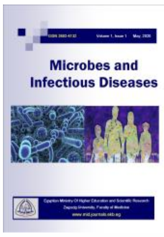
Microbes and Infectious Diseases 2022; 3(4): 842-851



Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Originalarticle

High SARS CoV2 antibody-prevalence among health care workers with variable exposure to COVID-19 patients: A cross-sectional university hospital study

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ARTICLE INFO

Article history:
Received4July2022
Received in revised form 4September2022
Accepted4 September 2022

Keywords:
COVID-19
HCWs
Egypt
Asymptomatic

ABSTRACT

Background: During the COVID-19 pandemic, the pattern of medical services changed to minimize transmission to health care workers (HCWs) or hospitalized patients. Despite the care of COVID-19 patients in a special ward, new cases are accidentally discovered. This study aimed at determining the antibody seroprevalence among asymptomatic HCWs and the associated risks. **Methods:** The study involved 190 participants, including physicians, nurses, technicians, and administrative staff. All were inquired for sociodemographic, specialty, previous isolation, and previous infection, and their blood was tested for SARS-CoV2 antibody. **Results:** Of 190 HCWs; 72,1% were females, the mean age was 32.6±7.9 years, 10.5% were smokers, and 15.8% reported co-morbid illness. SARS CoV2 antibodies were found in 68 (35.8%); being IgG, IgM and both IgM and IgG in 47 (69.1%), 10 (14.7%) and 11 (16.2%) participants respectively. The prevalence was higher (47.6%) among HCWs of the COVID unit, [OR=1.7 (95% CI: 0.69-4.3)] and HCWs with previous COVID-19, OR:1.61 (95% CI:0.88-2.94). The prevalence was significantly lower among smokers (p=0.049), OR:0.29 (95% CI:0.08-1.01), and significantly higher in HCWs who recalled cough (p=0.036) OR: 1.97 (95% CI: 1.05-3.69). The likelihood of antibody seropositivity increased in technicians [OR:2.02 (95% CI: 0.92-4.44)], followed by physicians [OR:1.7 (95% CI: 0.7-4.33)] while the odds ratio was low among nurses [OR:0.58 (95% CI: 0.32-1.07). **Conclusion:** A considerable proportion of antibody positive HCWs had evidence of past SARS CoV2. Provision of adequate personal protective equipment and periodic screening of HCWs are urgently needed to lessen the transmission within the health care settings.

Introduction: COVID-19 is a disease caused by a newly emerging human coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). The disease started in Wuhan, China, in late 2019 and within a few weeks involved most of the world [1].

Healthcare workers (HCWs) in the COVID-care units are at a high risk of infection compared to their colleagues in the other health care

DOI:10.21608/MID.2022.148952.1341
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unitsand individuals in the community [2]. Following the discovery of COVID cases by mid-March 2020, the Egyptian Covid-isolation hospitals adopted policies to protect their HCWs including the provision of adequate personal protective equipment (PPE), two-week-shift-system, periodic checking for symptoms, and subsequent screening for infection by nasopharyngeal swab for SARS CoV2-RNA or antigen. Moreover, strict infection control measures are followed [3]. Meanwhile, HCWs in non-COVID care units use less strict measures and contact with their family after daily work. The possibility of being infected from undiagnosed asymptomatic or pre-symptomatic patients or from the community is not remote [4].

In Suez Canal University Hospital, all patients admitted to the intensive care units or planned for surgery were initially screened for SARS COV2 infection. However, patients admitted to the other non-COVID wards were screened only if they show any manifestations suspicious of infection.

Despite occasional reporting of manifest COVID-19 cases among hospitalized patients and HCWs, a considerable proportion of mild, or asymptomatic cases were frequently reported. The lack of adequate disposable PPE and shortage of facilities for screening by nasal swab test for SARS CoV2 could be the underlying cause of unrevealing such cases that increase the spread of infection to the HCWs, patients, as well as their families [5,6].

In the health care settings, testing for the antibodies against SARS-Cov2 antigens can provide evidence of previous infection and immunity. In many reports, the antibody-prevalence ranged from 1.7% to11% and in a considerable proportion of such cases (38 to 48%), no symptom was reported [7-9].

As little is known about the prevalence of COVID-19 in Suez Canal University Hospital (SCUH), this study aimed to determine the seroprevalence of anti-SARS-CoV2 antibodies among HCWs at different workplaces and to identify factors that increase the likelihood of seropositivity.

