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Journal of Public Health Research 2021; volume 10:2102

Article

Asymptomatic SARS- CoV-2 infection among healthcare workers in a non-COVID-19 teaching university hospital

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Abstract

Introduction: During the COVID-19 pandemic, most of the published reports on COVID-19 emphasized that health care workers (HCWs) get infected more than the general population representing one of the most vulnerable groups. However, that the real percentage of HCWs infected by SARS-CoV2 in Egypt remains unknown. The researchers conducted the current study to assess seroprevalence of SARS-CoV-2 IgG among HCWs working in a hospital with no SARS-CoV-2 patients, and to identify the potential factors associated with SARS-CoV2 IgG seropositivity.

Design and Methods: The current study is a cross-sectional study carried out among 455 HCWs at Cairo University Hospital. The researchers administered a questionnaire shortly before the SARS-CoV-2 rapid test is performed using closed-ended question format to obtain information on demographic data of the study participants including age, sex, specialty, clinical information including questions about medical conditions, and. history of previous exposure with a confirmed or suspected case of COVID-19, and history of COVID-19- compatible symptoms during the previous 14 days (cough, sore throat, runny nose, fatigue, shortness of breath, fever, headache, vomiting, diarrhea, anosmia, ageusia, and chills).

Results: We screened 455 HCWs for SARS-CoV-2 antibodies, 31.4% were in the high-risk group, and 68.6% in the low-risk group. The overall IgG seroprevalence was, 36 (7.9%) (95% CI 5.8 to 10.8). The IgG seroprevalence was significantly higher in low-risk group 11% (35/312) *versus* high-risk group 0.7% (1/143, $p<0.001$.

Conclusion: Low seropositivity rates for SARS-CoV-2 among HCWs is suggestive of lack of immunity and we are still far from herd immunity.

Introduction

During Coronavirus Disease-2019 (COVID-19) pandemic, most of the published reports on COVID-19 emphasized that health care workers (HCWs) get infected more than the general population, representing one of the most vulnerable groups.[1,2] According to Keeling *et al*.,[3] HCWs represent 10% of overall cases and often more than 10% of any hospital's personnel are commonly infected. Unlike Severe Acute Respiratory Syndrome (SARS) or the Middle East Respiratory Syndrome (MERS), COVID-19 has a lower mortality rate.[2] Despite this lower mortality for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) the causative agent for COVID-19, its long incubation period resulted in a significant number of asymptomatic infected individuals.[4] A study done at the University of Cambridge in a large United Kingdom teaching hospital revealed that 3% of HCWs in the asymptomatic screening group tested positive for SARS-CoV-2.[5] Another study conducted among HCWs at a clinic in Chile. revealed that a 3.4% of positivity in asymptomatic HCWs.[6]

Given that the real percentage of HCWs infected by SARS-CoV2 in Egypt remains unknown, and in response to the increased number of infected and deceased HCWs in Egypt, the researchers conducted the current study to assess the seroprevalence of SARS-CoV-2 IgG among HCWs working in a hospital with no SARS-CoV-2 patients, and to identify the potential factors associated with SARS-CoV-2 IgGs.

Design and Methods

Study design, setting, and population

The current study is a cross-sectional study carried out among HCWs at Cairo University Hospital. The researchers defined the study population as those HCWs who deliver care and services to

Significance for public health

The current study emphasizes that the low seropositivity rates for SARS-CoV-2 among health care workers is suggestive of lack of immunity and we are still far from herd immunity.

patients, including physicians and nurses. Inclusion criteria included being an adult (>18 years) working at Cairo University Hospital. Exclusion criteria included: a) absenteeism from the workplace in the last 30 days, retirement, or end-of-contract, and working in a COVID hospital.

From a total number of 700 HCWs, 600 were eligible to take part in the study. We recruited 455, yielding a participation rate of 75%. All participants had worked at Cairo University Hospital for at least one month before study enrollment and were asymptomatic at the point of study recruitment. HCWs who were previously diagnosed with COVID-19 were excluded from the study. We divide health care workers into high risk and low-risk groups. High-risk HCWs are defined as those who are dealing with aerosol generating procedure pulmonary and included three departments (anesthesia, critical care, and pulmonary care). Low risk HCWs are those who are not involved in aerosol generating procedures.[7]

Procedures and data collection

Serum collection and self-administered questionnaire

Before serum collection, the researchers used an online short pre-screener questionnaire to determine the eligible HCWs and exclude those with history of confirmed COVID-19 infection. It included the following questions: name, email address, mobile phone, specialty, the most suitable day for sample collection, and the history of confirmed COVID-19.

