

BRIEF RESEARCH REPORT

Infectious Disease

Patient factors associated with SARS-CoV-2 in an admitted emergency department population

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Abstract

Background: The SARS-CoV-2 (COVID-19) virus has wide community spread. The aim of this study was to describe patient characteristics and to identify factors associated with COVID-19 among emergency department (ED) patients under investigation for COVID-19 who were admitted to the hospital.

Methods: This was a retrospective observational study from 8 EDs within a 9-hospital health system. Patients with COVID-19 testing around the time of hospital admission were included. The primary outcome measure was COVID-19 test result. Patient characteristics were described and a multivariable logistic regression model was used to identify factors associated with a positive COVID-19 test.

Results: During the study period from March 1, 2020 to April 8, 2020, 2182 admitted patients had a test result for COVID-19. Of these patients, 786 (36%) had a positive test result. For COVID-19-positive patients, 63 (8.1%) died during hospitalization. COVID-19-positive patients had lower pulse oximetry (0.91 [95% confidence interval, CI], [0.88–0.94]), higher temperatures (1.36 [1.26–1.47]), and lower leukocyte counts than negative patients (0.78 [0.75–0.82]). Chronic lung disease (odds

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ratio [OR] 0.68, [0.52–0.90]) and histories of alcohol (0.64 [0.42–0.99]) or substance abuse (0.39 [0.25–0.62]) were less likely to be associated with a positive COVID-19 result.

Conclusion: We observed a high percentage of positive results among an admitted ED cohort under investigation for COVID-19. Patient factors may be useful in early differentiation of patients with COVID-19 from similarly presenting respiratory illnesses although no single factor will serve this purpose.

KEYWORDS

COVID-19, emergency department, diagnosis

1 | INTRODUCTION

At the time of writing, the World Health Organization reports over 1.4 million COVID-19 cases globally, with significant associated morbidity.¹ The United States has over 420,000 reported cases.² COVID-19 testing speed and capacity remain a bottleneck in both emergency department care and in the study of disease epidemiology. There are also significant concerns about the clinical sensitivity and specificity of testing.³ Despite these limitations, COVID-19 testing in the emergency department (ED) will remain a cornerstone of acute patient care as it can be used to confirm diagnosis, enable inpatient cohorting, and drive discharge planning.

The clinical spectrum of COVID-19 disease is broad. While significant morbidity and mortality have been noted, there is a significant burden of asymptomatic or mildly symptomatic disease, with symptoms that mirror other respiratory illnesses.⁴ It is therefore challenging to establish likely COVID-19 status in the ED. Initially, travel screening was used to assess for suspected disease, but has since lost utility as local, community spread is now ubiquitous. Reports of COVID-19 patient characteristics have described variable symptoms and with few specific characteristics that can differentiate COVID-19 from other respiratory diseases. Early data from 138 hospitalized patients in Wuhan, China, suggested fever, cough, and fatigue were common symptoms and established lymphocytopenia as the most common laboratory abnormality.³ A larger cohort of 1099 positive patients across 522 Chinese hospitals showed that 43.8% of patients had fever on admission and 88.7% during hospitalization.⁵ Lymphocytopenia was common (83.2%), as was abnormal chest radiography (59.1%). This study and others have also shown that inflammatory markers including C-reactive protein (CRP), procalcitonin, and D-dimer can also be abnormal in patients with COVID-19 infection.

Little is understood, however, about demographics, vital signs, and diagnostic findings that may be used to differentiate COVID-19-positive patients from negative patients. Here, we sought to describe patient characteristics and identify factors associated with COVID-19 in an ED population under investigation for COVID-19 who were subsequently admitted for further care. We present data from 2182 ED visits for patients who had COVID-19 testing within a 72-hour window of ED presentation.

