Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

**Background.** Most individuals diagnosed with mild to moderate COVID-19 are no longer infectious after day 10 of symptom onset and those with severe or critical illness from COVID are typically not infected after day 20 of symptom onset. Recovered persons can continue to test positive for SARS-CoV-2 by PCR via detection of non-viable RNA in nasopharyngeal specimens for up to three months (or longer) after illness onset. It is also known that severely immunocompromised patients may produce replication-competent virus greater than 20 days from symptom onset and may require, per CDC recommendations, "additional testing and consultation with infectious diseases specialists and infection control experts." We aim to discuss four case studies of severely immunocompromised patients who exhibited signs of persistent COVID-19 infection of COVID and how we managed transmission-based precautions in our hospital through sequencing and evaluation of cycle thresholds (CT) values and subgenomic RNA detection.

**Methods.** Residual nasopharyngeal (NP) samples were collected on patients exhibiting persistent COVID-like symptoms. These samples underwent N gene and N gene subgenomic RNA (ngRNA) real-time reverse transcription polymerase chain reaction (RT-PCR) testing.

**Results.** Analysis of longitudinal SARS-CoV-2 sequence data demonstrated within-patient virus evolution, including mutations in the receptor binding domain and deletions in the N-terminal domain of the spike protein, which have been implicated in antibody escape. See Figures 1 and 2.

**Figure 1. Timelines of Identified Patients 1 and 2**

Patient 1: 46-year-old woman with recently diagnosed stage IV diffuse large B-cell lymphoma for which she was treated with 2 cycles of R-CHOP. Patient 2: 38-year-old woman with history of myelodysplastic syndrome, peripheral blood stem cell transplant with chronic graft versus host disease of the GI tract, skin, and eyes as well as CMV enteritis, and she was maintained on rituximab, mycophenolate mofetil, prednisone, and monthly IVIG without recent changes to her immunosuppression.

**Figure 2. Timeline of Identified Patients 3 and 4**

Patient 3: 44-year-old man with prior history of thymoma and thymectomy Patient 4: 46-year-old man who was initially diagnosed with marginal zone lymphoma approximately 2.5 years ago. He was initially treated with bendamustine and rituximab and achieved remission. He was then continued on maintenance rituximab without recent changes to his immunosuppression. Approximately 2.5 years ago, he was initially treated with bendamustine and rituximab and achieved remission. He was then continued on maintenance rituximab without recent changes to his immunosuppression.

**Conclusion.** Differentiating between prolonged viral shedding of non-infectious RNA and persistent replicating viable virus can be difficult to determine without full evaluation of a patient's clinical picture and timeline. Consultation between laboratory, infectious diseases, and infection prevention experts to provide appropriate level of guidance for precautions and treatment may be warranted. Testing by PCR and analysis of CT values may provide key findings of viral replication in immunocompromised hosts, indicating the need for evaluation of additional treatment and maintaining isolation status in healthcare settings.

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279. Clinical Characteristics of Critically Ill Patients with COVID-19 and Invasive Pulmonary Aspergillosis: A Case Series From Mexico City

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**Infectomed**

**Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes**

**Background.** COVID-19 has emerged as a global public health emergency and has been the main cause of intensive care admission during the pandemic. COVID-19-associated pulmonary aspergillosis (CAPA) has been reported in case series of critically ill patients. However, the criteria for CAPA diagnosis has been inconsistent among most of the reports. Mexico has been widely affected by SARS-CoV-2. We present a series of CAPA cases at a teaching hospital in Mexico City.

**Methods.** We performed a retrospective analysis of COVID-19 patients admitted to the ABC Medical Center from May 1st, 2020, to May 1st, 2021. Including only those with critical COVID-19 who required invasive mechanical ventilation (IMV). Patients with a diagnosis of CAPA were analyzed. We followed the 2020 ECMO/SHAM consensus criteria for CAPA diagnosis. Aspergillus antigen testing in tracheal aspirate and serum was done with Aspergillus-specific galactomannan protein (GP) ELISA (Euroimmun Medizinische Labordiagnostika).

