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Association of SARS-CoV-2 Viral load in COVID-19 at the Hospital Presentation

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The authors have no conflict of interest.

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Introduction

- The SARS-CoV-2 viral load and its association with COVID-19 severity remains a widely discussed topic with a little or no consensus.

Objective

- Our objective was to investigate SARS-CoV-2 viral load in the saliva/sputum in COVID-19 patients with varying severity levels at the hospital presentation.

Methods

Study design

- A single-center prospective cohort study at Ascension St John Hospital, conducted during early Jan. 2021 and Sept. 2021.
- We recruited 200 subjects with a PCR-confirmed COVID-19 who were ≥18 years of age. Enrolled subjects were divided into WHO-defined severity criteria upon hospital admission.

Sample Collection and Processing

- We collected sputum/saliva samples at the time of hospital admission. The CDC protocol (CDC-006-00019) was used to isolate total nucleic acid and measured them for SARS-CoV-2 viral load.
- In brief, we used the Qiagen QiAamp DSP Viral RNA mini kit, along with QIAGEN Qiacube to isolate the viral RNA from sputum/saliva sample.
- We used 140 ul of sample dissolved in equal amount of DTT to isolate 100 ul of total RNA, which was assayed using SARS-CoV-2 Research Use Only Primer and Probe Sets from Integrated DNA technologies and TaqPath™ 1-Step RT-qPCR Master Mix from Thermo Fisher. We used a human cell line as an isolation, as well as real-time PCR control.

Results

- We recruited 50 patients in each cohort, for a total of 200 patients. Our study cohort included 104 (52%) males and 96 (48%) females. Of the entire study population, 135 (67.5%) was black/African American.
- We observed COVID-19 related symptoms, inflammatory biomarker profile, C_T values and final disposition with respect to COVID-19 severity at the hospital presentation.

Table 1. **Study subject demographics and gender distribution**

		COVID-19 severity				
		Mild (N =50)	Moderate (N=50)	Severe (N=50)	Critical (N=50)	Total (N=200)
Sex	Male	31 (62%)	20 (40%)	28 (56%)	25 (50%)	104 (52%)
	Female	19 (38%)	30 (60%)	22 (44%)	25 (50%)	96 (48%)
Demographic	White	14 (28%)	16 (32%)	20 (40%)	11 (22%)	61 (30.5%)
	Black/ A.A.	34 (68%)	33 (66%)	30 (60%)	38 (76%)	135 (67.5%)
	Other	2 (4%)	1 (2%)	0	1 (2%)	4 (2%)

Table 2. **COVID-19 related symptoms at the hospital presentation**

	COVID-19 severity				
	Mild (N =50)	Moderate (N=50)	Severe (N=50)	Critical (N=50)	Total (N=200)
ICU admission	3 (6%)	3 (6.1%)	9 (18%)	10 (20%)	25 (12.6%)
Presented with encephalopathy	0 (0%)	0 (0%)	0 (0%)	10 (20%)	10 (5%)
Fever as symptom	14 (28%)	23 (46%)	22 (44%)	9 (22.5%)	68 (35.8%)
Sore Throat	5 (10%)	4 (8%)	6 (12%)	4 (10%)	19 (10%)
Headache	3 (6%)	11 (22%)	8 (16%)	4 (10%)	26 (13.7%)
Rash	0 (0%)	0 (0%)	1 (2%)	1 (2.5%)	2 (1.1%)
Cough	22 (44%)	35 (70%)	42 (84%)	25 (62.5%	124 (65.3%)
Shortness of breath	25 (50%)	35 (70%)	47 (94%)	23 (57.5%	130 (68.4%)
Chest Pain	12 (24%)	13 (26%)	5 (10%)	13 (26%)	43 (22.6%)
Fatigue or Malaise	15 (30%)	22 (44%)	24 (48%)	18 (45%)	79 (41.6%)
Myalgia	13 (26%)	25 (50%)	21 (42%)	10 (25%)	69 (36.3%)
Loss of Taste	5 (10%)	8 (16%)	9 (18%)	1 (2.5%)	23 (12.1%)
Loss of Smell	5 (10%)	10 (20%)	5 (10%)	0 (0%)	20 (10.5%)
Loss of Appetite	4 (8%)	13 (26%)	17 (34%)	13 (32.5%	47 (24.7%)
Nausea	9 (18%)	19 (38%)	16 (32%)	11 (27.5%	55 (28.9%)
Diarrhea	11 (22%)	14 (28%)	10 (20%)	16 (40%)	51 (26.8%)
Abdominal Pain	4 (8%)	6 (12%)	2 (4%)	7 (17.5%)	19 (10%)
Blood Cluture on Admission	11 (22%)	17 (34%)	18 (36%)	21 (42%)	67 (33.5%)
CXR on admission	44 (88%)	47 (94%)	46 (92%)	47 (94%)	184 (92%)
Venous duplex upper/lower extr showing DVT	1 (2%)	2 (4.1%)	7 (14%)	9 (18%)	19 (9.5%)

Table 3. **Inflammatory biomarker levels at the hospital presentation.**
Results are displayed as mean ± standard deviation.

