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Session: P-21. COVID-19 Research

Background. A major challenge to identifying effective treatments for COVID-19 has been the conflicting results offered by small, often underpowered clinical trials. The World Health Organization (WHO) Ordinal Scale (OS) has been used to measure clinical improvement among clinical trial participants and has the benefit of measuring effect across the spectrum of clinical illness. We modified the WHO OS to enable assessment of COVID-19 patient outcomes using electronic health record (EHR) data.

Methods. Employing the National COVID Cohort Collaborative (N3C) database of EHR data from 50 sites in the United States, we assessed patient outcomes, April 1, 2020 to March 31, 2021, among those with a SARS-CoV-2 diagnosis, using the following modification of the WHO OS: 1=Outpatient, 3=Hospitalized, 5=Required Oxygen (any), 7=Mechanical Ventilation, 9=Organ Support (pressors; ECMO), 11=Death. OS is defined over 4 weeks beginning at first diagnosis and recalculated each week using the patient's maximum OS value in the corresponding 7-day period. Modified OS distributions were compared across time using a Pearson Chi-Squared test.

Results. The study sample included 1,446,831 patients, 54.7% women, 14.7% Black, 14.6% Hispanic/Latinx. Pearson Chi-Sq $P < 0.0001$ was obtained comparing the distribution of 2nd Quarter 2020 OS with the distribution of later time points for Week 4.

Table 1. OS at week 1 and 4 by quarter

Modified OS	2 nd Quarter 2020		3 rd Quarter 2020		4 th Quarter 2020		1 st Quarter 2021	
	Week 1 N (%)	Week 4 N (%)	Week 1 N (%)	Week 4 N (%)	Week 1 N (%)	Week 4 N (%)	Week 1 N (%)	Week 4 N (%)
1 Outpatient	179,953 (83.31)	203,869 (94.38)	224,956 (90.72)	241,740 (97.49)	595,935 (90.94)	637,383 (97.27)	291,602 (89.02)	318,033 (97.09)
3 Hospitalized	26,437 (12.24)	5,200 (2.41)	18,369 (7.41)	3,456 (1.39)	45,782 (6.99)	8,561 (1.31)	27,612 (8.43)	4,679 (1.43)
5 Oxygen	2,792 (1.29)	386 (0.18)	1,761 (0.71)	212 (0.09)	6,706 (1.02)	721 (0.11)	4,182 (1.28)	402 (0.12)
7 Mechanical Ventilation	4,032 (1.87)	784 (0.36)	1,878 (0.76)	355 (0.14)	4,109 (0.63)	953 (0.15)	2,428 (0.74)	435 (0.13)
9 Organ Support	265 (0.12)	129 (0.06)	239 (0.1)	51 (0.02)	319 (0.05)	105 (0.02)	286 (0.09)	54 (0.02)
11 Death	2,529 (1.17)	5,640 (2.61)	764 (0.31)	2,153 (0.87)	2,442 (0.37)	7,570 (1.16)	1,453 (0.44)	3,960 (1.21)
Total N	216,008	216,008	247,967	247,967	655,293	655,293	327,563	327,563

The study sample included 1,446,831 patients, 54.7% women, 14.7% Black, 14.6% Hispanic/Latinx. Pearson Chi-Sq $P < 0.0001$ was obtained comparing the distribution of 2nd Quarter 2020 OS with the distribution of later time points for Week 4.

Conclusion. All Week 4 OS distributions significantly improved from the initial period (April-June 2020) compared with subsequent months, suggesting improved management. Further work is needed to determine which elements of care are driving the improved outcomes. Time series analyses must be included when assessing impact of therapeutic modalities across the COVID pandemic time frame.

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448. COVID-19 Acute Care at Home: A Substitution for Hospitalization in Patients with Mild Symptoms

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Background. Constraints on resources require healthcare systems to implement alternative and innovative means for delivering care. The COVID-19 pandemic amplified this issue throughout the world, leading to shortages of ventilators, hospital beds, and healthcare personnel. We report the results of an Acute Care at Home Program (ACHP) response to COVID-19, providing in-home hospital-level care to patients with mild symptoms, preserving in-hospital beds for more serious illness.

