461. Classical Antigen Presenting Cell Activation Correlates with T Cell Immunity and COVID-19 Severity

Zhongyan Lu, PhD[1]; Jarina Pena-DaMata, PhD[1]; Katherine Pohida, BS[2]; Camille Lake, PhD[1]; Nusrat J. Epsi, n/a[3]; Stephanie A. Richard, PhD, MHS[4]; Brian Agan, MD[5]; Simon Pollett, MBBS[1]; Mark P. Simons, Ph.D., MSPH[1]; Clifton Dalgard, PhD[6]; Paul W. Blair, MD MHS MSPH[7]; Josh Chenoweth, PhD[8]; Andrew L. Snow, Ph.D.[1]; Timothy Burgess, MD, MPH[9]; Allison M. Malloy, MD[1]; [1]Uniformed Services University of the Health Sciences, Bethesda, Maryland; [2]Uniformed Service University of the Health Sciences, Bethesda, Maryland; [3]HJF, Bethesda, Maryland; [4]Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, MD and Henry M. Jackson Foundation, Bethesda, MD, Bethesda, Maryland; [5]Infectious Disease Clinical Research Program, USU/HJF, Bethesda, Maryland; [6]The American Genome Center, Uniformed Services University of the Health Sciences, Bethesda, Maryland; [7]Uniformed Services University, Bethesda, Maryland; [8]Henry M. Jackson Foundation, Bethesda, Maryland; [9]Infectious Disease Clinical Research Program, Bethesda, Maryland

the EPICC Study Group

Session: P-21. COVID-19 Research

Background. The initial response of immune cells against respiratory viruses often determines the severity and duration of disease. The early trajectory of the immune response during infection with SARS-CoV-2 remains poorly understood. Dysregulation of innate immune factors that facilitate viral clearance and the adaptive response, such as type I interferons, have been implicated in severe COVID-19. However, collection of biological samples during the first seven days post-symptom onset has posed a logistical challenge, limiting our knowledge surrounding the immune responses that drive protection versus immunopathology.

Methods. From March 2020, Military Health System beneficiaries presenting with a positive SARS-CoV-2 test, a COVID-19 like illness, or a high-risk SARS-CoV-2 exposure at nine military medical treatment facilities across the United States were eligible for enrollment in our longitudinal cohort study, which included collection of respiratory sample, sera, plasma, and peripheral blood mononuclear cells (PBMCs). Twenty-five SARS-CoV-2 infected study participants provided samples with in the first seven days of symptom onset, fifteen of whom were hospitalized with COVID-19. We employed multiparameter spectral flow cytometry to comprehensively analyze the early trajectory of the innate and adaptive immune responses.

Results. We discovered that early activation of critical antigen presenting cell subsets was impaired upon comparing inpatients with outpatients, correlating with decreased antigen-experienced T cell responses. Specifically, we noted reduced expression of key costimulatory molecules, CD80 and CD86, on conventional dendritic cells that are required for viral antigen-specific T cell priming. Reduction in CD38, a marker of activation was also observed on inpatient dendritic cell subsets.

Conclusion. Reduced antigen presenting cell activation and expression of ligands that facilitate T cell engagement may impede the efficient clearance of SARS-CoV-2, coinciding with more severe disease in our cohort. Further analysis of the functional activation of early innate immune responses triggered by SARS-CoV-2 may unveil new immune biomarkers and therapeutic targets to predict and prevent severe disease associated with inadequate T cell immunity.

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462. Differences in the Humoral Response to SARS-CoV-2 Infection in Children vs. Adult

Girlande Mentor, MD[1]; Olivier Drouin, MDCM MsC MPH[2]; Silvie Valois, RN[3]; Suzanne Taillefer, PhD[3]; Christian Renaud, MD[4]; Fatima Kakkar, MD MPH[2]; [1]Universite de Montreal, Montreal, Quebec, Canada; [2]CHU Sainte-Justine, Montreal, Quebec, Canada; [3]Centre D'infectiologie Mere Enfant, Montreal, Quebec, Canada; [4]Departement De Microbiologie, Infectiologie, Immunologie, Faculte De Medecine, Universite De Montreal, Montreal, Quebec, Canada

Session: P-21. COVID-19 Research

Background. One of the most striking observations of the COVID-19 pandemic has been the difference in infection among children vs. adults. Overall, children with SARS-CoV-2 infection generally had milder disease compared to adults, though the cause is not clear.

The objective of this study was to compare the humoral response to infection in children vs. adults of a same family.

Methods. We performed a prospective cohort study at Sainte-Justine University Health Center in Montreal, Canada from July 2020 to March 2021. Children with a positive SARS-CoV-2 PCR were recruited from the COVID-19 clinic (index case), enrollment was offered to all household members. Serum IgG against SARS-CoV-2 native S1/S2 spike proteins was measured using the Diasorin (Liaison XL) assay, 4-6 months following a positive PCR. A mean antibody threshold of 15 Arbitrary unit per ml (AU/ml) was considered seropositive, with 94.4% positive agreement to plaque reduction neutralization tests (PRNT90) at a 1:40 ratio. Antibody titer was compared between children and adults.

