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Sero-prevalence of anti-SARS-CoV-2 antibodies among healthcare workers: A multicenter study from Egypt



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ABSTRACT

Background: Healthcare workers (HCWs) are at a high risk for disease exposure. Given the limited availability of nucleic acid testing by PCR in low resource settings, serological assays can provide useful data on the proportion of HCWs who have recently or previously been infected. Therefore, in this study, we conducted an immunologic study to determine the seroprevalence of anti-SARS-CoV-2 antibodies in two university hospitals in Egypt.

Methods: in this cross sectional study, HCWs who were working in SARS-CoV-2 Isolation Hospitals were interviewed. Estimating specific antibodies (IgM and IgG) against SARS-CoV-2 was carried out using an enzyme-linked immunosorbent assay targeting the Spike antigen of SARS-CoV-2 virus.

Results: Out of 111, 82 (74%) HCWs accepted to participate with a mean age of 31.5 ± 8.5 years. Anti-SARS-CoV-2 antibodies were detected in 38/82 (46.3%) of cases with a mean age of 31 years and female HCWs constituted 57.6% of cases. The highest rate of seropositivity was from the nurses (60.5%), and physicians (31.6%) with only (7.9%) technicians. Only 28/82 (34.1%) HCWs reported previous history of COVID-19. We reported a statistically significant difference in the timing of exposure ($p = 0.010$) and the frequency of contact with COVID-19 cases ($p = 0.040$) between previously infected and on-infected HCWs. Longer time of recovery was reported from IgG positive HCWs ($p = 0.036$).

Conclusion: The high frequency of seropositive HCWs in investigated hospitals is alarming, especially among asymptomatic personnel. Confirmation of diseased HCWs (among seropositive ones) are warranted.

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Introduction

Coronavirus disease 2019 (COVID-19), which emerged in Wuhan, China in December 2019, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has become a major global public health concern [1]. On March 10, 2020, COVID-19 had

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been declared a pandemic by the WHO (World Health Organization, 2020) [2].

Health care workers are at exceptionally high risk of infection as they work on the frontline of this pandemic. Assessing the prevalence of infection (either past or recent) among HCWs is valuable in identifying the exposure level and determining the high risk groups [3]. Positive detection of SARS-CoV-2 RNA in nasopharyngeal swab samples, sputum samples or bronchoalveolar lavage samples by reverse transcriptase polymerase chain reaction (RT-PCR) has been used to confirm SARS-CoV-2 infection. Recently, positive detection of IgM and IgG antibodies specific to SARS-CoV-2 has also been recognized as deterministic evidence for confirmed SARS-CoV-2 infection [4,5].

On February 24, 2020, Egypt announced the first case of COVID-19 [6]. In Egypt, from 3 January to 26 May 2021, there have been 256,124 confirmed cases of COVID 19 with 14,807 deaths reported to WHO [7]. The infection proportion among HCWs in Egypt was reported in earlier reports ranging from 3.7% to 20% in different healthcare settings [8–11], with anticipated underestimation of the total number of cases, as clarified by the Egyptian health authorities [12].

Determining the seroprevalence of COVID19 among HCWs is essential to gain a better understanding of COVID-19's spread across healthcare facilities as well as to evaluate the effectiveness of implementing the health-care associated interventions in the hospital wards. This will enable better establishment of health care place policies and procedures, and probably alleviate the transmission among different healthcare places [13,14]. Therefore, we aimed to determine the sero-prevalence of anti-SARS-CoV-2 antibodies (IgM and IgG) among HCWs at 2 Egyptian isolation hospitals.

Methods

Study settings and design

We conducted a cross sectional study at both Zagazig and Assiut University, Egypt. Data was collected from October 2020 to December 2020. At that time, the health system policy was to admit COVID-19 cases to certain equipped hospitals. The diagnosis of infected cases was done according to the Egyptian national guidelines [15].

Ethical approval

Institutional Review Board (IRB) Committees of Zagazig and Assiut Universities, Faculty of Medicine approved the current work (IRB numbers Zu-IRB #6414-16-9-2020 and 17300453, respectively). An informed written consent was obtained from all subjects. The work was done according to the revised declaration of Helsinki.

Recruitment of the study subjects

This study included 82 HCWs who were working in SARS-CoV-2 Isolation Hospitals either in Zagazig and Assiut Universities during the period from April to June 2020. Enrolled HCWs were asked to fill a data collection sheet. A blood sample was collected for serological assays [16].