Methods. Patients with COVID-19 were selected for ACHP after undergoing risk stratification for severe disease, including oxygen evaluation, time course of illness, and evaluation of comorbidities. Patients admitted to ACH met inpatient criteria, required oxygen supplementation of ≤ 4 liters, and received insurance approval. Services were provided consistent with best practice of inpatient care, including 24/7 provider availability via TeleMedicine, bedside care provided by paramedics and nurses, respiratory therapy, radiology and laboratory services, pulse oximetry monitoring, and administration of medications. Protocols existed for patient transfer to hospital in the event of clinical deterioration.

Results. Our initial cohort included 62 patients enrolled October 1, 2020 – May 31, 2021. Of these, 57 patients were discharged successfully from ACHP. Patients presented with initial oxygen requirements of 0-4 liters. Average length-of-stay in ACHP was 5.4 days. Five patients required hospitalization after enrollment in ACHP; one

subsequently expired, two were discharged home, one returned to ACHP after inpatient hospitalization, and one remains hospitalized. One additional patient that was successfully discharged home from ACHP was later readmitted and expired in a subsequent hospitalization. The patients that expired had significant immunocompromising conditions that may have contributed to their outcomes.

Conclusion. ACHP can provide care equivalent to hospitalization for select COVID-19 patients. Immunocompromised hosts with COVID-19 may represent a subset of patients in which in-house hospitalization must be carefully considered, even with mild oxygen requirements. Health systems should consider ACHP as a substitution for hospitalization for COVID-19 patients with mild symptoms.

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449. Performance of the Brighton Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C) Among a Large Single Center Cohort

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Background. Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare, life-threatening, hyperinflammatory condition presumed to follow SARS-CoV-2 infection. Whether MIS-C can also follow SARS-CoV-2 vaccination is not clear, making MIS-C an adverse event of special interest following immunization. Monitoring for post-vaccine MIS-C is complicated by the clinical overlap of MIS-C with numerous other inflammatory conditions including Kawasaki Disease, toxic shock syndrome, and viral myocarditis. A case definition for MIS-C was recently created with the Brighton Collaboration (BC). We aimed to determine the performance of the BC MIS-C case definition among a large, single-center MIS-C cohort.

Methods. Retrospective review was performed for the first 100 MIS-C cases at our institution (May 2020-February 2021). All cases met the Centers for Disease Control and Prevention (CDC) case definition. Data on age, presentation, laboratory results and cardiac studies were collected and used to determine cases that fulfilled the BC case definition for MIS-C (see figure).

Case Definition: Definite Case



Results. Of 100 children (age < 21 years) diagnosed with MIS-C using the CDC case definition, 93 patients also fulfilled the BC definition. All 100 patients had elevated laboratory markers of inflammation and positive SARS-CoV-2 antibodies. However, 1 patient was excluded for significant respiratory symptoms (pulmonary hemorrhage), 5 were excluded due to only 1 clinical feature, and an additional patient was excluded for having none of the measures of disease activity. Among the 93 patients fulfilling the revised case definition, 88 (95%) met criteria for a definite case. Five of the 93 patients (5%) were considered probable cases. 1 reported only 1 day of fever and 4 had only 1 measure of disease activity.

Conclusion. The original case definitions for MIS-C were created rapidly following the first emerging reports of this hyperinflammatory state. Knowledge of the varied clinical presentations of this disorder has grown substantially. Modification of the case definition to include features truly representative of MIS-C will allow for more precise diagnosis in the face of conditions which mimic MIS-C, and for accurate and reliable monitoring for adverse events following immunization.

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450. Type I Interferon Autoantibodies Are Detected in Those with Critical COVID-19, Including a Young Female Patient

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EPICC Study Group

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Background. Approximately 10-20% of patients with critical COVID-19 harbor neutralizing autoantibodies (auto-Abs) that target type I interferons (IFN), a family of cytokines that induce critical innate immune defense mechanisms upon viral infection. Studies to date indicate that these auto-Abs are mostly detected in men over age 65.

