Clinical Characteristics and Laboratory Biomarkers for Patients with Suspected COVID19 Infection Within HCA Healthcare

Scott Gutovitz, MD; Justin Hanson, DO; Christian Vandever MS; and Dietrich Jehle, MD

Grand Strand Medical Center

Background

The 2019 coronavirus pandemic (COVID-19) caused by SARS-CoV-2 spread rapidly and caused significant illness around the world. Most infections caused mild symptoms, however, a small percentage of patients developed respiratory failure, organ failure, or died. A few international or local case series have been reported showing common patient characteristics, clinical variables, and laboratory findings.[1,2]

Objective

We examined a large American population of patients who were tested for COVID-19 to find differences in patient characteristics, clinical variables, and laboratory findings in those who tested positive for COVID-19. Additionally, we examined COVID-19 patients to see if they had similar findings or had differences among those with severe and non-severe infections.

Methods

We retrospectively accessed a central database containing data from 162 ED's of a multihospital system in the United States of America. HCA Healthcare owns facilities in 18 states. we were able to collect demographic data including the subject's age, gender, race or ethnicity. Clinical variables collected included first day vital signs, ED status (admission or discharge home), type of inpatient ward (floor, step down unit, or intensive care unit (ICU)), final diagnoses (via ICD-10 codes), and final status (discharged from ED, discharged from hospital, deceased, or still admitted at time of data pull).

Laboratory biomarkers collected included routine tests (complete blood count with differential counts, chemistry analysis, lactic acid, troponin-I, and pregnancy test), coagulation tests (activated partial thromboplastin time (PTT), prothrombin time (PT), international normalized ratio (INR), d-dimer, fibrinogen), and markers of inflammation (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin, interleukin-6, ferritin, and lactic acid dehydrogenase (LDH)). Results from the SARS-CoV-2 test were also collected.

The subjects were divided into groups for analysis. The first group composed of subjects that tested negative vs. positive for SARS-CoV-2. The positive group was subdivided into non-severe (either discharged home from the ED or admitted to the hospital) vs. severe infections. (ICU or or had final diagnosis codes for severe sepsis, septic shock, systemic inflammatory response syndrome with organ dysfunction, adult respiratory distress syndrome, or acute respiratory failure.

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Results

Table 1: Baseline characteristics of patients tested for SARS-CoV-2

	Total (n=44,807)	COVID - (n=38,649)	COVID + (n=6158)	P value
Gender				
Female	23680 (52.8)	20691 (53.5)	2989 (48.5)	
Male	21127 (47.2)	17958 (46.5)	3169 (51.5)	p<0.001
Ages				
Ages 18-29		4168 (89.7)	480 (10.3)	
Ages 30-39		4728 (87.2)	695 (12.8)	
Ages 40-49		4627 (83.1)	944 (16.9)	ϕ
Ages 50-59		6324 (84.7)	1145 (15.3)	*
Ages 60-69		7325 (85.9)	1205 (14.1)	
Ages 70-79		6719 (87.2)	986 (12.8)	
Ages >80		4758 (87.1)	703 (12.9)	
Race				
White	29317 (65.4)	26527 (68.6)	2790 (45.3)	#
African American	8417 (18.8)	6732 (17.4)	1685 (27.4)	#
Other	6142 (13.7)	4666 (12.1)	1476 (24.0)	#
Asian	932 (2.1)	724 (1.9)	207 (3.4)	
Ethnicity				
Hispanic	8000 (17.9)	6338 (16.4)	1662 (27.0)	p<0.001
Non-Hispanic	36807 (82.1)	32311 (83.6)	4496 (73.0)	
Comorbidities				
Hypertension	17900 (39.9)	15205 (39.3)	2695 (43.8)	p<0.001
Cardiovascular Disease	17164 (38.3)	15375 (39.8)	1789 (29.1)	p<0.001
Hypercholesterolemia	14938 (33.3)	13024 (33.7)	1914 (31.1)	p<0.001
Diabetes	13150 (29.3)	11152 (28.9)	1998 (32.4)	p<0.001
COPD	13750 (30.7)	12579 (32.5)	1171 (19.0)	p<0.001
Malignancy	5282 (11.8)	4826 (12.5)	456 (7.4)	p<0.001
Chronic Kidney Disease	7675 (17.1)	6747 (17.4)	928 (15.1)	p<0.001
Chronic Liver Disease	2194 (4.9)	2010 (5.2)	184 (3.0)	p<0.001