We classified the participants into 4 categories [17]:

Mild Illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.

Moderate Illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO₂) \geq 94% on room air at sea level.

Severe Illness: Individuals who have SpO₂ <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%.

Critical Illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Collection of data

Data was collected by a sheet developed after review of literature [18,19]. It included: age, sex, occupation, comorbidities (bronchial asthma, allergic rhinitis, chronic sinusitis, ischemic heart diseases, hypertension, cerebrovascular accidents), duration of work in the isolation hospital, start of work in the isolation hospital, frequency of contact with SARS-CoV-2 patients, the used personal protective equipment (PPE), previous SARS-CoV-2 infection, symptoms SARS-CoV-2 infections, laboratory data at infection time ((complete blood count (CBC), serum ferritin, lactate dehydrogenase, D-dimer, kidney function tests, liver function tests, arterial blood gases) radiological findings at time of infection and the duration of viral shedding at time of infection. The latter is the number of days from the first positive nasopharyngeal sample to the last positive sample based on RT-PCR testing (followed by a negative RT-PCR result on two sequential tests) [20].

Sample collection

All laboratory tests were carried out in the Medical Microbiology and Immunology Departments in Zagazig and Assiut. Five ml blood were collected by venipuncture under complete aseptic conditions. Samples were allowed to clot then centrifuged at 1000 × g for 15 min. Sera were collected and stored at −20 °C. Sera were used to estimate SARS-CoV-2 antibodies.

Detection of SARS-CoV-2 antibodies

Estimating specific antibodies (IgM and IgG) against SARS-CoV-2 was carried out using an enzyme-linked immunosorbent assay (ELISA SARS-CoV-2 IgM/IgG Screen, Imbian Lab, Novosibirsk Regoin, Russia) according to the manufacturer's instructions. It is an indirect two stage ELISA targeting the Spike antigen of SARS-CoV-2 virus.

Data management and statistical analysis

Data were reviewed and cleared for any missing values. Then the participant was categorized according to their reported infection status and comparison of their characteristics were performed. Then analysis of IgG positive cases was performed according to their reported infection status. Lastly, comparison of previously infected participants according to their serological status was performed.

Statistical analyses were performed using IBM SPSS Statistics version 20 (SPSS Inc., Chicago, IL, USA). Categorical data were presented as numbers and percentages and compared by chi-square and Fisher exact tests, while continuous data were reported as means \pm SD and tested for normality using the Shapiro-Wilkes test. When quantitative data is normally distributed student's *t*-test was used while not normally distributed data Mann Whitney test was used. In all statistical tests *p*-value <0.05 was considered statistically significant.

Results

Among the total number (111) of staff members in both hospitals, 82 (74%) accepted to participate. The mean age of participants was 31.5 \pm 8.5 years, a similar frequency of male and females was

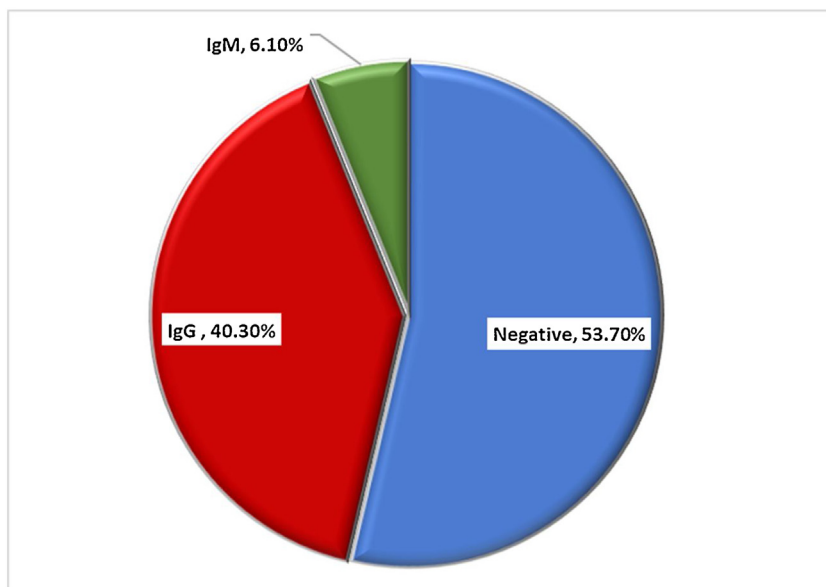


Fig. 1. Seroprevalence of anti-SARS-CoV-2 antibodies among participants (n = 82).

