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ORIGINAL ARTICLE

COVID-19 seroprevalence in primary and secondary healthcare workers (HCWs)

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Abstract

Professional anxiety existed early in the coronavirus disease 2019 (COVID-19) pandemic with challenging infection prevention and control support. The aims of this study were to compare epidemiological features of healthcare workers (HCWs) within primary and secondary care with their serological evidence of infection.
A prospective observational cohort of 1,916 HCWs completed a questionnaire, and their sera were assayed for detectable antibody to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleoprotein in the first wave of the pandemic. Datasets were compared between the two sub-cohorts in primary and secondary care and between the combined seropositive and seronegative cohorts.
Curiosity of antibody status was high. Detectable antibody was 7% in the primary care and 5% in the secondary care workers at a time of 1.7% in the general community. Inappropriate personal protective equipment (PPE) was more common in primary care, and detectable antibody was twice as prevalent in HCWs who felt they did not have appropriate PPE. Contact tracing was perceived to be inadequate although it was more commonly performed in the seropositive cohort suggesting appropriate prioritisation. Both temperature and symptom checking alerts and work exclusion were significantly more prevalent in the seropositive cohort.
The seroprevalence data support increased risk for HCWs, the importance of appropriate PPE and the usefulness of the daily temperature and symptom checks, particularly in primary care.

Keywords: *healthcare workers*; *infection control*; *seroprevalence*; *COVID-19*; *Ireland*

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The novel coronavirus that emerged in Wuhan, China, in 2019 was declared as a pandemic by the World Health Organization (WHO) in 2020 and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with the clinical infection named coronavirus disease (COVID-19) in February 2020 (1). Occupational exposure to SARS-CoV-2 is inherent to the clinical practice of healthcare workers (HCWs) requiring identification and mitigation of hazards and risk through various infection prevention and control (IPC) modalities and involves both rights and responsibilities (2). Limited personal protective equipment (PPE) early in the pandemic increased the fear of COVID-19 both in the public and healthcare workplaces due to the significantly high polymerase chain reaction (PCR) positivity rates amongst HCWs, with peak percentages of up to 40% in May 2020 in Ireland, later falling to 15% in February 2021 (3). Little is known about the HCW COVID-19 seroprevalence experience in primary care community settings compared to secondary care in hospital practice, and to our knowledge, this is the first HCW seroprevalence study to specifically compare HCWs in primary care with those in secondary care.

Methods

This prospective observational cohort study was named the COVID-19 Antibody Surveillance Study in Healthcare

Table 1. Questionnaire responses (positive responses/total answered), with seroprevalence and primary or secondary care workplace (% in brackets)