Results. 111 participants (52 adults and 59 children) were recruited from 50 separate families. Characteristic of participants and their clinical symptoms are described in Table 1. Among all participants, 76.3% children were SARS-CoV-2 seropositive vs. 51.9% of adults (p=0.007). Median antibody titer was significantly higher in children vs. adults (82.8 AU, [IQR: 18.4-130], vs 17.0 AU, [IQR: 6.8-77.8], p=0.006); findings were similar among SARS-CoV-2 PCR positive participants only. Overall, 13 participants were PCR positive but seronegative, 7 were PCR negative and seropositive, while 61 were both PCR positive and seropositive. Older participants and those with any comorbidity. Among the PCR positive group, the seropositive participants were younger (median age 31±17 vs 19±17 years, p=0.003) and more likely to have comorbidity (69% vs 29%, p=0.007).

Table 1: **Clinical characteristics and antibody response among participants**

	All Participants(n=111)			Only participants with Positive SARS-CoV-2 PCR (n=73)		
	Adult n=52	Child n=59	p-value	Adult n=30	Child n=43	p-value
Age (years, mean±SD)	41.5±10.6	8.5±5.5		40.2±11.9	8.6±5.7	
Sex (male)	19 (36.5%)	24 (40.7%)	0.66	10 (33.3%)	18 (41.8%)	0.46
SARS-CoV-2 PCR						
Positive	30 (57.7%)	44 (74.5%)	0.10	30	43	NA
Negative	18 (34.6%)	13 (22.0%)		0	0	NA
Not Done	4 (7.7%)	2 (3.4%)		0	0	NA
DISEASE SEVERITY						
Asymptomatic	14 (26.9%)	18 (30.5%)	0.67	5 (16.7%)	9 (20.9%)	0.37
Mild disease	27 (51.9%)	38 (64.4%)	0.18	15 (50%)	31 (72%)	**0.05**
Moderate disease	7 (13.5%)	3 (5.8%)	0.11	6 (20%)	3 (7.0%)	0.1
Severe disease	3 (5.8%)	0	0.1	3 (10%)	6 (14.0%)	0.72
Critical disease	1 (1.9%)	0	0.5	1 (3%)	0	0.41
SEROLOGY						
Time between SARS-CoV-2 PCR and Serology (Mean ± SD)	137 ±51	133±45	0.64	139 ±47	139 ±42	0.76
Seropositive (Cut off >=15 AU/ml)	27 (51.9%)	45 (76.3%)	**0.007**	21 (70%)	39 (90.7%)	**0.02**
Titer (AU/ml) (median, IQR)	17 [6.8-77.8]	82.8 [18.4-130]	**0.006**	32.8 [12.9-108]	93.2 [49.8-148]	**0.03**

Conclusion. These results suggest that children have a stronger antibody response to SARS-CoV-2 infection than adults, and that older age and presence of comorbidity are associated with a less robust humoral response. Further work on the differences in response between children and adults may help elucidate mechanisms underlying the severity of disease

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463. Factors of Social Determinants of Health Associated with Length of Stay in COVID-19 Patients with Multimorbidity in Southwest Georgia, United States

Sahand Golpayegany, PharmD Candidate[1]; Sharmon P. Osae, Pharm.D., BCACP[1]; Geren Thomas, Pharm.D., BCPS[2]; Henry N. Young, Ph.D.[1]; Andrés F. Henao Martínez, MD[3]; Carlos Franco-Paredes[4]; Daniel B. Chastain, Pharm.D., BCIDP, AAHIVP[1]; [1]University of Georgia College of Pharmacy, Albany, Georgia; [2]John D. Archbold Memorial Hospital, Thomasville, Georgia; [3]University of Colorado Anschutz Medical Campus, Aurora, Colorado; [4]University of Colorado Denver, School of Medicine, Aurora, CO

Session: P-22. COVID-19 Social Determinants of Health

Background. Previous studies have observed that multimorbidity, defined as two or more comorbidities, is associated with longer lengths of stay (LOS) and higher mortality in patients with COVID-19. In addition, inequality in social determinants of health (SDOH), dictated by economic stability, education access and quality, healthcare access and quality, neighborhoods and built environment, and social and community context have only added to disparities in morbidity and mortality associated with COVID-19. However, the relationship between SDOH and LOS in COVID-19 patients with multimorbidity is poorly characterized. Analyzing the effect SDOH have on LOS can help identify patients at high risk for prolonged hospitalization and allow prioritization of treatment and supportive measures to promote safe and expeditious discharge.

Methods. This study was a multicenter, retrospective analysis of adult patients with multimorbidity who were hospitalized with COVID-19. The primary outcome was to determine the LOS in these patients. The secondary outcome was to evaluate the role that SDOH play in LOS. Poisson regression analyses were performed to examine associations between individual SDOH and LOS.

Results. A total of 370 patients were included with a median age of 65 years (IQR 55-74), of which 57% were female and 77% were African American. Median Charlson Comorbidity Index was 4 (IQR 2-6) with hypertension (77%) and diabetes (51%) being the most common, while in-hospital mortality was 23%. Overall, median length of stay was 7 days (IQR 4-13). White race (-0.16, 95% CI -0.27 to -0.05, p=0.003) and residence in a single-family home (-0.28, 95% CI -0.38 to -0.17, p< 0.001) or nursing home/long term care facility (-0.36, 95% CI -0.51 to -0.21, p< 0.001) were associated with decreased LOS, while Medicare (0.24, 95% CI 0.10 to 0.38, p=0.001) and part-time (0.35, 95% CI 0.13 to 0.57, p=0.002) or full-time (0.25, 95% CI 0.12 to 0.38, p< 0.001) employment were associated with increased LOS.