Demographic and clinical correlates of acute and convalescent SARS-CoV-2 infection among patients of a U.S. emergency department

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ABSTRACT

Background: Emergency Departments (EDs) have served as critical surveillance sites for infectious diseases. We sought to determine the prevalence and temporal trends of acute (by PCR) and convalescent (by antibody [Ab]) SARS-CoV-2 infection during the earliest phase of the pandemic among patients in an urban ED in Baltimore City.

Methods: We tested remnant blood samples from 3255 unique ED patients, collected between March 16th and May 31st 2020 for SARS-CoV-2 Ab. PCR for acute SARS-CoV-2 infection from nasopharyngeal swabs was obtained on any patients based on clinical suspicion. Hospital records were abstracted and factors associated with SARS-CoV-2 infection were assessed.

Results: Of 3255 ED patients, 8.2% (95%CI: 7.3%, 9.2%) individuals had evidence of SARS-CoV-2 infection; 155 PCR +, 78 Ab+, and 35 who were both PCR+ and Ab+. Prevalence of disease increased throughout the study period, ranging from 3.2% (95%CI: 1.8%, 5.2%) PCR+ and 0.6% (95%CI: 0.1%, 1.8%) Ab+ in March, to 6.2% (95%CI: 5.1%, 7.4%) PCR+ and 4.2% (95%CI: 3.3%, 5.3%) Ab+ in May. The highest SARS-CoV-2 prevalence was found in Hispanic individuals who made up 8.4% (95%CI: 7.4%, 9.4%) of individuals screened, but 35% (95%CI: 29%, 41%) of infections (PCR and/or Ab+). Demographic and clinical factors independently associated with acute infection included Hispanic ethnicity, loss of smell or taste, subjective fever, cough, muscle ache and fever. Factors independently associated with convalescent infection were Hispanic ethnicity and low oxygen saturation.

Conclusions: The burden of COVID-19 in Baltimore City increased dramatically over the 11-week study period and was disproportionately higher among Hispanic individuals. ED-based surveillance methods are important for identifying both acute and convalescent SARS-CoV-2 infections and provides important information regarding demographic and clinical correlates of disease in the local community.

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1. Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the respiratory illness Coronavirus disease-19 (COVID-19) [1]. By the spring of 2020, COVID-19 had progressed into a global pandemic [2]. Accurate estimates of the prevalence of SARS-CoV-2 infection are needed to determine the burden of disease, temporal trends, and demographic and clinical correlates of disease, all of which are important for designing and assessing the impact of public health interventions [3]. Critical to these estimates is the ability to accurately estimate disease burden [4,5]. Methods and sampling frameworks for estimating disease prevalence during the pandemic have proven difficult, particularly early in the pandemic, when infection rates were low, and relatively limited and biased population-based surveillance data existed [6]. While serologic assays have proven to be an important tool for estimating population-level prevalence [7], gaps exist in regard to the populations they have been applied.

While a number of serosurveys have been conducted in health care workers [8-10], demonstrating a higher burden of disease than the general population, relatively few have been carried out in broad patient populations. One national study which focused on dialysis patients in July 2020 reported a seroprevalence of antibodies to SARS-CoV-2 of <10%, among a cohort of nearly 30,000 patients [11]. Emergency Departments (EDs) are potentially unique sites for conducting SARS-CoV-2 serosurveillance, providing a 'window' into the community. Historically, EDs have played a critical role in prior public health epidemics and pandemics, including HIV, hepatitis C, HSV-2 and influenza H1N1 [12-14], and more recently, in detecting racial/ethnic disparities for COVID-19 [15].

In the current study, we first validated a serologic algorithm to detect the prevalence of antibodies to SARS-CoV-2 infection. The validated algorithm was then applied to remnant samples from Johns Hopkins Hospital Emergency Department (JHHED) patients collected between March 16th and May 31st 2020. Patient records were abstracted to determine signs, symptoms and PCR status for active SARS-CoV-2 infection. Finally, factors associated with acute [PCR+] and convalescent [Ab+] SARS-CoV-2 infection were assessed.

2. Methods

2.1. Study population

To estimate the prevalence of antibodies to SARS-CoV-2 infection among patients attending the JHHED, we conducted an identity-unlinked seroprevalence study from March 16 to May 31, 2020. The study ED, located in Baltimore, Maryland is an urban academic adult ED with 66,000 annual visits in 2019. It serves a mainly underserved minority population including Black or African Americans (65%) and Latinx (8%), from the surrounding neighborhoods and the general Baltimore metropolitan area. During the study period, approximately 5% and 1% of the ED patients were homeless or residents of a skilled nursing facility, respectively. As in a previous identity-unlinked seroprevalence study from the JHHED [12,16], all available remnant blood from hematology samples from ED patients aged >17 years were collected during the study period. For each sample, a unique study code was assigned, processed, and stored at −80 °C. For all samples, basic patient demographic characteristics (age, sex, race, ethnicity, and residential zip code), clinical information (month of ED visit, COVID-19 related symptoms: loss of smell or taste, subjective fever, cough, sore throat, fatigue, diarrhea, chest pain, short of breath, muscle ache, headache, chills, and congestion) and triage vital signs (temperature, heart rate, respiratory rate, and oxygen saturation) were abstracted from medical records, and all identifiers and protected health information removed from the dataset. Laboratory testing was then performed on stored specimens after delinking the demographic/clinical dataset. The SARS-CoV-2 serostatus was merged to the demographic/clinical dataset using the

unique study code. The first time point of individuals who visited the ED multiple times was analyzed. The study was approved by The Johns Hopkins University School of Medicine Institutional Review Board (IRB00083646, CIR00016268) and conducted by the ethical standards of the Helsinki Declaration of the World Medical Association.