Participants and Methods

This cross-sectional study included 190 HCWs from 12 different disciplines; one COVID-isolation unit and 11 other clinical settings (diagnostic, outpatient, emergency, in-patients) and administration.

Sample size

Calculation of the sample size was done using Raosoft sample size calculator [10] taking into consideration the following: a margin of error of 5% and confidence level of 95%, an eligible population of 1500 HCWs, an attack rate of COVID-19 of 11.7% within the HCWs [11]. The sample size was 144 and increased to 190 to compensate for possible dropout.

Selection of the target population

All the studied HCWs were selected from the different health care units of SCUH using systematic random sampling.

Inclusion and exclusion criteria

The work was carried out between March and June 2021, corresponding to late wave 2 and early wave 3 of the COVID pandemic in Egypt. All the HCWs were eligible including HCWs in the COVID-isolation units, the other clinical departments, the diagnostic units, and the administration staff. However, the study excluded individuals who had evidence of confirmed SARS CoV2 infection, were vaccinated or were suffering from manifestations suspicious of COVID-19 at the time of the interview.

Methodology

The study was approved by the Research Ethical Committee of the Faculty of Medicine, Suez Canal University (approval No.: 4481). The objectives and benefits of the study were explained to each HCW before approval and assigning written informed consent. All participants were inquired for the following: their sociodemographic data, co-morbid illness, previous care or exposure to COVID-19 cases, and previous isolation for being a contact of confirmed COVID-19 cases within the family or workplace previous experience of manifestations suspicious of COVID-19.

Screening of SARS CoV2 infection

Blood samples from participants were collected in BD vacutainer serum tubes. After centrifugation serum was collected and analyzed as soon as possible and in case of delayed analysis sera were stored at – 20°C.SARS CoV2 qualitative test was first done to diagnose antibody seropositive individuals . In sera of the later group A rapid test was done to detect IgM and/or IgG antibodies. antibodies were tested using the Elecsys anti-SARS-

CoV-2 assay on the Cobas e411(Roche Diagnostics) for the qualitative detection of antibodies to a recombinant protein representing the nucleocapsid (N) antigen in a double-antigen sandwich electrochemiluminescence immunoassay, which favors detection of high- affinity antibodies against SARS-CoV-2.

Study outcomes

The previous possibility of COVID-19 is considered if a HCW recalled two or more symptoms suggestive of infection with SARS CoV2. In absence of vaccination, past infection is suggested if IgG is positive while ongoing or resolving infection is considered if the candidate is positive to IgM or both IgM and IgG.

Statistical analysis

Patients were stratified according to clinical suspicion of COVID-19 and seropositivity to anti-SARS CoV2 antibodies. Continuous variables were presented as a range, mean, and standard deviation and categorical data were presented as numbers and percentages. Groups were compared by unpaired t-test for continuous data and by a Chi-square or Fischer's exact test for categorical data. The odds ratio was calculated for the estimation of risk with a 95% confidence interval. The *p*-value was considered significant if less than 0.05.

Results

This study included 190 HCWs; their mean age was 32.6±7.9 years; 137 (72.1 %) were females, 138 (72.6 %) were married and 66.9% were living in urban areas. Of all, 20 (10.5%) were active smokers and 30 (15.8%) recalled co-morbid chronic disease; mainly hypertension in 12 (6.3%) and diabetes mellitus in 8 (4.2%). The studied population was 21(11.1%) physicians, 119 (62.6 %) nurses, and 30 (15.8%) technicians working in three diagnostic departments (laboratory, radiology, and endoscopy units) and 20 administrative staff workers (10.5%).

The overall prevalence of antibody seropositivity was 35.8% (68/190). IgG, IgM, and combined IgM and IgG were positive in sera of 47 (24.74%), 10 (5.32%), and 11 (5.79%) of the participants respectively. Among 78 HCWs who recalled a history of two or more symptoms suggestive of previous COVID-19 infection, antibody positivity was encountered in 33 (42.3%).

Two or more symptoms were present in, 26/47 (55.3%) IgG positive, 2/10 (20%) IgM positive, and 5/11 (45.5%) seroreactive to both IgM and IgG.

