Table 1: Demographics

	n (%) or median [IQR]			
	All patients n=259	Non severe n=166 (%)	Severe group n=93 (%)	p-value
Median [IQR] age in years	62[51,73]	61[49,72]	65[56,74]	0.0254*
Gender				0.5251
Male	138	86(51.8)	52(55.9)	
Female	121	80(48.2)	41(44.1)	
Race/Ethnicity				0.1142
NH African Americans	48	24 (14.5)	24 (25.8)	
NH White Caucasians	124	82 (49.4)	42 (45.2)	
NH Others	12	7 (4.2)	5 (5.4)	
Hispanic / Latino[#]	75	53 (31.9)	22 (23.7)	
Health care worker				0.5057
Yes	15	11(6.6)	4(4.3)	
No	178	116(69.9)	62(66.7)	
Unknown	66	39(23.5)	27(29.0)	
SNF				0.0094*
Yes	60	30(18.1)	30(32.3)	
No	199	136(81.9)	63(67.7)	

SNF: Rehabilitation and skilled nursing facility; NH: Non- Hispanics; *p-values of <0.05
[#]5 African Americans also identified themselves as Hispanic/ Latino. They were excluded from NH African American group and included in Hispanic/ Latino group only.

Results: Of 259 patients, 166 (64%) had non-severe disease, and 93 (36%) severe disease; median age [IQR] was 62 [51,73]. There were 138(53%) males and 75 (29%) Hispanics. Among non-Hispanics,124(48%) were White, 48(19%) African Americans, and 12(5%) other races. Sixty (23%) were admitted from a nursing facility and the in-hospital mortality rate was 15% (38/259). Severe COVID-19 was associated with older age (p=0.02), admission from nursing facility (p=0.009), increased BMI (p=0.03), diabetes mellitus (p=0.0002), and COPD (p=0.03). At the time of presentation, severe COVID-19 was associated with tachypnea, hypoxia, hypotension (all p< 0.0001), elevated BUN (p=0.002) and AST (p=0.001), and acute or chronic kidney injury (p=0.01). Median hospital stay [IQR] was 11 days [7,18] in the severe vs. 6 days [3,11] in the non-severe group. In the severe group, 72% required ICU admission and 39% died.

Table 2: Medical comorbidities

	n (%) or median [IQR]			
	All patients n=259	Non severe n=166(%)	Severe group n=93(%)	p-value
Smoking (ever)	93	59(35.5)	34(36.6)	0.8700
Median BMI[#] [IQR]	30[26,34]	29[25,34]	30[27,35]	0.0347*
BMI>30 kg/m^2	114	66(39.8)	48(51.6)	0.0652
Hypertension	164	100(60.2)	64(68.8)	0.1695
Diabetes mellitus	100	50(30.1)	50(53.8)	0.0002*
Pre-diabetes	38	27(16.3)	11(11.8)	0.3330
Hyperlipidemia	134	84(50.6)	50(53.8)	0.6253
Coronary artery disease	38	27(16.3)	11(11.8)	0.3330
Peripheral vascular disease	10	5(3.0)	5(5.4)	0.3434
COPD	25	11(6.6)	14(15.1)	0.0276*
Asthma	30	20(12.0)	10(10.8)	0.7546
Chronic kidney disease	46	27(16.3)	19(20.4)	0.4001
Congestive heart failure	37	20(12.1)	17(18.3)	0.1692
Chronic liver disease	16	11(6.6)	5(5.4)	0.6885
Neurological diseases	53	30(18.1)	23(24.7)	0.2026
Autoimmune disease	10	8(4.8)	2(2.2)	0.2849
Organ transplant	10	6(3.6)	4(4.3)	0.7832
HIV	5	1(0.61)	4(4.4)	0.0650
Malignancy	29	18(10.8)	11(11.8)	0.8095
Immunosuppression secondary to medications	25	13(7.8)	12(12.9)	0.1848

#BMI was only reported in 248, out of which 156 were non-severe and 92 were severe.

Table 3: Presenting symptoms and signs in the first 48 hours of admission

	n (%) or median [IQR]			
	All patients n=259	Non severe n=166(%)	Severe group n=93(%)	p-value
Subjective				
GI symptoms	127	86(51.8)	41(44.1)	0.2331
Respiratory symptoms	223	138(83.1)	85(91.4)	0.0651
Systemic symptoms	209	134(80.7)	75(80.7)	0.9879
Objective				
Fever	153	94(56.6)	59(63.4)	0.2846
Hypothermia	30	15(9.0)	15(16.1)	0.0871
Tachycardia	138	83(50.0)	55(59.1)	0.1573
Tachypnea	191	107(64.5)	84(90.3)	<.0001*
Hypoxia	202	112(67.5)	90(96.8)	<.0001*
Hypotension	44	14(8.4)	30(32.3)	<.0001*