2 | METHODS

2.1 | Study design, setting, data collection, and processing

This was an observational, retrospective study of patients admitted from the ED with COVID-19 testing. We included patients who had testing between 48 hours before and 24 hours after ED presentation. Testing before presentation was included if test results were not available in the ED. The window was extended to 24 hours after presentation because institutional practices initially restricted testing within the hospital to inpatient wards and not the ED. The healthcare system comprised a mix of pediatric ($n = 1$), suburban community ($n = 6$), urban community ($n = 2$), and urban academic ($n = 1$) EDs with approximately 300,000 total visits per year. Testing for COVID-19 was performed at local and/or reference laboratories by nucleic acid detection methods using oropharyngeal (OP), nasopharyngeal (NP), or a combination OP/NP swab. This observational study was approved by our local institutional review board (IRB# 2000027747). Patients who explicitly opted out of research were excluded from analysis ($n < 5$). We adhered to the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (<http://www.equator-network.org/reporting-guidelines/strobe/>).

Patient demographics, summarized medical histories, vital signs, and laboratory results available during the ED encounter were extracted from our local Observational Medical Outcomes Partnership (OMOP) data repository and analyzed within our computational health platform.^{6,7} OMOP is a common data model for electronic health records in widespread use that leverages data standards to facilitate large-scale systematic analyses. Data included visits from March 1, 2020 through April 7, 2020 as our institution's first COVID-19 tests were ordered after March 1, 2020. Data were transformed into an analysis-ready data set using custom scripts in PySpark (version 2.4.5), a Python programming language interface into a fast and general cluster computing system for big data. Non-physiologic values (likely related to data entry errors) for vital signs were converted to missing values based on expert-guided rules. Medical histories were generated by using diagnoses before the date

of admission to exclude new diagnoses. These medical histories in the form of ICD-10 codes were mapped to Elixhauser comorbidity groups and mortality indices using H-CUP Software and Tools (*hcuppy* package, version 0.0.7).^{8,9} The Elixhauser mortality index is generated based on a point-system from the combination of the individual comorbidities.

2.2 | Outcome measures

We selected COVID-19 test result from initial testing as the primary outcome measure. During the study period, based on institutional protocols, testing for ED patients was restricted to only those admitted and suspected of COVID-19 based on symptoms and provider judgment.

2.3 | Statistical analyses

Standard descriptive analyses were performed on data stratified by COVID-19 result. Categorical data were summarized as numbers with percentages and continuous data are presented as means with standard deviations or medians with interquartile ranges (IQR) based on the normality of the underlying distribution. To examine the association between demographics, vitals, and laboratory features and the COVID-19 result, logistic regression was performed using all available features. Missing data were imputed using multiple imputation with chain equations (MICE) using 20 imputed datasets.¹⁰ The overall performance of the model was assessed with the Hosmer-Lemeshow statistic. Multicollinearity was checked by variance inflation factor (VIF) and influential variables and additional outliers by Cook's distance. Results from the logistic regression are presented as odds ratio (OR) with 95% confidence intervals (CIs). Given the descriptive nature of the analyses and consideration of ease of interpretation for readers, adjustments of confidence intervals for multiple comparisons were not made.

3 | RESULTS

Between March 1, 2020 and April 7, 2020, there were a total of 2182 ED visits for patients with COVID-19 testing ordered within the 72-hour window around presentation (48 hours before and 24 hours after presentation). Of these, 782 patients (36%) had a positive COVID-19 test. Population characteristics including demographics and comorbidities for the study are shown in Table 1. Outcomes for COVID-19-positive patients are reported in Table 2. The total comorbidity burden of the study population was high, with only 292 (13.4%) admitted patients having no comorbidities. We observed a bimodal distribution in Elixhauser comorbidity mortality indices among COVID-19-positive patients (Figure 1). Pair-plots displaying vital sign relationships stratified by COVID-19 status are presented in Figure 2.