Antibody prevalence was higher [47.6% (10/21)] of HCWs in the COVID-Care unit compared to 34.3% (58/169) of the other clinical units, p=0.23, [OR=1.7 (95% CI: 0.69-4.3)]. The prevalence was high among technicians working in the diagnostic units (50%) and physicians (47.6%), and less frequent in nurses (31.1%), and the administrative staff (30%), (p>0.05) **(Table 1).**

The prevalence of antibodies among workers in the diagnostic units was in the radiology staff (66.7%) compared to the laboratory (38.9%) and endoscopy unit (30.8%). In the non-COVID clinical wards, the prevalence varied in different specialties and settings; being 60% in family medicine, 57.1% in gynecology and obstetrics, 40% in the outpatient clinics, 36% in pediatrics, 26.7% in internal medicine and least in the emergency department (18.8%) **(Figure 1).**

The study also shows the previous isolation of 46/190 (24.2%) studied HCWs following exposure to confirmed COVID-19 cases; 4/12 (33.3%) in the COVID-care unit and 42/178 (23.6%) from the other departments (p=0.44). A month or more before the study, HCWs recalled fever, cough, difficulty in breathing, body aches, fatigue, diarrhea, loss of smell in 30.5%, 31.6%, 18.9%, 37.4%, 14.7%%, 17.9%, and 19.5 % respectively. Of 78 who had two or more symptom suggestive of previous COVID-19, 33 (42.3%) were antibody positive compared to 35 of 112 (31.3%) asymptomatic participants (p=0.127). The type of immune globulins in both groups is shown in **table (2).** The probability of antibody seropositivity increased with having two or more symptoms [OR 1.61 (95% CI =0.88-2.94], history of diarrhea [OR 2.37 (95% CI =1.05-5.35)], loss of smell [2.06 (95% CI =0.97-4.36)], cough [1.97 (95% CI =1.05-3.69)], dyspnea [1.57 (95% CI =0.75-3.28)], body aches [1.56 (95% CI =0.85-2.87)] and fever [1.1 (95% CI=0.6-2.17)]. The differences in the prevalence of antibody seropositivity in relation to these symptoms were not significant except for that of cough (p=0.036).

Among the job category of HCWs, technicians working in the diagnostic units had the highest probability of SARS CoV2 antibody seroreactivity [OR=2.02 (95% CI =0.92-4.44)], followed by physicians [OR=1.7, (CI=0.7-4.33)]. On the other hand, nurses were associated with a low likelihood of seropositivity [OR=0.58 (CI= 0.32-

1.07)]. It is worth noting that only 15% of active smokers were antibody-positive compared to 38.2% of non-smokers active smoking [OR=0.29, (95% CI=0.08-1.01)], *p*=0.049.

The prevalence of antibody positivity was similar in females (37%) and males (35.8% each), [OR=1 (95% CI= 0.52-1.94)]. [OR=0.29, (95% CI=0.08-1.01)]. The mean age of antibody positive HCWs was significantly higher compared to antibody negative group (34.3±1.0 vs. 31.66±0.67), p=0.025 and antibody seropositivity was more frequent among HCWs ≥40 years (42.3%) compared to <40 (32.5%) [OR=1.8 (95% CI=0.98-3.27), among non-married than married (40.1% and 37% respectively), [OR=1.21 (95% CI=0.61-2.34)] and in HCWs with comorbidity (40%) compared to those without (33.75%), [OR=1.24 (95% CI=0.56-2.75)]. The sero-reactivity to COVID-19 antibody was also more frequent among HCWs who were isolated after contact to confirmed COVID cases (41.3%) compared to others (34%),[OR=1.36, (95% CI=0.7-2.69) **(Figure 2).**

Table 1. Characteristics of the studied health care workers.