Query	All respondents	Antibody detected	Antibody not detected	Primary care (GP)	Secondary care (hospital)
Would you like to know the result of your antibody test?	1,911/1,916 (99.74)	131/132 (100)	1,778/1,783 (99.72)	1,454/1,457 (99.8)	457/459 (99.6)
Do you expect to have a positive response?	325/1,912 (17)	86/131 (65.65)	239/1,780 (13.43)	258/1,455 (17.7)	67/457 (14.7)
Do you hope to have a positive antibody response?	1,069/1,899 (56.29)	98/130 (75.68)	971/1,768 (54.92)	874/1,447 (60.4)	195/452 (43.1)
Have you suffered a COVID-19-like illness in the last 6 months?	751/1,917 (39.18)	109/130 (83.85)	641/1,786 (35.89)	635/1,459 (43.5)	116/458 (25.3)
Would you categorise your symptoms 'moderate to severe'?	277/718 (38.58)	43/100 (43)	234/617 (37.93)	228/607 (37.6)	49/111 (44.1)
Did your illness require interruption of usual activities?	418/1,050 (39.81)	83/113 (73.45)	334/936 (35.68)	343/854 (40.1)	75/196 (38.3)
Was your illness confirmed as COVID-19?	78/824 (9.47)	70/111 (63.06)	8/712 (1.12)	62/676 (9.2)	16/148 (10.8)
Was your illness suspected as COVID-19?	160/824 (19.42)	20/111 (18.02)	140/712 (19.66)	134/676 (19.8)	26/148 (17.6)
Have you looked after or been exposed to suspected or unknown COVID-19 patients with appropriate PPE?	698/1,900 (36.74)	45/130 (34.62)	652/1,769 (36.86)	537/1,443 (37.2)	132/457 (28.9)
Have you looked after or been exposed to suspected or unknown COVID-19 patients without appropriate PPE?	227/1,900 (11.95)	28/130 (21.54)	199/1,769 (11.25)	175/1,443 (12.1)	23/457 (5)
Which was your highest risk exposure? – known COVID-19	467/1,938 (25.41)	40/125 (32)	426/1,712 (24.88)	372/1,399 (26.6)	95/439 (21.6)
Which was your highest risk exposure? – Suspected COVID-19	515/1,838 (28.02)	36/125 (2.8)	479/1,712 (27.98)	412/1,399 (29.5)	103/439 (23.5)
Which was your highest risk exposure? – Not suspected	856/1,838 (46.57)	49/125 (39.2)	807/1,712 (47.14)	615/1,399 (44)	241/439 (54.9)
Have you had a community contact in the last 6 months? (Confirmed or Suspected Case)	370/1,893 (19.55)	47/127 (37.01)	323/1,765 (18.3)	327/1,440 (22.7)	43/453 (9.5)
Have you had a community contact in the last 6 months? (International Travel)	113/1,893 (5.97)	15/127 (11.81)	98/1,765 (5.55)	92/1,440 (6.4)	21/453 (4.6)
Have you had a hospital or GP practice contact? (Known or Suspected)	674/1,885 (35.76)	63/129 (48.84)	610/1,755 (34.86)	605/1,428 (42.4)	69/457 (15.1)
If you had community, GP or hospital contact, were you contacted by a contact tracing team (hospital or public health)?	71/247 (28.74)	20/28 (71.43)	51/219 (23.29)	66/235 (28.1)	5/12 (41.7)
Have you been excluded from work for COVID-19 symptoms in the last 6 months?	341/1,910 (17.85)	87/130 (66.92)	254/1,779 (14.28)	278/1,451 (19.2)	63/459 (13.7)
Have you had a temperature ≥37.5°C at the screening station on 1 or more occasions?	100/1,641 (6.09)	28/103 (27.18)	72/1,537 (4.68)	85/1,192 (7.1)	15/449 (3.3)
Did you feel well enough to come to work?	74/164 (45.12)	14/38 (36.84)	60/126 (47.62)	58/139 (41.7)	16/25 (64)
Have you answered 'YES' to any of the questions in the daily COVID-19 assessment questionnaire?	438/1,366 (32.06)	50/78 (64.1)	388/1,288 (30.12)	377/978 (38.6)	61/388 (15.7)

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Staff (CASSIS Study) and employed a questionnaire on attitudes, perceptions, exposure, morbidity and IPC, and an antibody assay. All hospital staff in a private 196-bedded secondary care hospital (33% single rooms) in Dublin, Ireland, were invited to participate through an all-users email. Additionally, staff from those primary care practices who refer patients to this hospital were also posted an invitation to participate. To minimise exclusion bias, the antibody test was offered free to all whether they decided to enter the study or not. Those who entered in the study gave a written informed consent and 5–10 ml serum. The test was offered to all employees of any referring general practice (GP) staff. The data were completed between the months of June and August 2020 in an environment with no vaccine availability. 35% of the overall hospital staff complement were entered in the study, and although the exact denominator datum was not known for the primary care cohort, 684 general practitioners were emailed, of which 410 opened their email invitation. Table 1 shows the variables in the questionnaire, and the questions are available in the Supplementary Appendix. The results of the antibody test and the questionnaire were collated and anonymised for analysis. Those HCWs in both groups who demonstrated detectable antibody and wished to know their result were personally telephoned and counselled on the test significance. Those with no detectable antibody were given results on request. Participation was voluntary, and the study was approved by the Beacon Hospital Research and Ethics Committee.

Sera were measured against SARS-CoV-2-nucleoprotein (N), using the Elecsys Anti-SARS-CoV-2 (Roche Diagnostics, Burgess Hill, UK) and run on the Roche 8000 series platform. The assay uses a recombinant protein representing the nucleocapsid (N) antigen in a double-antigen sandwich assay format and is intended to qualitatively detect pan-Ig antibodies against SARS-CoV-2.

Anonymised data were entered into an Excel spreadsheet (Microsoft, Redmond, WA, USA), collated, and then analysed using the Excel data analysis tools package to derive percentages. Statistical significance was derived using the Chi square or Fisher's exact test. The Fisher's exact test was used to examine relationships with those respondents of question 1 who answered 'no' because of the small sample sizes. A Chi square test of independence was used to examine the relationship for the remaining questions. Data from those tested but who did not sign the consent form were removed from the data analysis.