To better understand the association of demographic, comorbidity, vital sign, and laboratory factors to COVID-19 positivity, we generated

The Bottom Line

This study from 8 US emergency departments evaluated features of 2182 admitted patients tested for COVID-19. Those who were COVID-19 positive (N = 786) had higher temperatures, lower pulse oximetry, lower leukocyte counts and less chronic lung disease, alcohol or substance abuse. This is one of the largest US series to affirm patterns of clinical findings observed in COVID-19.

odds ratios using a multivariable logistic regression model (Figure 3, Table 3). Age (OR [95% CI], 1.03 [1.02–1.04] per year) was positively associated with COVID-19 outcome. Patients with chronic lung disease (0.68 [0.52–0.90]) and histories of alcohol (0.64 [0.42–0.99]) or substance abuse (0.39 [0.25–0.82]) were less likely to be COVID-19 positive.

Among vital signs pulse oximetry (0.91 [0.88–0.94]/% O₂) and body temperature (1.36 [1.26–1.47]/°F) were associated with COVID-19 outcome. Notable associated laboratory factors included white blood cell counts (0.78 [0.75–0.82]/×1000/μL), hemoglobin (1.23 [1.14–1.32]/g/dL), and total bilirubin (0.68 [0.49–0.95]/mg/dL). CRP, D-dimer, ferritin, and procalcitonin were less commonly ordered within our cohort (see Table 1 for missingness) and were not statistically associated with our primary outcome.

4 | LIMITATIONS

Within our health system during the study period, hospital-based COVID-19 testing was not being performed within the ED on discharged ED patients or patients without findings concerning for possible COVID-19 infection, so they were not included in this cohort. It is important to highlight that features identified in our restricted cohort may not align with general population features due to spectrum bias. In addition, we did not consider the possibility of second/repeat tests ordered on patients or the effect of false-positive or -negative results. Method of oxygenation (ie, room air, nasal cannula) was not available at the time of data analysis. Furthermore, the data in this study were observational data provided from a single health system and so may not be generalizable based on local testing and admissions practices. Our data were extracted from an electronic health record, which is associated with known limitations including propagation of old or incomplete data. Our choice of primary outcome (COVID-19 test result) is inherently limited by the characteristics of testing.³ Inflammatory markers were less commonly ordered in our cohort and it is possible that missingness impacted our analysis (see Table 1). Also, given the lack of adjustment for multiple comparisons within the logistic regression, we highlight the potential for false discovery of associated features.

TABLE 1 Characteristics of ED admitted patients evaluated for COVID-19

Variable	Category	COVID-19 test result		
		Missing	Negative	Positive
			n = 1396	n = 786
Age		0	65.0 [51.0,78.2]	66.0 [53.0,78.0]
Sex	Male		692 (49.6)	441 (56.1)
Ethnicity	Not Hispanic or Latino	5	1160 (83.3)	570 (72.6)
	Hispanic or Latino		216 (15.5)	194 (24.7)
Race	White	0	901 (64.5)	352 (44.8)
	Black or African American		269 (19.3)	219 (27.9)
Comorbidities				
	Mortality score		15.0 [3.0,28.0]	6.0 [0.0,21.0]
	Hypothyroidism		332 (23.8)	149 (19.0)
	Metastatic disease		164 (11.7)	64 (8.1)
	Other neurologic disorders		601 (43.1)	227 (28.9)
	Renal disease		391 (28.0)	159 (20.2)
	Congestive heart failure		461 (33.0)	141 (17.9)
	Depression		580 (41.5)	193 (24.6)
	Chronic pulmonary disease		714 (51.1)	249 (31.7)
	Hypertension with complications		556 (39.8)	203 (25.8)
	Valvular disease		496 (35.5)	175 (22.3)
	Anemia from blood loss		148 (10.6)	53 (6.7)
	Peripheral vascular disease		423 (30.3)	172 (21.9)
	Fluid and electrolyte disorders		810 (58.0)	299 (38.0)
	Psychoses		294 (21.1)	79 (10.1)
	Rheumatoid arthritis/collagen vascular		173 (12.4)	67 (8.5)
	Diabetes with chronic complications		446 (31.9)	217 (27.6)
	Weight loss		335 (24.0)	123 (15.6)
	Deficiency anemias		648 (46.4)	253 (32.2)
	Obesity		455 (32.6)	233 (29.6)
	Diabetes without chronic complications		119 (8.5)	95 (12.1)
	Alcohol abuse		239 (17.1)	55 (7.0)
	Drug abuse		276 (19.8)	49 (6.2)
	Liver disease		294 (21.1)	100 (12.7)
	Coagulation deficiency		278 (19.9)	87 (11.1)
	Hypertension		445 (31.9)	290 (36.9)
	Solid tumor without metastasis		154 (11.0)	79 (10.1)
	Paralysis		129 (9.2)	47 (6.0)
	Chronic peptic ulcer disease		109 (7.8)	43 (5.5)
	Pulmonary circulation disorders		187 (13.4)	62 (7.9)
	Lymphoma		46 (3.3)	14 (1.8)
	AIDS		25 (1.8)	18 (2.3)
Vitals				
	Systolic blood pressure	56	134.0 [117.0,155.0]	135.0 [121.0,149.0]
	Heart rate	50	96.0 [80.0,111.0]	96.0 [82.0,110.0]
	Respiratory rate	50	18.0 [18.0,22.0]	20.0 [18.0,22.0]

