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COVID-19 infection among emergency department healthcare providers in a large tertiary academic medical center following the peak of the pandemic

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ABSTRACT

The COVID-19 pandemic has spread through the US during the last few months exposing healthcare providers to possible infection. Here we report testing of emergency department (ED) healthcare providers (HCP) for exposure to COVID-19 through lateral flow point of care (POC) and lab-based enzyme-linked immunosorbent assay (ELISA), and RTq-PCR for evidence of acute infection.

138 ED HCP were tested between May 26th (approximately one month after the peak of COVID-19 first wave of cases) and June 14th. Enrolled ED HCP represented about 70% of the total ED HCP workforce during the study period. Subjects were tested with a POC COVID-19 antibody test, and standard ELISA performed by a university-based research lab. Subjects also provided a mid-turbinate swab and a saliva specimen for RTq-PCR. All subjects provided demographic information, past medical history, information about personal protective equipment (PPE) use, COVID-19 symptoms, as well as potential COVID-19 exposures during the previous 4 weeks, both in the ED, and outside the clinical setting.

None of the HCP had positive RT-PCR results; 7 HCP (5%) had positive IgG for COVID-19; there was strong agreement between the lab-based ELISA (reference test) and the POC Ab test ($P \leq 0.0001$). For the POC Ab test there were no false negatives and only one false positive among the 138 participants. There was no significant difference in demographic/ethnic variables, past medical history, hours worked in the ED, PPE use, or concerning exposures between seropositive and seronegative individuals. Moreover, there was no significant difference in reported symptoms between the two groups during the previous four weeks.

The rate of COVID-19 seroconversion in our ED was 5% during the month following the pandemic's first wave. Based on questionnaire responses, differences in demographics/ethnicity, medical history, COVID-19 exposures, and PPE use were not associated with ED HCP having been infected with SARS-CoV-2. In the setting of our limited cohort of subjects the COVID-19 POC Ab test performed comparably to the ELISA lab-based standard.

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1. Introduction

The COVID-19 pandemic has put healthcare workers at risk the world over with a report of about 153,000 infections as of the end of May 2020 [1] which grew to over 500,000 in the Americas alone by August 2020 [2]. Reports of rates of COVID-19 infections of HCPs have varied widely from 1.6% to 44% [3–6]. The reasons for higher rates of transmission among certain groups of healthcare providers [5,7] remain unclear. A large number of reports appear to show a rate of HCP

infection of 1–5%, with frontline HCP consistently at the higher end of the range [3,4,6,8–12]. While there are reports of significant rates of COVID-19 infection among HCPs that appear unrelated to intensity of exposure [13], other reports highlight the importance of the degree of infection in the community as key to the risk posed to HCPs [14,15]. One such report, based upon extensive modeling, concludes that infection among US HCPs is about 10 times the rate of documented COVID-19 infection in the community [14]. Assuming 5,800,000 diagnosed US cases at the end of August 2020—1.8% of the population—that would suggest 18% of frontline HCP in the US had been infected. A recent screening study of HCP in Britain employed COVID-19 serology in addition to RT-PCR, reported 18% infection rate in a large cohort of healthcare workers from two London hospitals, at a time when the

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estimates of COVID-19 prevalence in the surrounding area was about 0.3% [16]. Antibody testing of ED HCP in an urban hospital in mid-April 2020 found a COVID-19 prevalence of 5–10% at a time when the incidence of COVID-19 in the surrounding community was 0.1% [17]. While reports of prevalence of COVID-19 among HCP far greater than that of the surrounding community argues strongly for occupational exposure, some recent reports have asserted that occupational exposure in HCP is a minor factor, and COVID-19 among HCP reflect the exposure to the disease in the surrounding community [14,18].

To address this question in a single busy, urban emergency department (ED) we undertook to test a high proportion of frontline HCPs during a period of two weeks starting one month following the peak of the pandemic's first wave in Washington, DC. Like the US, to date about 1.8% of the population of Washington, DC has tested positive for COVID-19. We reasoned that a single cohort of HCP equally exposed to COVID-19 would provide a reliable basis for assessing occupational risks of caring for these patients in the emergency setting. To test ED HCP, Multiple different testing modalities were employed including a point of care (POC) lateral flow antibody test, ELISA serology performed by a university research lab, and two different COVID-19 RT-PCR tests: a mid-turbinate nasal swab and a saliva sample.