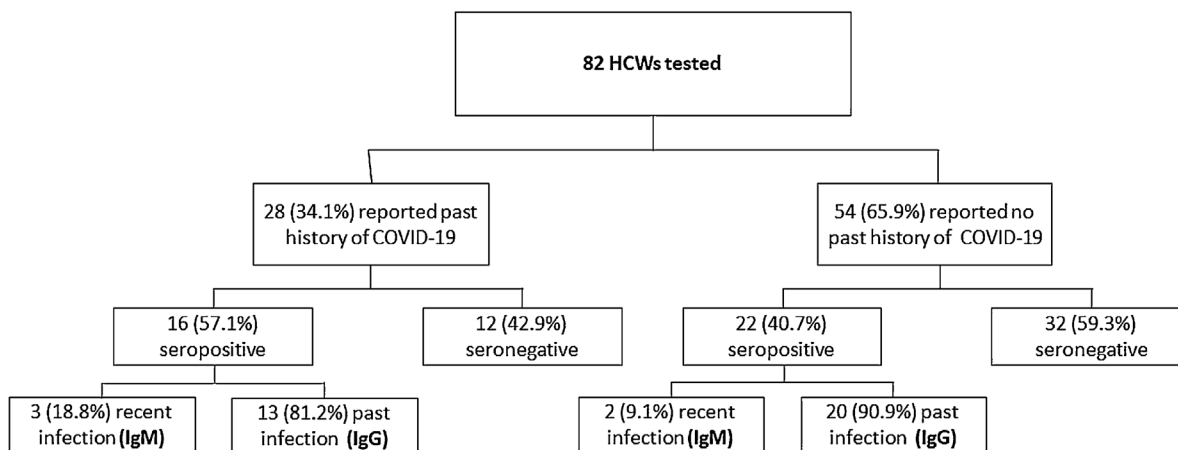


Fig. 2. COVID-19 status of study participants.

reported, and most participants were from the chest department followed by internal medicine and anesthesia departments (45.1%, 31.7%, and 23.2% respectively).

The seroprevalence of anti-SARS-CoV-2 antibodies was demonstrated in Fig. 1, as 53.7% of participants were seronegative, 40.3% IgG positive and 6% IgM positive. Out of 82 HCWs, 28 (34.1%) reported previous COVID-19 during their work at isolation hospitals (Fig. 2).

When we compared between infected and non-infected participants, they were comparable in most of the demographic data. We reported a statistically significant difference in the timing of exposure ($p = 0.010$) and the frequency of contact with COVID-19 cases ($p = 0.040$) (Table 1). Of our study group, there was 17.1% of them have a comorbidity and most reported was hypertension (Fig. 3).

For IgG positive participants, there was a statistically significant difference in occupation of infected and non-infected personnel as physicians were more in infected participant ($p = 0.044$). However, all non-infected participant were worked at isolation hospital from more than 3 months compared to 92.3% of infected group ($p = 0.024$) (Table 2).

Among infected participants, IgG positive group show longer time for symptoms start, recovery time, time from symptoms and recovery to ELISA test but it showed statistically significant differ-

ent from IgG negative group in time of recovery only ($p = 0.036$). There were no differences in clinical data during the course of disease among positive and negative group (Table 3).

Five of study participants (2 physicians, 2 nurses and 1 technician) have IgM antibodies, their age ranged from 24 to 51 years old and 3 of them were males. Three were reported they got infected during their work in isolation hospital and they had recovered from infection 3 months earlier than the current study work. Two of IgM positive HCWs did not with COVID-19 cases and all of them reported a proper use of PPE.

Discussion

Asymptomatic and pre-symptomatic portion of SARS-CoV2 infection is estimated to be up to 30% [21]. In addition, routine testing for antibodies for asymptomatic persons is not usually carried out. This study aimed to evaluate the seroprevalence of anti-SARS-CoV2 antibodies in two university hospitals.

In our report, 34.1% of HCWs self-reported a previous positive COVID-19 status. This rate is higher than earlier reports in Egypt [8–11]. This may be the target group in our report in isolation hospitals, where a higher risk of exposure existed. Earlier

Table 1
Characteristics of participants according to COVID-19 status (n = 82).