(Continues)

TABLE 1 (Continued)

Variable	Category	COVID-19 test result		
		Missing	Negative	Positive
	Pulse oximetry	55	97.0 [95.0,99.0]	95.0 [92.0,97.0]
	Temperature	69	98.3 [97.6,99.3]	99.4 [98.3,100.9]
Labs				
	Sodium	58	138.0 [135.0,140.0]	137.0 [134.0,139.0]
	Chloride	77	101.0 [97.0,104.0]	100.0 [96.2,103.0]
	Potassium	84	4.1 [3.7,4.5]	4.0 [3.7,4.3]
	Bicarbonate	60	24.0 [21.0,27.0]	24.0 [22.0,26.0]
	BUN	60	19.0 [13.0,31.0]	17.0 [12.0,26.0]
	Calcium	58	9.0 [8.1,9.5]	8.7 [8.2,9.1]
	Glucose	57	123.5 [103.0,163.0]	122.0 [105.0,162.0]
	Creatinine	66	1.0 [0.8,1.6]	1.0 [0.8,1.4]
	White blood cell count	61	9.7 [7.2,13.6]	6.2 [4.9,8.4]
	Hemoglobin	93	12.4 [10.6,13.9]	13.3 [11.8,14.4]
	Platelets	62	237.0 [180.0,305.0]	196.0 [153.0,247.2]
	Aspartate aminotransferase (AST)	571	30.0 [21.0,48.0]	44.0 [30.0,63.0]
	Alanine aminotransferase (ALT)	554	24.0 [16.0,42.0]	30.0 [20.0,48.0]
	Alkaline phosphatase	548	92.0 [71.0,126.0]	77.0 [61.0,100.0]
	Total protein	628	7.3 [6.8,7.8]	7.4 [6.9,7.8]
	Total bilirubin	585	0.5 [0.3,0.8]	0.5 [0.3,0.6]
	Lactate	688	1.7 [1.2,2.6]	1.3 [1.0,2.0]
	C-Reactive protein	1591	19.3 [5.7,73.8]	68.2 [19.9,137.8]
	D-Dimer	1499	1.2 [0.6,3.2]	0.9 [0.5,1.7]
	Ferritin	1468	199.0 [92.2,422.5]	563.5 [293.0,1135.2]
	Procalcitonin	1127	0.2 [0.1,0.7]	0.1 [0.1,0.3]
	Troponin I	1404	0.0 [0.0,0.1]	0.0 [0.0,0.1]

Categorical data are summarized as numbers with percentages and continuous data as medians with interquartile ranges (IQR). ED, emergency department.