ϕ p<0.001 between this age group and all others except 50-59.
* p<0.001 between this age group and all others except 40-49 or 60-69.
# p<0.001 between White, African America, and Other races

Table 2: Vital signs and clinical characteristics of ED patients who tested for SARS-CoV-2

	Total Tested (n=44,807)	COVID -	COVID +	t-test P value	Chi-squared P value
Heart Rate (n=44,358), median beats per min (IQR)		97 (83-112)	98 (86-110)	p=0.64	
Systolic Blood Pressure (n=44,287), median mmHg (IQR)		145 (130-165)	142 (129-157)	p<0.001	
Diastolic Blood Pressure (n=44,287), median mmHg (IQR)		84 (75-92)	82 (75-90)	p<0.001	
Oxygen saturation (n=43,975), median % (IQR)		95 (92-97)	94 (90-96)	p<0.001	
Respiratory Rate (n=44,146), median breaths per min (IQR)		19 (18-23)	20 (18-24)	p<0.001	
Temperature (n=44,113), median ºC (IQR)		37.0 (36.8-37.4)	37.5 (37.0-38.4)	p<0.001	
Admitted to ICU, No. (%)	9805 (21.9)	8144 (21.1)	1661 (27.0)		p<0.001
SIRS without organ dysfunction, No. (%)	11239 (25.1)	9153 (23.7)	2086 (33.9)		p<0.001
SIRS with organ dysfunction, severe sepsis, or septic shock, No. (%)	5207 (11.6)	4226 (10.9)	981 (15.9)		p<0.001
ARF, No. (%)	12274 (27.4)	9712 (25.1)	2562 (41.6)		p<0.001
ARDS, No. (%)	417 (0.9)	128 (0.3)	289 (4.7)		p<0.001

*** n = number of subjects with that recorded vital sign (some data was missing)**
*** Abbreviations: Interquartile Range (IQR), Celsius (C), Intensive Care Unit (ICU), Systemic Inflammatory Response Syndrome (SIRS), Acute Renal Failure (ARF), Acute Respiratory Distress Syndrome (ARDS)**

Table 3: Laboratory biomarkers of COVID+ patients on admission to hospital, median (IQR)