2.2. Laboratory testing

SARS-CoV-2 antibody testing was performed using the anti-SARS-CoV-2 ELISA IgG (Euroimmun, Germany) according to the manufacturer's protocol. ELISA outcomes are described in a signal to cutoff ratio (S/C), where values ≥1.1 are considered positive, <1.1 to ≥0.8 as indeterminate, and < 0.8 as negative. The Coronachek COVID-19 IgG/IgM Rapid Test Cassette (Hangzhou Biotest Biotech Co. Ltd., Hangzhou China), a point of care test, was performed according to the manufacture's protocol with the following modification: 10ul of plasma was pipetted onto the sample well instead of whole blood [17]. Any visible band on the CoronaChek was considered a positive result. The testing algorithm used an initial screen of the Euroimmun IgG ELISA followed by confirmatory testing of any initial indeterminate or positive result with the CoronaChek rapid test. The overall performance of this testing algorithm was 100% (24/24) sensitivity among hospitalized individuals 14 days after symptom onset; sensitivity was found to be 84% (111/133) among samples from plasma donors 50 days after positive PCR, and overall a specificity of 100% (95% CI 99.3, 100 [554/554]). Performance of serologic algorithm is presented in detail in Supplemental Methods. ED patients were tested for SARS-CoV-2 by PCR, based on presenting signs and symptoms and/or at the discretion of the treating ED clinician. With the evolving epidemic of COVID-19 and the increasing capacity of hospital SARS-CoV-2 PCR testing, the study institution granted PCR testing for ED patients with asymptomatic admission to Psychiatry or the Surgical/Procedural services in mid-April and for all asymptomatic admission patients in mid-May.

2.3. Statistical analyses

Descriptive statistical analysis was performed first including missing data which ranged from 0.1% to 2.0% for demographic or clinical characteristics out of 3255 unique patients, followed by comparison of subjects by SARS-CoV-2 PCR testing status (i.e. no evidence of infection, SARS-CoV-2 PCR+ only, and SARS-CoV-2 Ab+), and PCR and antibody status among those with evidence of infection (PCR+ only, both PCR+ and Ab+, PCR- but Ab+, and Ab+ but without PCR testing) using chi-square or Fisher's exact tests. Only PCR testing ordered in the ED were analyzed. Age was categorized into 3 groups (18–44, 45–64, and ≥ 65 years). Group-specific prevalence was assessed using a composite variable of sex and race/ethnicity to categorize Hispanic female, Hispanic male, non-Hispanic white female, non-Hispanic white male, non-Hispanic Black female, non-Hispanic Black male, other female, and other male groups. Residential zip codes of subjects were categorized by the most common individual 5 zip codes (representing approximately 5% or more of the patients analyzed) and the remaining zip codes categorized as 'other'. Residential zip code was also linked to ZIP code tabulation area (ZCTA) data from the 2018 American Community Survey of 5-year estimates for proportion living below the poverty level which was categorized into <10%, 10–20%, 20–30%, ≥ 30%, or missing [18,19]. All prevalence point estimates were presented with their corresponding 95% confidence intervals (CIs).

Associations of SARS-CoV-2 positivity with demographic and ED visit symptoms, and triage vital signs were initially performed for each variable independently using modified Poisson regression. Variables with *p*-value <0.2 in the bivariate analysis were included in the multivariable regression. Month of ED visit was collapsed to 2 categories (March or April versus May) and the zip code variable was further collapsed to 3 categories (Zip Code A, B and other) with consideration of sample size in each cell. Stepwise variable selection for the

multivariable regression analysis was used to select variables in the final model to estimate the adjusted prevalence ratios, adjusted for zip code clustering effects. All prevalence ratios were presented with their corresponding 95% CIs. An identical regression modeling analysis approach was employed to determine the variables associated with the presence of SARS-CoV-2 Ab. All data analyses were performed using SAS V.9.4 (SAS Institute Inc., Cary, North Carolina) and a two-sided p-value less than 0.05 was considered statistically significant. Sensitivity analysis was performed to estimate overall and age-, sex-, race-, and ethnicity-specific infection rates according to sensitivity and specificity of the serologic algorithm.

Comparisons of the proportion of cumulative patients with evidence of SARS-CoV-2 infection (SARS-CoV-2 PCR+ or Ab+) in the ED to that of the cumulative COVID-19 reported cases in Baltimore City per 1000 residents were performed by race and ethnicity (black, white, and Hispanic) every 10 days from March 31 to May 31. The ratio between two proportions for each group at each time point was also calculated. The cumulative Baltimore City COVID-19 reported case rate per 1000 residents by race and ethnicity were abstracted from Baltimore City COVID-19 Dashboard (https://coronavirus.baltimorecity.gov/).

3. Results

During the 11-week study period, there were 9049 visits of 7037 unique individuals to the JHHED. There were 3830 remnant blood samples came from a total of 3255 unique individuals. Of these 3255 individuals, 55% (1798/3255) were tested for SARS-CoV-2 by PCR at their first ED visit, among whom 5.8% (190/1798) were positive. The overall seroprevalence for antibodies to SARS-CoV-2 at the first ED visit was 3.5% (113/3255) [95% CI: 2.9%, 4.2%], and was similar in the populations who had PCR testing for active SARS-CoV-2 infection (3.7% [66/1798, 95% CI: 2.9, 4.6]) compared to the population that was not tested by PCR (3.2% [47/1457, 95% CI: 2.4, 4.3]) (Supplemental Table S1).

The frequency of SARS-CoV-2 infection, as assessed by either PCR+ and/or Ab+, increased from 3.6% in March to 9.1% in May. The prevalence of SARS-CoV-2 seropositivity was lower than PCR positivity over the duration of the study (Fig. 1A). Hispanic individuals made up <9% of the population visiting the JHHED between March and May, but represented 39% (61/155) of all acute (PCR+/Ab-) and 29% (33/113) of all

Ab+ SARS-CoV-2 infections (Table 1). There was a significantly higher prevalence of SARS-CoV-2 infection among Hispanic women and men than in Black or White women and men (Fig. 1B). For Hispanic women and men, the frequency of any evidence of SARS-CoV-2 infection (either PCR+ and/or Ab+) increased from 7% (95% CI: 0, 34) and 11% (95% CI: 1, 35) in March to 38% (95% CI: 27, 49) and 35% (95% CI: 25, 47) in May, respectively. Similarly, Hispanic men had an increase in any evidence of SARS-CoV-2 infection from in March to in May. Similar upward trends were observed for Black women and men. In contrast, the prevalence in White women and men did not significantly change over the study period. Sensitivity analysis based on the performance of serologic algorithm found that the overall infection rate was 11.2% (95% CI: 10.1%, 12.2%). Zip codes associated with high poverty rates were not significantly associated with increased disease prevalence. Demographic-specific infection rates by the sensitivity analysis are presented in Supplemental Table S2.

