Diagnosed and Undiagnosed COVID-19 in US Emergency Department Healthcare Personnel: A Cross-Sectional Analysis

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Abstract

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Objective: To determine the percentage of diagnosed and undiagnosed SARS-CoV-2 infection among a sample of US ED health care personnel (HCP) before July 2020.

Methods: Cross-sectional analysis of ED HCP in 20 geographically diverse university-affiliated EDs from May to July 2020, including case counts of prior laboratory-confirmed COVID-19 diagnoses among all ED HCP, then serology (with confirmatory testing) and reverse transcriptase-polymerase chain reaction (RT-PCR) testing in a sample of volunteers without a previous COVID-19 diagnosis. HCP were categorized as clinical (physicians, advanced practice providers, and nurses) and non-clinical staff (clerks, social workers, and case managers). Previously undiagnosed infection was based on positive SARS-CoV-2 serology or RT-PCR among HCP without prior diagnosis.

Results: Diagnosed COVID-19 occurred in 2.8% (193/6,788) HCP, and the prevalence was similar for nonclinical and clinical staff (3.8% vs. 2.7%; odds ratio, OR 1.5, 95% confidence interval, 95% CI 0.7–3.2). Among 1,606 HCP without previously diagnosed COVID-19, 29 (1.8%) had evidence of current or past SARS-CoV-2 infection. Most (62%, 18/29) who were seropositive did not think they had been infected, 76% (19/25) recalled COVID-19-compatible symptoms, and 89% (17/19) continued to work while symptomatic. Accounting for both diagnosed and undiagnosed infections, 4.6% (95% CI 2.8–7.5%) of ED HCP were estimated to have been infected with SARS-CoV-2, with 38% of those infections undiagnosed.

Conclusions: The estimated prevalence of SARS-CoV-2 infection was 4.6%, and over one-third of infections were undiagnosed. Undiagnosed SARS-CoV-2 infection may pose substantial risk for transmission to other staff and patients.

Introduction

Background

SARS-CoV-2 spreads primarily through close personal contact[1,2], and an analysis of self-reported US and UK data identified that HCP had higher risk of COVID-19 than non-HCP (hazard ratio 3.4). As of November 1, 2020, the Centers for Disease Control and Prevention (CDC) has identified over 200,000 U.S. HCP who have contracted COVID-19.[2,3] These findings parallel data from the 2003 SARS-1 outbreak that documented HCP transmission—especially for those performing aerosol-generating airway procedures.[4]

Importance

Emergency department (ED) HCP may be at particularly high risk since they perform resuscitation procedures and frequently treat patients with unknown infection status.[5] Population-based seroprevalence studies provide evidence that SARS-CoV-2 infection is frequently undiagnosed.[6–8] Undiagnosed infection among HCP may pose a threat of infection transmission to patients and other HCP.

Goals of This Investigation

We describe the prevalence of diagnosed and undiagnosed COVID-19 among US HCP working at 20 geographically diverse US EDs prior to July 2020.

Methods

Design, Setting, and Selection of Participants

COVID-19 Evaluation of Risks in Emergency Departments (COVERED) is a multicenter prospective surveillance of HCP for SARS-CoV-2 infection at 20 geographically diverse high-volume university-affiliated US hospital EDs (in 15 states, all sites are listed in Acknowledgements) that included assessment of baseline cross-sectional seroprevalence. We collected total COVID-19 case counts identified from among all HCP in participating EDs, then we enrolled a sample of physicians, nurses, advanced practice providers (APPs), and non-clinical HCP (clerks, social workers, case managers, and others without routine patient contact who worked in the ED) not previously diagnosed with COVID-19. This activity was determined to meet the requirements of public health surveillance because it was authorized by a public health authority for assessing risk to HCP in the COVID-19 pandemic as defined in 45 CFR 46.102(l)(2)[9], and participating HCP provided informed consent. This paper is reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[10]

Recruitment and Data Collection

We collected ED facility-level data, including counts of employees' COVID-19 diagnoses from occupational health reports. Additionally, 20 local teams recruited approximately 80 volunteer HCP at each site who had not been diagnosed with COVID-19: 40 physicians/APPs, 20 nurses, and 20 non-clinical staff (20.8% of eligible employees). The sample size was determined from the parent study to detect an attributable risk of COVID-19 acquisition of 4% (α=0.05, power=0.9). Participants completed a survey about their job and COVID-19 exposures[11] and provided a blood sample and a proctored self-collected nasal swab for baseline serology and SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) testing, respectively. After these initial results were reported, we asked participants with positive results to provide information about symptoms and exposures since December 31, 2019. We collected COVID-19 community cumulative incidence from public health reports for the health service area (HSA) of each facility as of June 29, 2020.

