR). Categorical variables were reported as numbers (percentages).
- To explore any statistically significant differences between the group of patients with (IP) and without underlying immunocompromising conditions (N-NP) across the available characteristics, Chi-squared or Fisher's Exact test for categorical variables and Wilcoxon rank sum test for continuous variables were performed.

Results

- A total of 82 patients with AI were identified during the study period according to the results of the PCR assay.
- Of these, 30 (36.6%) patients were immunocompromised patients and 52 (63.4%) non-neutropenic patients.
- Immunocompromised patients included 7 people living with HIV, 15 haematological/oncology patients and 8 transplant patients.
- Overall, males accounted for 68.3% of individuals. The median age was 66 years and the most frequent comorbidity was cardiovascular (34.1%). SARS-CoV-2 and tracheostomy occurred in 20.7% and 52.4%, of subjects, respectively. Mortality within 28 days occurred in 45.1% of patients.

Table 1 Demographic characteristics of patients with AI, overall and by immunocompromise status

Characteristics	Overall N = 82[1]	IP[1]	N-NP[1]	p-value[2]
		N = 30 (36.6%)[1]	N = 52 (63.4%)[1]	
Sex				0.027
Female	26 (31.7%)	14 (46.7%)	12 (23.1%)	
Male	56 (68.3%)	16 (53.3%)	40 (76.9%)	
Age	66 (57.3, 75.0)	60.5 (51.5, 72.0)	71.0 (62.0, 77.0)	0.02

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test; Wilcoxon rank sum test

- Compared with N-NP, IP with AI were more likely to be females (46.7% vs 23.1%, p=0.027), with lower age (60.5 vs 71 years, p=0.02) and with no SARS-CoV-2 concomitant infection (40% vs 9.6 %,p=0.001)

Table 2 Clinical characteristics of patients with AI, overall and by immunocompromise status

Characteristc	Overall, N = 82[1]	IP[1]	N-NP[1]	p-value[2]
		N = 30 (36.6%)[1]	N = 52 (63.4%)[1]	
Comorbidities				0.1
Respiratory	10 (12.2%)	4 (13.3%)	6 (11.5%)	
Cardiovascular	28 (34.1%)	6 (20.0%)	22 (42.3%)	
Neurological	1 (1.2%)	0 (0.0%)	1 (1.9%)	
Other	13 (15.9%)	4 (13.3%)	9 (17.3%)	
No	30 (36.6%)	16 (53.3%)	14 (26.9%)	
SARS-CoV-2				0.001
Yes	17 (20.7%)	18 (60.0%)	47 (90.4%)	
No	65 (79.3%)	12 (40%)	5 (9.6%)	
Tracheostomy				0.6
Yes	43 (52.4%)	17 (56.7%)	26 (50.0%)	
No	39 (47.6%)	13 (43.3%)	26 (50%)	
Year of AI				0.032
2021	16 (19.5%)	2 (6.7%)	14 (26.9%)	
2022	41 (50.0%)	20 (66.7%)	21 (40.4%)	
2023	25 (30.5%)	8 (26.7%)	17 (32.7%)	

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test;Fisher's exact test

- No statistically significant difference in length of stay and mortality within 28 days was observed between the group of patients with and without underlying immunocompromising conditions (Table 1-3).
- Overall, simultaneous evidence of AI was detected in 31 (37.8%), 13 (15.9%) and 14 (17.1%) patients for GALAG, BDGLU and culture, respectively.

Table 3 Clinical outcome of patients with AI, overall and by immunocompromise status

Characteristics	Overall, N = 82[1]	IP[1]	N-NP[1]	p-value[2]
		N = 30 (36.6%)[1]	N = 52 (63.4%)[1]	
Lenght of stay (days)	20 (10, 38)	21 (9.8, 38.8)	18 (10.5, 32.5)	0.4
Mortality within 28 days	37 (45.1%)	13 (43.3%)	24 (46.2%)	0.8

[1] n (%); Median (IQR)
[2] Wilcoxon rank sum test

- The concordance results between PCR, Galactomannan and 1-3 Beta-D-glucan are described in Table 4.

Table 4 Microbiology of patients with AI, overall and by immunocompromise status

Microbiology	Overall N = 82[1]	IP[1]	N-NP[1]	p-value[2]
		N = 30 (36.6%)[1]	N = 52 (63.4%)[1]	
Positivity to PCR and Galactomannan	31 (37.8%)	9 (30%)	22 (42.3%)	0.3
Positivity to PCR and 1-3 Beta-D-Glucan	13 (15.9%)	7 (23.3%)	6 (11.5%)	0.2
Positivity to PCR and Culture	14 (17.1%)	4 (13.3%)	10 (19.2%)	0.2
Positivity to PCR, Galactomannan and 1-3 Beta-D-Glucan	7 (8.5%)	4 (13.3%)	3 (5.8%)	0.3
Positivity to PCR, Galactomannan, 1-3 Beta-D-Glucan and Culture	3 (3.7%)	1 (3.3%)	2 (3.8%)	>0.9
PCR samples				
BAL (Broncho-Alveolar Lavage)	63 (76.8%)	24 (80.0%)	39 (75.0%)	0.3
BAS (Cronchoaspirate)	16 (19.5%)	4 (13.3%)	12 (23.1%)	
Other	3 (3.7%)	2 (6.7%)	1 (1.9%)	
Galactomannan samples				0.032
BAL (Broncho-Alveolar Lavage)	21 (25.6%)	6 (20%)	15 (28.8%)	
BAS (Cronchoaspirate)	5 (6.1%)	0 (0.0%)	5 (9.6%)	
Serum	3 (3.7%)	3 (10%)	0 (0.0%)	
Not available	53 (64.6%)	21 (70%)	32 (61.5%)	

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test;Fisher's exact test

Conclusion

- The study suggests that IP, particularly those who are female, younger in age, and uninfected with SARS-CoV-2, are more likely to develop AI, compared to N-NP.
- There wasn't a significant difference in outcomes and mortality rates between IP and N-NP.
- Notably, the study reports a higher incidence of GALAG positivity in the BAL of N-NP compared to IP. These observations highlight the importance of reevaluating the utility of the GALAG test in diagnosing AI in IP in the future.

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