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Seroprevalence study of SARS-CoV-2 antibodies in healthcare workers following the first wave of the COVID-19 pandemic in a tertiary-level hospital in the south of Ireland

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ABSTRACT

Objective This study investigated seroprevalence of SARS-CoV-2-specific IgG antibodies, using the Abbott antinucleocapsid IgG chemiluminescent microparticle immunoassay (CMIA) assay, in five prespecified healthcare worker (HCW) subgroups following the first wave of the COVID-19 pandemic.

Setting An 800-bed tertiary-level teaching hospital in the south of Ireland.

Participants Serum was collected for anti-SARS-CoV-2 nucleocapsid IgG using the Abbott ARCHITECT SARS-CoV-2 IgG CMIA qualitative assay, as per the manufacturer's specifications.

The groups were as follows: (1) HCWs who had real-time PCR (RT-PCR) confirmed COVID-19 infection (>1-month postpositive RT-PCR); (2) HCWs identified as close contacts of persons with COVID-19 infection and who subsequently developed symptoms (virus not detected by RT-PCR on oropharyngeal/nasopharyngeal swab); (3) HCWs identified as close contacts of COVID-19 cases and who remained asymptomatic (not screened by RT-PCR); (4) HCWs not included in the aforementioned groups working in areas determined as high-risk clinical areas; and (5) HCWs not included in the aforementioned groups working in areas determined as low-risk clinical areas.

Results Six of 404 (1.49%) HCWs not previously diagnosed with SARS-CoV-2 infection (groups 2–5) were seropositive for SARS-CoV-2 at the time of recruitment into the study.

Out of the 99 participants in group 1, 72 had detectable IgG to SARS-CoV-2 on laboratory testing (73%). Antibody positivity correlated with shorter length of time between RT-PCR positivity and antibody testing.

Quantification cycle value on RT-PCR was not found to be correlated with antibody positivity.

Conclusions Seroprevalence of SARS-CoV-2 antibodies in HCWs who had not previously tested RT-PCR positive for COVID-19 was low compared with similar studies.

Strengths and limitations of this study

- ► We successfully recruited the numbers that we had aimed for in each of the prespecified groups.
- ► This was a single-centre study in an area of relatively low SARS-CoV-2 prevalence.
- ► Enrolment began 8 weeks after peak regional prevalence, and therefore, IgG antibodies may have become undetectable in a proportion of participants.
- ► Recruitment of groups 3–5 was by self-selection and therefore was not a true random sample of these groups.
- ► Quantification cycle (C_q) values were only available for 69 of the 99 participants who were real-time PCR positive, including only 12 of whom were IgG negative. It is therefore difficult to draw any firm conclusion as regards the correlation between C_q value and antibody positivity.

INTRODUCTION

Healthcare workers (HCWs) at the front line treating patients with suspected or confirmed COVID-19 have been heavily impacted by the pandemic. Due to potential occupational exposures, HCWs are at higher risk of infection from patients or from other HCWs than the general population. In a study published in July 2020, there was an estimated HR of 3.40 for COVID-19 infection in HCWs compared with risk of infection in the general population.[1] Indeed, as of November 2020 in Ireland, the Health Protection and Surveillance Centre put the number of HCW infections at 10 976, accounting for 16.6% of total infections.[2]

The first case of SARS-CoV-2 infection was reported in Ireland on 29 February 2020 relating to travel. On 5 March, a patient was diagnosed with SARS-CoV-2 infection who had been ventilated in the intensive care unit of Cork University Hospital (CUH) with atypical pneumonia despite having no epidemiological link to a known case or area of high prevalence. This was the first documented community acquisition of SARS-CoV-2 in Ireland and was an indication of potential widespread community transmission.[3] From this date, additional infection prevention measures were instituted in CUH, including testing and contact tracing of all symptomatic patients and staff, changes in hospital operations and provision of personal protective equipment (PPE).

Seroprevalence studies can provide relevant information on the proportion of a population who have experienced a recent or past infection. Monitoring the prevalence of infection among HCWs is useful for assessing the level of exposure and identifying high-risk areas.