	Total	**Seropositive**	**Seronegative**	**OR**	**95% CI**
Age (mean) in years	32.6±7.9 years	34.3±1.0	31.66±0.67**	--	--
Male	53	19 (35.8%)	34 (64.2%)	1.004	
Female	137	49 (35.8%)	88 (64.2%)		0.52-1.94
Married	138	51 (37%)	87 (63%)	1.21	
Non-married	42	17 (40.1%)	25 (59.9%)		0.61-2.34
≥40	97	41 (42.3%)	56 (57.7%)	1.8	
<40	83	27 (32.5%)	56 (67.5%)		0.98-3.27
Smoking	20	3 (15%)	17 (85%)	0.29#	0.08-1.01
Co-morbidity	30	12 (40%)	18 (60%)	1.24	0.56-2.75
Previous isolation	46	19 (41.3%)	27 (58.7%)	1.36	0.7-2.69
Fever	58	22 (36.9%)	36 (62.1%)	1.1	0.6-2.17
Cough	60	28 (46.67%)	32 (53.33)	1.97*	1.05-3.69
Dyspnea	36	16 (44.4%)	20 (55.6%)	1.57	0.75-3.28
Body aches	71	30 (42.25%)	41 (57.75%)	1.56	0.85-2.87
Diarrhea	28	15 (53.6%)	13 (46.3%)	2.37	1.05-5.35
Loss of smell	34	17 (50%)	17 (50%)	2.06	0.97-4.36
≥2 symptom	78	33 (42.3%)	45 (57.7%)	1.61	0.88-2.94
Physicians	21	10 (47.6%)	11 (52.4%)	1.7	0.7-4.33
Nurse	119	37 (31.1%)	82 (68.9%)	0.58	0.32-1.07
Workers in diagnostic units	30	15 (50)	15 (50%)	2.02	0.92-4.44

#*p*= 0.049 *P=0.036 (significant) ***p*=0.025

Table 2. Pattern of anti-SARS COV2 antibodies in relation of clinical suspicious of COVID-19.

	Total	COVID suspect*	Non-COVID-suspect**	*p*-value
IgG	47/68 (69.11%)	26/78 (33.3%)	21/112 (18.75%)	0.12
IgM	10/68(14.7%)	2/78 (2.54%)	8/112 (7.14%)	
IgM and G	11/68 (16.2%)	5/78 (6.4%)	6/112 (5.35%)	

68 antibody seropositive HCWs, 33 with previous COVID symptoms and 35 without*78HCWs reported previous COVID symptoms
**112 HCWs reported no symptoms suggestive of previous COVID

Figure 1. The incidence of anti-SARS CoV2 antibodies among the studied health care according to specialty or workplace.

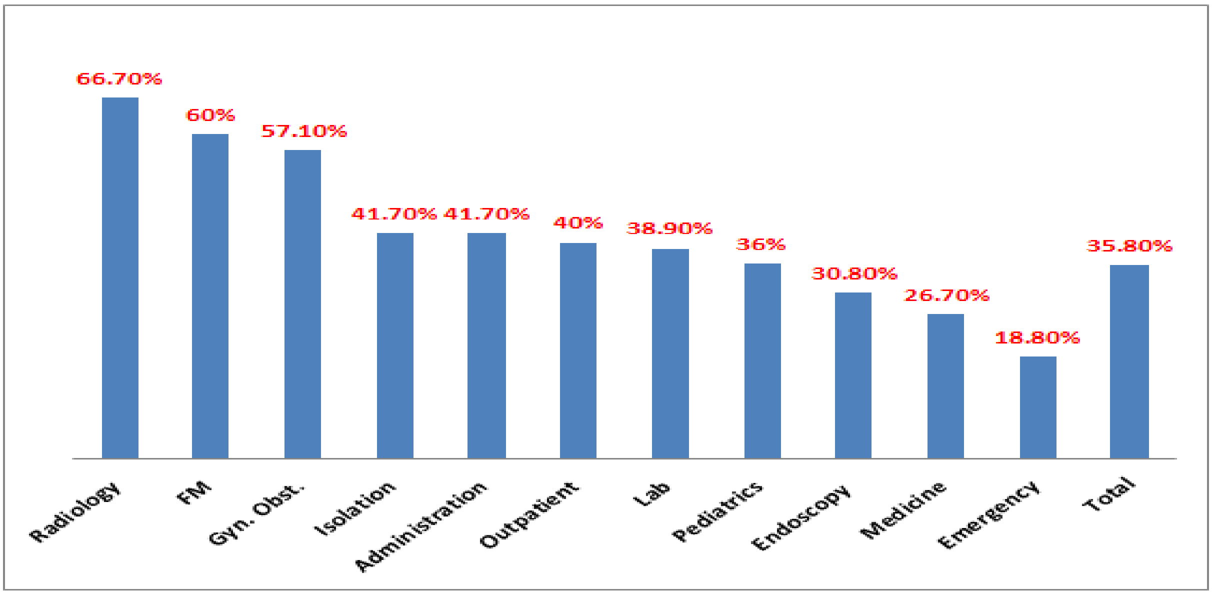
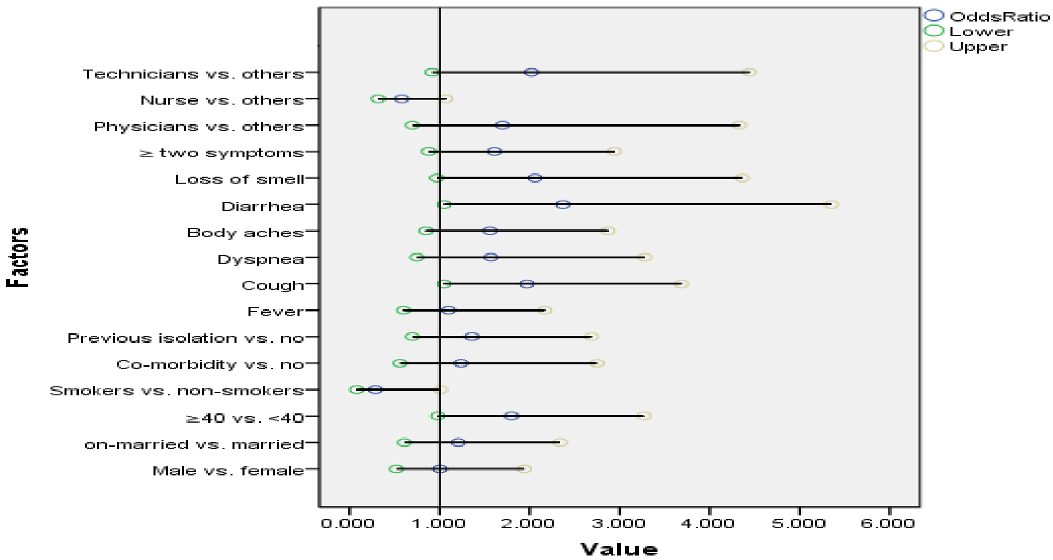