Methods. We screened for type I IFN serum auto-Abs in sera collected < 21 days post-symptom onset in a subset of 103 COVID-19 inpatients and 24 outpatients drawn from a large prospective cohort study of SARS-CoV-2 infected patients enrolled across U.S. Military Treatment Facilities. The mean age of this n = 127 subset of study participants was 55.2 years (SD = 15.2 years, range 7.7 – 86.2 years), and 86/127 (67.7%) were male.

Results. Among those hospitalized 49/103 (47.6%) had severe COVID-19 (required at least high flow oxygen), and nine subjects died. We detected neutralizing auto-Abs against IFN- α , IFN- ω , or both, in four inpatients (3.9%, 8.2% of severe cases), with no auto-Abs detected in outpatients. Three of these patients were white males over the age of 62, all with multiple comorbidities; two of whom died and the third requiring high flow oxygen therapy. The fourth patient was a 36-year-old Hispanic female with a history of obesity who required mechanical ventilation during her admission for COVID-19.

Conclusion. These findings support the association between type I IFN auto-antibody production and life-threatening COVID-19. With further validation, reliable high-throughput screening for type I IFN auto-Abs may inform diagnosis, pathogenesis and treatment strategies for COVID-19, particularly in older males. Our finding of type I IFN auto-Ab production in a younger female prompts further study of this autoimmune phenotype in a broader population.

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451. Is Antibody to Nucleocapsid More Prevalent in Individuals with Severe COVID-19?

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Background. Virus-specific antibodies help to understand the prevalence of infections and the course of the immune response. Humans produce antibodies against the spike and nucleocapsid proteins of SARS-CoV-2 virus. Patients with COVID-19 who recover from the infections have higher levels of antibodies to spike proteins. Our study aimed to find the levels of antibodies to spike and nucleocapsid proteins in severe COVID-19.

Methods. A single center prospective study was done at Ascension St John Hospital, Detroit, MI. We included COVID-19 cases diagnosed by reverse-transcriptase polymerase-chain-reaction (RT-PCR). Quantitative measurements of plasma or serum antibodies to nucleocapsid and spike proteins were done in hospitalized

patients with acute COVID-19. Using the electronic medical record, we collected data on demographic and clinical information.

Results. A total 24 patients were studied. Of which, 15 patients were suffering from severe and critical COVID 19 and 9 patients were suffering from mild to moderate COVID 19. The mean age (standard deviation) of our cohort was 69 \pm 10 years and 60% were males. Common comorbid conditions were hypertension, obesity, and type 2 diabetes. We also noted that severe to critical COVID 19 expressed higher level of antibody to nucleocapsid.

Conclusion. These results display the seroconversion in COVID 19 patients. Our study shows antibody level remain high in severe COVID 19 patients but those are against nucleocapsid protein instead of spike protein.

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452. Correlation of Charleston Comorbidity Index Score as the COVID-19 Pandemic Surged Throughout HCA Healthcare Facilities and Patient Outcomes

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Background. As the COVID-19 pandemic raged throughout the United States, the healthcare system was strained due to a sudden increase in demand. Testing was initially limited, and the perception was that patients with high comorbidity burden were at higher risk for poor outcomes. The Charleston Comorbidity Index (CCI) is widely used as a predictor of prognosis and one-year mortality for a wide range of pathologies. This study aims to assess whether a correlation exists between CCI score, COVID-19 incidence throughout the pandemic and patient outcomes.

Charleston Comorbidity Index Score

Charleston Comorbidity Index (CCI)	
Condition	Score
Myocardial infarction	1
Congestive Heart Failure	1
Peripheral Vascular Disease (including aortic aneurysm >6cm)	1
TIA or Cerebrovascular disease with mild of no residua	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Peptic ulcer disease	1
Mild liver disease without portal HTN	1
Diabetes without end-organ damage	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with end-organ damage	2
Tumor without metastases (diagnosed <5years ago)	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS	6

Scoring system for Charleston Comorbidity Index (CCI). Plus 1 point for every decade age 50 years and over, maximum 4 points. Higher scores indicate a more severe condition and consequently, a worse prognosis.

Methods. Multicenter, retrospective review of patients diagnosed with COVID-19 from January 2020 to September 2020 throughout the HCA Healthcare system. The percent of total encounters that were COVID-19 positive by state was calculated along