Having a fever was observed in only 3.3% (110/3255) of the population entering the JHHED over the study period, but was present in 35% (38/110) of individuals acutely infected (PCR+/Ab-) with SARS-CoV-2. Similarly, symptoms such as loss of smell or taste was uncommon among patients overall (3%, 96/3255), but was present in 31% (30/96) of patients who were acutely infected with SARS-CoV-2. The most common symptom among individuals with either active or convalescent evidence of SARS-CoV-2 infection was shortness of breath at 48% (130/268). A minority of individuals had symptoms of loss of smell or taste (37/256), and the majority of those were acutely infected (30/37). When comparing the four different groups of individuals who had evidence of current and previous SARS-CoV-2 infection (Table 2), we noted distinct differences between the groups. Comparing acutely infected (PCR+/Ab-) with convalescent (PCR- or missing PCR/Ab+) individuals, significant differences were observed based on presenting signs and symptoms. The most common symptoms among those acutely infected were cough (63.2%), fever (58.7%) and shortness of breath (54.8%); the most common signs at triage was tachycardia (38.1%), which were significantly less frequent in the convalescent individuals.

When subjects with acute or convalescent infection were compared to their uninfected counterparts in the multivariate regression analysis, Hispanic ethnicity or attending the ED in May versus March and April
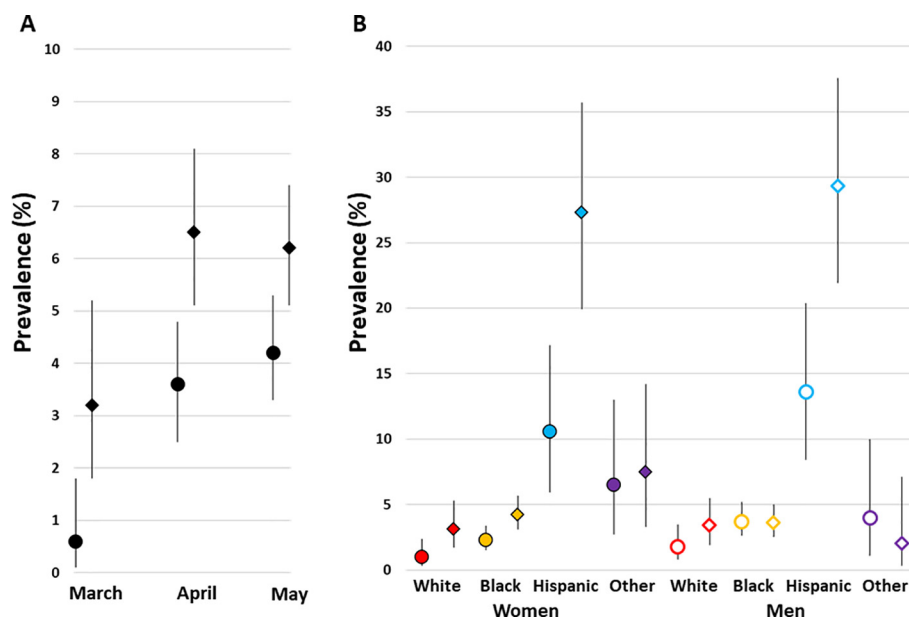

Fig. 1. Prevalence of SARS-CoV-2 Antibody and PCR Results by Month, Sex, Race and Ethnicity among Patients Attending the Johns Hopkins Hospital Emergency Department. Antibody prevalence is denoted by a circle, while PCR positivity is represented by a diamond. Panel A denotes the prevalence by month of survey. Panel B shows the prevalence by sex, race and ethnicity.

Table 1
Characteristics of emergency department patients by SARS-CoV-2 infection status.