After that, the researchers administered a questionnaire shortly before the SARS-CoV-2 rapid test is performed using closed-ended question format to obtain information on:

a. Demographic data of the study participants including age, sex, specialty,

b. Clinical information including questions about medical conditions (chest diseases, cardiovascular diseases, diabetes, *etc*.), surgical history, medication intake such as (anticoagulant, immunosuppression, chemotherapy, steroids, antiepileptic, and vitamins), and smoking history,

c. History of previous exposure with a confirmed or suspected case of COVID-19, and history of COVID-19- compatible symptoms during the previous 14 days (cough, sore throat, runny nose, fatigue, shortness of breath, fever, headache, vomiting, diarrhea, anosmia, ageusia, and chills).

The questionnaire was based on Health workers exposure risk assessment and management in the context of COVID-19 virus.[8]

Detecting serum IgG against SARS-CoV-2

Samples were tested immediately by lateral flow immunoassay (SD-Biosensor, Korea). The STANDARD Q COVID-19 IgM/IgG Duo Test showed according to the manufacturer's insert this test has a sensitivity 94% and specificity 95%. Validation of the results was done using iFlash-SARS-CoV-2 IgG chemiluminescent

Table 1. Comparison between high risk and low risk health care workers regarding demographic, clinical information, exposure information, and COVID-19 like symptoms (n=455).

Demographic characteristics	All subjects	Health care workers		p
		High risk group n=143	Low risk group n=312	
Age (mean ±SD)	32.8 ± 8.3	33.7 ± 8	32.4 ± 8.4	0.110
Gender (n, %)				
Male	239 (52.5%)	92 (64.3%)	147 (47.1%)	0.001*
Clinical history (n, %)				
Past surgical history	118 (25.9%)	59 (41.3%)	59 (18.9 %)	<0.001*
Past medical history	89 (19.6%)	30 (21%)	59 (18.9%)	0.606
Hypertension	25 (5.5%)	11(7.7%)	14 (4.5%)	0.164
Diabetes	9 (2.0%)	2(1.4%)	7 (2.2%)	0.726
Asthma	19 (4.2%)	8 (5.6%)	11 (3.5%)	0.306
Allergy	16(3.5%)	5(3.5%)	11 (3.5%)	0.988
Other medical conditions #	25 (5.5%)	10 (7.0%)	15 (4.8%)	0.342
Medication intake	99 (21.8%)	32 (22.4%)	67(21.5%)	0.828
Smoking history (n, %)				
Current smoker	24 (5.3%)	5 (3.5%)	19 (6.1%)	0.251
Ex-smoker	62 (13.6%)	15 (10.5 %)	47 (15.1%)	0.187
Exposure information (n, %)				
Direct contact with the environment where the confirmed COVID-19 was cared for	187 (41.1%)	74 (51.7%)	113 (36.2%)	0.002 *
History of travelling in proximity with confirmed COVID-19 patient	100 (22%)	14 (9.8%)	36 (11.5%)	0.580
Family member with COVID-19 diagnosis	24 (5.3%)	6 (4.2%)	18(5.8%)	0.486
Family member with pneumonia diagnosis	11 (2.4%)	4 (2.8%)	7 (2.2%)	0.747
Symptoms compatible with COVID-19 in the past 2 weeks (n, %)				
Flu-like illness	108 (23.7%)	50 (35%)	58 (18.6%)	<0.001*
Wheezing	42 (9.2%)	15 (10.5%)	27(8.7%)	0.530
Fever	61 (13.4%)	25 (17.5%)	36 (11.5%)	0.084
Gastroenteritis	96 (21.1%)	34(23.8%)	62(19.9%)	0.343
Sore throat	133 (29.2%)	61(42.7%)	72(23,1%)	<0.001*
Muscle aches	81(17.8%)	34(23.8%)	47(15.1%)	0.024 *
IgG seroprevalence				
+VE	36 (7.9) [5.8-10.8]	1 ,0.7	35 ,11.2	<0.001*

#Liver disease, renal disease, cancers and autoimmune and other immunological disorders; *statistically significant.

immunoassay kit (LOT 20200307; REF C86095G; YHLO Biotech, Shenzhen). Per manufactures' instructions, the sensitivity and specificity of the kits were 90% and 95% respectively for IgG, In this assay the nucleocapsid (N) protein was combined with the spike (S) glycoprotein antigens to increase the sensitivity. The levels of IgG antibodies were positively correlated with the relative luminescence unit (RLU) and were evaluated as arbitrary units per milliliter (AU/mL)

The study researchers via short message informed participants who tested positive for SARS-CoV-2 antibodies.