TABLE 2 Outcomes of COVID-19-positive patients

Outcome	n = 786
In-hospital mortality	63 (8.1)
Mechanical ventilation	142 (18)
Intensive care unit	196 (25)
Discharged	667 (85)
Still in hospital	56 (7.1)

5 | DISCUSSION

This study aimed to characterize admitted patients tested for COVID-19 and identify features associated with a positive test outcome in a large ED cohort. This is both one of the largest studies of COVID-19 positive patients to date and one of the few to focus on ED presentation. During the study period, COVID-19 testing was nearly ubiquitous

for patients with respiratory complaints or fever within our health system. Thus, we hypothesize that our observations reflect a general, hospitalized symptomatic patient population.

We noted that while the majority of cohort self-identified as white (57.4%), black patients appeared more likely to have a positive test result (44.9% vs 28.1%). While black or African American race was not associated with COVID-19 positive results after adjustment, patients self-identifying as white had a lower risk of having COVID-19 (0.62 [0.40–0.96]). These data suggest that there are potential racial and socioeconomic risk factors in our testing cohort that will require further investigation.

Our study population appeared to have a significant burden of chronic illness with only 13.4% of patients having no Elixhauser comorbidities. As population, COVID-19-positive patients appeared to have fewer risk factors than test-negative patients. In the multivariable analysis, patients with chronic lung disease had less risk of COVID-19. We hypothesize that lung disease is not mechanistically protective, but

