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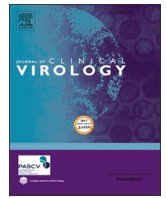
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SARS-CoV-2 RT-PCR positivity and antibody prevalence among asymptomatic hospital-based health care workers

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ABSTRACT

Background: The level of asymptomatic infection with SARS-CoV-2 could be substantial and among health care workers (HCWs) a source of continuing transmission of the virus to patients and co-workers.

Objectives: Measure the period prevalence of SARS-CoV-2 PCR positivity and seroprevalence of SARS-CoV-2 IgG antibodies among a random sample of asymptomatic health system hospital-based health care workers (HCWs) 6½ -15½ weeks after 4/5/2020, the peak of the first surge of COVID-19 admissions.

Results: Of 524 eligible and consented participants from four metropolitan hospitals, nasopharyngeal swabs were obtained from 439 (83.8 %) and blood from 374 (71.4 %). Using PCR nucleic acid-based amplification (NAAT) methods, the period prevalence of SARS-CoV-2 infection was 0.23 % (95 % confidence interval (CI) 0.01 %–1.28 %; 1/439) from 5/21/20–7/16/20. The seroprevalence of SARS-CoV-2 IgG antibodies from June 17–July 24, 2020 was 2.41 % (95 % CI 1.27 %–4.51 %; 9/374). Those who were reactive were younger (median age 36 versus 44 years; $p = 0.050$), and those with self-reported Hispanic/Latino ethnicity had a higher seroprevalence (2/12 = 16.7 % versus 7/352 = 2.0 %; $p = 0.051$). There were no significant differences by sex, race, residence, hospital, unit or job type. The one employee who was found to be PCR test positive in this study was also reactive for IgG antibodies, tested 27 days later.

Conclusions: The period prevalence of PCR positivity to SARS-CoV-2 and IgG seroprevalence was unexpectedly low in asymptomatic HCWs after a peak in COVID-19 admissions and the establishment of state and institutional infection control policies, suggesting that routine screening tests while community prevalence is relatively low would produce a minimal yield.

1. Background

As the novel SARS COV-2 virus began its sweep across the world in late 2019, health care workers (HCWs) were at risk of COVID-19 morbidity and mortality through work and community exposure as well as being potential transmission sources of nosocomial infection for patients and co-workers [1,2]. Metropolitan Detroit, Michigan developed as a “hot spot” in March 2020, with the first two cases in the state confirmed on 3/10/20, statewide polices on social distancing and stay-in-place for non-essential workers mandated on 3/23/20, and the highest number of cases reached in early April 2020 [3]. Henry Ford

Health System (HFHS) had a peak number of COVID-19 inpatients ($n = 603$) in its four metropolitan Detroit hospitals on 4/5/20. Stringent infection control policies were put in place as the pandemic progressed, including a universal masking policy on 4/7/20 [4]. The number of inpatients dropped markedly until reaching lower rates in May 2020 (average COVID-19 bed census 68.4; 95 % confidence interval (CI) 64.5–72.4). A recent meta-analysis of COVID-19 screening studies among asymptomatic HCWs across the world yielded an estimated pooled prevalence of 5% (95 % confidence interval (CI) of 1–13), but the analysis included time periods of both peak and low community disease activity [5].