Statistical analysis

The researchers used the Statistical Package of Social Science Software program (IBM SPSS Statistics for Windows, Ver. 25.0; IBM Corp., Armonk, NY, USA). We summarized the data using range, mean, and standard deviation for quantitative variables and frequency and percentage for qualitative ones. We performed the comparison between groups for qualitative variables using Chi-square or Fisher's exact tests, while for quantitative variables we conducted the comparison using Independent *t*-test; p-values less than 0.05 were considered statistically significant.

Results

Between 20 /5/ 2020 and 11/6/ 2020, we screened a total number of 455 HCWs for the SARS-CoV-2 IgG antibody. Among them, 143 (31.4%) were in the high-risk group and 312 (68,6%) in the low-risk group. We present the demographic characteristics of the two groups in Table 1. Out of 455 HCWs, 36 tested positive by both IgG rapid test and chemiluminescent immunoassay; this corresponds to an overall seroprevalence estimate of 7.9% (95% CI 5.8 to 10.8). The prevalence of IgG against SARS-CoV2 among the high-risk group was 1 (0.7%), in contrast, the seroprevalence was significantly higher in the low-risk group 11% (35/312) p<0.001. Direct contact with an environment where the confirmed COVID-19 cared, was significantly higher in the high risk compared to the low-risk group odds ratio (95% confidence interval) OR [95% CI]: 1.9 [1.3-2.8], p<0.0001.

The researchers also compared the subjects' characteristics between those with anti-SARS-CoV-2 IgG positive and negative. Demographic data, clinical information, and smoking history were comparable between both groups Regarding symptoms compatible with COVID-19 in the past two weeks, 141(31%) did not report any COVID-19 like symptoms. One third (29%) reported having a sore throat, followed by Flu-like illness 104 (23%), and muscle aches 82 (18%). However, there was no significant difference between study participants who tested positive and those who were tested negative (Table 2).

Discussion

The main outcome of the present study that the overall seroprevalence among HCWs is low; 7.9%. Moreover, IgG seropositivity was less prevalent among the high-risk group compared to the low-risk group. In the current study, the seroprevalence among HCWs was 7.9%. Consistent with the current study finding, several studies found that the seroprevalence among healthcare workers was low and varied from 0% to 8.6% .[9,10]

We conducted the present study in a large non-COVID -19 university teaching hospital aiming at predicting the real prevalence of asymptomatic COVID-19 disease among the general population. Interestingly, the author supposed at the start of research that the seroprevalence would be high among HCWs. However, the low prevalence rate among HCWs (7.9%) may suggest lower rates among the general population. Several recent larger-scale studies

Table 2. Association between demographic characteristics, clinical history, exposure information and COVID-19 IgG seroprevalence (n=455).

Demographic characteristics	IgG		p
	+VE n=36	-VE n=419	
Age (mean ± SD)	33.4 ± 9.3	32.8 ± 8.2	0.707
Gender (n, %)			
Male	16 (44.4%)	223 (53.2%)	0.312
Clinical history (n, %)			
Past surgical history (n, %)	12 (33.3%)	106 (25.3%)	0.291
Past medical history (n, %)	8 (22.2%)	81 (19.3%)	0.675
Hypertension	2 (5.6%)	23 (5.5%)	1.000
Diabetes	0 (0)	9 (2.1%)	1.000
Asthma	1 (2.8%)	18 (4.3%)	1.000
Allergy	1 (2.8%)	15 (3.6%)	1.000
Other medical conditions[#]	3 (8.3%)	22 (5.3%)	0.436
Medication intake (n, %)	9 (25%)	90 (21.5%)	0.623
Smoking history (n, %)			
Current smoker	2 (5.6%)	22 (5.3%)	1.000
Ex-smoker	6 (16.7%)	56 (13.4%)	0.611
Non-smoker	28 (77.8%)	341 (81.4%)	0.596
Symptoms in the past 2 weeks (n, %)			
Flu-like illness	8 (22.2%)	100 (23.9%)	0.824
Wheezing	6 (16.7%)	36 (8.6%)	0.127
Fever	5 (13.9%)	56 (13.4%)	1.000
Gastroenteritis	8 (22.2%)	88 (21%)	0.863
Sore throat	9 (25%)	124 (29.6%)	0.561
Muscle aches	10 (27.8%)	71 (16.9%)	0.103