Results

The number of staff in all the referring primary care practices was unknown, but amongst the hospital staff, 779/1,419 (54.89%) took up the offer of the test and 492 of these (63.16%) gave full informed consent and were entered in the study, that is, 34.67% of total hospital staff. Minor differences in denominators within groups reflect some questions not being answered by all respondents. Overall, a higher seroprevalence was found amongst primary care (6.9%) than secondary care (5.4%) HCWs, but this was not significant ($P = 0.19$).

Table 1 shows the affirmative proportions of respondents' questions in total and within the sub-cohorts based on seroprevalence and primary or secondary care. The Fisher's exact test for question 1 was 0.3452, showing no significant difference at $P < 0.05$ between the two HCW groups. Comparing the antibody detected and antibody not detected cohorts of all HCWs, of the total 1,916 HCWs entered in the study, 99.74% wished to know the result of their antibody test and 56.29% hoped to have antibodies; 75.68% of those who had detectable antibodies had also expressed the hope that they would have antibodies compared to 54.92% with no detectable antibody who had hoped to have antibodies ($P < 0.001$). Only 17% expected to have antibodies, but of those who were positive, 65.65% of them expected this as compared to only 13.43% of those who were negative but expected to be positive ($P < 0.0001$). 39.18% of HCWs surveyed had suffered a subjective COVID-19 illness, which was characterised as an illness which the HCW's thought was consistent with COVID-19 symptoms. 83.85% with a positive antibody response had suffered a COVID-19 like illness, and 35.89% with no detectable antibody felt that they had suffered a COVID-19 illness ($P < 0.001$). Those who had moderate to severe symptoms (38.58%) were of equally distributed percentages between seropositive and seronegative groups. Almost 39.81% had to interrupt their usual activities, and the proportion was much higher (73.45%) in the positive group than in the negative group (35.68%, $P < 0.00001$). 9.47% of all respondents had known confirmed COVID-19, and of these, 63.06% had antibody and 1.12% had no detectable antibody ($P < 0.0001$). The date of illness onset had not been requested. 19.42% were suspected to have COVID-19, but within this group, there was no significant difference between those who had antibody (18.02%) and those who had no antibody (19.66%).

Those HCWs who had appropriate PPE showed no significant difference in seroprevalence, but amongst the 11.95% who did not have appropriate PPE twice as many were seropositive (21.54% vs. 11.25%, $P < 0.0005$). HCWs assessed their highest risk exposure incidents to be amongst patients not suspected of having COVID-19 (46.57%), with equal amounts believing their highest exposure risks were amongst known COVID-19 or suspected COVID-19 patients (25.41% and 28.02%, respectively). Of the 19.55% who had a community contact, twice as many had detectable antibody, 37.01%, compared to 18.3% who had no detectable antibody ($P < 0.0001$). 35.76% had a known or suspected contact in either hospital or GP, and again more

of these were seropositive (48.84%) than seronegative (34.86%, $P < 0.001$). Only 28.74% of those who felt they had a contact were contact traced, but this was much higher in the positive group (71.43%) compared to the negative group (23.29%, $P < 0.0001$).

Overall, 17.85% had been excluded from work because of COVID-19 symptoms and again this was much higher in the seropositive group (66.92%) than in the seronegative group (14.28%, $P < 0.00001$). Only 6.09% of HCWs had been excluded from work because of a temperature of >37.5°C, and of this group, more were in the seropositive group (27.18%) than in the seronegative group (4.68%, $P < 0.00001$). There was no significant difference in HCW seroprevalence based on whether they felt well enough to come to work. One-third (32.06%) had answered yes to any of the screening symptom questions with twice as many in the seropositive group (64.1%) compared to the seronegative group (30.12%, $P < 0.00001$).

Secondly, comparing the primary and secondary care cohorts, there was no difference in the curiosity level of their antibody status or in their expectations of having detectable antibody. More in primary care (60.4%) than secondary care (43.1%), hoped to have detectable antibody ($P < 0.00001$). More primary care HCWs (43.5%) than secondary care workers (25.3%) believed they had suffered a COVID-19 like illness ($P < 0.000010$), although there was no difference in either their known confirmed rates or severity or antibody prevalence. With regards to PPE, more primary care HCWs (37.2%) than secondary care HCWs (28.9%, $P < 0.01$) perceived that they had appropriate PPE; however, more in primary care reported being without appropriate PPE (12.1%) than in secondary care, (5%, $P < 0.0001$) and as stated earlier, there was a higher antibody seroprevalence in those reporting inappropriate PPE.