There have been a number of studies that have attempted to characterise the immunological response to COVID-19. Median time to seroconversion is estimated at 9–12 days following onset of symptoms depending on the antibody measured, with up to 100% developing antibodies by day 21.[4] Sensitivity of assays measuring the antinucleocapsid antibodies has been shown to decline from 60 days following PCR positivity.[5] However, correlation between seropositivity or antibody levels and protection against reinfection remains to be fully determined.[6 7]

The aim of this study was to investigate seroprevalence of SARS-CoV-2-specific IgG antibodies, using the Abbott antinucleocapsid IgG chemiluminescent microparticle immunoassay (CMIA), in five prespecified HCW subgroups following the first surge of the pandemic in a region of relative low prevalence of COVID-19 infection.

METHODS

Study design and participants

This study was undertaken over a 6-week period from the 27 May 2020 to 7 July 2020 in CUH, an 800-bed university teaching hospital. CUH is the tertiary referral centre in the South West of Ireland serving a population of 1.1 million people. The study was designed to recruit 100 HCWs from five prespecified subgroups as outlined as follows.

HCW subgroups

1. HCWs who had real-time PCR (RT-PCR) confirmed COVID-19 infection (>1-month postpositive RT-PCR).
2. HCWs identified as close contacts of persons with COVID-19 infection and who subsequently developed symptoms (virus not detected by RT-PCR on oropharyngeal/nasopharyngeal swab).
3. HCWs identified as close contacts of COVID-19 cases and who remained asymptomatic (not screened by RT-PCR).
4. HCWs not included in the aforementioned groups working in areas determined as high-risk clinical areas.
5. HCWs not included in the aforementioned groups working in areas determined as low-risk clinical areas.

Basic demographic data including age, gender, occupation and comorbid illness were collected by means of a self-administered questionnaire (online supplemental appendix 1).

HCWs from groups 1 (previous confirmed RT-PCR COVID-19 infection) and group 2 (close contact of COVID-19 case with virus not detected by RT-PCR on oropharyngeal/nasopharyngeal swab when symptomatic) were contacted by the occupational health department. As there were fewer than 100 HCWs with RT-PCR-confirmed COVID-19 in CUH, HCWs with RT-PCR-confirmed COVID-19 from affiliated regional centres were invited to participate.

HCWs from group 3–5 were recruited by open invitation, and group allocation was confirmed by recruiting investigators.

Inclusion criteria

HCWs aged 18 years or over, fluent in English working in CUH or affiliated centres in the region were eligible to participate. HCWs were defined as those who deliver care and services to patients, either directly as physicians or nurses, healthcare attendants, or other support staff (porters, administrative officers, cleaning, maintenance, etc).

Exclusion criteria

HCWs who tested positive by RT-PCR for SARS-CoV-2 within 30 days of recruitment to the study or reporting symptoms of COVID-19 at time of recruitment were deemed ineligible to participate. However, there were no diagnosed infections among staff in our institution in the 30 days prior to enrolment.

Patient and public involvement

Patients and the public were not involved in the design of this study; however, feedback was enlisted on the sampling procedures and appropriateness of sampling modalities that the researchers used as part of the study (venepuncture for antinucleocapsid antigen as well as saliva and point of care testing used in the validation of other testing modalities not included in this paper).

Laboratory procedures

Serological testing

Serum was collected for anti-SARS-CoV-2 nucleocapsid IgG using the Abbott ARCHITECT SARS-CoV-2 IgG CMIA qualitative assay, as per the manufacturer's specifications. The Abbott Elisa Kit (Abbott Diagnostics) uses a nucleocapsid protein as the antigen and reported a 100% concordance (95% CI 95.89% to 100%) with their RT-PCR positive panel >14 days after symptom onset and 99.6% negative on their historical pre-COVID-19 controls (95% CI 98.98% to 99.89%)[8]

 Faller E, et al. BMJ Open 2021;11:e051415. doi:10.1136/bmjopen-2021-051415

qRT-PCR for SARS-CoV-2

HCWs from group 1 and group 2 who had close contact with a case of COVID-19 infection and developed symptoms had a combined oropharyngeal/nasopharyngeal swab undertaken as part of clinical care. Laboratory confirmation of SARS-CoV-2 infection was performed using the MagNA Pure 24/MagNA Pure LC (Roche Diagnostics) extraction system and Realstar (Altona Diagnostics, Hamburg, Germany) or EURORealTime (EUROIMMUN, Lübeck, Germany) SARS-CoV-2 qRT-PCR kits, as per the manufacturer's instructions. Target detection was reported on a LightCycler 480 Instrument II (Roche) if the quantification cycle (C_q) value was <40. In the absence of assay standardisation with RNA copy number controls, the C_q value was used as a relative quantitative indication of viral load.