Characteristics	Category	Number	No. of Patients (%)			p-value
			No Infection	PCR+ but Ab-	Ab+	
		n = 3255	n = 2987 (91.8)	n = 155 (4.8)	n = 113 (3.5)	
Age	18–44 years	1522 (46.8)	1399 (46.8)	80 (51.6)	43 (38.1)	0.111
	45–64 years	1162 (35.7)	1072 (35.9)	42 (27.1)	48 (42.5)	
	≥65 years	568 (17.5)	513 (17.2)	33 (21.3)	22 (19.5)	
	Missing	3 (0.1)	3 (0.1)	0 (0.0)	0 (0.0)	
Sex/Race/Ethnicity	NH White Female	417 (12.8)	401 (14.0)	12 (7.7)	4 (3.5)	<0.001
	NH Black Female	998 (30.7)	940 (31.5)	35 (22.6)	23 (20.4)	
	Hispanic Female	132 (4.1)	89 (3.0)	29 (18.7)	14 (12.4)	
	Other Female	107 (3.3)	94 (3.2)	6 (3.9)	7 (6.2)	
	NH White Male	447 (13.7)	424 (14.2)	15 (9.7)	8 (7.1)	
	NH Black Male	915 (28.1)	857 (28.7)	24 (15.5)	34 (30.1)	
	Hispanic Male	140 (4.3)	89 (3.0)	32 (20.7)	19 (16.8)	
	Other Male	99 (3.0)	93 (3.1)	2 (1.3)	4 (3.5)	
Month of Visit	March	475 (14.6)	458 (15.3)	14 (9.0)	3 (2.7)	<0.001
	April	1096 (33.7)	999 (33.4)	58 (37.4)	39 (34.5)	
	May	1684 (51.7)	1530 (51.2)	83 (55.6)	71 (62.8)	
Zip Code	A	312 (9.6)	300 (10.0)	8 (5.2)	4 (3.5)	<0.001
	B	223 (6.9)	174 (5.8)	32 (20.7)	17 (15.0)	
	C	216 (6.6)	199 (6.7)	12 (7.7)	5 (4.4)	
	D	172 (5.3)	162 (5.4)	5 (3.2)	5 (4.4)	
	E	151 (4.6)	139 (4.7)	7 (4.5)	5 (4.4)	
	Other	2181 (67.0)	2013 (67.4)	91 (58.7)	77 (68.1)	
Symptoms						
Loss of Sense	Yes	96 (3.0)	59 (2.0)	30 (19.4)	7 (6.2)	<0.001
	No	3159 (97.1)	2928 (98.0)	125 (80.7)	106 (93.8)	
Fever	Yes	477 (14.7)	357 (12.0)	91 (58.7)	29 (25.7)	<0.001
	No	2778 (85.4)	2630 (88.1)	64 (41.3)	84 (74.3)	
Cough	Yes	669 (20.6)	533 (17.8)	98 (63.2)	38 (33.6)	<0.001
	No	2586 (79.5)	2454 (82.2)	57 (36.8)	75 (66.4)	
Sore Throat	Yes	234 (7.2)	184 (6.2)	39 (25.2)	11 (9.7)	<0.001
	No	3021 (92.8)	2803 (93.8)	116 (74.8)	102 (90.3)	
Diarrhea	Yes	355 (10.9)	301 (10.1)	38 (24.5)	16 (14.2)	<0.001
	No	2900 (89.1)	2686 (89.9)	117 (75.5)	97 (85.8)	
Fatigue	Yes	296 (9.1)	242 (8.1)	43 (27.7)	11 (9.7)	<0.001
	No	2959 (90.9)	2745 (91.9)	112 (72.3)	102 (90.3)	
Chest Pain	Yes	592 (18.2)	529 (17.7)	35 (22.6)	28 (24.8)	0.056
	No	2663 (81.8)	2458 (82.3)	120 (77.4)	85 (75.2)	
Short of Breath	Yes	918 (28.2)	788 (26.4)	85 (54.8)	45 (39.8)	<0.001
	No	2337 (71.8)	2199 (73.6)	70 (45.2)	68 (60.2)	
Muscle Ache	Yes	359 (11.0)	272 (9.1)	67 (43.2)	20 (17.7)	<0.001
	No	2896 (89.0)	2715 (90.9)	88 (56.8)	93 (82.3)	
Headache	Yes	490 (15.1)	414 (13.9)	57 (36.8)	19 (16.8)	<0.001
	No	2765 (85.0)	2573 (86.1)	98 (63.2)	94 (83.2)	
Chills	Yes	258 (7.9)	205 (6.9)	40 (25.8)	13 (11.5)	<0.001
	No	2997 (92.1)	2782 (93.1)	115 (74.2)	100 (88.5)	
Congestion	Yes	77 (2.4)	72 (2.4)	3 (1.9)	2 (1.8)	0.851
	No	3178 (97.6)	2915 (97.6)	152 (98.1)	111 (98.2)	
Signs at Triage						
Temperature ≥ 100.4 °F	Yes	110 (3.4)	65 (2.2)	38 (24.5)	7 (6.2)	<0.001
	No	3081 (94.7)	2863 (95.8)	115 (74.2)	103 (91.2)	
	Missing	64 (2.0)	59 (2.0)	2 (1.3)	3 (2.7)	
Heart Rate > 100/min	Yes	893 (27.4)	801 (26.8)	59 (38.1)	33 (29.2)	0.002
	No	2335 (71.7)	2163 (72.4)	96 (61.9)	76 (67.3)	
	Missing	27 (0.8)	23 (0.8)	0 (0.0)	4 (3.5)	
Respiratory Rate > 20/min	Yes	251 (7.7)	206 (6.9)	24 (15.5)	21 (18.6)	<0.001
	No	2946 (90.5)	2728 (91.3)	128 (82.6)	90 (79.6)	
	Missing	58 (1.8)	53 (1.8)	3 (1.9)	2 (1.8)	
Oxygen Saturation < 94%	Yes	110 (3.4)	82 (2.7)	16 (10.3)	12 (10.6)	<0.001
	No	3097 (95.1)	2863 (95.8)	139 (89.7)	95 (84.1)	
	Missing	48 (1.5)	42 (1.4)	0 (0.0)	6 (5.3)	

were significantly associated with SARS-CoV-2 infection (Fig. 2, Supplemental Tables S3 and S4). Signs and symptoms frequently associated with COVID-19 infection (i.e. loss of smell or taste, fever, cough, and muscle ache) were all independently associated with being PCR positive for SARS-CoV-2 in our population (Fig. 2A). Hispanic ethnicity and low oxygen saturation were independently associated with convalescent infection. (Fig. 2B).

During the same time period of surveillance in the JHHED, active surveillance for acute SARS-CoV-2 infection by PCR was reported to the Baltimore City Health Department (BCHD) from multiple screening sites (Fig. 3). As shown in the Figure, acute SARS-CoV-2 infection steadily rose over time in both the community screening sites as well as in the JHHED. When combining both positive PCR and antibody results in patients attending the JHHED, a much greater rate of increase was

Table 2
Characteristics 268 patients with a laboratory evidence of SARS-CoV-2 infection PCR and antibody status.