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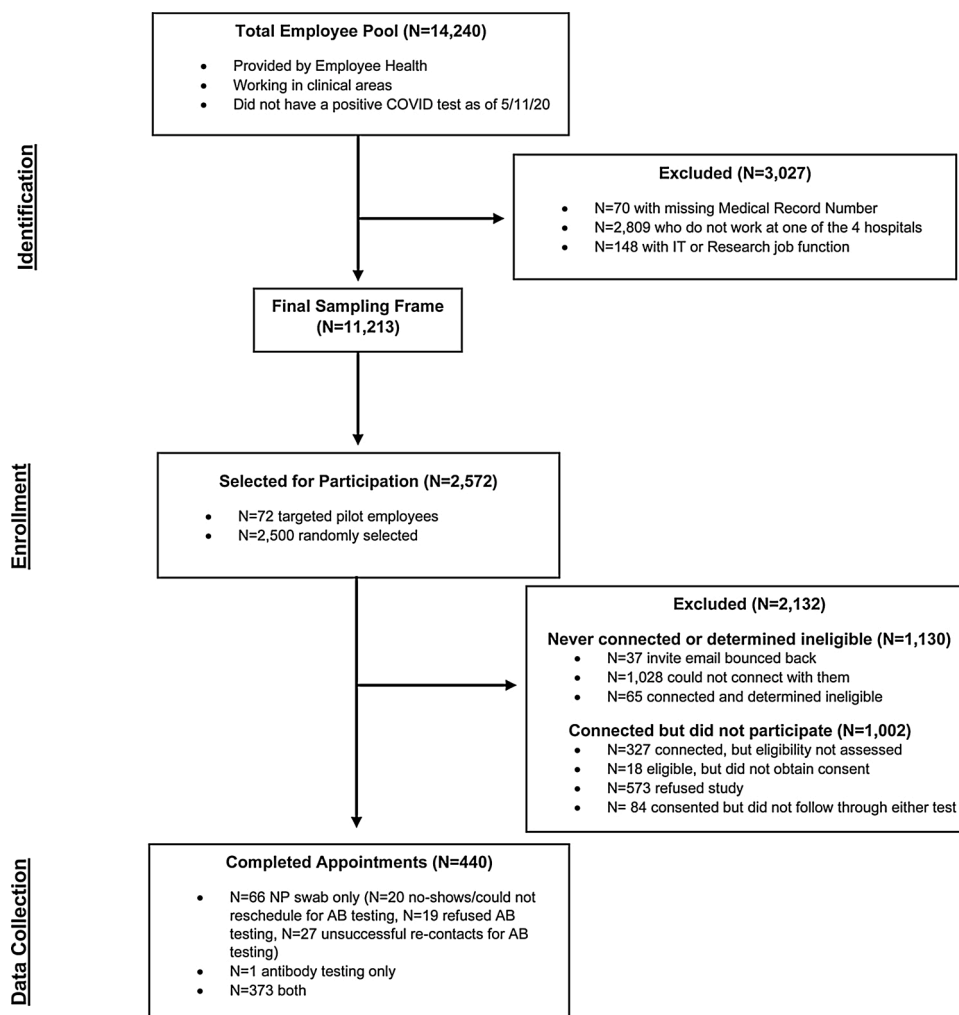


Fig. 1. Disposition of Study Recruitment and Enrollment.

2. Objectives

To address concerns about hospital-based transmission, a study was designed to determine whether the prevalence of detectable SARS-CoV-2 among asymptomatic HCWs, during a post-surge period and as regular hospital activities resumed, justified the need for routine screening. After the study started, a serology test became available, which was also offered to participants to evaluate the seroprevalence of IgG antibodies to the virus.

3. Study design

A list of employees actively working at the HFHS academic hospital and its 3 Detroit-area community hospitals in patient-facing clinical areas was created that included names, occupation, work location, email and phone number. A random sample was selected and invited to undergo testing for SARS-CoV-2 through the collection of nasopharyngeal (NP) swabs. Starting on 5/27/20, following a pilot study that began on 5/20/20, recruitment emails were sent in batches, followed by reminder emails and repeated phone contacts. Employees with any history of a COVID-19 diagnosis were ineligible. As of 6/15/20, the SARS-CoV-2 IgG antibodies test was also offered to new participants and those who had already provided NP swabs.

The NP swabs were collected in saline transport vials and tested for SARS-CoV-2 using real-time reverse-transcriptase RT-PCR NAAT on the NeumoDx 288 platform (NeumoDx Molecular Systems, Ann Arbor, MI)

which was approved for SARS-CoV-2 testing under the FDA Emergency Use Authorization (EUA). The assay detected dual SARS-CoV-2 targets, the NSP-2 and the N gene. Testing for IgG was performed on serum samples using the Access SARS-CoV-2 IgG antibodies assay (Beckman Coulter, Chaska, MN).

Non-parametric tests (Fisher's exact test and Kruskal-Wallis test), were used to assess differences between participants and non-participants and populations with positive versus negative test results. Prevalence estimates and 95 % CIs were calculated [6].

All study processes and procedures were approved by the HFHS Institutional Review Board (IRB #13,878) and electronic informed consents obtained.

4. Results

4.1. Study population

After initial exclusions, our final sampling frame included 11,213 individuals (Fig. 1).

A sample of 72 HCWs was selected for the pilot study followed by a random sample of 2,500. Of these, 1,130 could not be contacted or were determined to be ineligible. Of the remaining 1,442, 1,002 were contacted but did not enroll, while 440 (31 %) consented and received at least one test. Statistically significant differences were found by hospital of employment and job function between those eligible and consented ($n = 524$), those not successfully contacted ($n = 1,065$), and those

Table 1
Characteristics of HCWs by IgG reactivity.