Odds ratios for Covid Positive Test Result

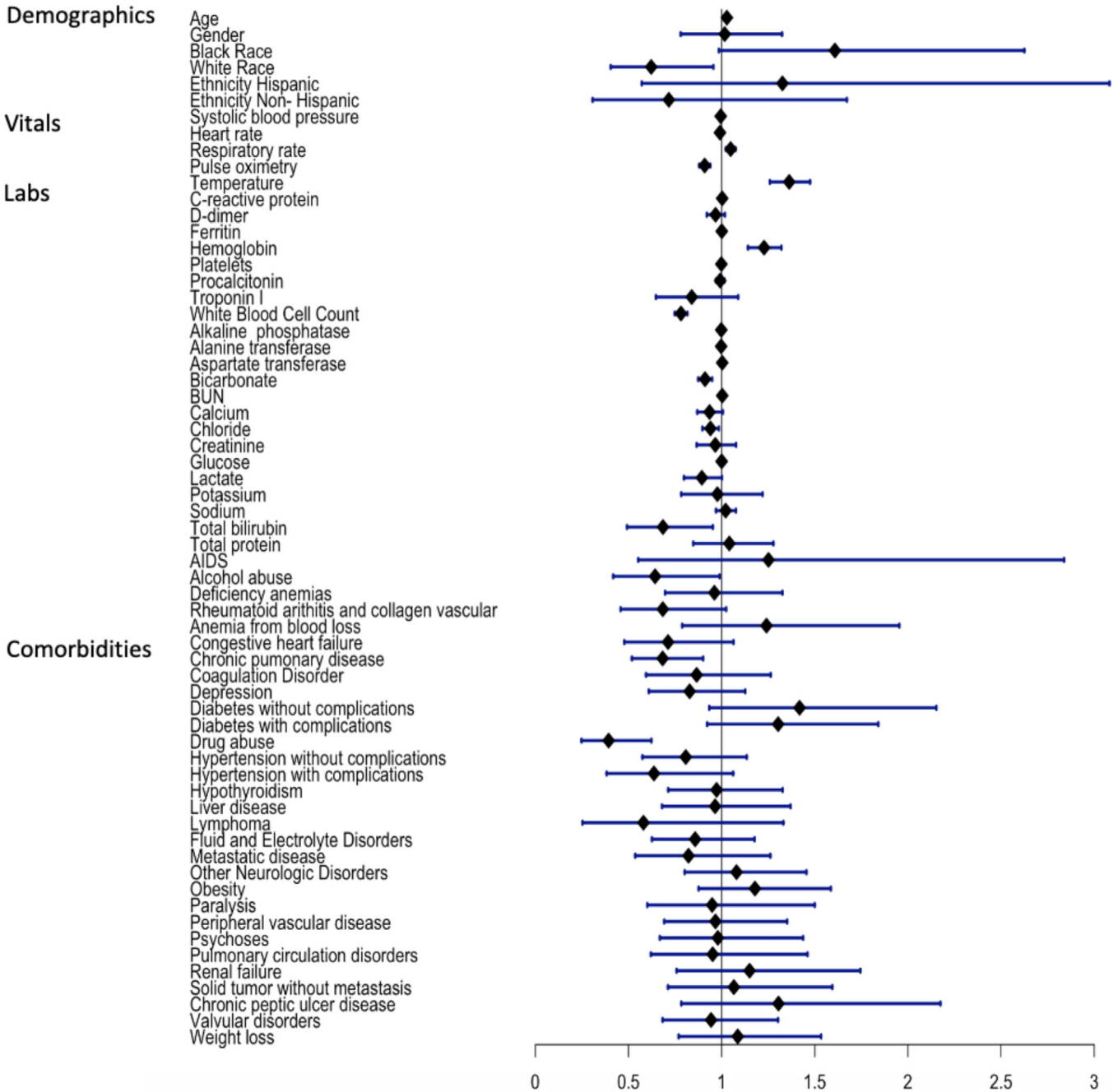


FIGURE 1 Kernel density estimate distribution plot for Elixhauser comorbidity scores stratified by COVID-19 outcome. Y axis represents the probability for a particular Elixhauser comorbidity score value. X axis represents the Elixhauser comorbidity score. Higher values represent higher risk of mortality

rather that these patients are being admitted for symptoms related to their chronic disease process and being subsequently tested. Similarly, patients with histories of substance use disorders were also less likely to test positive, which may be related to patients being admitted in the setting of loss of outpatient care options.

These findings reinforce the expectation that patients with chronic diseases will continue to experience sequelae of their underlying disease during the COVID-19 pandemic. While further research is required to better understand the individual effects of specific comor-

bidities (eg, asthma, chronic obstructive pulmonary disease) on disease risk, our observations also highlight the challenges of treating patient populations with multiple potential symptom etiologies at a time of growing population disease burden.

There is significant interest in using vital signs and laboratory evidence to help establish a pretest probability of disease. Consistent with prior knowledge about the clinical syndrome, relative hyperthermia, tachypnea, and hypoxemia increased likelihood of positive testing. The small mean differences in these factors may limit their utility. Similarly,

TABLE 3 Odds ratios for characteristics of ED admitted patients evaluated for COVID-19

	Odds ratio	95% CI lower bound	95% CI upper bound
Age	1.03	1.02	1.04
Sex	1.02	0.78	1.32
Black race	1.61	0.98	2.62
White race	0.62	0.40	0.96
Ethnicity Hispanic	1.33	0.57	3.08
Ethnicity non-Hispanic	0.72	0.31	1.67
Systolic blood pressure	0.99	0.99	1.00
Heart rate	0.99	0.98	1.00
Respiratory rate	1.05	1.02	1.07
Pulse oximetry	0.91	0.88	0.94
Temperature	1.36	1.26	1.47
C-Reactive protein	1.00	1.00	1.01
D-Dimer	0.97	0.92	1.02
Ferritin	1.00	1.00	1.00
Hemoglobin	1.23	1.14	1.32
Platelets	1.00	1.00	1.00
Procalcitonin	0.99	0.97	1.01
Troponin I	0.84	0.65	1.09
White blood cell count	0.78	0.75	0.82
Alkaline phosphatase	1.00	0.99	1.00
Alanine transferase	1.00	0.99	1.00
Aspartate transferase	1.00	1.00	1.00
Bicarbonate	0.91	0.87	0.95
BUN	1.00	0.99	1.01
Calcium	0.93	0.87	1.01
Chloride	0.94	0.90	0.98
Creatinine	0.97	0.87	1.08
Glucose	1.00	1.00	1.00
Lactate	0.89	0.80	1.00
Potassium	0.98	0.78	1.22
Sodium	1.02	0.97	1.08
Total bilirubin	0.68	0.49	0.95
Total protein	1.04	0.85	1.28
AIDS	1.25	0.55	2.84
Alcohol abuse	0.64	0.42	0.99
Deficiency anemias	0.96	0.70	1.33
Rheumatoid arthritis and collagen vascular	0.68	0.46	1.02
Anemia from blood loss	1.24	0.79	1.95
Congestive heart failure	0.71	0.48	1.06
Chronic pulmonary disease	0.68	0.52	0.90
Coagulation Disorder	0.87	0.59	1.26
Depression	0.83	0.61	1.13