Fever was defined as the highest temp of >38C; hypothermia as the lowest temp of <36C; tachycardia was defined as having a heart rate of >100 beats per minute; tachypnea was defined as having a respiratory rate of >20 breaths per minute; hypoxia was defined as having an O2 saturation of <95% on room air; hypotension was having a systolic blood pressure of <90mm Hg. Symptoms of cough, shortness of breath, chest pain, sore throat, and congestion were grouped as respiratory; GI symptoms were nausea, vomiting, diarrhea, abdominal pain; systemic symptoms were fever, myalgias, rash, encephalopathy, dizziness.
*p-values of <0.05

Table 4: Basic labs in the first 24 hours

	n (%) or median [IQR]			
	All patients n=259	Non severe n=166(%)	Severe group n=93(%)	p-value
Leukocytosis	37	19(11.6)	18(19.6)	0.1157
Leucopenia	25	14(8.5)	11(12.0)	
Normal WBC	194	131(79.9)	63(68.5)	
Elevated BUN	80	38(23.2)	42(45.7)	0.0002*
AKI/ CKD	68	35(21.3)	33(35.9)	0.0116*
ALT> 42 IU/L[#]	51	30(22.1)	21(26.9)	0.4215
AST> 45 IU/L[#]	62	29(21.3)	33(42.3)	0.0011*

Leukocytosis is defined as WBC> 11x10exp9/L; leucopenia is defined as WBC< 3.5x10exp9/L; elevated BUN defined as >24 mg/dl; AKI/ CKD defined as serum creatinine >1.27 mg/dl
#ALT, AST in first 24 hours was only available for 214 patients. WBC count was missing in 3 patients.
*p-values of <0.05

Conclusion: In this cohort of patients with COVID-19, specific comorbidities, and vital signs at presentation were associated with severe COVID-19. These findings help clinicians with early identification and triage of high risk patients.

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

519. Immune responses and COVID-19 severity

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Session: P-19. COVID-19 Research

Background: The coronavirus-19-disease (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread to >200 countries and surpassed 7 million cases. There is a broad range of COVID-19 illness, ranging from milder disease to a rapidly progressive respiratory disease and ARDS. The causes of this different clinical course and the drivers for severe disease are currently unknown. A fulminant increase of pro-inflammatory cytokines is thought to play a role in causing a rapid disease evolution, however the immune correlates of severe COVID-19 remain unclear.

Methods: To gain insight into relationship between immune responses and disease severity we built a longitudinal cohort of 40 adult patients with known COVID-19. Samples were collected at diagnosis and every 7 days until hospital discharge or death. As controls we also included a group of convalescent patients, and subjects who tested negative for COVID-19 by PCR. Clinical and laboratory data and were also collected. Multicolor flow cytometry was used to determine the presence and phenotype of B, T and natural killer (NK) cells. We also identified specific sub-populations (Tfh, activated/cytotoxic CD8 and NK) and assessed lymphoid exhaustion of different cell types such as naïve, memory T cells, or NK over time. Anti-Sars-CoV2 IgG and IgM antibody were detected using lateral flow method.

Results: We found that the absolute number of lymphocytes and monocytes was decreased starting at diagnosis and correlated with disease severity. Disease severity correlated with decreased NK and T cell. In severe COVID-19 cases, NK cell populations were strongly decreased over time in intubated patients while they recovered in patients who improved and were discharged. CD8+ were also decreased at disease onset and seemed to correlate with disease severity. A high percentage of CD4+ and CD8+ T cells showed an exhausted phenotype. All patients tested at admission had IgM antibody responses irrespective of the course of the disease. Further analyses are ongoing.

Conclusion: The characterization and role of the immune responses in COVID-19 evolution is still under investigation. Further characterization of viral and immune factors will help in identifying subjects at high risk of severe disease and targets for intervention.

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520. Longitudinal Analysis of SARS-CoV-2 Viruses in Hospitalized Adults

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Session: P-19. COVID-19 Research

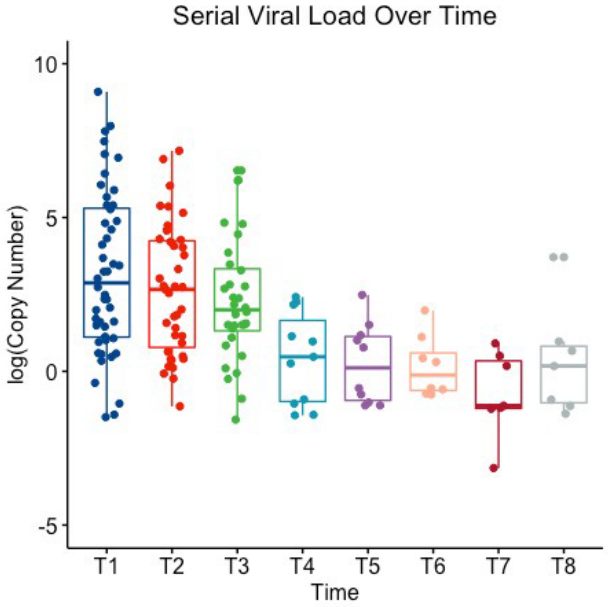
Background: The rapid spread of SARS-CoV-2, the causative agent of Coronavirus disease 2019 (COVID-19), has been accompanied by the emergence of viral mutations, some of which may have distinct virological and clinical consequences. While whole genome sequencing efforts have worked to map this viral diversity at the population level, little is known about how SARS-CoV-2 may diversify within a host over time. This is particularly important for understanding the emergence

of viral resistance to therapeutic interventions and immune pressure. The goal of this study was to assess the change in viral load and viral genome sequence within patients over time and determine if these changes correlate with clinical and/or demographic parameters.

