# Invasive aspergillosis in COVID-19 patients in an intensive care unit in Mexico City

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## Background

- COVID-19 causes a wide variety of clinical manifestations, ranging from **asymptomatic to acute respiratory distress syndrome**.
- Invasive pulmonary aspergillosis (**IPA**) usually develops in immunosuppressed patients.
- IPA has also been described in patients with **severe viral pneumonia**, including COVID-19.
- At the beginning of the pandemic **tocilizumab** was used widely, presenting questionable results.
- Tocilizumab has been associated with the development of **opportunistic infections** caused by mycobacteria, Pneumocystis carinii and fungi such as Candida sp. and Aspergillus.
- Another treatment for COVID-19 were **high dose glucocorticoids**, they are also considered a traditional risk factor for the development of IPA when used for prolonged periods of time.

## Methods

- Cohort study with the COVID-19 registry of the ABC Medical Center.
- COVID-19 was diagnosed based on the presence of clinical manifestations and a **positive PCR for SARS-CoV2** or **CT scan** with characteristic findings.
- Inclusion criteria: admission March 15th-July 10th, admission to **the ICU, serum or bronchoalveolar lavage fluid galactomannan.**
- Exclusion criteria: missing data on diagnostic criteria and outcomes.
- IPA was confirmed using the **Schauwvlieghe criteria**.
- The local ethics committee approved the study (ABC-20-26).

## Results

- Out of a total of 198 patients, we included 83 patients.
- We identified 16 patients (19.2%) with IPA.
- Mycological criteria were met with: positive galactomannan (87.5%), and with positive cultures for Aspergillus sp (12.5%).
- There were no significant differences between the two groups in regard to the proportion or dose of glucocorticoids (1.3 mg/kg of prednisone or equivalent), tocilizumab, lopinavir, ritonavir, azythromicin or hydroxicloroquine.
- All IPA patients required IMV vs. 84% of the non-IPA group (p=0.09).
- 5 deaths (31%) in the IPA group vs. 9 (13%) in the non-IPA (p=0.08).
- All patients with IPA were promptly treated with antifungals.

## Results: Baseline characteristics

| Variable | IPA (n=16) | Controls (n=67) | p-value |
|---|---|---|---|
| Age (years), mean (SD) | 64 (10) | 55 (15) | <0.001 |
| Female sex | 16 (22) | 15 (22) | 0.47 |
| PaFIO2, median (IQR) | 122 (84-166) | 108 (82-160) | 0.76 |
| **Comorbidities** | | | |
| Overweight | 8 (50) | 33 (49) | 0.39 |
| Obesity | 6 (38) | 19 (28) | 0.39 |
| COPD | 1 (6) | 3 (4) | 0.77 |
| Hypertension | 4 (25) | 22 (33) | 0.57 |
| Diabetes mellitus | 5 (31) | 13 (19) | 0.30 |
| Cancer | 3 (19) | 3 (4) | 0.05 |
| **Laboratory data, median (IQR)** | | | |
| Leucocytes | 9 (6-10) | 8 (6-12.5) | 0.94 |
| Lymphocytes | 0.93 (0.62-1.27) | 0.88 (0.54-1.10) | 0.65 |
| Platelets | 205 (135-257) | 192 (139-298) | 0.66 |
| D-Dimer | 1088 (714-2795) | 1072 (648-2085) | 0.68 |
| C Reactive Protein | 18 (5-26) | 17 (9-30) | 0.39 |
| Interleukin 6 | 15 (9-88) | 44 (12.5-77) | 0.60 |
| Ferritin | 1756 (1027-2387) | 1178 (722-2089) | 0.18 |
| **Severity scales** | | | |
| NEWS, mean (SD) | 7.1 (2.47) | 6.84 (2.45) | <0.001 |
| CALL, median (IQR) | 10 (8.5-11.5) | 9 (7-11) | 0.21 |
| MuLBSTA, median (IQR) | 12 (11-12) | 9 (7-12) | 0.26 |
| **Positive Bacterial Isolates** | | | |
| CVC culture | 5 (31) | 4 (6) | 0.01 |
| Endotracheal tube culture | 3 (19) | 7 (10) | 0.39 |
| Sputum culture | 1 (6) | 3 (4) | 1.00 |

**Table 1:** Here we show the comparison of the baseline characteristics amongst patients with ant without IPA. Patients with IPA tended to be older, have a history of cancer and to have higher scores in the NEWS scale. Patients with IPA had microbiological isolates found on their CVCs more often than patients without IPA. All values are N(%) unless otherwise noted. Abbreviations: COPD: Chronic Obstructive Pulmonary Disease, CRP: C-reactive protein, CVC: Central venous catheter, IL-6: Interleukin-6.

## Results: COVID-19 treatment received

| All patients | IPA (n=16) | Controls (n=67) | p-value |
|---|---|---|---|
| Hidroxicloroquine | 14 (88) | 56 (84) | 0.71 |
| Lopinavir/Ritonavir | 11 (69) | 45 (67) | 0.91 |
| Azithromycin | 12 (75) | 56 (84) | 0.43 |
| Steroids | 2 (13) | 22 (33) | 0.34 |
| Tocilizumab | 12 (75) | 43 (64) | 0.52 |

**Table 2:** Here we show the COVID-19 treatment received by each group. There were no significant differences in the frequencies in which COVID-19 treatment was administered amongst both groups. All values are N(%)

## Results: Clinical outcomes

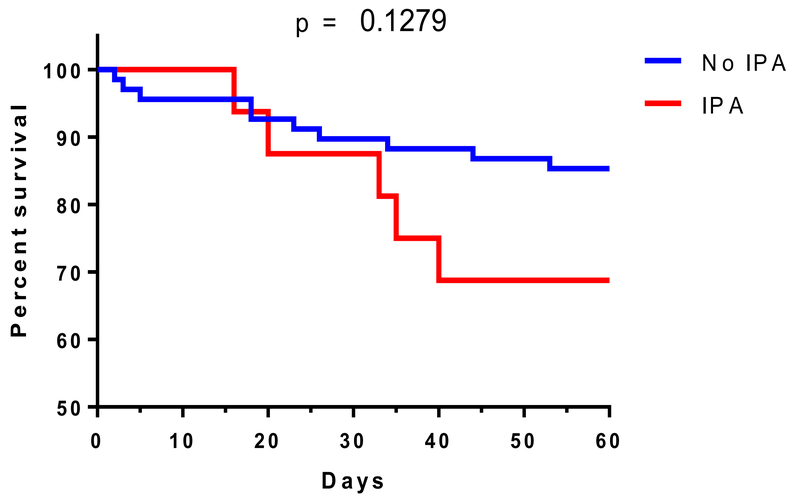


**Figure 1:** Here we show the survival of both groups. Mortality tended to be more frequent in the IPA group, although it did not reach statistical significance.

## Conclusions

Older age and a history of cancer were associated with the development of IPA in COVID-19 patients. None of the treatments used for COVID-19 were associated with an increased risk of IPA. The proportion of worst clinical outcomes are more frequent in IPA patients, this sample is small to prove differences between groups, we need more studies to see consistency with ours.