(Continues)

TABLE 3 (Continued)

	Odds ratio	95% CI lower bound	95% CI upper bound
Diabetes without complications	1.42	0.93	2.15
Diabetes with complications	1.30	0.92	1.84
Drug abuse	0.39	0.25	0.62
Hypertension without complications	0.81	0.57	1.13
Hypertension with complications	0.64	0.38	1.06
Hypothyroidism	0.97	0.71	1.33
Liver disease	0.96	0.68	1.37
Lymphoma	0.58	0.25	1.33
Fluid and electrolyte disorders	0.86	0.63	1.18
Metastatic disease	0.82	0.54	1.26
Other neurologic disorders	1.08	0.80	1.45
Obesity	1.18	0.88	1.59
Paralysis	0.95	0.60	1.50
Peripheral vascular disease	0.97	0.69	1.35
Psychoses	0.98	0.67	1.44
Pulmonary circulation disorders	0.95	0.62	1.46
Renal failure	1.15	0.76	1.74
Solid tumor without metastasis	1.06	0.71	1.59
Chronic peptic ulcer disease	1.30	0.78	2.17
Valvular disorders	0.94	0.68	1.30
Weight loss	1.09	0.77	1.53

CI, confidence interval; ED, emergency department.

the COVID-19-positive cohort had lower lymphocyte counts as compared to the negative group. Our analysis of inflammatory markers was limited by missing data, but we were unable to establish clinically significant associations in these markers. At this time, it is increasingly clear that no single laboratory result will define disease. We hypothesize that there will be more success using a laboratory phenotype as defined by multiple biologically linked findings.

