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Epidemiology, Immunology and Clinical Characteristics of Emerging Infectious Diseases with Pandemic Potential (EPICC) Study Group

Session: P-18. COVID-19 Pathogenesis

Background: While the majority of illness due to COVID-19 does not require hospitalization, little has been described about the host inflammatory response in the ambulatory setting. Differences in the levels of inflammatory signaling proteins between outpatient and hospitalized populations could identify key maladaptive immune responses during COVID-19.

Methods: Samples were collected from 76 participants (41% female, mean 46.8 years of age) enrolled at five military treatment facilities between March 20, 2020 and June 17, 2020 in an ongoing prospective COVID-19 cohort. This analysis was restricted to those with positive SARS-CoV-2 (severe acute respiratory syndrome–coronavirus 2) RT-PCR testing and included hospitalized (N=29; 10 requiring an ICU stay) and non-hospitalized (N=43) participants. Severity markers (IL6, D-dimer, procalcitonin, ferritin, ICAM-1, IL5, lipocalin, RAGE, TNFR, VEGFA, IFNγ, IL1β) were measured in plasma (mg/dL) using the Ella immunoassay and natural log transformed. Univariate negative binomial regression was performed to determine relative risk of hospitalization. Using the full marker panel, we performed a Principal Component Analysis (PCA) to determine directions of maximal variance in the data. Pearson's correlation coefficient was determined between analytes and each axis.

Results: Participants requiring ambulatory-, hospital-, and ICU-level care had samples collected at 44.0 (IQR: 35.0–51.0), 40.0 (13.0–51.0), and 47.5 (21.0–54.0) days, respectively. Higher unadjusted levels of IL6, D-dimer, procalcitonin, or ferritin were each associated with hospitalization (Table 1). The PCA showed a separation along axes between level of care and duration of symptoms (Fig 1). While significant correlations were noted with a number of biomarkers, PC1 most correlated with TNFR1 (r=0.88) and PC2 most correlated with IL6Ra (r=0.95). PC1 axis variation accounted for 36.5% of variance and the PC2 axis accounted for 20.0% of variance.

Figure 1. Principal Component Analysis (PCA) of biomarkers by level of care and symptom duration.

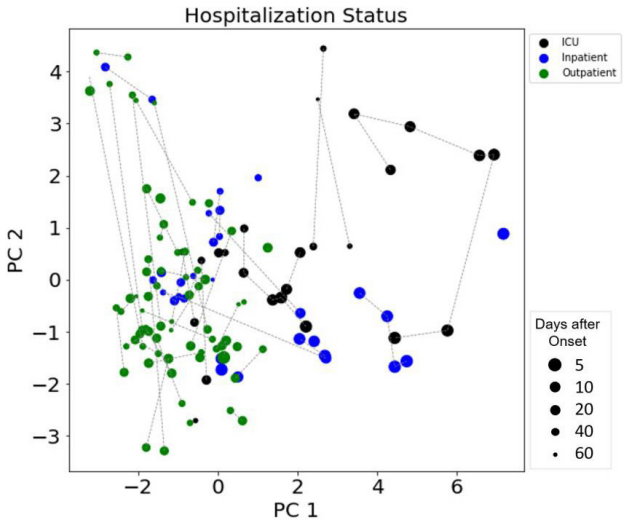

Table 1. Inflammation biomarker levels between level of care requirements.

Biomarker analyte (units)	Ambulatory care (median, IQR) (pg/mL)	Required hospitalization (median, IQR) (pg/mL)	Received ICU care (median, IQR) (pg/mL)	RR of hospitalization (95% CI) (per natural log pg/ml)
D-dimer	313,489 (193,814-652,718)	891,014 (479,005-1.8e+06)	964,282 (611,300-1.5e+06)	1.72 (1.2, 2.4)
IL6	1.2 (0.7-1.7)	2.4 (2.0-6.4)	4.5 (2.1-17.5)	1.5 (1.2, 1.8)
Ferritin	76,430 (22,431-169,441)	188,417 (64,865-450,179)	270,657 (111,496-601,828)	1.33 (0.99, 1.8)
Procalcitonin	46.5 (33.3-80.6)	69.4 (40.1-99.8)	139.5 (67.9-256.0)	1.37 (1.1, 1.8)

RR: relative risk; IQR: interquartile range

Conclusion: TNFR1 and IL6Ra levels correlated with differences in the proinflammatory states between hospitalized and non-hospitalized individuals including time points late in the course of illness. Further analysis of these preliminary findings is needed to evaluate for differences by stages of illness.