Characteristics	Category	Number	PCR+/Ab−	PCR+/Ab+	PCR−/Ab+	No PCR/Ab+	p-value
		n = 268	n = 155 (57.8)	n = 35 (13.1)	n = 31 (11.6)	n = 47 (17.5)	
Age	18–44 years	123 (45.9)	80 (51.6)	10 (28.6)	14 (45.2)	19 (40.4)	0.017
	45–64 years	90 (33.6)	42 (27.1)	13 (37.1)	15 (48.4)	20 (42.6)	
	≥65 years	55 (20.5)	33 (21.3)	12 (34.3)	2 (6.5)	8 (17.0)	
Sex	Female	130 (48.5)	82 (52.9)	17 (48.6)	13 (41.9)	18 (38.3)	0.296
	Male or Other	138 (51.5)	73 (47.1)	18 (51.4)	18 (58.1)	29 (61.7)	
Race	Black or African American	119 (44.4)	59 (38.1)	18 (51.4)	16 (51.6)	26 (55.3)	0.164
	White	40 (14.9)	27 (17.4)	2 (5.7)	6 (19.4)	5 (10.6)	
	Other or Unknown	109 (40.7)	69 (44.5)	15 (42.9)	9 (29.0)	16 (34.0)	
Ethnicity	Hispanic	94 (35.1)	61 (39.4)	16 (45.7)	6 (19.4)	11 (23.4)	0.027
	Non-Hispanic or Unknown	174 (64.9)	94 (60.7)	19 (54.3)	25 (80.7)	36 (76.6)	
Sex/Race/Ethnicity	NH White Female	16 (6.0)	12 (7.7)	1 (2.9)	3 (9.7)	0 (0.0)	0.068
	NH Black Female	58 (21.6)	35 (22.6)	7 (20.0)	5 (16.1)	11 (23.4)	
	Hispanic Female	43 (16.0)	29 (18.7)	7 (20.0)	3 (9.7)	4 (8.5)	
	Other Female	13 (4.9)	6 (3.9)	2 (5.7)	2 (6.5)	3 (6.4)	
	NH White Male	23 (8.6)	15 (9.7)	0 (0.0)	3 (9.7)	5 (10.6)	
	NH Black Male	58 (21.6)	24 (15.5)	9 (25.7)	11 (25.5)	14 (29.8)	
	Hispanic Male	51 (19.0)	32 (20.7)	9 (25.7)	3 (9.7)	7 (14.9)	
	Other Male	6 (2.2)	2 (1.3)	0 (0.0)	1 (3.2)	3 (6.4)	
Month of Visit	March	17 (6.3)	14 (9.0)	1 (2.9)	0 (0.0)	2 (4.2)	0.335
	April	97 (36.2)	58 (37.4)	13 (37.1)	8 (25.8)	18 (38.3)	
	May	154 (57.5)	83 (53.6)	21 (60.0)	23 (74.2)	27 (57.5)	
Zip Code	A	12 (4.5)	8 (5.2)	1 (2.9)	1 (3.2)	2 (4.3)	0.694
	B	49 (18.3)	32 (20.7)	8 (22.9)	2 (6.5)	7 (14.9)	
	C	17 (6.3)	12 (7.7)	0 (0.0)	1 (3.2)	4 (8.5)	
	D	10 (3.7)	5 (3.2)	1 (2.9)	1 (3.2)	3 (6.4)	
	E	12 (4.5)	7 (4.5)	1 (2.9)	1 (3.2)	3 (6.4)	
	Other	168 (62.7)	91 (58.7)	24 (68.6)	25 (80.7)	28 (59.6)	
ZCTA Poverty Level	<10%	61 (22.8)	35 (22.6)	8 (22.9)	6 (19.4)	12 (25.5)	0.792
	10% to <20%	104 (38.8)	63 (40.6)	16 (45.7)	10 (32.3)	15 (31.9)	
	20% to <30%	56 (20.9)	27 (17.4)	7 (20.0)	11 (35.5)	11 (23.4)	
	≥30%	39 (14.6)	25 (16.1)	3 (8.6)	3 (9.7)	8 (17.0)	
	missing	8 (3.0)	5 (3.2)	1 (2.9)	1 (3.2)	1 (2.1)	
Symptoms							
Loss of Sense	Yes	37 (13.8)	30 (19.4)	5 (14.3)	1 (3.2)	1 (2.1)	0.003
	No	231 (86.2)	125 (80.7)	30 (85.7)	30 (80.7)	46 (97.9)	
Fever	Yes	120 (44.8)	91 (58.7)	21 (60.0)	4 (12.9)	4 (8.5)	<0.001
	No	148 (55.2)	64 (41.3)	14 (40.0)	27 (87.1)	43 (91.5)	
Cough	Yes	136 (50.8)	98 (63.2)	21 (60.0)	7 (22.6)	10 (21.3)	<0.001
	No	132 (49.3)	57 (36.8)	14 (40.0)	24 (77.4)	37 (78.7)	
Sore Throat	Yes	50 (18.7)	39 (25.2)	6 (17.1)	5 (16.1)	0 (0.0)	0.002
	No	218 (81.3)	116 (74.8)	5 (82.9)	26 (83.9)	47 (100)	
Diarrhea	Yes	54 (20.2)	38 (24.5)	9 (25.7)	6 (19.4)	1 (2.1)	0.007
	No	214 (79.9)	117 (75.5)	26 (74.3)	25 (80.7)	46 (97.9)	
Fatigue	Yes	54 (20.2)	43 (27.7)	7 (20.0)	3 (9.7)	1 (2.1)	<0.001
	No	214 (79.9)	112 (72.3)	28 (80.0)	28 (90.3)	46 (97.9)	
Chest Pain	Yes	63 (23.5)	35 (22.6)	8 (22.9)	6 (19.4)	14 (29.8)	0.703
	No	205 (76.5)	120 (77.4)	27 (77.1)	25 (80.7)	33 (70.2)	
Short of Breath	Yes	130 (48.5)	85 (54.8)	23 (65.7)	7 (22.6)	15 (31.9)	<0.001
	No	138 (51.5)	70 (45.2)	12 (34.3)	24 (77.4)	32 (68.1)	
Muscle Ache	Yes	87 (32.5)	67 (43.2)	11 (31.4)	4 (12.9)	5 (10.6)	<0.001
	No	181 (67.5)	88 (56.8)	24 (68.6)	27 (87.1)	42 (89.4)	
Headache	Yes	76 (28.4)	57 (36.8)	8 (22.9)	4 (12.9)	7 (14.9)	0.003
	No	192 (71.6)	98 (63.2)	27 (77.1)	27 (87.1)	40 (85.1)	
Chills	Yes	53 (19.8)	40 (25.8)	8 (22.9)	2 (6.5)	3 (6.4)	0.006
	No	215 (80.2)	115 (74.2)	27 (77.1)	29 (93.6)	44 (93.6)	
Congestion	Yes	5 (1.9)	3 (1.9)	0 (0.0)	0 (0.0)	2 (4.3)	0.472
	No	263 (98.1)	152 (98.1)	35 (100)	31 (100)	45 (95.7)	
Vomiting	Yes	20 (7.5)	15 (9.7)	1 (2.9)	3 (9.7)	1 (2.1)	0.240
	No	248 (92.5)	140 (90.3)	34 (97.1)	28 (90.3)	46 (97.9)	
Signs at Triage							
Temperature ≥ 100.4 °F	Yes	45 (16.8)	38 (24.5)	3 (8.6)	2 (6.5)	2 (4.3)	0.003
	No	218 (81.3)	115 (74.2)	31 (88.6)	28 (90.3)	44 (93.6)	
	Missing	5 (1.9)	2 (1.3)	1 (2.9)	1 (3.2)	1 (2.1)	
Heart Rate > 100/min	Yes	92 (34.3)	59 (38.1)	14 (40.0)	8 (25.8)	11 (23.4)	0.026
	No	172 (64.2)	96 (61.9)	21 (60.0)	21 (67.7)	34 (72.3)	
	Missing	4 (1.5)	0 (0.0)	0 (0.0)	2 (3.1)	2 (4.3)	
Respiratory Rate > 20/min	Yes	45 (16.8)	24 (15.5)	11 (31.4)	2 (6.5)	8 (17.0)	0.157
	No	218 (81.3)	128 (82.6)	24 (68.6)	28 (90.3)	38 (80.9)	
	Missing	5 (1.9)	3 (1.9)	0 (0.0)	1 (3.2)	1 (2.1)	