Statistical analysis

SPSS V.26.0 and GraphPad Prism V.8 were used for statistical analysis. χ^2 test was used to compare categorical variables. Independent samples t-test was used to compare means of independent scale variables where frequencies were normally distributed and Mann-Whitney U test was used to compare continuous variables where frequencies were non-normally distributed. Results were deemed to be significant if the p value is <0.05.

RESULTS

Sample characteristics

Of 4500 staff employed directly in CUH, 503 HCWs were recruited to the study. Baseline demographics of participants are outlined in table 1.

The age range of participants was 20–65 years (IQR 30–47 years), and 77% were female. There were no significant between-group differences in age profiles. Nurses were the most represented professional group (41.7%) followed by doctors (35.0%).

Overall level of comorbidity was low across the groups, with 58.8% of the study population reporting no known/current medical issues. There were a significantly greater number of ex-smokers among participants in group 1 compared with other groups (p<0.001) and a significantly greater number of current smokers in group 2 (p=0.021). There was no significant between-group difference for any of the other comorbidities listed.

Of the participants, 187 (187/503, 37.2%) worked in high-risk settings. These were deemed to be areas in which HCWs were having daily contact with patients with confirmed or suspected COVID-19 infection during the peak of the local epidemic.

Of the participants, 469 (469/503, 93.2%) were working in CUH, the institution in which the study was conducted with 34 participants (all from group 1) recruited from affiliated institutions within the South/Southwest Hospital Group.

Seroprevalence

Overall, 78 of 503 (15.5%) HCWs who participated in the study were seropositive for SARS-CoV-2 at time of recruitment into the study. Table 2 presents serology results by the HCW group.

Out of the 99 participants in group 1, 72 had detectable IgG to SARS-CoV-2 on laboratory testing (73%). Longitudinal IgG detection from date of positive RT-PCR is displayed in figure 1. The mean period of time from RT-PCR positivity to IgG testing was significantly shorter in the IgG-positive group, with a mean of 69.3 days compared with 77.0 days in those who were antibody negative (p=0.025). There was no correlation noted between antibody seropositivity and age (p=0.63), gender (p=0.416) or presence of one or more comorbidities (p=0.935).

Only 1 of 99 HCWs with RT-PCR-confirmed COVID-19 required hospitalisation for management of infection, with the vast majority experiencing mild symptoms.

RT-PCR C_q values were available for 69 of the participants in group 1. This included 57 participants who were IgG positive and 12 who were IgG negative. There was no correlation found between RT-PCR C_q values and SARS-CoV-2 IgG detection (p=0.943).

Overall seroprevalence was low among groups 2–5, with IgG antibodies detected in only 6 out of 404 participants (1.49%). Prevalence was comparable between the four groups with IgG antibodies detected in two participants in group 2 (1.9%), one in group 3 (1.1%), one in group 4 (1.0%) and two in group 5 (1.9%).

DISCUSSION

Of 99 HCWs with RT-PCR-confirmed SARS-CoV-2 infection, 73% (72) had detectable antinucleocapsid IgG antibodies to SARS-CoV-2. A single factor, time interval from positive RT-PCR was associated with antibody detection. This is consistent with much of the wider literature in indicating that antinucleocapsid IgG antibodies to SARS-CoV-2 begin to decline from day 60 following positive PCR, particularly in individuals with mild or asymptomatic primary infection.[7 9 10] Although a higher sensitivity has been reported for this assay,[11] our data indicate that sensitivity drops over time, potentially limiting usefulness of this assay over the longer term.

We report a seroprevalence of SARS-CoV-2 IgG in HCWs in our institution not previously diagnosed with COVID-19 by RT-PCR of 1.49%. The (SCOPI) conducted over the same period estimated overall seroprevalence in the general population at 1.7%,[12] with regional differences between urban Dublin (3.1%) and rural Sligo (0.6%). In Cork and Kerry, the two main counties served by our hospital, HCW infections represented 23% of total infections during the first wave. This was a smaller percentage than the figure seen nationally of 32.1% and would indicate that there was a lower proportion of HCW infected in Cork.[13]

Seroprevalence in HCWs without previously diagnosed COVID-19 is lower than in the majority of published international studies that report seroprevalence among