Figure 2. The odds ratio (and 95% confidence interval) of SARS CoV2 antibody positivity in relation to characteristics of the studied HCWs. Only cough was a significant risk factor (*p*=0.036) while smoking was a protective factor (*p*=0.049).



Discussion

This study revealed a high prevalence of antibodies to SARS CoV2 antigen (35.8%) in asymptomatic HCWs in a university hospital in Ismailia City, Egypt. In a non-vaccinated individual, past infection is suggested if IgG is positive while ongoing or resolving infection is interpreted when IgM alone or with IgG is positive [12].

In this study, the majority of antibody-positive HCWs had IgG alone (69.1%) is suggestive of past exposure. Meanwhile, IgM alone or with IgG were found in 30.9%, a finding that might submit an ongoing or resolving COVID infection. This rate of seroconversion reflects the cumulative attack rate in the studied population from mid-March 2020 to the time of the study; early wave 3. In the earlier time of the pandemic, a lower prevalence of seroconversion has been reported. In Cairo University hospitals, the incidence of seroreactivity was lower than ours; being 7.9%, 10.6%, and 11.7% respectively in three reports during wave 1 [11,13,14]. Meanwhile, the incidence of COVID-19 among HCWs also reflects the degree of spread of SARS CoV2 in the population. For example, in Iran, a high rate of seroconversion was reported during the devastating wave 1 with a predominance of IgG antibodies (34%) compared to IgM (5.6%) [15].

Except for HCWs in the COVID-care unit of our hospital, routine screening for COVID-19 was not a policy for asymptomatic HCWs, and the availability of the complete sets of PPE was limited. Furthermore, most of the HCWs in the non-COVID clinical units were exposed daily to their household contacts. At the COVID-care units, HCWs had a two-week-shift followed by a similar duration for isolation before joining their families.

The differences in the seroprevalence of COVID-19 could also be contributed to the test used whether nasal swab PCR or serology, the difference in sensitivity of the serology test, and the use of different study designs [16, 17].

It is worth nothing that our study population did not suffer from any of the manifestations of COVID-19 at the time of the study and none of them had received the vaccination. However, 51.5% of the antibody-positive HCWs did not recall previous symptoms suggestive of the illness. In a COVID-referral hospital in Cairo, more than two-thirds of the antibody-positive HCWs (68.6%) were asymptomatic [11]. Such individuals represent a real risk of transmission to their contacts in the workplace and the community outside. According to the Misnistry of Health, the prevalence of confirmed COVID-19 in the general population is far below that revealed in HCWs in many reports from Egypt including our study [18]. This could be due to the low rate of screening of the population. Meanwhile, a considerable proportion of COVID cases were diagnosed outside the public health sector.