The POC antibody test was included as it is a rapid, easy-to-use, free standing testing platform which greatly decreases obstacles to implementation, and thus, if accurate, has the potential to facilitate efficient screening for COVID-19 exposure among groups of frontline HCP, and/or, other groups. Lateral flow POC COVID-19 Ab tests were recently reported to show good positive predictive value in a large scale study of HCP [16], tracking the performance of ELISA serology reasonable closely.

2. Methods

ED HCP were defined as any ED staff that come into close contact with ED patients while delivering medical care. Roles included in the study were physicians, advanced practice providers, nurses, and technicians. About 200 ED HCP were eligible for inclusion in the study; 138 consented and were enrolled over a 2-week period. Study was approved by the IRB of George Washington University. Participants answered a standardized survey which included: Past Medical History, Smoking History, Tested positive for COVID-19 in last four weeks, Symptoms of COVID-19 in last 4 weeks (fever, fatigue, dry cough, anorexia, body aches, dyspnea, sputum, sore throat, diarrhea, nausea, dizziness, headache, vomiting, and abdominal pain). Personal Protective Equipment usage was surveyed including: consistency of wearing surgical masks, frequency of surgical mask change, consistency of wearing N95, frequency of N95 mask change, consistency of Powered Air Purifying Respirator (PAPR). We also surveyed if participant was not wearing proper PPE and exposed to a patient with COVID-19, and if they had an exposure outside of work to COVID-19.

2.1. Sample collection

Three samples were collected from each ED HCP. Self-collected mid-turbinate samples were collected using a 3D printed lattice swab (Resolution Medical). Participants were instructed to insert swabs to the mid-turbinate and rotate slowly for 5–10 s and repeat for both nostrils. Swabs were collected then placed into DNA/RNA Shield (Zymo Research). Participants self-collected at least 1 mL of saliva into a sterile cup. Venous blood was collected into BD Vacutainer Mononuclear Cell Preparation Tubes containing sodium heparin (Becton Dickinson).

2.2. Detection of SARS-CoV-2 RNA by Reverse Transcriptase Quantitative Real-Time PCR (RTq-PCR)

RNA was extracted from a 50 μ L aliquot of each RTq-PCR specimen (saliva/mid-turbinate swab) using the MagMax-96 Viral RNA Isolation Kit (Thermo Fisher) with a 50 μ L elution volume. SARS-CoV-2 genomic

RNA was detected using the CDC 2019-nCoV EUA RTq-PCR test (Integrated DNA Technologies). The targets in this panel are two SARS-CoV-2 nucleocapsid genes (N1 and N2) and the human RNase P gene. The CDC 2019-nCoV EUA test was performed with qScript One-Step RTq-PCR reagents (Quantabio) on a LightCycler 480 Real-Time PCR Instrument (Roche). Cq values were assigned using the maximum second derivative method and a sample was considered positive for SARS-CoV-2 if both the N1 and N2 targets were detected. Performance testing with inactivated SARS-CoV-2 virus (BEI Resources) established the lower limit of detection at 12.5 copies/ μ L.

2.3. Detection of IgG and IgM antibodies against SARS-CoV-2 receptor binding domain by Enzyme-Linked Immunosorbent Assay (ELISA)

Blood samples were spun down at 500 xg at room temperature for 15 min with the brake on 1 to separate blood components. Up to 3 mL of plasma from each tube were aliquoted to cryotubes and heat-inactivated for one hour at 56 °C prior to analysis.

Detection of IgG and IgM antibodies against SARS-CoV-2 receptor binding domain (RBD) in human plasma was performed by a modified enzyme-linked immunosorbent assay protocol [19] using purified RBD protein expressed from a pCAGGS plasmid vector containing recombinant RBD (BEI Resources; NR-52309), anti-RBD antibody (Absolute Antibody; Ab01680-10.0), and anti-human IgG and IgM antibodies (Jackson ImmunoResearch; 109-035-006, 109-035-043). Receiver Operating Characteristic Curve (ROC) analysis using the Youden index provided positive cutoff values for 100% specificity for both IgG and IgM. Sensitivity at these cutoff values was determined to be 88.8% (95% CI 82.8–92.9%) for IgG and 83.7% (95% CI 75.1–89.7%) for IgM for patients who are more than 10 days post symptom onset [20] > An inconclusive IgM level was re-categorized as positive if the accompanying IgG test was positive.