Laboratory Testing

Nasal swabs were analyzed by SARS-CoV-2 RT-PCR (limit of detection 0.009 median tissue culture infectious dose [$TCID_{50}$]/mL). Anti-SARS-CoV-2 IgG (nucleocapsid phosphoprotein; sensitivity 100% and specificity 99.6%) was measured using the Architect i2000 (Abbott Laboratories, Chicago, Illinois), with positive serology results confirmed by orthogonal testing using a spike glycoprotein (sensitivity 90% and specificity 100%) ELISA assay (EUROIMMUN, Lubeck, Germany). We designated HCP as testing positive for prior SARS-CoV-2 infection if they had: (1) positive results on *both* the nucleocapsid and spike IgG assays, or (2) positive nasal PCR.

Analysis

We calculated summary statistics as counts and percentages (with 95% confidence intervals, adjusted for clustering by site) for categorical variables, and we used medians and IQRs for continuous variables. We calculated odds ratios with adjusted 95% confidence intervals adjusted for clustering by site to compare COVID-19 prevalence between strata of interest. We calculated the *percentage of diagnosed infections* (documented by testing prior to the start of this project) as the ratio of the number of occupational health-reported infections among all ED HCP (from December 31, 2019 to site enrollment) and the total number of ED HCP at participating sites. We calculated the *conditional percentage of undiagnosed infections* as the ratio of participants in the prospective seroprevalence project with positive test results and the number of tested HCP participants at the time of their baseline evaluation. We estimated the *number of ED HCP with undiagnosed infection* by multiplying the percentage of test-positive participants in each job classification at each site by the number of site-specific ED HCP in that classification (including non-participating personnel) not previously diagnosed with COVID-19. We estimated the *community population cumulative incidence* across all sites as the mean of the HSA-specific population cumulative incidence weighted by the number of total employees in each participating ED. We estimated unadjusted odds ratios to describe the probability of infection by job category.

Results

Figure 1 shows the percentage of HCP with diagnosed and undiagnosed infections in the 20 US EDs at the time of enrollment (May 13 to July 8, 2020). Across all centers, the aggregate number of ED HCP with previously diagnosed COVID-19 from December 31, 2019 to enrollment was 193 of 6,788 (2.8%). Diagnosed COVID-19 was reported to occupational health clinics in 3.8% (38/993) nonclinical vs. 2.7% (155/5,795) clinical staff (OR 1.5). During this period, the population cumulative incidence of diagnosed COVID-19 ranged from 214 to 2,778 per 100,000 population, with a weighted population cumulative incidence of 1,058 per 100,000 (1.1%) (Figure 1).

Among 1,606 selected participants without prior COVID-19 diagnosis who had baseline serology and PCR testing, 29 (1.8%) had evidence of undiagnosed SARS-CoV-2 infection (28 by serology and 1 by PCR; Figure 1). Table 1 shows factors associated with SARS-CoV-2 infection. Across all sites, the estimated combined prevalence of diagnosed and undiagnosed COVID-19 was 4.6% (95% CI 2.8–7.5%), with 38% being undiagnosed. Two sites had prevalence of prior infection above 10%. Total estimated infections were highest for nonclinical staff and lowest for nursing staff (6.2% vs. 4.0%, respectively; OR 1.6; 95% CI 1.1–2.4; Table 2).

Participants who tested negative for COVID-19 were more likely to believe that they had not been infected (88% [1,398/1,577] seronegative vs. 62% [18/29] seropositive). Among 25 respondents with evidence of undiagnosed SARS-CoV-2 infection (86% response rate to additional survey), 19 (76%) reported prior symptoms compatible with COVID-19. Six participants (24%) had nasopharyngeal testing performed (all negative, Table 3), and 17 (89%) of those who reported symptoms worked in the ED while symptomatic (median 3 days; IQR 2–4).