**Results.** Among the 230 admitted patients who required IMV, we identified 49 (21.3%) cases of CAPA. 46 probable CAPA and 3 proven CAPA. Nineteen (38%) of those died in the hospital. The mean age was 64.5 ± 12.6 years and 11 were female. Proven CAPA was diagnosed with culture in three cases (one A. niger, one A. terreus and one A. fumigatus). Probable CAPA was diagnosed by a positive serum GP in 27 (55.1%) patients and by a positive bronchoalveolar lavage (BAL) GP in 29 (59.2%) cases. Seven patients had both serum and BAL positive GP. Forty-six (93.9%) patients received corticosteroids, and 22 (49.9%) were treated with tocilizumab before CAPA diagnosis. All but one received isavuconazole as CAPA treatment. We detected 35 (71.4%) patients who had a bacterial co-infection. Eighteen of those died (51.4%) compared to only one dead in the subgroup without coinfections (7.1%). The mean time from hospital admission to CAPA diagnosis was 6.2 days (SD 7.1) among those who survived compared to 13.2 (SD 6.3) days in those who died p<0.01.

**Conclusion.** CAPA had a lower prevalence than previously reported in other series. However, it appears to be linked to higher mortality. A specific time when it occurs with other bacterial coinfections and when it is diagnosed late from admission.

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280. Burden of Hyperglycemia in Patients Receiving Dexamethasone for Severe COVID-19

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**Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes**

**Background.** Previous studies demonstrated the adverse impact corticosteroids can have on blood glucose homeostasis in both diabetics and non-diabetics. This raises concerns for corticosteroid use in severe COVID-19 where the population is enriched for those at highest risk of severe disease, such as diabetics and patients with obesity. Previous studies of dexamethasone in COVID-19 were limited by the inability to assess steroid-induced hyperglycemia or the impact of hyperglycemia on hospital resources.

**Objective.** The study aimed to describe the clinical characteristics, management, and outcomes related to hyperglycemia, before and after dexamethasone therapy was used as the standard of care in patients with severe COVID-19.

**Methods.** We performed a pre/post retrospective study of patients with severe COVID-19 pneumonia admitted from May to July 2020 to Harbor-UCLA Medical Center. 126 patients were evaluated. 64 received dexamethasone and 62 did not. To quantify the effect of dexamethasone on diabetic vs. non-diabetic patients, we documented the average blood gluoses and frequency of correctional insulin doses required by each patient group (diabetic with and without dexamethasone, non-diabetic with and without dexamethasone).

**Results.** While dexamethasone was associated with higher median blood glucose values and more frequent correctional insulin dosing in diabetic patients, there was minimal effect of dexamethasone on hyperglycemia in non-diabetic patients. Furthermore, while non-diabetic patients receiving dexamethasone required more doses of correctional insulin per day vs non-diabetic patients not receiving dexamethasone (0.3 doses per day vs 0.1 doses per day), the frequency of correctional insulin doses required by non-diabetics on dexamethasone remained low at 0.3 doses per day.

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Disclosures.

Conclusion.

Table 1. Baseline Characteristics

|          | No dexamethasone (n=62) | Dexamethasone (n=64) |
|----------|--------------------------|----------------------|
| Age, median (range) | 53 (24-87) | 56.5 (23-84) |
| Female, n (%) | 29 (46.8) | 26 (40.6) |
| Ethnicity, n (%) | 1 (1.6) | 1 (1.6) |
| Black | 4 (6.5) | 6 (9) |
| White, non-Hispanic | 1 (1.6) | 1 (1.6) |
| Hispanic/Latinx | 56 (89) | 49 (76.6) |
| Other | 2 (3.2) | 8 (12.5) |
| BMI, mean (range) | 31 (18.3 - 57) | 32.2 (16.0 - 65.6) |
| Prior diagnosis of DM, n (%) | 26 (42) | 35 (55) |
| HgbA1C, mean% (STD, n) | 9.3% (2.9%, n=29) | 8.9% (2.6%, n=36) |
| Highest required O2 Supplemental | 27 (43.5) | 22 (34.4) |
| Low flow, n (%) | 17 (27.4) | 29 (45.3) |
| High flow nasal canula, n (%) | 18 (29.0) | 13 (20.3) |
| Mechanical ventilation, n (%) | 8 (5-13) | 8 (5.5-13) |
| Days on dexamethasone, median (IQR) | 0 | 7.5 (4.5-10) |