2.4. Detection of IgG and IgM antibodies against SARS-CoV-2 receptor binding domain by Enzyme-Linked Immunosorbent Assay by Lateral flow Point of Care Test

The Biolidics POC antibody test employs solid-phase immunochromatography; SARS-CoV-2 specific IgM and IgG antibodies in blood samples bind to colloidal gold-labeled SARS-CoV-2 antigens impregnated into the test strip. Mouse anti-human IgM antibody and mouse anti-human IgG antibodies are impregnated in discrete bands in the test strip. If present in blood, SARS-CoV-2 Ab binds with cognate antigens, and the resulting Ab/Ag complexes flow along the nitrocellulose test strip through capillary force until bound by the respective anti-human mouse Ab generating a red colored line corresponding to IgM or IgG. The manufacturers report test sensitivity of 91% (95% CI: 87–95%), and specificity of 97% (95%CI: 95–98%) Others have reported a sensitivity of 92%; specificity 100% for IgG [21].

Demographic, clinical, and exposure characteristics were compared by antibody positivity using the Fisher's exact test for categorical variables, and Wilcoxon signed rank test for continuous variables.

3. Results

A total of 138 health care workers were enrolled: 37% were nurses; 22% Residents/Advanced practitioners; 20% Attending physicians; 12% ED Technicians; 9% other (Respiratory technicians, pharmacists, etc.). 7 subjects (4 nurses, 2 Attending, and one Resident/Advanced practitioner) tested positive for IgG with Point of Care (POC) testing, and all were confirmed with ELISA Serology performed by a university research lab. Of the 7 that were IgG antibody positive, 3 had IgM titer's that were detectable; another subject tested positive for IgM on laboratory testing (but not POC testing)—repeat lab-based serology in this subject were negative for both IgG and IgM. This subject never had any symptoms suggestive of COVID-19. Of the 138 health care workers enrolled, 133

had Nasal swab testing with 4 having insufficient sample, and one specimen not collected; none tested positive for SARS-CoV-2. Saliva specimens were tested with COVID-19 qRT-PCR on 137 individuals with one insufficient specimen—none were found to be positive for SARS-CoV-2.

In the 138 surveyed, 47 (34%) reported at least one symptom suspicious for COVID-19 in the previous 4 weeks (see Table 1), with only one seropositive subject reporting symptoms (see Table 2). The average hours worked per week in SARS-CoV-2 IgG positive was 34 vs. 41 h for those with negative serology. Of the 7 found to be SARS-CoV-2 IgG positive, 3 were known positives prior to testing; the other 4 subjects with positive serology had no previous knowledge of infection (see Table 3). N95 respirator usage was surveyed and no significant difference between those with positive serology versus those with negative serology (see Table 2). Powered air-purifying respirator (PAPR) use was 14% among seropositive subjects, versus 31% of those that were seronegative. 54% of study subjects reported having at least one work exposure in the previous 4 weeks without appropriate PPE; no significant difference in unprotected clinical exposures was found between seropositive and seronegative patients. Similarly, 21 subjects reported at least one unprotected community exposure in the previous 4 weeks without any difference between seropositive and seronegative patients.