	COVID-19 severity			
	Mild (N =50)	Moderate (N=50)	Severe (N=50)	Critical (N=50)
CRP	34.99 ± 41.35	72.37 ± 7.76	90.31 ± 73.06	82.83 ± 84.11
LDH	228.77 ± 60.83	341 ± 109.52	440.22 ± 188.31	616.75 ± 548.77
PT	14.91 ± 2.37	16.83 ± 7.31	15.10 ± 3.55	14.99 ± 1.98
D-Dimer	1561.49 ± 3215.059	1584.26 ± 1713.199	2350 ± 3920.196	3728.89 ± 5612.500
Ferritin	629.68 ± 1015.235	752.26 ± 1054.079	1414.23 ± 2990.297	643.09 ± 633.093
Procalcitonin	0.2569 ± 0.23048	0.1565 ± 0.29252	0.4333 ± 0.66137	1.3210 ± 3.97355
Troponin	0.0308 ± 0.00487	0.0311 ±0.00577	0.0659 ± 0.09887	0.0750 ± 0.12588
CPK	236.44 ± 236.44	162.31 ± 151.217	260.05 ± 296.275	1265.14 ± 1826.734

Table 4.**The real-time PCR C_T values from SARS-CoV-2 assay in patient sputum/saliva sample at hospital presentation.**
Results are displayed as mean ± standard deviation.

	COVID-19 severity			
	Mild (N =50)	Moderate (N=50)	Severe (N=50)	Critical (N=50)
N1 Gene in Saliva CT Value	26.75 ± 7.39	26.94 ± 7.54	23.91 ± 6.62	26.41 ± 5.63
N2 Gene in Saliva CT Value	30.07 ± 8.55	30.79 ± 8.76	27.33 ± 7.57	29.43 ± 6.66
RNase P Gene in Saliva CT Value	26.53 ± 3.00	27.24 ± 3.87	26.51 ± 3.54	26.87 ± 3.80

Table 5. **Final Disposition of study participants across all severity of COVID-19**

		COVID-19 severity				
		Mild (N =50)	Moderate (N=50)	Severe (N=50)	Critical (N=50)	Total (N=200)
Final Disposition	Died	2 (4%)	2 (4%)	12 (24%)	10 (20%)	26 (13%)
	Survived	48 (96%)	48 (96%)	38 (76%)	40 (80%)	174 (87%)

List of Abbreviations

Abbreviation	Defination	Abbreviation	Defination
COVID-19	Coronavirus Disease 2019	DTT	Dithiothreitol
WHO	World Health Organization	CXR	Chest X-Ray
CDC	Center of Disease Contol	DVT	Deep Vein Thrombosis
PCR	Polymerase Chain Reaction	CRP	C-Reactive Protein
RNA	Ribonucleic Acid	LDH	Lactate dehydrogenase
RT	Reverse transcription	PT	Prothrombin time
qPCR	Quantitative Polymerase Chain Reaction	CPK	Creatine phosphokinase

Discussion

- Our results indicate that COVID-19 related symptoms, inflammatory biomarkers and SARS-CoV-2 viral load at the hospital presentation correlated with varying severity of COVID-19. However, individual symptoms or biomarkers were inadequate to represent the entire spectrum of COVID-19 severity.
- We observed loss of appetite & taste, shortness of breath, cough, DVT, CRP, LDH, and ferritin levels at hospital presentation correlated well with mild, moderate, and severe degree of COVID-19.
- In the severe COVID-19 cohort, we observed the lowest C_T value i.e., highest SARS-CoV-2 viral load when compared to other cohorts, including the critical COVID-19 cohort.

Conclusions

- We noted SARS-CoV-2 viral load on admission was significant enough to tell it apart from severe COVID-19.
- SARS-CoV-2 viral load can be assessed in conjunction with loss of appetite & taste, shortness of breath, cough, DVT, CRP, LDH, and ferritin levels for prognostic assessment. This can provide a supportive utility for the identification of patient suffering from severe COVID-19.
- These findings provide a system level insight into association between viral load assessment and disease severity.

References

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