Limitations

Our most significant limitation is the risk of applying an estimate of undiagnosed infection from a sample of volunteers to the entire HCP population. Because we did not randomly select HCP for participation in our surveillance testing, our volunteer participants may have been more likely or less likely to include the highest-risk HCP. Our estimates of the burden of undiagnosed infection come from extrapolation to the larger ED HCP population, but this sampling method introduces uncertainty into our estimate of disease.

Additionally, participating sites were academic centers with infection control programs in place, which may not be fully representative of all US EDs. Our project is further limited by the occupational health data used to tabulate diagnosed COVID-19 cases. Our reliance on occupational health records may have undercounted infections among the non-participating HCP. Recall bias may have affected the quality of data in seropositive participants. The strengths of this project include geographic diversity and rigorous high-accuracy testing procedures.

Discussion

SARS-CoV-2 infection occurred among an estimated 4.6% of US ED HCP and many infections were undiagnosed. Single-site studies of US HCP have shown SARS-CoV-2 seropositivity rates between 0.4% and 46%,[5,12] and a recent multisite seroprevalence survey of frontline HCP estimated a seropositivity at 6%.[13] Our methods differ from the prior multisite study in that we enrolled both clinical and non-clinical staff in EDs only, reported occupational health data, and used an orthogonal serology testing strategy specifically designed to limit false positive tests. That one-third of infections were undiagnosed highlights the importance of infection control strategies not only to prevent HCP infections (e.g., use of personal protective equipment [PPE]) but also to limit spread from HCP to others (e.g., universal use of masks).[14]

Recognition of SARS-CoV-2 infection by HCP was unreliable, with over 60% of those infected unaware that they had COVID-19. Many of these HCP worked during a period when they had COVID-compatible symptoms, either because their infection was early in the pandemic, symptoms were perceived as trivial, or negative PCR testing reassured them it was safe to work. Additionally, about one-quarter of infections appeared to be asymptomatic. Enhanced PPE use by HCP, HCP surveillance for infection, non-punitive workplace illness measures, and priority access to potential vaccine may decrease the risk of viral transmission from HCP to vulnerable patients and help maintain an effective frontline healthcare workforce. Ultimately, COVERED is an ongoing prospective surveillance project determining rates of new infections among clinical and non-clinical ED HCP that will collect information on specific exposures, infection control practices, PPE use, and community and household contacts to better determine the attributable risk of ED patient care.

We did not find a higher prevalence of infection in clinical compared to nonclinical staff, suggesting that the risk from direct ED patient care in these sites may be relatively small.

The nonclinical infection risk suggests that either reduced PPE use put them at risk or there are additional non-occupational community risks. Non-frontline HCP have previously been shown to have higher rates of COVID-19 infection, possibly related to less infection control vigilance and PPE use.[15]

In conclusion, the estimated percentage of SARS-CoV-2 infection among HCP in a sample of 20 high-volume US EDs in the late spring and early summer of 2020 was approximately 4.6%, with 38% of those infections undiagnosed.

Acknowledgements

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A.

Percentage (%) / Population Cumulative Incidence (cases per 100,000 population)

Legend:
- ■ Undiagnosed Infection
- ☐ Diagnosed Infection (gray)
- ☐ Cumulative Community COVID-19 Incidence

Site (1–20)

B.

Percentage (%)

Legend:
- ■ Undiagnosed Infection
- ☐ Diagnosed Infection (gray)