Methods: Hospitalized patients admitted to Northwestern Memorial Hospital with a positive SARS-CoV-2 test were enrolled in a longitudinal study for the serial collection of nasopharyngeal specimens. Swabs were administered to patients by hospital staff every 4 ± 1 days for up to 32 days or until the patients were discharged. RNA was extracted from each specimen and viral loads were calculated by quantitative reverse transcriptase PCR (qRT-PCR). Specimens with qRT-PCR cycle threshold values less than or equal to 30 were subject to whole viral genome sequencing by reverse transcription, multiplex PCR, and deep sequencing. Variant populations sizes were estimated and subject to phylogenetic analysis relative to publicly available SARS-CoV-2 sequences. Sequence and viral load data were subsequently correlated to available demographic and clinical data.

Results: 60 patients were enrolled from March 26th to June 20th, 2020. We observed an overall decrease in nasopharyngeal viral load over time across all patients. However, the temporal dynamics of viral load differed on a patient-by-patient basis. Several mutations were also observed to have emerged within patients over time.

Distribution of SARS-CoV-2 viral loads in serially collected nasopharyngeal swabs in hospitalized adults as determined by qRT-PCR. Samples were collected every 4 ± 1 days (T#1–8) and viral load is displayed by log(copy number).



Conclusion: These data indicate that SARS-CoV-2 viral loads in the nasopharynx decrease over time and that the virus can accumulate mutations during replication within individual patients. Future studies will examine if some of these mutations may provide fitness advantages in the presence of therapeutic and/or immune selective pressures.

Disclosures: Michael G. Ison, MD MS, AlloVir (Consultant)

521. Similarities and Differences in Transcriptomic Host Response between SARS-CoV-2 and Other Viral Infections

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Session: P-19. COVID-19 Research

Background: COVID-19 is a pandemic caused by the SARS-CoV-2 virus that shares and differs in clinical characteristics of known viral infections.

Methods: We obtained RNAseq profiles of 62 prospectively enrolled COVID-19 patients and 24 healthy controls (HC). We collected 23 independent studies profiling 1,855 blood samples from patients covering six viruses (influenza, RSV, HRV, Ebola, Dengue and SARS-CoV-1). We studied host whole-blood transcriptomic responses in COVID-19 compared to non-COVID-19 viral infections to understand similarities and differences in host response. Gene signature threshold was absolute effect size ≥1, FDR ≤ 0.05%.

Results: Differential gene expression of COVID-19 vs HC are highly correlated with non-COVID-19 vs HC (r=0.74, p< 0.001). We discovered two gene signatures: COVID-19 vs HC (2002 genes) (COVIDsig) and non-COVID-19 vs HC (635 genes) (nonCOVIDsig). Pathway analysis of over-expressed signature genes in COVIDsig or nonCOVIDsig identified similar pathways including neutrophil activation, innate immune response, immune response to viral infection and cytokine production. Conversely, for under-expressed genes, pathways indicated repression of lymphocyte differentiation and activation (Fig1).

Intersecting the two gene signatures found two genes significantly oppositely regulated (*ACO1*, *ATL3)*. We derived a third gene signature using COCONUT to compare COVID-19 to non-COVID-19 viral infections (416 genes) (Fig2). Pathway analysis did not result in significant enrichment, suggesting identification of novel biology (Fig1).

Statistical deconvolution of bulk transcriptomic data found M1 macrophages, plasmacytoid dendritic cells, CD14+ monocytes, CD4+ T cells and total B cells changed in the same direction across COVID-19 and non-COVID-19 infections. Cell types that increased in COVID-19 relative to non-COVID-19 were $CD56^{bright}$ NK cells, M2 macrophages and total NK cells. Those that decreased in non-COVID-19 relative to COVID-19 were $CD56^{dim}$ NK cells & memory B cells and eosinophils (Fig3).

Figure 1

Fig1. Heatmap of the significance level in each gene set of interest including COVID-19 vs HC (+) and (-), non-COVID-19 viral vs HC (+) and (-), and COVID-19 vs non-COVID-19 viral (+) and (-) and combinations of the intersect of COVID-19 vs HC with non-COVID-19 viral. Scale in heatmap is from 1 to 10 for the significance level.