	Total (n = 82)	Previously infected (n = 28)	Not infected (n = 54)	p-Value*
Age (years)	31.5 ± 5.2	29.2 ± 5.4	32.6 ± 9.6	0.081
Gender				
Male	42 (51.2%)	12 (42.9%)	30 (55.6%)	0.391
Female	40 (48.8%)	16 (57.1%)	24 (44.4%)	
Work area				
Internal medicine/Tropical	26 (31.7%)	10 (35.7%)	16 (29.6%)	0.340
Chest	37 (45.1%)	11 (39.3%)	26 (48.1%)	
Anesthesia	19 (23.2%)	7 (25.0%)	12 (22.2%)	
Job title				
Physician	32 (39.0%)	15 (53.6%)	17 (31.5%)	0.093
Nurse	47 (57.3%)	13 (46.4%)	34 (63.0%)	
Technician	3 (3.7%)	0	3 (5.6%)	
Any comorbidity	14 (17.1%)	4 (14.3%)	10 (18.5%)	0.826
Serological result				
Negative	44 (53.7%)	12 (42.9%)	32 (59.3%)	0.245
IgM	5 (6.1%)	3 (10.7%)	2 (3.7%)	
IgG	33 (40.2%)	13 (46.4%)	20 (37.0%)	
Start exposure to COVID-19 patients in isolation hospital				
≤3 months from exposure to catching infection	12 (14.6%)	8 (28.6%)	4 (7.4%)	0.010***
>3 months from exposure to catching infection	70 (85.4%)	20 (71.4%)	50 (92.6%)	
Duration of work in isolation hospital				
<2 weeks	16 (19.5%)	3 (10.7%)	13 (24.1%)	0.148
≥2 weeks	66 (80.5%)	25 (89.3%)	41 (75.9%)	
Contact with COVID-19 patients				
No**	10 (12.2%)	3 (10.7%)	7 (13.0%)	0.700
Yes	72 (87.8%)	25 (89.3%)	47 (87.0%)	
Frequency of contact (n = 72)				
Once daily	56 (77.8%)	16 (64.0%)	40 (85.1%)	0.040***
Once weekly	16 (22.2%)	9 (36.0%)	7 (14.9%)	
Distance of contact (n = 72)				
≤2 m	55 (76.4%)	20 (80.0%)	35 (74.5%)	0.599
>2 m	17 (23.6%)	5 (20.0%)	12 (25.5%)	

* Student's T-test, Fisher exact & chi-square test were used.

** Allocated tasks inside the hospital did not necessitate contact with COVID-19 patients.

*** Significant p-value.

studies calculated the rates from HCWs regardless of their workplace nature. A study of COVID-19 infection among HCWs at the gastroenterology department, Al-Manial University Hospital (Cairo University, Egypt) reported that 10/74 (13.5%) tested positive for viral nucleic acid and 9/74 (12.2%) had anti SARS-CoV-2 antibodies [22]. Previous research in developed countries recorded varying infection rates among HCWs. In Germany a study in a large university hospital showed that 52/957 of employees (5.4%) were positive for COVID-19 infection by PCR [23]. A similar frequency was also observed in a study that was carried out in the Netherlands during the early phase of the pandemic in 2 teaching hospitals and involved 9705 HCWs, of which 18% males and 14% females suffered from COVID-19 symptoms and were tested for infection by PCR. About 6% of the suspected employees were positive for COVID-19 which represent 1% of all enrolled HCWs [24]. In Milano (Italy), 138/1573 HCWs (8.8%) showed positive SARS-CoV-2 PCR [25]. A higher rate of infection among HCWs was observed in studies from the Spain where 791/2085 (38%) were positive for SARS-CoV-2 infection [26].

Among the participants, 53.7% were seronegative, 40.3% IgG positive and 6% IgM positive. These results are comparable to those obtained in other studies performed on frontline HCWs, with IgG serology coupled with IgA and/or IgM serology [27,28]. In the current study, 46% of the included, apparently healthy persons were sero-positive for anti-SARS-CoV-2 antibodies (with 6% IgM and 40% IgG). This drives the attention to the possibility of silent transmission of COVID-19. A significant proportion of asymptomatic COVID-19 cases transmitting the SARS-CoV-2 was reported in earlier studies and the relatively high seroprevalence of SARS-CoV-2 infections among frontline HCWs recommend the routine use of screening strategies based on symptoms alone may not be effective in preventing the introduction and spread of SARS-CoV-2 in a hospital setting [29–31].