Table 2 (*continued*).

| Characteristics	Category	Number	No. of Patients (%)				p-value
			PCR+/Ab-	PCR+/Ab+	PCR−/Ab+	No PCR/Ab+	
		n = 268	n = 155 (57.8)	n = 35 (13.1)	n = 31 (11.6)	n = 47 (17.5)	
Oxygen Saturation < 94%	Yes	28 (10.5)	16 (10.3)	5 (14.3)	2 (6.5)	5 (10.6)	0.013
	No	234 (87.3)	139 (89.7)	30 (85.7)	26 (83.9)	39 (83.0)	
	Missing	6 (2.2)	0 (0.0)	0 (0.0)	3 (9.7)	3 (6.4)	

observed over time versus that reported by the BCHD. Furthermore, a nearly 10-fold difference in the overall case rate per 1000 population was evident in the ED population compared to what was reported from general community surveillance for acute infection by PCR alone.

4. Discussion

One of the distinct strengths of our study from other serosurveys is that we were able to use SARS-CoV-2 PCR testing data to track active infections and to detect disparities or patterns in clinical presentations. In this large urban ED patient serosurvey conducted from mid-March to May 2020, the overall SARS-CoV-2 seroprevalence was 3.5%; during that same time period selective PCR testing found a positivity rate of 5.8%. SARS-CoV-2 seroprevalence increased from 0.6% in March to 4.2% in May, while the prevalence of PCR+ individuals rose from 3.2% to 6.2%. This rise in infection observed in the ED over 11 weeks paralleled rise in acute SARS-CoV-2 infection which was reported in Baltimore City. Notably, the detailed demographic analysis from our ED revealed early on that the burden of SARS-CoV-2 was disproportionately higher among Hispanic individuals than individuals with other ethnicity, and was the single strongest predictor of being either PCR+ or Ab

+ for SARS-CoV-2. These findings corroborated the disproportional burden of SARS-CoV-2 which has been observed in the Hispanic population in other studies in the United States [20-23]. In those studies, which also demonstrated a higher burden of disease among minority populations, the authors attributed the high infection to be due to social inequities, including living in high density multi-generational households and employment in 'essential' labor as one's means of income. These early observations, contributed to informing varied focused educational interventions for clinicians regarding testing and care, including developing improved outpatient services for those populations at highest risk [24].