	Non- Reactive N = 365 N (Row %) or Median [Q1; Q3]	Reactive N = 9 N (Row %) or Median [Q1; Q3]	p- value ^a	N
Age at Consent	44.0 [34.8;55.0]	36.0 [29.8;42.5]	0.050	364
Sex:			0.697	373
Female	273 (97.8 %)	6 (2.15 %)		
Male	91 (96.8 %)	3 (3.19 %)		
Race:			1.000	374
White	282 (97.6 %)	7 (2.42 %)		
Black	35 (97.2 %)	1 (2.78 %)		
Other	45 (97.8 %)	1 (2.17 %)		
Refused/Missing	3 (100 %)	0 (0.00 %)		
Hispanic/Latino Ancestry:			0.051	374
Yes	10 (83.3 %)	2 (16.7 %)		
No	345 (98.0 %)	7 (1.99 %)		
Refused/Missing	10 (100 %)	0 (0.00 %)		
Middle Eastern Ancestry:			1.000	374
Yes	30 (100 %)	0 (0.00 %)		
No	325 (97.3 %)	9 (2.69 %)		
Refused/Missing	10 (100 %)	0 (0.00 %)		
Lives within Detroit City Limits:			1.000	373
No	338 (97.4 %)	9 (2.59 %)		
Yes	26 (100 %)	0 (0.00 %)		
Work Location:			0.643	374
Henry Ford Hospital	178 (97.8 %)	4 (2.20 %)		
West Bloomfield Community Hospital	83 (96.5 %)	3 (3.49 %)		
Macomb Community Hospital	57 (96.6 %)	2 (3.39 %)		
Wyandotte Community Hospital	47 (100 %)	0 (0.00 %)		
Job Function:			0.258	374
Nursing	136 (96.5 %)	5 (3.55 %)		
Physicians	54 (98.2 %)	1 (1.82 %)		
Leadership/Management	30 (93.8 %)	2 (6.25 %)		
Admin Support/Business	26 (100 %)	0 (0.00 %)		
Allied	85 (100 %)	0 (0.00 %)		
Other	34 (97.1 %)	1 (2.86 %)		
Where do you spend the majority of your work day?:			0.972	373
ED	12 (100 %)	0 (0.00 %)		
ICU	29 (100 %)	0 (0.00 %)		
COVID-19 Care or Testing Area	10 (100 %)	0 (0.00 %)		
Inpatient Unit	86 (96.6 %)	3 (3.37 %)		
Outpatient Clinic	46 (97.9 %)	1 (2.13 %)		
Other	181 (97.3 %)	5 (2.69 %)		
Have you been exposed to anyone diagnosed with COVID-19 confirmed by laboratory testing?:			1.000	374
No	107 (98.2 %)	2 (1.83 %)		
Yes	258 (97.4 %)	7 (2.64 %)		
Do you live with anyone who was diagnosed with COVID-19 confirmed by laboratory testing?:			1.000	373
No	360 (97.6 %)	9 (2.44 %)		
Yes	4 (100 %)	0 (0.00 %)		
On a typical day, how many other people live in your home (Not including yourself)?	2.00 [1.00;3.00]	2.00 [1.00;3.00]	0.734	372

Table 1 (continued)

	Non- Reactive N = 365 N (Row %) or Median [Q1; Q3]	Reactive N = 9 N (Row %) or Median [Q1; Q3]	p- value ^a	N
Do you have direct contact with patients?:			0.693	371
No	74 (98.7 %)	1 (1.33 %)		
Yes	288 (97.3 %)	8 (2.70 %)		
Do you work in an area categorized as direct COVID- 19 Care?:			1.000	370
No	187 (97.4 %)	5 (2.60 %)		
Yes	174 (97.8 %)	4 (2.25 %)		
Do you potentially come into contact with COVID-19 contaminated items or enter rooms where COVID-19 patients are bedded?:			0.282	373
No	118 (99.2 %)	1 (0.84 %)		
Yes	246 (96.9 %)	8 (3.15 %)		
Month of Antibody Testing:			0.503	365
June	126 (98.4 %)	2 (1.56 %)		
July	230 (97.0 %)	7 (2.95 %)		

^a Chi-squared or Fisher's exact test when the expected frequencies is less than 5 in some cells for categorical covariates; Kruskal-Wallis test for continuous covariates.

contacted who did not participate (n = 918), both p < 0.001. Nurses were the most difficult to contact, and managers and allied health staff were more likely to participate, while facility/security staff were less likely. Males were less likely to participate than females (p = 0.059). A total of 373 had both tests completed (average of 18 days between NP swab and blood draw); 66 had only an NP swab collected and one participant only had a serology test.