4. Discussion

To date population-wide assessment of infection with COVID-19 is limited by a combination of factors, including a high proportion of

Table 1 ED healthcare providers demographic, roles, and COVID-19 exposure.

| Characteristic | Total | % |
|--|-------|------|
| Female, n | 98 | 71% |
| Male, n | 41 | 29% |
| Average age (years) | 35 | |
| At least one chronic medical condition | 30 | 22% |
| Immunocompromised | 1 | 0.7% |
| Present or former tobacco smoker | 9 | 7% |
| Ethnicity | | |
| Asian | 15 | 11% |
| Black or African American | 11 | 8% |
| Hispanic or Latino | 7 | 5% |
| White | 102 | 76% |
| Role | | |
| Attending physician | 28 | 20% |
| Resident physician/Advanced Practitioner | 30 | 22% |
| Nurse | 51 | 37% |
| ED technician | 17 | 12% |
| Miscellaneous | 12 | 9% |
| Number different COVID-19-type symptoms in the last 4 weeks | | |
| 0 | 91 | 66% |
| 1 | 2 | 16% |
| 2 | 3 | 11% |
| 3 | 4 | 6% |
| 4 | 1 | 1% |
| Use of N-95 Mask | | |
| Not using | 1 | 1% |
| Only for select patients | 20 | 14% |
| Every patient | 40 | 29% |
| Entire shift including ED common areas | 77 | 56% |
| Number of ED COVID-19 exposures without PPE over last 4 weeks | | |
| 0 | 62 | 45% |
| 1 | 30 | 22% |
| 2–5 | 29 | 21% |
| >5 | 13 | 12% |
| Number of community COVID-19 exposures without PPE over last 4 weeks | | |
| 0 | 114 | 84% |
| 1 | 5 | 4% |
| 2–5 | 12 | 9% |
| >5 | 4 | 3% |

Table 2 COVID-19 negative versus COVID-19 positive patients—demographics and exposures.

| | COVID-19 negative (n = 131) | COVID-19 positive (n = 7) | |
|--|-----------------------------|---------------------------|----|
| Average age (years) | 35 | 34 | ns |
| Female | 71% | 71% | ns |
| White ethnicity | 73% | 100% | ns |
| History tobacco use | 5% | 14% | ns |
| COVID-19-like symptoms last 4 weeks | 35% | 14% | ns |
| Average weekly hours worked last 4 weeks | 41 | 34 | ns |
| N95 only for selected patients | 14% | 29% | ns |
| N95 every patient | 29% | 15% | ns |
| N95 entire shift including ED common areas | 53% | 58% | ns |
| PAPR use at some time | 31% | 14% | ns |
| Concerning clinical COVID-19 exposures | | | |
| None | 44% | 43% | ns |
| 1 exposure | 20% | 42% | ns |
| 2–5 exposures | 22% | 15% | ns |
| more than 5 exposures | 12% | 0% | ns |
| Concerning community COVID-19 exposures | | | |
| None | 79% | 85% | ns |
| 1 exposure | 6% | 0% | ns |
| 2–5 exposures | 10% | 15% | ns |
| More than 5 exposures | 5% | 0% | ns |

ns = not statistically significant.

asymptomatic infection [22], and imperfections in the available tests. Indeed, the production of antibodies against COVID-19 was reported in over 80% of those with moderate to severe COVID-19, but only about 15% of exposed contacts who tested positive via RTq-PCR but had mild or asymptomatic infection [23]. What's more, evidence for immunity to COVID-19 has been reported in individuals that otherwise had negative RTq-PCR, and serology [24]. This combination of factors has made it impossible to accurately determine population-level prevalence of infection with COVID-19. Be that as it may, serology provides the only practical means available at present for obtaining a longitudinal snapshot of COVID-19 within a given population. And, since positive serology is associated with more severe infection, it also provides information about the vulnerability of that population to clinically significant disease. What serology cannot tell us is the incidence of infection and, by extension, the risk of transmission, over time, within a population.

In those who have antibody responses, they are generally measurable by 3 weeks after symptoms onset; the median time for ongoing viral shedding after seroconversion has been reported as 2 weeks [25]. Since we were testing a cohort of ED HCP about one month to six weeks after the peak of the pandemic's first wave, the combination of RTq-PCR for acute disease and serology for resolved COVID-19 infection was considered adequate for evaluating the burden of disease in our subjects. At the time of testing none of the study subjects had ongoing symptoms suggestive of COVID-19, meaning that the likelihood of our missing COVID-19 was low, and, in any case, there is not at present practical means for identifying all COVID-19 infections.