Table 1 Participant demographics and comorbidities

Characteristic	Total n=503	Group 1* n=99	Group 2† n=106	Group 3‡ n=91	Group 4§ n=100	Group 5¶ n=107
Gender						
Male	115 (22.9)	24 (24.2)	20 (18.9)	26 (28.6)	29 (29.0)	16 (15.0)
Female	388 (77.1)	75 (75.8)	86 (81.1)	65 (71.4)	71 (71.0)	91 (85.0)
Age						
Range (years)	20–65	20–65	22–64	21–61	20–56	21–62
IQR	29.5–47.0	31.0–49.0	30.0–46.0	28.8–48.0	28.0–42.0	30.0–47.0
20–29	125 (24.9)	20 (20.2)	25 (23.6)	24 (26.4)	32 (32.0)	24 (22.4)
30–39	164 (32.6)	27 (27.3)	41 (38.7)	29 (31.9)	33 (33.0)	34 (31.8)
40–49	122 (24.3)	30 (30.3)	24 (22.6)	19 (20.9)	23 (23.0)	27 (25.2)
50–59	80 (15.9)	16 (16.2)	14 (13.2)	17 (18.7)	12 (12.0)	21 (19.6)
60–69	9 (1.8)	6 (6.1)	1 (0.9)	1 (1.1)	0 (0.0)	1 (0.9)
Occupation						
Medical	176 (35.0)	18 (18.2)	29 (27.4)	38 (41.8)	55 (55.0)	36 (33.6)
Nursing	210 (41.7)	43 (43.4)	55 (51.9)	32 (35.2)	29 (29.0)	51 (47.7)
Healthcare assistant	27 (5.4)	11 (11.1)	7 (6.6)	3 (3.3)	4 (4.0)	2 (1.9)
Physiotherapy	15 (3.0)	5 (5.1)	1 (0.9)	5 (5.5)	3 (3.0)	1 (0.9)
Pharmacy	17 (3.4)	6 (6.1)	6 (5.7)	4 (3.8)	1 (1.0)	0 (0.0)
Other allied health professional	11 (2.2)	3 (3.0)	2 (1.9)	3 (3.3)	0 (0.0)	3 (2.8)
Administrative	12 (2.4)	4 (4.0)	1 (0.9)	1 (1.1)	0 (0.0)	6 (5.6)
Auxiliary staff	23 (4.6)	9 (9.1)	2 (1.9)	3 (3.3)	6 (6.0)	3 (2.8)
Other/not documented	12 (2.2)	0 (0.0)	3 (2.8)	2 (2.2)	2 (2.0)	5 (4.7)
Comorbidity						
Smoker	29 (5.8)	3 (3.0)	13 (12.3)	5 (5.5)	5 (5.0)	3 (2.8)
Ex-smoker	81 (16.1)	32 (32.3)	14 (13.2)	11 (12.1)	15 (15.0)	9 (8.4)
Hypertension	30 (6.0)	8 (8.1)	5 (4.7)	5 (5.5)	5 (5.0)	7 (6.5)
COPD	5 (1.0)	1 (1.0)	3 (2.8)	0 (0.0)	1 (1.0)	0 (0.0)
Asthma	70 (13.9)	14 (14.1)	14 (13.2)	8 (8.8)	17 (17.0)	17 (15.9)
Diabetes mellitus	10 (2.0)	0 (0.0)	4 (3.8)	1 (1.1)	2 (2.0)	3 (2.8)
Heart disease	4 (0.8)	0 (0.0)	0 (0.0)	2 (2.2)	1 (1.0)	1 (0.9)
Other metabolic conditions	22 (4.4)	1 (1.0)	8 (7.5)	2 (2.2)	6 (6.0)	5 (4.7)
Chronic kidney disease	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)
Chronic liver disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immunosuppressed	9 (1.8)	0 (0.0)	4 (3.8)	0 (0.0)	1 (1.0)	4 (3.7)
Blood disorder	5 (1.0)	0 (0.0)	2 (1.9)	0 (0.0)	1 (1.0)	2 (1.9)
Active cancer diagnosis	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)
Neurological condition	7 (1.4)	1 (1.0)	2 (1.9)	2 (2.2)	1 (1.0)	1 (0.9)
None of the above	296 (58.8)	52 (52.5)	61 (57.5)	62 (68.1)	55 (55.0)	66 (61.7)
Risk profile by area of work						
High risk	187 (37.2)	10 (10.1)	43 (40.6)	34 (37.4)	100 (100)	0 (0.0)
Low risk	316 (62.8)	89 (89.9)	63 (59.4)	57 (62.6)	0 (0.0)	107 (100)
Institution						
Cork University Hospital	469 (93.2)	65 (65.7)	106 (100)	91 (100)	100 (100)	107 (100)
Other institution	34 (6.8)	34 (34.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Data are presented as n (% of total displayed at top of individual columns) unless otherwise stated.
*RT-PCR-confirmed COVID-19 infection (>1-month postpositive RT-PCR).
†Close contacts of persons with COVID-19 infection and who subsequently developed symptoms (virus not detected by RT-PCR on oro/nasopharyngeal swab).
‡Close contacts of COVID-19 cases and who remained asymptomatic.
§HCWs working in areas determined as high-risk clinical areas.
¶HCWs working in areas determined as low-risk clinical areas.
COPD, chronic obstructive pulmonary disease; RT-PCR, real-time PCR.