4.2. PCR testing

There was one HCW with a positive NAAT test of 439 tested from 5/21/20–7/16/20. The period prevalence of positive NAAT tests among asymptomatic HCWs was 0.23 % (95 % CI 0.01 %–1.28 %).

4.3. Serology testing

Table 1 presents the characteristics of the 374 participants who provided blood samples from 6/17/20–7/24/20. Nine HCWs were reactive, corresponding to a seroprevalence of IgG to SARS-CoV-2 of 2.41 % (95 % CI 1.27 %–4.51 %). Those who were reactive were younger (median age 36 years versus 44 years; p = 0.050), and those self-identified as Hispanic had higher reactivity (16.7 % versus 1.99 %; p = 0.051). There were no differences by sex, race, Middle Eastern ancestry, city residence, hospital of employment, job, or direct contact with COVID-19 patients.

The specimen of the one participant who had a positive NAAT test was collected in the end of May 2020, followed by a blood draw for an IgG antibodies test 27 days later, which was also positive. The SARS anti-IgG assay we used demonstrated 100 % PPV at 14 days post-PCR at our overall PCR positive rate of 5.9 % during assay validation (data not shown). The low prevalence of PCR positivity in our asymptomatic HCW population of 0.23 % would reduce the PPV to approximately 22 %, with an NPV of 100 %.

Table 2
Studies of SARS-CoV-2 detection by RT-PCR and IgG antibody seroprevalence among asymptomatic HCWs.

First Author, Publication Date	Location	Setting	N of asymptomatics tested	Period	Positivity (%)	Antibody Prevalence (%)
Rivett L [2] (5/2020)	Cambridge, UK	Teaching hospital; screening asymptomatic HCWs from high risk areas; low community prevalence	1032	4/6/20–4/24/20	0.6*	NA
Korth J [7] (5/2020)	Essen, Germany	University hospital, 2–3 weeks pre-peak, HCW with varying levels of contact, detected 5 asymptomatic cases but 4 reported previous symptoms	316	3/25/20–4/21/2020	NA	1.6 (0.32 if exclude those with previous symptoms)
Treibel TA (5/2020) [8]	London, UK	Consortium of hospitals following a cohort of asymptomatic HCW volunteers	400	3/23–3/29 (baseline) 3/30–4/5 4/6–4/12 4/13–4/19 4/20–4/26	7.1 4.9 1.5 1.5 1.1	NA
Martin C [9] (6/2020)	Brussels, Belgium	Tertiary hospital, cohort of staff working in units with COVID patients or ED to be followed longitudinally; peak admits 3/31/20	270	4–15-20 to ~5–3-20	0.7	4.8
Al-zoubi NA [10] (6/2020)	Irbid, Jordan	University hospital, all staff assigned; peak admits on 5/1/20	370	4/22/20-4/29/20	0	NA
Lahner E [11] (6/2020)	Rome, Italy	Teaching hospital; calculated asymptomatic %; low incidence region	2115 NP 1084 Serology	NP: 3/18/20–4/27/20 Serology:4/0720–4/27/20	0.9	0.7
Garcia-Basteiro AL [12] (7/2020)	Barcelona, Spain	Tertiary hospital; cohort of random sample of HCWs at baseline to be followed; epidemic rapidly growing in community	368	3/28/20–4/9/20	0.8	3.0**
Brant-Zawadzki M [13] (7/2020)	Orange County CA, USA	Regional hospital, all employees invited to participate, to be followed; low community prevalence	2920	May-June 2020	NA	0.86
Vahidy FS [14] (7/2020)	Houston, TX, USA	Academic medical center and 7 affiliated community hospitals	2787	3/11/20–4/19/20	3.9	NA
Blairon L [15] (8/2020)	Brussels, Belgium	Public hospital network, peak on 4/10/20	630	5/25/20–6/19/20	0.0***	7.1
Grant JJ [16] (9/2020)	London, UK	Health care system, self-referred HCWs	973	5/15/2020–6/5/2020	NA	14 %
Martin C [17] (11/2020)	Leicester, UK	University hospitals	7828	5/29/2020–7/13/2020	NA	6.6
Martin C [18] (12/2020)	Leicester, UK	University hospitals, low community prevalence	1150	7/20/20–8/14/2020	0.0	NA
Varona JF [19] (1/2021)	Spain	17 hospitals, all employees invited	5589	4/15/2020–6/30/2020	0.4	4.7
Kantele A [20] (1–2/2021)	Helsinki, Finland	Secondary/tertiary university hospital; samples of selected wards/units	1095	4/22/20–5/15/20	2.8	3.0
Piccoli L [21] (2/2021)	Canton of Ticino, Switzerland	5 hospitals, all employees invited	1089	4/16/2020–4/30/2020	NA	2.4
Trieu, M [22] 2/2021	Bergen, Norway	Hospitals/EDs testing and treating COVID-19 patients, cohort of asymptomatic HCWs followed through first pandemic wave	607	4/2020–5/2020	1.3	3.0

* Self collected nose and throat swab.