There was no perceived significant difference in risk exposure for known or suspected COVID-19, but there was a higher perceived exposure to not suspected COVID-19 patients in secondary care (54.9%) than in primary care (44%, $P < 0.0001$). Perhaps by definition, more primary care HCWs had a community contact (22.7% vs. 9.5%, $P < 0.00001$) and a professional contact (42.4% vs. 15.1%, $P < 0.00001$), but there was no significant difference for contacts through international travel (6.4% vs. 4.6%). Again, contact tracing was low after a perceived exposure, 28.1% in primary care and 41.7% in secondary care (NS), but this may only reflect the perceptions of the HCW of an exposure. With respect to daily symptom checking, more HCWs in primary care had answered yes to any symptom check questions (38.6% vs. 15.7%, $P < 0.0001$), and more had been excluded from work (19.2% in primary care vs. 13.7% in secondary care, $P < 0.01$) and less in primary care felt well enough to come to work (41.7% vs. 64%, NS).

Discussion

To our knowledge, this is the first COVID-19 seroprevalence study to specifically compare HCWs working within primary care surgeries with a hospital-based HCW cohort. HCWs appreciate IPC support and access to diagnostics such as antibody status. The higher seroprevalence found in primary care than secondary care was not significant, but both levels were much higher than the background level found in another contemporary study, 1.7% (4). Other studies have reported higher first wave seroprevalences of up to 24% in a UK hospital (5), and 4–15% in two other hospitals in Ireland (6), perhaps reflecting busier wards with greater caseloads and less single room infrastructure.

Two-thirds of those HCWs with an antibody response had expected this. A UK study found that 49% of HCWs had overestimated COVID-19 infection and were seronegative (7). During the telephone feedback in our study to those staff with detectable antibody, most believed that they had been exposed in mid-March 2020 in the first wave. None of those asymptomatic and surprised by a positive result was concerned about future loss of detectable antibody. A mean half-life of immunoglobulin G (IgG) of 36 days has been reported (8), and the ongoing SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study in the UK is starting to elucidate the protective effect of previous infection observing 84% lower infection at 7 months (9). Those who had already known that they had positive PCR results during their illness had still wished to know their antibody status.

This study has identified a cohort of HCWs in the first wave with perceived incomplete PPE support and a greater level of detectable antibody in their serum compared to the general population, which may support their concerns. Consistent with this is the lack of difference in seroprevalence amongst the cohorts who felt they did have full appropriate PPE. This observation is significantly greater in the primary care HCW cohort and perhaps reinforced by their greater belief that they had suffered a COVID-19-like illness. Not only were there shortages of PPE (10) in the first wave, but also conflicting IPC advice existed as it evolved, and some HCWs were even advised by their hospital management not to speak to the media. Employers may need clear occupational health advice regarding their legal responsibilities to provide PPE and governments to perhaps not to be so dependent on international supplies.

Another deficiency in pandemic preparedness identified here was the surprisingly low level of contact tracing reported at 28.74%, although this rose to 71.43% amongst those with serological evidence of infection, perhaps suggesting appropriate prioritisation. Commentary has been published on the limitations in the UK test trace and isolate programme suggesting only 8% of symptomatic cases

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might be identified (11), further supporting the need for HCW diagnostics as critical in the healthcare workplace.

This study also promotes the usefulness of symptom and temperature screening as positive alerts were more prevalent in those with detectable antibody, and a greater percentage excluded from work was seen in those with antibody. Also, a greater percentage of screening alerts was observed in primary care than in secondary care; however, a weakness is that evolving differences in symptom screen designs may have been used in primary care than in our hospital, and this could affect how respondents answer the screening questions. A separate study group is analysing the temperature range in a different database of daily temperature measurements of the hospital sub-cohort of HCWs to assess the optimum screening temperature as 37.5°C, which may not achieve optimal specificity. Loss of sense of taste or smell has been shown to be the most useful predictor of infection in symptom screening at least with the prevalent first wave genotype (12).

A major limitation of the current study is the self-reported nature of the data captured in the questionnaire, perhaps mitigated by the HCW level of symptom knowledge compared to such use in the general public. A volunteering bias could also be active although this may be mitigated by the free access to the antibody assay independent of consenting to enter the study. Other limitations may be unknown individual circumstances, such as age, immune suppression or pregnancy, which were not captured. These results are also subject to the limitations of this commercial assay using a single antigen. Although the manufacturer reported 100% specificity and 99.8% sensitivity, a lower sensitivity (86.1%) was found at >14 days post-exposure by an independent evaluation (13). In addition, individual variability in antibody seroconversion, degree of antibody production, the role of circulating antibody compared to neutralising antibody and its unknown role in protection or transmission are limitations to any conclusions. Another study is ongoing in Northern Ireland and the UK but uses a capillary blood sample, which may not have the same performance characteristics, and the epidemiological data capture of this study may not be as detailed (14).