[#]Liver disease, renal disease, cancers, and autoimmune and other immunological disorders.

documented low prevalence among the general population. The Spanish study, which included over 60,000 participants, showed a nationwide seroprevalence of 5.0% (population-based seroepidemiological study).[11] We got similar numbers across the 2766 participants in the Swiss study, with seroprevalence data from Geneva reaching 10·8%.[12] All these findings from the current study and others documented that most of the population appears to have remained unexposed to SARS-CoV-2, even in areas with widespread virus circulation.

The second main finding was that the IgG seropositivity was more prevalent among low-risk HCWs than high risk HCW. Inconsistent with the present study finding, a recent study conducted in Germany found that the seroprevalence was low in the high-risk HCWs (1.2%) versus the low-risk group (5.2%).[12] Out of 42,600 HCWs caring for COVID-19 patients in the second half of the China epidemic, none was infected, suggesting that sufficient precautions and rigorous enforcement of PPE are the major determinants for eliminating COVID-19 infection,[9] and consistent with data suggesting that HCWs in hospitals involved in COVID-19 care could have a lower burden of infection than those not taking part in COVID-19 care. [11] Contradicting results are noted in a large study from Madrid where the SARS-CoV-2 prevalence is higher in HCW working in areas with exposure to COVID-19 (34%) compared with the low-risk area (26%) and external workers (30%) in Madrid.[13] and to a recent study conducted among frontline HCWs during the peak of COVID-19 pandemic in a tertiary care hospital in Egypt with higher prevalence (14.3%).[14] The possible explanation of the current study finding was that the high-risk group had a high perception of increased risk of SARS- CoV-2 transmission leading to more careful practices and more use of PPE thus, a lower risk of acquiring the infection.[14]

The current study findings should be viewed with respect to the following limitations: First, this study was limited to one hospital, so its findings may not be generalizable to HCWs in other workplaces, however, the current study was conducted to explore the situation in this new area of inquiry. Second, detection of SARS-CoV-2 IgG antibody in a single sample may miss any SARS-CoV-2 infected HCW yet to seroconvert, although this is likely to be minimal.

In conclusion, the IgG seroprevalence among the enrolled HCWs of a tertiary non-COVID hospital in Egypt was 7.9%. The low seropositivity against SARS CoV-2 among HCWs who have not been exposed to COVID-19 patients suggests that we are far behind from herd immunity.

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Key words: COVID-19; seroprevalence; IgG; asymptomatic; health care workers.

Contributions: AM, conceived the study and performed data analysis; MA, contributed to managing the literature searches, study design, data management and writing; AE, EA, MH, DG, contributed in sample collection, processing and analysis of results; MRS, contributed in data management and writing; MO, contributed to managing the literature searches, and writing. All authors shared in writing, drafting, and approving the final manuscript and all approve equal share in the study.

Acknowledgments: The authors are thankful for all study participants.

Clinical trial: The study was submitted to Clinicaltrials.gov under identifier NCT04354792.

Availability of data and materials: The datasets are available upon request.

Conflict of interest: All authors declare that they have no conflict of interest.

Funding: Research grant from Cairo University [N-31-2020] supported this work.

Ethical approval: The Ethical Review Committee in the Faculty of Medicine, Cairo University revised and approved the research with the research ethical approval number: N-31-2020. All procedures for data collection were treated with confidentiality according to Helsinki declarations of biomedical ethics. The researchers obtained written informed consent directly from each HCW included in the study before data collection, and after explaining the study objectives and importance. All administrative permissions were obtained from the hospital manager and the heads of the included departments.

Received for publication: 6 January 2021.
Accepted for publication: 6 March 2021.

Journal of Public Health Research 2021;10:2102
doi:10.4081/jphr.2021.2102

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