** Either IgA, IgM or IgG reactive.

*** 7 were positive but uncertain whether these individuals previously symptomatic or not; all cultured and negative.

5. Discussion

The period prevalence study of SARS-CoV-2 detection and IgG seroprevalence among a random sample of HCWs in an academic hospital and three affiliated community hospitals 45–109 days post the peak number of COVID-19 admissions demonstrated unexpectedly low estimates. However, a literature review [2,7–22] indicates that most studies of asymptomatic HCWs show similarly low estimates (Table 2). Consideration of the timing of testing related to the phase of the epidemic locally is critical, [9] as is the timing related to the ready availability and compliant use of personal protective equipment (PPE) [1]. The community prevalence during the study period was also low, with a proportion of positive tests for SARS-CoV-2 for the entire state of Michigan of 0.6 % (95 % CI 0.59–0.61) [3], commensurate with that of the HCW's estimate in this study. Also, over the same dates as this study, the average daily COVID-19 inpatient census was 26.5 (95 % CI 24.3–28.7) and the prevalence estimates for asymptomatic patients being screened for COVID-19 prior to undergoing surgeries, non-surgical procedures, or delivering a baby at HFHS were 0.9 %, 0.3 % and 1.5 %,

respectively.

Like others, we found a higher prevalence in younger HCWs. [11,13] One other US study of both symptomatic and asymptomatic HCWs reported a higher prevalence of SARS-CoV-2 IgG antibodies among Hispanic/Latinos employees, [13] perhaps reflecting the higher community COVID-19 incidence in this group.[23,24] Direct COVID-19 patient exposure was not associated with prevalence; that and an infection prevalence similar to the community implies the effectiveness of infection control policies. Some have reported increased detection of SARS antibodies by combining IgM and IgG results from separate assays [25]. In similar fashion, using a dual serology algorithmic approach may increase detection capability. At the time of this study, the IgG assay used was the only COVID-19 antibody assay in our laboratory. Since then, we have added testing for total SARS antibodies (IgG + IgM) using the Cobas SARS-CoV-2 Total antibodies assay and automated high-throughput e801 analyzers (Roche Diagnostics, Indianapolis, IN). Early findings in a study of initial and sustained antibodies to COVID-19 have demonstrated 98.6 % agreement of the two serologic assays, making a dual testing approach of minimal value in our setting (data not

shown).

Limitations of this study included a longer time to enroll participants than expected, stretching out the period of prevalence, an inability to contact many of those selected to participate and a higher than expected number of refusals. We suspect that many of those who could not be contacted were passive refusers. At the time of the study, it is probable that HCWs felt less fearful of being infected, as well as fatigued from research requests and COVID-related concerns. The low prevalence of COVID-19 in our asymptomatic HCWs also means that some of the observed serology positives might in fact be false positive results. Strengths of the study were the exclusion of individuals with any previous COVID-19 symptoms, diagnoses or positive tests, the use of CLIA certified and FDA approved diagnostic tests, and the random sampling design deployed in a large diverse health care workforce typical of other US metropolitan hospitals.

These results demonstrate that the prevalence of COVID among asymptomatic HCW's after a local pandemic surge and after implementation of COVID protection policies was similar or even lower to that seen in the community. These results support others recommending that at times of low community prevalence of SARS CoV-2, and given the need to conserve testing supplies and reagents to maintain a reserve capacity along with the high potential for false-positive tests; it is not effective to routinely screen asymptomatic HCWs as long as COVID-19 protection policies are in place [18,26,27].

Authors' contributions

Study concept and design: Johnson, Muma, Weinmann and Samuel. Acquisition of data: Coleman, Leon, Cook, Muma, Tibbetts and Samuel. Analysis and interpretation of data: Johnson, Coleman, Sitarik, Cook, Weinmann, Tibbetts, Samuel. Drafting of the manuscript: Johnson. Critical revision of the manuscript for important intellectual content and final approval of the manuscript: Johnson, Coleman, Sitarik, Leon, Tibbetts, Cook, Muma, Weinmann and Samuel. Statistical analysis: Sitarik. Obtained funding: Muma. Administrative, technical, and material support: Coleman, Cook, Leon, Tibbetts, Samuel. Study supervision: Johnson, Coleman.

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Declaration of Competing Interest

The authors report no declarations of interest.

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