Unlike other serologic surveys conducted in the U.S., this ED-based study found that PCR+ individuals for SARS-CoV-2 infection outnumbered Ab+ individuals. The ratio of PCR+ to Ab+ individuals ranged from 4.7:1 to 1.5:1 over the observed study period which is notably higher than the 1:10 ratio seen in other serosurveys performed in the United States during the same study period [25]. The ED population represents a distinctive group for carrying out infectious diseases epidemiologic and clinical research, given the fact that these are individuals who are seeking care for acute illnesses, and in some cases for primary health care, while serosurveys conducted in other settings, typically
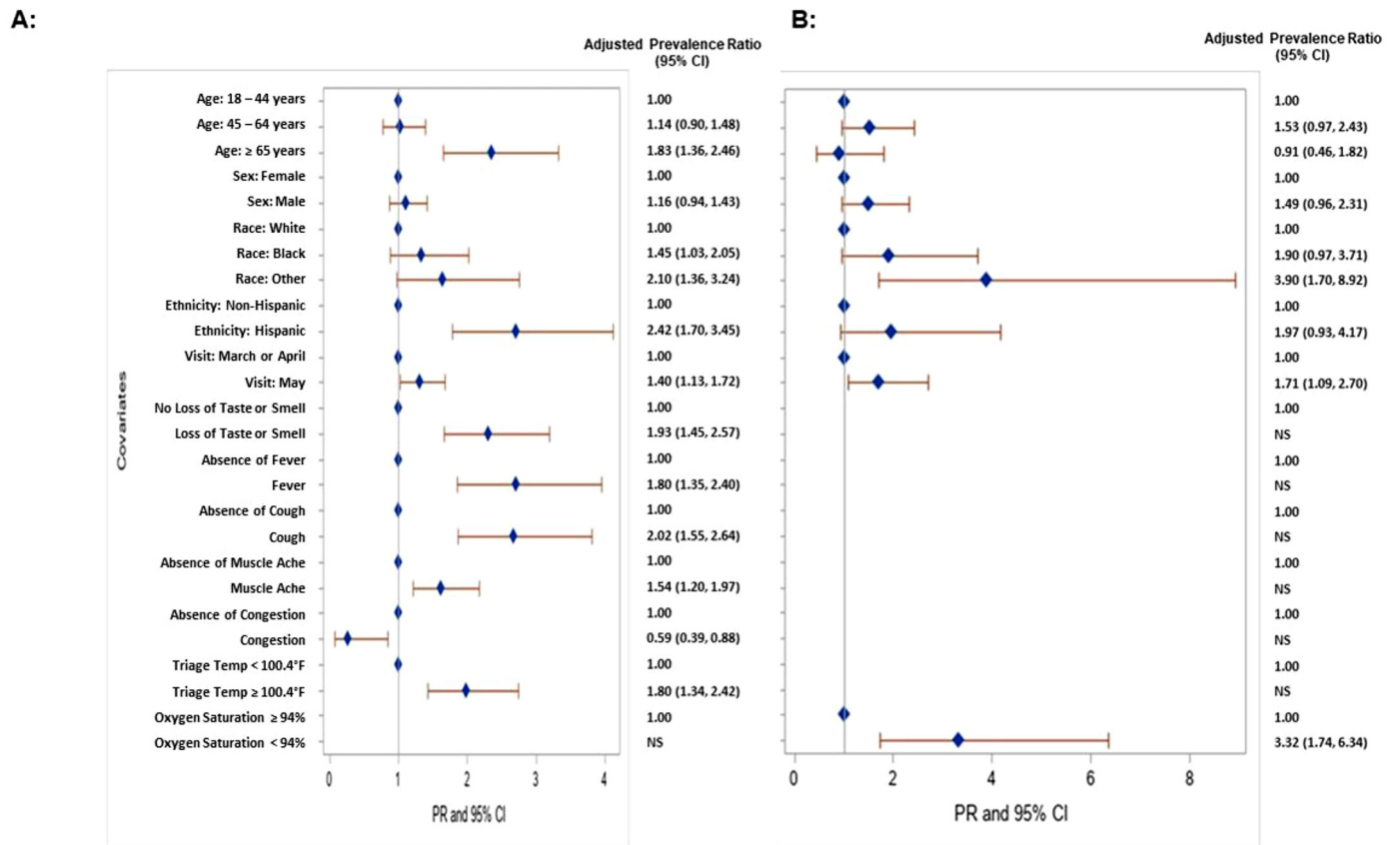
* excluding those who were SARS-CoV-2 PCR positive

Fig. 2. Forest plots of Prevalence Ratios Associated with PCR-Positive acute SARS-CoV-2 Infection (A) and Those Who Had SARS-CoV-2 in the Past as Indicated by Seropositivity (B).
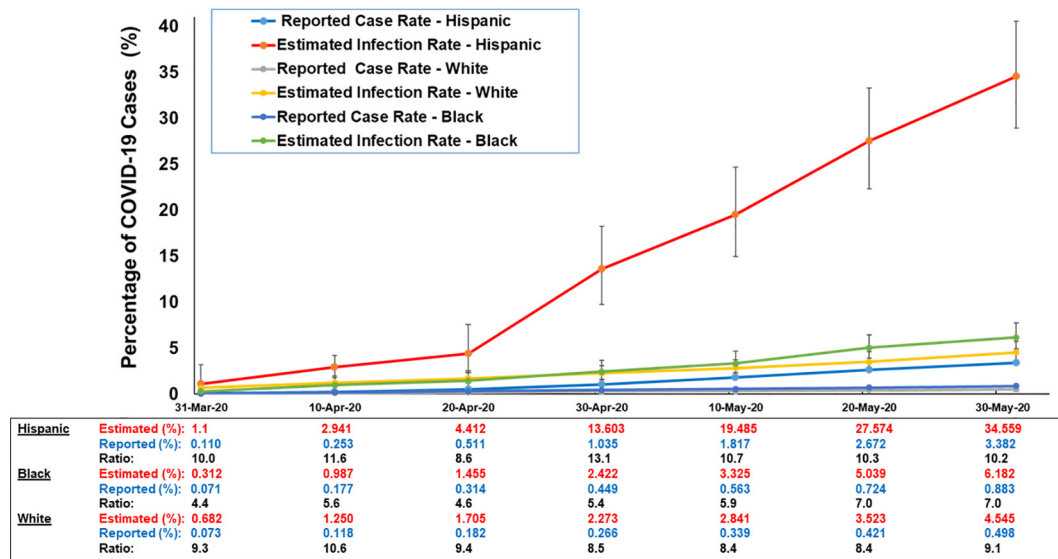
Percentage of COVID-19 Cases (%)

Legend:
- Reported Case Rate - Hispanic
- Estimated Infection Rate - Hispanic
- Reported Case Rate - White
- Estimated Infection Rate - White
- Reported Case Rate - Black
- Estimated Infection Rate - Black

		31-Mar-20	10-Apr-20	20-Apr-20	30-Apr-20	10-May-20	20-May-20	30-May-20
Hispanic	Estimated (%):	1.1	2.941	4.412	13.603	19.485	27.574	34.559
	Reported (%):	0.110	0.253	0.511	1.035	1.817	2.672	3.382
	Ratio:	10.0	11.6	8.6	13.1	10.7	10.3	10.2
Black	Estimated (%):	0.312	0.987	1.455	2.422	3.325	5.039	6.182
	Reported (%):	0.071	0.177	0.314	0.449	0.563	0.724	0.883
	Ratio:	4.4	5.6	4.6	5.4	5.9	7.0	7.0
White	Estimated (%):	0.682	1.250	1.705	2.273	2.841	3.523	4.545
	Reported (%):	0.073	0.118	0.182	0.266	0.339	0.421	0.498
	Ratio:	9.3	10.6	9.4	8.5	8.4	8.4	9.1

Fig. 3. Cumulative Reported COVID-19 Case Rate and Cumulative Estimated Infection Rate in Residents Aged 20 Years and Older in Baltimore City.

have represented asymptomatic community-based populations [7,11,26]. The access to ED patients who are acutely ill as well as those who were previously infected provides a unique window into the frequency of an infection in the community, which we believe will be helpful to temporally track trends associated with various waves of pandemic, and could thus be helpful to understand the impact of local and regional interventions. Further, our identity unlinked testing method permits detailed collection of paired clinical and demographic data helpful for contextualizing the associated characteristics of those who are actively infected, and/or have been infected. These data can be revealing for example with regard to chronic effects of the disease, such as long term respiratory (i.e. persistent hypoxemia) or cardiac complications [27], which were detected in our study as well. As the pandemic and the long term consequences of SARS-CoV-2 infections are uncovered, the ED will likely be an important site both for characterizing the prevalence of those complications and developing effective methods for intervening.