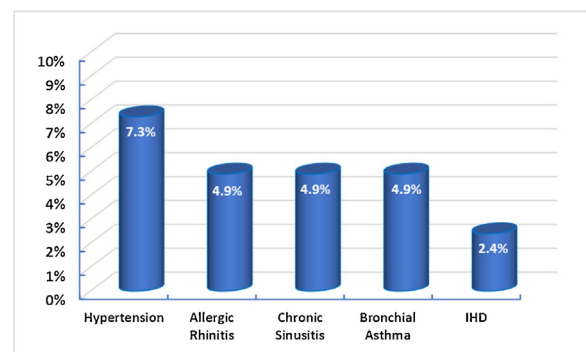


Fig. 3. Distribution of self-reported comorbidities among the studied group (n = 82).

Many studies have investigated the factors associated with SARS-CoV-2 antibody positivity. Similar to our observations, previous studies did not find associations for the proposed variables. Blairon, Mokrane analyzed the serological characters of the HCWs in a 4-site public hospital in Belgium and did not find an association [32]. Similarly, Martin, Montesinos showed that working as a physician/nurse was not a risk-factor for COVID-19 [33]. In New York City, immunologic testing was carried out for HCWs during the pandemic and showed that neither age nor sex was associated with presence of antibodies to SARS-CoV-2 [34]. In Spain, a study on 578 HCWs reported that sex, presence of comorbidities, profession, previous working in SARS-CoV-2 units, daily and close contact with COVID-19 patients were not associated significantly with development of antibodies [27].

Knowing the strength and duration of immunity after SARS-CoV-2 infection would allow a better assessment of individual

Table 2
Characteristics of IgG positive group according to COVID-19 status.

	Total (n = 33)	Previous COVID-19 (n = 13)	No previous COVID-19 (n = 20)	p-Value*
Age (years)	31.2 ± 7.8	28.8 ± 4.0	32.8 ± 9.3	0.151
Gender				
Male	14 (42.4%)	6 (46.2%)	8 (40.0%)	0.727
Female	19 (57.6%)	7 (53.8%)	12 (60.0%)	
Work area				
Internal medicine/Tropical	10 (30.3%)	5 (38.5%)	5 (25.0%)	0.253
Chest	17 (51.5%)	5 (38.5%)	12 (60.0%)	
Anesthesia	6 (18.2%)	3 (23.1%)	3 (15.0%)	
Job title				
Physician	10 (30.3%)	7 (53.8%)	3 (15.0%)	0.044**
Nurse	21 (63.6%)	6 (46.2%)	15 (75.0%)	
Technician	2 (6.1%)	0	2 (10.0%)	
Any comorbidity	3 (9.1%)	1 (7.7%)	2 (10.0%)	0.822
Start exposure to COVID-19 patients in isolation hospital				
≤3 months from serologic testing	3 (9.1%)	3 (23.1%)	0	0.024**
>3 months from serologic testing	30 (90.9%)	10 (76.9%)	20 (100%)	
Duration of work in isolation hospital				
<2 weeks	7 (21.2%)	1 (7.7%)	6 (30.0%)	0.126
≥2 weeks	26 (78.8%)	12 (92.3%)	14 (70.0%)	
Contact with COVID-19 patients				
No direct contact	1 (3.0%)	1 (7.7%)	0	0.208
Direct contact	32 (97.0%)	12 (92.3%)	20 (100%)	
Frequency of contact (n = 32)				
Once daily	24 (75.0%)	8 (66.7%)	16 (80.0%)	0.399
Once weekly	8 (25.0%)	4 (33.3%)	4 (20.0%)	
Distance of contact (n = 32)				
≤2 m	24 (75.0%)	9 (75.0%)	15 (75.0%)	1.00
>2 m	8 (25.0%)	3 (25.0%)	5 (25.0%)	

* Student's T-test & chi-square test was used.

** Significant p-value.

Table 3
Clinical data of previously infected participants.