	Normal Range	Non-Severe Covid Infections	Severe Covid Infections	P value
White blood cell count (n=826), x10^9/L	3.6-11.0	5.7 (4.5-7.7)	7.53 (5.5-9.7)	p<0.001
Neutrophil count (n=625), x10^9/L	1.6-8.2	4.2 (3.2-5.7)	4.9 (3.5-7.5)	p<0.001
Lymphocyte count (n=694), x10^9/L	1.1-4.7	1.13 (0.85-1.6)	0.94 (0.6-1.3)	p=0.259
Platelet count (n=885), x10^9/L	150-400	204 (161.5-255)	203 (160-266)	p=0.106
Hemoglobin (n=919), g/dL	12.0-16.0	13.2 (12.0-14.5)	13.4 (11.9-14.7)	p=0.784
Activated partial thromboplastin time (n=284), s	25.1-36.5	29.8 (27.7-32.9)	30.2 (27.5-34.0)	p=0.055
Prothrombin time (n=383), s	9.4-12.5	12.2 (10.9-13.8)	12.4 (11.0-13.8)	p=0.875
International Normalized Ratio (n=182), U	1-1.4	1.1 (1.0-1.2)	1.1 (1.0-1.3)	p=0.507
D-dimer (n=163), mg/L FEU	<500	820 (504-1,400)	1,248 (620-2,640)	p=0.023
Sodium (n=900), mmol/L	136-145	137 (134-139)	136 (133-139)	p=0.478
Potassium (n=927), mmol/L	3.5-5.1	3.8 (3.6-4.1)	3.9 (3.5-4.3)	p=0.151
Chloride (n=846), mmol/L	98-107	103 (100-106)	103 (99-107)	p=0.334
Bicarbonate (n=1057), mmol/L	21-32	25 (23-27)	24 (22-27)	p=0.008
Blood urea nitrogen (n=880), mg/dL	7-18	13 (9-19)	18 (12-29)	p<0.001
Creatinine (n=901), mg/dL	0.6-1.3	0.98 (0.77-1.21)	1.10 (0.81-1.59)	p=0.088
Blood Urea Nitrogen/Creatinine (n=176), ratio	9.3-24.4	15 (10.8-20.8)	16 (12.4-20)	p=0.981
Glomerular filtration rate (n=672), mL/min	>60	60 (60-60)	60 (50-60)	p<0.001
Glucose (n=1027), mg/dL	70-110	117 (101-161)	125 (104-182)	p=0.002
Lactic acid (n=705), mmol/L	0.4-2.0	1.2 (0.9-1.6)	1.6 (1.2-2.2)	p<0.001
Troponin-I (n=668), ng/dL	<0.034	0.015 (0.012-0.020)	0.02 (0.015-0.065)	p=0.163
Aspartate aminotransferase (n=689), U/L	15-37	35 (26-50)	45 (28-69.5)	p<0.001
Alanine aminotransferase (n=730), U/L	10-60	35 (24-54)	36 (23-61)	p=0.312
Lactic acid dehydrogenase (n=237), U/L	84-246	260 (204-310)	334 (251-473)	p<0.001
C-reactive protein (n=261), mg/L	<1.0	5.10 (2.23-9.16)	9.28 (5.00-16.05)	p=0.004
Erythrocyte Sedimentation Rate (n=43), mm/hr	<20	33 (4-59)	49 (33-72)	p=0.166
Procalcitonin (n=189), ng/mL	<0.50	0.08 (0.05-0.24)	0.14 (0.05-0.42)	p=0.257
Ferritin (n=203), ng/mL	8-388	373 (195-718)	623 (208-1283)	p=0.173
Fibrinogen (n=21), mg/dL	200-393	370 (358-424)	523 (439-604)	p=0.269
Interleukin-6 (n=14), pg/mL	<15.5	91 (20-163)	79 (41-261)	p=0.604

*** n = number of COVID+ subjects with that laboratory test, first value if multiple**
*** Abbreviations: Interquartile Range (IQR), liters (L), seconds (s), grams (g), milligrams (mg), units (U), fibrinogen equivalent units (FEU), millimoles (mmol), deciliters (dL), minutes (min), nanograms (ng), millimeters (mm), hours (hr), picograms (pg).**

Discussion

The patients who tested COVID+ were more likely to be male and older. (40-69 yrs) May be due to older males having severe disease requiring ED visit. Similar trends were found in China, United States, and Italy.[1-4] Our study found similarities to prior studies who identified hypertension and diabetes mellitus as common in COVID-19 patients. However, our patients with a history of cardiovascular disease, hypercholesterolemia, COPD, malignancy, chronic kidney disease, or chronic liver disease were more likely to test negative for SARS-CoV-2. Our database also confirmed the previous reports that COVID-19 illness is more likely to occur in minority or ethnic demographic groups versus caucasians.[4-6]

Our study found COVID+ patients were more likely to be febrile (temperature > 38 °C), hypoxic (SpO2 < 93% on room air) and tachypneic (respiratory rate >16). Lastly, our results add to prior research showing inflammatory markers are elevated with severe illness and indicated a risk of mortality.[8-15] Our study found higher levels of total WBC, neutrophil count, BUN, glucose, lactic acid, AST, LDH, D-dimer, and CRP in severe disease. Of these, LDH and CRP had the strongest correlation to severe illness (p<0.001) and D-dimer showed the third strongest correlation to severe illness (p=0.023). Other inflammatory markers show less correlation. Other studies showed elevated levels of ESR, procalcitonin, ferritin, fibrinogen, and Interleukin-6 may be associated with severe infections.[8-15]

Conclusion

This large multi-state database of American Emergency Departments confirmed common baseline characteristics, clinical variables, and laboratory biomarkers of patients with SARS-CoV-2 found internationally. Male gender, non-Caucasian minority and ethnic groups, patients aged 40-69, and those with a history of hypertension or diabetes were most associated with testing positive for SARS-CoV-2. Confirmed cases were mo1re likely to be febrile, tachypneic, or hypoxic. And lastly, those with severe COVID-19 disease were more likely to have elevated levels of many biomarkers, with LDH and CRP showing the strongest correlation.

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