Table 2 SARS-CoV-2 IgG seropositivity by study group		
Study group	**Total**	**IgG positive**
Group 1*	99	72 (72.7)
Group 2†	106	2 (1.9)
Group 3‡	91	1 (1.1)
Group 4§	100	1 (1.0)
Group 5¶	107	2 (1.9)
Total	503	78 (15.5)

Data are presented as n (%) or total in first column.
*RT-PCR-confirmed COVID-19 infection (>1 month postpositive RT-PCR).
†Close contacts of persons with COVID-19 infection and who subsequently developed symptoms (virus not detected by RT-PCR on oropharyngeal/nasopharyngeal swab).
‡Close contacts of COVID-19 cases and who remained asymptomatic.
§HCWs working in areas determined as high-risk clinical areas.
¶HCWs working in areas determined as low-risk clinical areas.
HCW, healthcare worker; RT-PCR, real-time PCR.

HCWs not previously diagnosed with COVID-19 (groups 2–5) of anywhere between 1.6% and 9.0%.[14–19]

In the USA, a study of a multistate hospital network reported 6% seropositivity in 3248 HCWs across 13 geographically diverse institutions. Notably, 69% of those who were antibody-positive did not have a prior diagnosis of COVID-19 infection.[15] A study of 46 117 HCWs in the greater New York City area across 52 sites revealed a 13.7% total seropositivity to SARS-CoV-2-specific IgG antibodies. 10.3% of those who had previously tested RT-PCR negative and 9.0% of those who had never been previously tested were seropositive.[20] In Madrid, a large tertiary-level institution reported a seroprevalence of 11.2% in a random sample of HCWs at the peak of the first wave in Europe (28 March–9 April 2020). Of this cohort, 40.0% had not had previously diagnosed COVID-19 infection.[14] However, one smaller-scale study of 316 HCWs in Essen in Germany found just 5 (1.6%) were seropositive, none of whom had previously tested positive.[16]

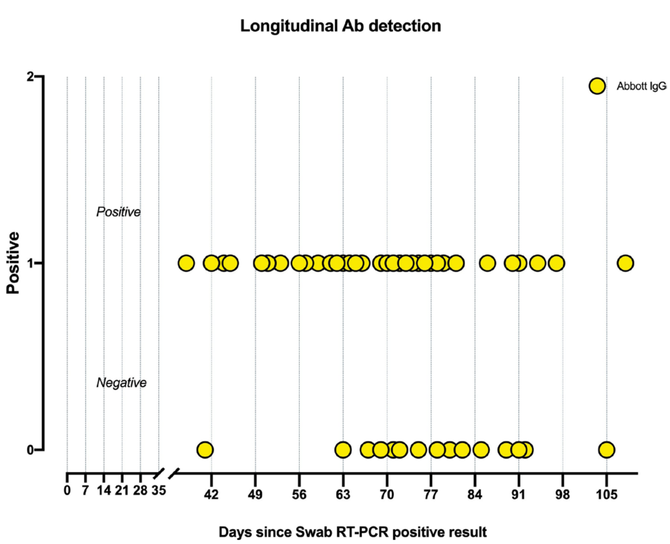

Figure 1 Group one longitudinal SARS-CoV-2 IgG detection since date of positive RT-PCR. n=99.

This was particularly surprising given that rate of asymptomatic infection in COVID-19 is thought to be about 15%.[21] Only 6 out of 105 participants (5.7%) in our study with laboratory evidence of SARS-CoV-2 infection were not diagnosed at time of infection. This was despite guidelines applicable early in the pandemic which dictated that only symptomatic individuals be tested for COVID-19.