COVID-19 seroconversion in our cohort was 5%. This falls into the range most widely reported for HCP across a broad range of studies [3,6,8–11,16]. For reasons noted above, the actual incidence of infection in our cohort was probably higher, however, the seroconversion rate allows us to draw comparisons with other populations, similarly studied, and estimate the ongoing risk of significant COVID-19 disease to similar cohorts of HCP going forward. The seroconversion rate in our cohort, like that in most other reports, is higher than that in the surrounding community, supporting the conclusion that for frontline HCP, the risk is mostly occupational. At the time of testing the background prevalence of Covid-19 in our area was estimated at 1.8%. While reported estimates

Table 3
Characteristic of Covid positive subjects' PCR and serology

| Role | Nasal Swab PCR | Saliva PCR | Anti-SARS-CoV-2 IgG | IgG titer (mg/mL) | Anti-SARS-CoV-2 IgM | IgM titer (mg/mL) | Date diagnosed if previously known positive |
|--|----------------|--------------|---------------------|-------------------|---------------------|-------------------|---|
| Subject 1 Nurse | Not detected | Not detected | Positive | 3.03 | Not detected | | 03/27/2020 |
| Subject 2 Nurse | Not detected | Not detected | Positive | 1.58 | Positive | 0.76 | |
| Subject 3 Nurse | Not detected | Not detected | Positive | 1.63 | Not detected | | |
| Subject 4 Attending physician | Not detected | Not detected | Positive | >10 | Positive | 1.32 | |
| Subject 5 Resident/advanced practitioner | Not detected | Not detected | Positive | 1.34 | Not detected | | 04/27/2020 |
| Subject 6 Nurse | Not detected | Not detected | Positive | 2.20 | Not detected | | 04/01/2020 |
| Subject 7 Attending physician | Not detected | Not detected | Positive | 1.41 | Positive | 1.98 | |

for the risk of Covid-19 in HCPs range as high as ten times the level in the surrounding community [14], others report that occupational factors accounted for only 27% of the risk for Covid-19 among HCPs. Based upon the prevalence of Covid-19 in our community at the time of testing, 5% positivity among ED HCPs would seem to be accounted for by neither model. Positivity ranging around 5% percent, however, has been reported in many recent studies of Covid 19 among HCPs, as noted above, while at the same time scattered reports of much higher incidences of Covid-19 among HCPs has also been reported. This suggests that the kinetics of transmission of Covid-19 to HCPs may be a complex phenomenon difficult to predict on the basis of a small number of parameters.

The reported history of COVID-19-like symptoms in our cohort during the weeks prior to testing was not different in those that were seropositive compared to those seronegative. There was also no difference in reported PPE use, or concerning exposures between these two groups. Taken together one way of interpreting these findings is that with prudent use of PPE and hygienic measures currently employed in our ED and many others, a small number of HCP will become infected as the result of random variation in risk/exposure which are not eliminated by current infection-control practices [26,27].

Performance of a lateral flow POC Ab detection device in our study demonstrates that this convenient, inexpensive, easy-to-use device may be deployed to assess COVID-19 seroprevalence within populations of interests with minimal technical obstacles. While not a gold standard for COVID-19 serology, these devices provide some information about the penetrance of the disease within a population, which can be invaluable for comparative and public health purposes [28,29]. The device used in our study, as was recently reported for another device [16], performed with little less precision than the lab-based gold-standard ELISA.

5. Conclusion

Following the Covid-19 pandemics first wave ED HCPs were found to have 5% seropositivity; comparable to similar reports in the literature. In our cohort Covid 19 seropositivity was not predicted by the experience of symptoms during the previous 4 weeks, use of PPE, or subjects' assessments of potential exposures. Convenient POC devices for assessing seropositivity are available, and perform similarly to the ELISA gold standard.

Credit author statement

JL designed, enrolled subjects, lab work, analyzed data, wrote text.
EM designed, enrolled subjects, lab work analyzed data, wrote text.

AG enrolled subjects, lab work analyzed data.
MP enrolled subjects, lab work.
CG enrolled subjects, lab work.
DEP lab procedures, wrote text.
JV lab procedures, wrote text.
CL lab procedures.
IT designed, analyzed data, wrote text.

Declaration of Competing Interest

The authors declare no conflict of interest.

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