Direct exposure to SARS-CoV-2 patients has been identified as the most common risk factor in mental health outcomes other than occupational burnout (15), and 85% of HCWs have been reported to fear self-infection with SARS-CoV-2 (16). The experience with Zika virus has shown that infection control knowledge is significantly correlated with infection-control attitude and infection control practices in a study on student nurses' attitudes to Zika virus (17). However, altruism is also inherent in this occupational group. Although media anxiety may contribute to HCW affect, it should be counterbalanced by the cognitive awareness resulting from their professional training and should empower the HCW with increased confidence. We have personal experience in our hospital of observing this confidence growth throughout the experience of working with COVID-19 patients, but this was not measured in this study. Social support and group coherence with interventions such as group self-reflection, for example, problem-based learning, may empower action and goal realisation in the workplace (18). The emotional value of testing for antibody should not be overlooked as a HCW support. Perceptions of assumed immunity, or lack of it, to COVID-19 may affect safety behaviour and further enhance the risks of exhaustion and professional burn-out. Although continued adherence to IPC practice and vaccination are crucial, additional organisational interventions and support could be useful, and the nuanced needs of sub-cohort analysis must not be forgotten, particularly in the community.

Further studies are required to assess the value of specific interventions within different workplace cohorts such as greater access to higher quality laboratory diagnostics, more efficient contact tracing support and improved IPC and PPE to support and help optimise HCW workforce management. None of this is difficult with appropriate funding, some of it achievable within existing resources and with prudent preparedness may lead to system optimisation for future wave peaks, new variants of concern or the inevitable next pandemic.

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Conflict of interest and funding

None of the authors wish to declare any conflict of interest other than their attendance/employment at Beacon Hospital, Dublin Ireland.

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Appendix: Questionnaire completed by all included participants

CASSIS Study

Covid-19 Antibody Surveillance Survey in healthcare Staff

Thank you for volunteering your blood sample to this investigation of our local healthcare worker SARS-CoV-2 seroprevalence in both primary and secondary care staff. Please circle or underline your answers and attach your completed questionnaire to your blood sample, (5-10 ml clotted blood), and submit to: The Laboratory, Beacon Hospital.

Name DOB Contact telephone

1. Would you like to know the result of your antibody test?
   Yes No

2. Do you expect to have a positive response?
   Yes No Neither yes or no

3. Do you hope to have a positive antibody response?
   Yes No Neither yes or no

4. Have you suffered a Covid-19-like illness in the last 6 months?
   (Fever, new cough, new SOB, myalgia, tiredness, loss of smell or taste, headache)
   No Yes
   If yes would you categorise it as: Mild Moderate Severe

5. If you suffered a Covid-19-like illness in the last 6 months did your illness require interruption of usual activities?
   Yes No

6. If you suffered a covid-19 like illness in the last 6 months was your illness confirmed or suspected as Covid-19 ?
   Confirmed Covid-19 Suspected Covid-19 Not considered to be due to Covid-19

7. What is your clinical role / department?
   Hospital :
   Consultant NCHD GP Clinical Nurse Allied health care
   Administration Housekeeping Catering Other
   GP:
   Doctor Nurse Reception Other

8. Have you looked after or been exposed to Covid-19 Patients, (suspected/known)?
   No Yes with appropriate PPE Yes without appropriate PPE

9. Which was your highest risk exposure?
   Suspected Covid19 Known Covid19 Not suspected

10. Have you had a community contact in the last 6 months?
    Yes, a confirmed contact Yes, a suspected contact International travel

    No, I have not had a community contact

11. Have you had a hospital or GP Practice contact?
    Yes, a known contact Yes a suspected contact

    No, I did not have a hospital or GP contact

12. Were you contacted by a contact tracing team?
    No Yes, Hospital contact tracing team. Yes, HSE Public Health contact tracing team.

13. Have you been excluded from work for Covid-19 symptoms in last 6 months?
    Yes No

14. Have you had a temperature ≥ 37.5°C at the screening station on 1 or more occasions
    Yes No Not applicable

    If yes, did you feel well enough to come to work

    Yes No Not applicable

15. Have you answered yes to any of the questions in the daily Covid-19 assessment questionnaire?
    Yes No Not applicable

    Thank you for your cooperation.

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