Categories: MD, Nurses, Non-clinical
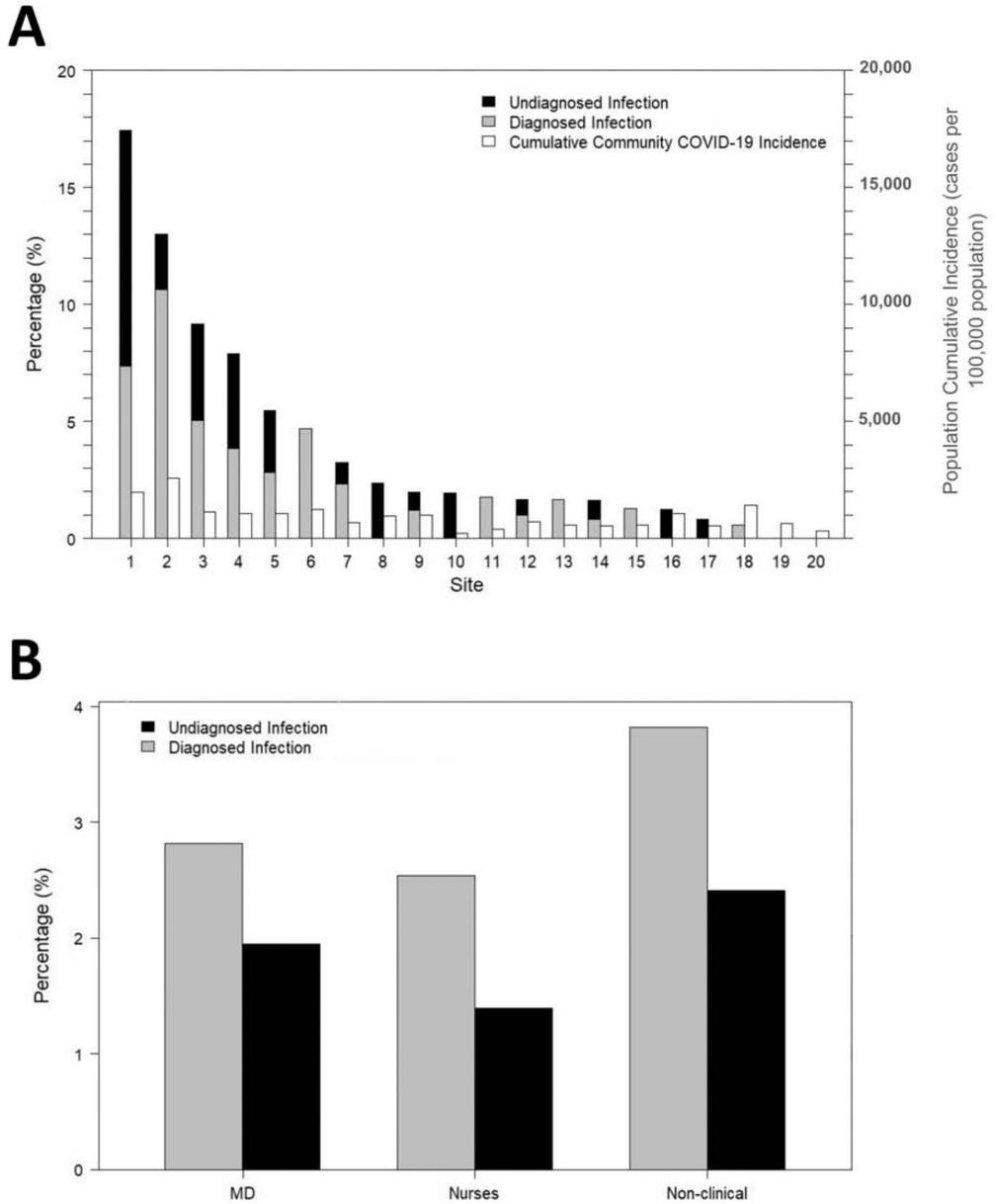
Figure 1. Prevalence of Diagnosed and Estimated Undiagnosed SARS-CoV-2 Infections in US Emergency Department Health Care Personnel, July 2020, by site.

A. This figure shows the percentage of health care personnel (HCP) with diagnosed and undiagnosed infections in a sample of 20 US emergency departments (EDs) at the time of enrollment (May 13 to July 8, 2020). Gray bars represent the percentage of diagnosed infections as recorded in occupational health reports at the beginning of the enrollment period. Black bars represent undiagnosed infections estimated from a sample of previously undiagnosed volunteer HCP in whom serology and nasal RT-PCR testing was performed (Table 2). White bars show the cumulative community COVID-19 incidence (June 29, 2020, right vertical axis). In total, 38% of all infections among ED HCP were undiagnosed prior to PCR and serology testing. **B.** The relationship between the percentage of recognized and

estimated unrecognized infections in this sample, stratified by job classification. Gray bars represent diagnosed infections, and black bars represent undiagnosed infections.

Table 1.

Characteristics of 1,606 US Emergency Department Health Care Personnel, Stratified by Baseline SARS-CoV-2 Serology Results.

This table shows the percentage of health care personnel in each category at the time of project enrollment (May 13 to July 8, 2020).