Disclosures: **All Authors**: No reported disclosures

509. Comparision of CD4+ T Cells in Patients with Severe vs Critical COVID -19

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Session: P-18. COVID-19 Pathogenesis

Background: Over the past few years, it has been shown that T cells play an essential role in antiviral immunity, in the course of the COVID-19 pandemic some studies reported an association between lymphocytopenia and exhaustion of the surviving remaining T cells which are apparently functional in patients with acute COVID-19, specially in those with severe forms of presentation. Some studies have reported an association where less than 800 CD4 + T cells are negatively related to the survival of seriously ill patients with COVID -19.

Methods: We included 19 patients admitted to our hospital (ABC Medical Center) from May 7 to 15, 2020 with a confirmed diagnosis of COVID-19 and were randomized into 2 groups according to the severity of the presentation (severe or critical) A determination of CD4 + T cells was made at admission, we also reported the need for invasive mechanical ventilation at some point of the hospitalization for each group, all patients were followed until their hospital discharge. One patient was excluded because he was still admitted at the time of the analysis.

Results: Of the 18 patients included, 9 (50%) fulfilled criteria of severe and 9 (50%) of critical. The mean of CD4 + T cell was 455 (256–697) for the severe and 285.44 (145–430) for the critical (CI 95% P 0.46), the determination of CD8+ T cell was 212 (88–392) for the severe and 201 (59–534) for the critical (CI 95% P 1.19), of the critical patients 8 (88.9%) required invasive mechanical ventilation and only one non-invasive mechanical ventilation, while the severe patients only required support with supplemental oxygen by nasal cannula (9 (100%)).The mean lenght of hospitalization was 12.73 days (3–34) and all the patients survived until they were discharged home.

Conclusion: As it has been reported in some studies, the pathogenesis of SARS-CoV-2 infection in humans is associated with a reduction and functional exhaustion of T cells in patients with COVID-19.In this study we presume that lower levels of CD4+T cells can be associated with critical forms of COVID 19 as the majority of critical patients in our report had < 300 CD4 +T cell count, while we need further studies with a greater number of patients and follow-up to establish reliable determinations, we propose than the levels of CD4+T cell count could be use as a good predictor of severity in COVID-19

Disclosures: **All Authors**: No reported disclosures

510. Elevated IL-1β level as a predictor of inflammation and death in COVID-19

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Session: P-18. COVID-19 Pathogenesis

Background: SARS-Cov-2 (severe acute respiratory disease coronavirus 2) causes Coronavirus Disease 2019 (COVID19) and is associated with respiratory failure and death in severe disease. This is associated with high levels of cytokines such as IL-6, IL-8 and TNF-alpha which are predictors of severe outcomes. SARS-CoV-2 leads to activation of the NLRP3 inflammasome which results in secretion of

the cytokine IL-1ß. While high levels of IL-1ß are not observed in most patients with severe COVID-19, there is a subset of patients with high IL-1ß levels. Here we sought to characterize these patients and determine whether high IL-1ß levels are associated with adverse outcomes and death in COVID-19.

Methods: We identified 90 patients with high IL-1ß levels (greater or equal to 2 pg/ml) and laboratory confirmed COVID-19 hospitalized in our hospital system in New York March 12 and May 8, 2020. We collected baseline clinical characteristics, laboratory values, COVID-19 treatment, and outcomes from this group and the group with IL-1ß levels below 2 pg/ml. Baseline clinical characteristics and outcomes were compared.

Results: Comparing patients by IL-1ß level had similar demographics (age, sex, race/ethnicity, smoking status and comorbid disease prevalence). The group had comparable levels of adverse markers of disease severity but the patients with high IL-1ß had increased inflammatory biomarkers including IL-8 (629 vs. 68 pg/ml, p< 0.0001), TNF-alpha (30 vs. 51 pg/ml, p< 0.0001), IL-6 (173 vs. 5075 pg/ml, p< 0.0001), CRP (141 vs. 178, p=0.0007), d-dimer (2.6 vs. 4 p=0.0002), and increased rates of death (30% vs. 20%, p=0.008).