In general, signs and symptoms obtained at triage for SARS-CoV-2 were not a precise indicator of acute SARS-CoV-2 infection. The great majority of patients who had symptoms (including loss of smell or taste, fever, cough, sore throat, or shortness of breath) or signs (elevated temperature, reparations, or decreased oxygen saturation) did not have any evidence of SARS-CoV-2 infection. One intriguing finding from our study was the statistically increased prevalence of low oxygen saturation present in convalescent seropositive patients. This is suggestive of the pronounced chronic effects following COVID-19 in many people, and is of growing concern given the potential ongoing medical utilizations needs over time associated with this disease [28,29]. Given that the ED has, and will likely continue to serve as a common site of follow-up for SARS-CoV-2 patients who are initially diagnosed in the ED (particularly those who are marginalized or at increased risk for not receiving primary care services) further research to corroborate and explain this observation is needed.

With increasing number of Americans who have received at least 1 dose of COVID-19 vaccine [30], future serosurveys of SARS-CoV-2 infection that use conventional SARS-CoV-2 antibody assays will not truly reflect prevalence of current or past infection in the community, unless more complicated specialized serologic assays that can differentiate natural and vaccine-induced immunity are performed [31]. On the other hand, our study presents an ED-based active surveillance model that uses PCR-based testing data for active infection surveillance in order to provide rapid public health responses in given vulnerable

resource-limited communities, especially during the time when more individuals have received COVID-19 vaccine. With active infection surveillance data at hand, EDs could partner with local health departments and community-based organizations to prioritize targeted geographical testing, contact tracing, and vaccine distribution without stigmatizing or targeting racial, ethnic, or other groups [32,33].

There are a number of limitations to our study. First, the population that was screened is composed of ED patients and therefore highly enriched for symptomatic individuals. Second, antibody testing was only performed on 46% of all individuals attending the JHHED during the study period, as samples were limited only to those individuals who required a blood draw for CBC testing. Third, only 55% of the subjects tested for antibody had been tested for acute SARS-CoV-2 at their ED visit. Fourth, the ability to detect the neighborhood effects of local hotspots and poverty level on SARS-CoV-2 infection in the multivariate regression model is somewhat limited due to the use of zip code-level data in the model rather than census block data which could provide more granular neighborhood data. However, census block data were not available. Similarly, we were not able to identify the difference between mono-lingual Spanish/indigenous Latino patients and bilingual patients within the heterogeneous Latinx community in Baltimore since language information was not collected in this study. Fifth, the sensitivity of the serologic algorithm was less than 100%, although the specificity was 100%. This is consistent with most other serologic studies in which the sensitivity of antibody tests among non-hospitalized patients has been demonstrated to be approximately 85%. This lower sensitivity is due to the finding that a proportion of non-hospitalized individuals fail to make an antibody response to SAR-CoV-2 infection [34]. Finally, the sensitivity of PCR on nasopharyngeal samples is at best 80% for symptomatic individuals three to five days post infection, and drops significantly after that time [35]. Together these results indicate that the burden of SARS-CoV-2 infection would be underestimated in ours or any surveillance study which uses this algorithm. By using both PCR and serologic assays for antibody, one can however estimate longitudinal epidemiologic patterns within a particular population.

Regardless of these limitations, we demonstrate here the important role of ED-based surveillance studies to measure the local burden in SARS-CoV-2 infection in a population, and characterize demographic and clinical correlates of the SARS-CoV-2 infection, particularly for populations that may be disproportionately impacted. There is a strong historical precedence for EDs serving as surveillance sites for other transmissible infectious diseases threats, most notably HIV, hepatitis B

and C viruses, and influenza, and it is anticipated the ED will continue to serve an important role in advancing our understanding of the evolving SARS-CoV-2 pandemic. An abbreviated version of representative, multi-site serosurvey that only collects basic demographics along with SARS-CoV-2 PCR testing results could quickly identify hotspots and the most vulnerable subgroups of population. This could supplement current public health surveillance strategies and help inform approaches combating the COVID-19 pandemic. The EDs can serve as the frontline for both monitoring the pandemic and developing focused interventions for the communities that they serve.

Author's contribution

OL, Y-HH, RER, GDK, TCQ designed the study. GD, REF, HAS, JM, MK, EK, CSK, ORB, RW, IVL, MY, SR, MK, RK, ER, YJE, DA, and JH, had primary responsibility for the remnant blood specimen and data collection. REF, HAS, JM, MK, EK, CSK, ORB performed laboratory testing. GD and ER supervised data collection. OL and REF supervised laboratory testing. OL and Y-HH performed data analyses. OL, Y-HH, RER, GDK, EUP, AART, and TCQ primarily interpreted results. OL, Y-HH, RER, and TCQ primarily drafted the manuscript. TK, GDK, WC, EUP, and AART performed critical editing of the manuscript. GD, REF, HAS, JM, MK, EK, CSK, ORB, RW, IVL, MY, SR, MK, RK, ER, YJE, DA, and JH reviewed and approved the manuscript.

Funding

Ethics committee approval

The study was approved by the Johns Hopkins University School of Medicine Institutional Review Board.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2021.04.081.

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