Table 2. Results

|          | No dexamethasone (n=62) | Dexamethasone (n=64) | P value |
|----------|--------------------------|----------------------|---------|
| 10-day average blood glucose, median (IQR) | 117 mg/dL (105-176.6) | 175 mg/dL (122.2-249) | <0.005* |
| 10-day average BG with diabetes, median (IQR) | 176.3 mg/dL (138.6-209.7) | 234.4 mg/dL (206.1-273.8) | <0.005* |
| 10-day average BG without diabetes, median (IQR) | 106.9 mg/dL (96-113.6) | 118.8 mg/dL (111.1-143.6) | <0.005* |

Correctional Insulin

| Number of days with ≥7 correctional dose per days hospitalized on or dexamethasone | No Diabetes | Diabetes |
|---------------------------------------------|-------------|---------|
| 10-day average correctional dose per day on dexamethasone | 8 doses/223 days (CI: 0.02/day - 0.07/day) | 18 doses/197 days (CI: 0.05/day - 0.1/day) |

Sensitivity analysis using only positive diagnostic test to define influenza cases

Conclusion.

281. Prevalence of Influenza Co-infection in a Real-world Cohort of COVID-19 Patients in the U.S.
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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. Over 29 million people have been infected with COVID-19 in the U.S. alone. While COVID-19 carries serious morbidity and mortality, potential for co-infection with other respiratory infections remains unclear. We aimed to: (1) estimate co-infection prevalence of COVID-19 and influenza, and (2) compare demographics and clinical outcomes of co-infected patients to those of COVID-19 singly-infected patients using U.S. electronic health records (EHR).

Methods. Patients in the Optum De-identified COVID-19 EHR database diagnosed with COVID-19 (lab-confirmed or ICD code) between February 2020 and January 2021 were eligible. Influenza co-infection was defined as an influenza diagnosis (lab-confirmed or ICD code) within ±10 days of COVID-19 diagnosis. We report co-infection prevalence for all COVID-19 patients and for a subset of hospitalized COVID-19 patients.

Results. Among all COVID-19 patients (N = 549,532), 1,794 (0.3%) were co-infected with influenza. Among the hospitalized subset (N = 80,192), 242 (0.3%) were co-infected with influenza. In sensitivity analyses restricting to lab-confirmed influenza, co-infection prevalence was 0.1% overall and 0.2% among hospitalized patients. No meaningful differences were observed in baseline demographics between co-infected and singly-infected patients. Among hospitalized patients, univariate analysis suggested higher likelihood of invasive ventilation (12.8% vs. 9.8%; p=0.14), respiratory failure (56.2% vs. 46.6%; p<0.01), and ICU stay (27.3% vs. 23.1%; p=0.13), but no meaningful difference in mortality (13.3% vs. 13.0%; p=0.97), for co-infected as compared to singly-infected COVID-19 patients.

Table 1. Prevalence of influenza co-infection among COVID-19 patients, overall and hospitalized

|          | Total COVID-19 cohort | Co-infected with influenza |
|----------|-----------------------|---------------------------|
| Sensitivity analysis | Overall | 549,532 | 1,794 (0.3%) |
| Hospitalized | 80,192 | 242 (0.3%) |

Conclusion. In a real-world cohort, we observed a low proportion (0.3%) of COVID-19 patients co-infected with influenza. Co-infected patients had similar baseline characteristics but higher likelihood of hospitalization severity as compared to singly-infected COVID-19 patients. Limitations include low prevalence of circulating influenza and potential missing data bias.

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282. Risk Factors for Mortality in Severe COVID-19 Patients Admitted to the Intensive Care Unit: A Retrospective Single-Center Study in Saudi Arabia
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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. The first case of COVID-19 in the Kingdom of Saudi Arabia (KSA) was reported in March 2020. This study aims to describe the overall mortality in the ICU during the COVID-19 pandemic and to determine independent risk factors for overall survival & 29 days mortality.

Methods. This is a retrospective single-center study; data for adult patients admitted to the ICU with COVID-19 between 1st March 2020 to 31st December 2020 were extracted and reviewed. Overall survival was described using Kaplan-Meier curves with reporting of median overall survival and 29 days survival estimates. Multivariate analysis using ICD codes or positive diagnostic test to define influenza cases

Conclusion. NIH COVID-19 guidelines recommend administering dexamethasone only if the patient is in a monitored setting. Our data support the NIH concerns that outpatients with diabetes receiving steroids are at risk for hyperglycemic complications. However, contrary to the NIH guidelines, our data suggest that patients without diabetes receiving steroids are at low risk for complications due to hyperglycemia and a majority do not require monitoring.

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