	Total (n = 25)	IgG negative (n = 12)	IgG positive (n = 13)	p-Value*
Time of symptoms onset after start of isolation work (days)	15.4 ± 11.1	12.3 ± 12.2	17.6 ± 10.3	0.178
Time of recovery (days)	18.0 ± 17.0	10.5 ± 12.2	23.0 ± 18.3	0.036**
Time from symptom start to ELISA test (days)	135.4 ± 61.2	121.6 ± 72.1	145.8 ± 52.5	0.382
Time from recovery to ELISA test (days)	128.5 ± 62.8	115.8 ± 73.3	138.1 ± 55.0	0.435
Self reported symptoms ^a				
Fever	13 (46.4%)	5 (41.7%)	8 (61.5%)	0.320
Cough	6 (21.4%)	1 (8.3%)	5 (38.5%)	0.078
Dyspnea	6 (21.4%)	2 (16.7%)	4 (30.8%)	0.410
Sore throat	14 (50%)	6 (50%)	7 (53.8%)	0.848
Loss of smell and taste	7 (25.0%)	3 (25.0%)	3 (23.1%)	0.910
Myalgia	13 (46.4%)	5 (41.7%)	7 (53.8%)	0.543
Headache	5 (17.9%)	4 (33.3%)	1 (7.7%)	0.109
GIT symptoms	8 (28.6%)	4 (33.3%)	4 (30.8%)	0.891
Self-reported COVID-19 severity				
Asymptomatic	2 (7.1%)	2 (16.7%)	0	0.327
Mild	16 (57.1%)	6 (50.0%)	8 (61.5%)	
Moderate	5 (17.9%)	3 (25.0%)	2 (15.4%)	
Severe	5 (17.9%)	1 (8.3%)	3 (23.1%)	
Isolation place				
Home	21 (75.0%)	9 (75.0%)	10 (76.9%)	0.994
Hospital (ward)	4 (14.3%)	2 (16.7%)	2 (15.4%)	
Hospital (ICU)	3 (10.7%)	1 (8.3%)	1 (7.7%)	
Viral shedding duration (weeks)	2.9 ± 1.4	3.1 ± 1.4	2.8 ± 1.2	0.564

^a Symptoms of past history, Multiple responses were allowed.

* Mann-Whitney & chi-square tests were used.

** Significant p-value.

immune protection and aid in decision making on easing restrictions on physical distancing and wearing of a face mask. Several studies characterizing adaptive immune responses to SARS-CoV-2 infection have reported that most convalescents have detectable neutralizing antibodies, which correlate with the number of virus-specific T cells and decrease within 2 months after infection. Our results showed that IgG was associated with physicians and exposure to COVID-19 patients in isolation hospitals for longer durations (>3 months). Interestingly, Moscola, Sembajwe [35] showed that

self-reporting of high suspicion of SARS-CoV-2 exposure was associated with SARSCoV-2 antibody positivity. Similar observation was also shown by Self et al. [36] and Stubblefield et al. [37] who concluded that self-reported belief of previous SARSCoV-2 infection was associated with seropositivity. Another reported factor that was associated with higher IgG detection was the prolonged contact with patients who work in isolation units of COVID19 [2]. A meta-analysis involving 127,480 HCWs reported that male gender, patient-care related work, working in COVID19 areas to be

associated with seropositivity [38]. Interestingly, in another study higher frequencies were observed among health-care employees who have not contact with patients than that groups with direct patient contact (physicians and nurses) which was attributed to better implementation of the HCWs who has direct patient-care contact [39]. Screening of all workers in health-care facilities and proper training about infection control procedures should be considered even correct donning and doffing of PPE. Further, also the number of experienced symptoms of the COVID-19. Patient group did not correlate with immune response. In this respect, the lack of correlation of the number of symptoms with IgG titers might be explained, but the low number of COVID-19 positive patients in our study population must also be taken into account. This also reported in previous studies [2].

We found no correlation between the viral shedding period and seroprevalence. The same results was concluded by previous study that found a weak correlation between symptoms and viral shedding (viral titers from respiratory tract), despite difficulty of determining precise dates of symptoms onset, especially if the subjects were pauci-symptomatic or with atypical symptoms [21]. These data strengthen current recommendations for expanded screening of HCWs and the universal use of face masks for the whole population in general and HCWs in particular.

Conclusion

The high frequency of seropositive HCWs in investigated hospitals is alarming, especially among asymptomatic personnel. Confirmation of diseased HCWs (among seropositive ones) are warranted.

Limitations of the study

Data collected from participants are self-reported which make it liable to recall bias. The exposure of HCWs outside the hospital cannot be neither ignored nor controlled.

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Competing interests

None declared.

Ethical approval

Not required.

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