There are a number of factors that may have contributed to the low seroprevalence of SARS-CoV-2 IgG in the previously undiagnosed cohort.

The number of patients assessed or hospitalised with COVID-19 (n=150) at our institution was comparatively low during the first wave of the pandemic, and therefore staff may have been exposed to a lower number of COVID-19 patients than in other institutions. The regional prevalence was also comparatively low with a total of 1700 cases reported in Cork as of August 2020 with a peak incidence of 104 cases per 100 000 on 27 March 2020.[13]

At no stage during the surge was there an interruption in PPE supply in our institution, and high standards of infection prevention and control were employed throughout. At all times, the guideline-recommended PPE was available to staff for the assessment of COVID-19 confirmed and suspected patients.[22]

Public transport usage by CUH staff is comparatively low, and there is no tram or commuter rail service serving the hospital. This would potentially reduce overall exposure of staff to tightly congregated environments. There are some data to suggest that use of public transport is positively correlated with antibody positivity.[23]

Easily accessible RT-PCR testing and recommendation for quarantine of symptomatic staff members were implemented locally from identification of our first case of COVID-19 on 5 March 2020. This enabled diagnosis of the vast majority of symptomatic infections from the outset with isolation of these cases minimising risk of onward transmission to patients or other HCWs.

Given antibody positivity was only 73% in group 1, it is possible that HCWs in groups 2–5 were infected but have had undetectable antibodies at the time of sampling. This would result in a potential underestimate of previously infected individuals in these groups.

As well as within hospitals, similar targeted epidemiological studies would undoubtedly be useful in high-risk, high-prevalence settings such as universities, schools and other healthcare institutions to gain a better understanding of patterns of transmission.

Limitations of this study include its being a single-centre study undertaken in an area of relatively low prevalence of COVID-19. Enrolment began 8 weeks after peak regional prevalence, and therefore IgG antibodies may have become undetectable in a proportion of participants.[24] The assay used in the study, Abbott Architect SARS-CoV-2 IgG CMIA, is a qualitative assay, so therefore we were unable to quantify antibody levels in participants. Recruitment of groups 3–5 was by self-selection and therefore was not a true random sample of these groups.

Data regarding C_q were only available for 69 participants, of whom only 12 were IgG negative. Therefore, numbers would not be sufficient to draw a firm conclusion as to the lack of correlation between viral load and subsequent IgG positivity.

CONCLUSION

In the face of the ongoing COVID-19 pandemic, it is important to define the epidemiology of infection in the healthcare setting. Hospital-wide screening for antibodies to SARS-CoV-2 can profile transmission dynamics and inform infection control and prevention policies. With rollout of effective vaccination on the horizon, studies such as this may inform recommendations for prioritisation of immunisation in the context of potentially limited initial supplies.

It is essential that learning from experience of the initial surge of COVID-19 in the healthcare setting informs future practice and response to optimally protect HCWs and vulnerable patients.

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Contributors EF: study concept and design, protocol development; drafted the paper, helped organise logistics of the sample collection. AW: organised and oversaw sample collection for groups 2-5, edited and signed off on the paper. RB: edited and drafted sections of the paper pertaining to microbiological assays. KC, CE, PF, CF, EH, SL, AM-B, EM and DOS: sample collection, paper edits. GK and GOS: enlisted groups 1 and 2 for participation, paper edits. JAE: edits to the paper. DOS: validated and performed the Abbott assay for all these samples. CD: validated all the SARS-CoV-2 assays listed and personally performed many of the assays from March and April. JB: personally performed many of the assays from March and April. MP: study concept and design, protocol development. Finalised aspects of paper pertaining to microbiology. JG: study concept and design, protocol development; finalised aspects of paper pertaining to occupational health. JM: study concept and design, protocol development, substantial edits and input in all sections of paper. LJF: study concept and design, protocol development and substantial input in all sections of paper. SOR: study concept and design, protocol development, substantial edits and input in all sections of paper. MH: edited and helped finalise paper. CS: study concept and design, protocol development and substantial edits and input to all sections, finalised the paper. All authors approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Written informed consent was obtained from healthcare workers using the document contained in the online supplemental appendix 1. The clinical research ethics committee of the Cork Teaching Hospitals granted ethics approval for this study (ECM 4 (a) 16/06/2020).

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