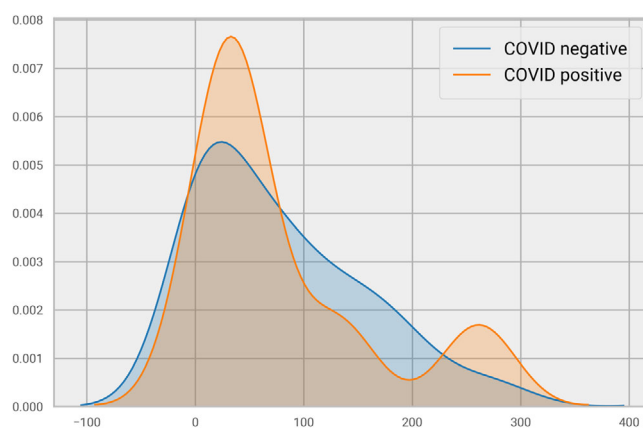


FIGURE 2 Pair-plot of vital signs stratified by COVID-19 outcome

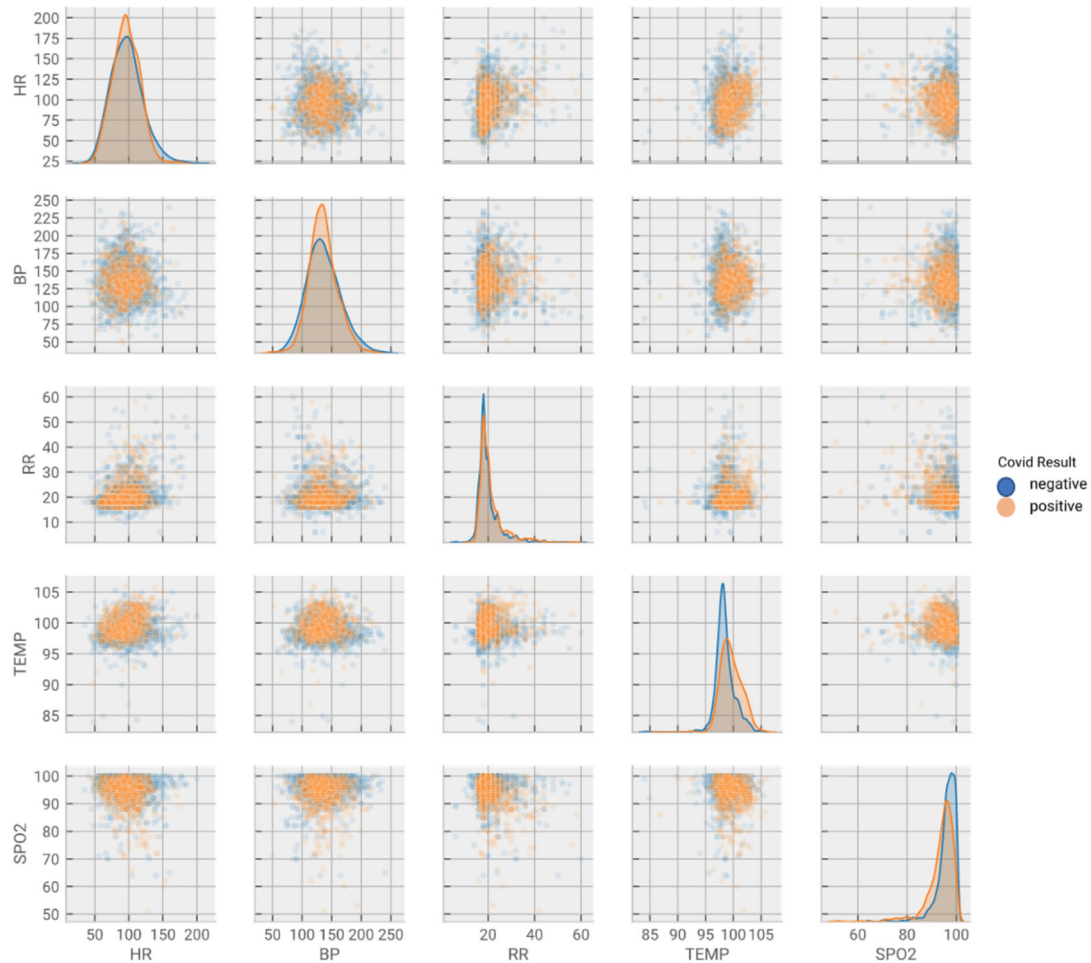


FIGURE 3 Forest plot of odds ratios for COVID-19 outcome from multivariable logistic regression

In conclusion, we found that 36% of patients tested positive for COVID-19 in our ED population. While we note several demographic, lab, and vital sign differences between tested patients with and without COVID-19 due to the overlap of these features with other disease etiologies, it is uncertain if these differences are clinically useful. We expect research in this area will continue to proceed rapidly, with increased emphasis on early diagnosis, risk stratification, and elucidation of COVID-19 test characteristics.

CONFLICTS OF INTEREST

The authors report no conflicts of interest relating to this work.

AUTHOR CONTRIBUTIONS

Adrian Haimovich, R. Andrew Taylor, and Wade Schulz conceived the study. R. Andrew Taylor, Wade Schulz, Frederick Warner, Guannan Gong, and H. Patrick Young supervised data collection and preprocessing. Neal G. Ravindra, Frederick Warner, Arijit Sehanobish, and David van Dijk performed statistical analysis. Adrian Haimovich and R. Andrew Taylor drafted the manuscript, and all authors contributed substantially to its revision. Richard Andrew Taylor takes responsibility of the paper as a whole.

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