Category	Baseline Negative Serology (n=1,577; n [%])	Baseline Positive Serology (n=29; n [%])
Job Classification		
Attending Physician	360 (23)	6 (21)
Resident Physician	264 (17)	8 (28)
Advanced Practice Provider (Physician Assistant, Nurse Practitioner)	155 (10)	1 (3)
Nurse	404 (26)	6 (21)
Non-Clinical Staff	394 (25)	8 (28)
Gender		
Male	569 (36)	12 (41)
Female	1001 (64)	17 (59)
Transgender/Non-Conforming	7 (0.4)	0 (0)
Race		
White	1,264 (80)	16 (55)
Black	118 (7)	13 (45)
Asian	132 (8)	2 (7)
Other	76 (5)	1 (3)
Ethnicity		
Hispanic/Latino	148 (10)	4 (14)
Age		
30 years or less	368 (23)	8 (28)
31–40 years	613 (39)	9 (31)
41–50 years	313 (20)	6 (21)
51–60 years	216 (14)	6 (21)
Over 60 years	67 (4)	0 (0)
Suspected Infection		
Do you believe that you have been personally infected with COVID-19? This includes presumed positive regardless of whether you had testing done. Yes	179 (11)	11 (38)

Table 2.

Diagnosed and projected undiagnosed cases in 20 US emergency departments.

	Physicians/APPs (%; 95% CI)	Nurses (%; 95% CI)	Non-clinical Staff (%; 95% CI)	Total (%; 95% CI)
Diagnosed, Cases/Total HCP	71/2506 (2.8%; 2.0–4.1 %)	84/3289 (2.6%; 1.2–5.4%)	38/993 (3.8%; 1.3–10.5%)	193/6788 (2.8%; 1.6–5.0%)
Undiagnosed, Projected Cases/Total HCP	49/2506 (2.0%; 0.9–4.0%)	46/3289 (1.4%; 0.6–3.1%)	24/993 (2.4%; 1.3–4.6%	119/6788 (1.8%; 1.0–3.1 %)
Total Diagnosed + Undiagnosed/Total HCP	120/2506 (4.8%; 3.1–7.3%)	130/3289 (4.0%; 2.0–7.7%)	62/993 (6.2%; 2.9–12.9%)	312/6788 (4.6%; 2.8–7.5%)
Projected Undiagnosed Cases/Total Projected Cases	49/120 (40.8%; 26.0–57.5%)	46/130 (35.4%; 20.2–54.3%)	24/ 62 (38.7%; 17.8–64.8%)	119/312 (38.1%; 25.9–52.1%)

APP, advanced practice provider; 95% CI, 95% confidence interval; HCP, health care personnel.

Table 3.

Recall of Symptoms and Work Behaviors among US Emergency Department Health Care Personnel with Undiagnosed SARS-CoV-2 Infection (n=25)[1].

Participants responded to this survey after results of their serology testing had been reported, in early July 2020.

Question	n (%)
Since December 31, 2019, have you had any symptoms that could be consistent with COVID-19 at any point? Yes	19 (76)
Since December 31, 2019, have you measured a fever (a temperature greater than 100.4°F or 38°C) at any point? Yes	2 (8)
To which of the following did you attribute your symptoms [select all that apply]?	
COVID-19	8 (42)
Common cold	8 (42)
Influenza	5 (26)
Seasonal allergies	7 (36)
Gastroenteritis/stomach flu	1 (5)
Exacerbation of a chronic medical condition	1 (5)
Medications	1 (5)
Asthma	2 (10)
Inadequate sleep, over-work, schedule changes, or stress	7 (36)
Other	1 (5)
Did you seek care of any health care provider for any of these symptoms? Yes	1 (5)
During the time period(s) that you had any symptoms (even minimal, minor, or atypical symptoms), did you go to work at your place of employment? Yes	17 (89)[2]
Have you had ANY COVID-19 testing (nasal test, blood test, or any other test) before participation in this project? Yes	6 (24)
Since December 31, 2019, estimate how many PATIENTS with confirmed COVID-19 infection you cared for at work without mask and gloves.	
0	9 (36)
1–5	9 (36)
6–10	2 (8)
Greater than 10	5 (20)
Since December 31, 2019, have you traveled outside the United States? Yes	2 (8)

[1] Among 29 participants with evidence of undiagnosed SARS CoV-2 infection, 28 had positive serology and 1 had positive nasal PCR.

[2] The percentage of those who worked while they had symptoms was calculated from among only those who had symptoms (17/19=89%).