Conclusion: Demographic and comorbid conditions are not effective at predicting high IL-1ß serum levels in COVID-19 patients, however those individuals with high levels are at risk for adverse outcomes of severe disease and death. Further investigation is required to probe the mechanism of NLRP3 inflammasome activation and IL-1ß signaling and the role of this cytokine in mediated inflammation and death in COVID-19.

Disclosures: Judith A. Aberg, MD, Theratechnology (Consultant)

511. Hospitalized COVID-19 Patients with Elevated Cardiac Troponin I Have Increased Length Of Stay But Similar Ventilation Time

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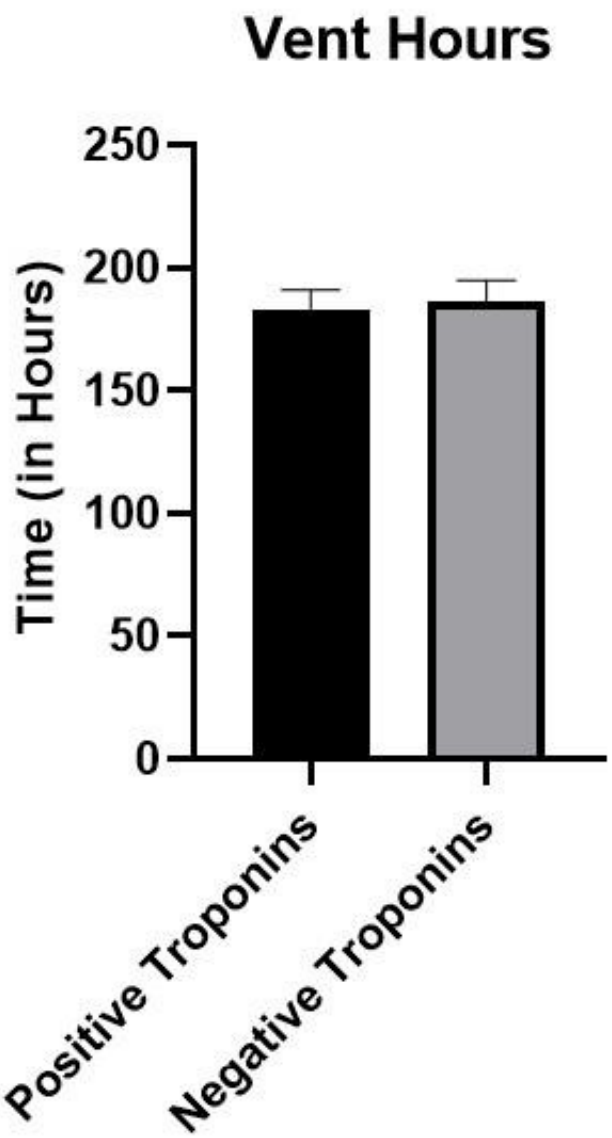
Session: P-18. COVID-19 Pathogenesis

Background: Coronavirus disease 2019 (COVID-19) causes increased mortality and morbidity in patients with underlying cardiovascular disease. Elevated cardiac troponin I (cTnI) can suggest either a co-concurrent myocarditis or acute myocardial infarction. Understanding how laboratory values predict disease severity is important for clinicians to guide therapy and triage patients.

Methods: A cross sectional study was performed utilizing the 184 hospital United States database of HCA. Patients were selected based on inpatient visits to HCA facilities from February 2020 to May 2020 with a COVID-19 diagnosis and at least one cTnI lab test. Patients were divided according to an elevated or normal cTnI value based on the 99th percentile reference range of the test. Outcomes, such as length of stay, disposition, and time on the ventilator, were compared.

Results: 3968 patients hospitalized with COVID-19 were identified. Of those, 3158 patients had at least one cTnI test throughout their hospitalization. 829 (26%) had at least one positive cTnI during their hospitalization. Patients with at least one positive cTnI were hospitalized on average for 8.7 days, whereas patients without positive cTnI were hospitalized on average for 6.3 days (p< 0.0001). 1499 patients without positive cTnI were sent home without health care, but only 196 with positive cTnI were discharged home without requiring home health (p < 0.0001). Need for mechanical ventilation was also higher in the elevated cTnI group. If intubated, patients in both groups required on average the same amount of ventilator time, 7 days (p = 0.7263).

Ventilation time between COVID-19 patients with and without elevated Troponins



Length of hospitalization stay between COVID-19 patient with and without elevated Troponins