The community source of SARS-CoV2 transmission could be from a newly admitted infected patient or workers' contacts outside the hospital, while the hospital source could be a colleague or a patient whether asymptomatic or during the pre-symptomatic phase of COVID. Contact of HCWs with their household family or friends is considered a risk factor for COVID-19 infection [19,20,16]. In a report from Omani Hospital, community-acquired transmission was more frequent than workplace transmission; 61.3% and 25.5% respecttively [21]. On contrary, in four British Teaching Hospitals: patients with hospital-acquired SARS CoV2 infection carried more risk of transmission to HCWs and other patients compared to the community-acquired transmission [22].

The current study shows equal seroprevalence of antibodies among male and female HCWs (OR=1); suggesting a similar susceptibility in the same workplace. The same conclusion was also reported in different countries [23,24]. However, the outcomes were reported to be different. Male patients are more likely to be admitted to intensive treatment units and more likely to die [24-26].

The current study also shows a wide range of antibody seropositivity between the studied units of the hospital; being lowest (18.8%) in the emergency unit and highest (66.7%) in the radiology units. In the COVID-care unit, the incidence 41.7%. However, In Saudi Arabia and China, the incidence of seroconversion of HCWs in COVID-referral hospitals was reported to be lower in non-COVID-referral hospitals [27,1]. This could be attributed to more availability of the PPE, periodic screening, better training for personal protection, and strict infection control measures than any other discipline.

In this study, 60% of the studied HCWs at the family medicine clinic were antibody-positive; denoting high exposure to early COVID-19 cases that might be asymptomatic or in the pre-symptomatic phase. Shortage of the PPE facilities is an additional possible factor [28].

During the early phases of the pandemic, the main concern of the surgical departments was limited to emergency cases including delivery. However, this study revealed high antibody seropositivity (57.1%) in the HCWs in the department of gynecology and obstetrics. This could reflect the magnitude of asymptomatic COVID pregnant ladies at delivery; a finding that was also reported in two hospitals in the USA[29,30].

In this study, the highest odds ratio for antibody seropositivity was found in technicians [OR: 20.2 (95% CI:0.92-4.44], followed by physicians [OR: 1.7 (95% CI:0.7-4.33] while that of nurses [OR:0.58 (95% CI:0.32-1.07] could be considered as protective. However, none of these odds ratios were significant. This difference according to the job could reflect the frequency of exposure to COVID-19 cases, the closeness between patients and the health care providers, and the time spend during practice. The high antibody seropositivity in physicians compared to nurses was also reported by other studies [1,15,21], In Belgium, the overall seroprevalence was 7.6% among HCWs of a public hospital with a higher seroprevalence in nurses (10.0%) than in physicians (6.4%), paramedical (6.0%), and administrative staff (2.9%) [31].The high prevalence of antibody reactivity among technicians working in our radiology unit (66.7%) was also reported in a German hospital; where most of the imaging done was X-ray chest and CT lung [32].

This study also emphasizes the importance of history taking in the prediction of seroreactivity to SARS CoV2 antigens. The combination of two or more symptoms also predicts antibody reactivity (OR: 1.61). The likelihood of antibody positivity was highest if there is diarrhea (OR: 2.37), loss of smell (OR: 2.1), cough (OR: 1.97), dyspnea (OR: 1.57), and body aches (OR: 1.56). The least likelihoods were for fever (OR: 1.1). The differences in the odds ratio for antibody seropositivity concerning these symptoms were not statistically significant except for that of cough (p=0.036) which could be considered as a risk factor for SARS CoV2 infection.

In this study, the prevalence of antibody seroreactivity was significantly lower among smokers compared to non-smokers (15% vs. 38.2%, p=0.049) with an odds ratio of 0.29, (95% CI=0.08-1.01). The same finding was also reported by other report. However, the impact of smoking on the severity of COVID-19, which is not our topic, is unsettled and shows great debate[33,34,35].

Conclusion

A considerable proportion of antibody-positive HCWs had evidence of past SARS CoV2 infection while asymptomatic ongoing or resolving infection was not uncommon. Periodic screening of HCWs is urgently needed to lessen the source of transmission within the health care settings. Further study with a different design is recommended to determine the source of infection whether community or health care related.

Limitations of the study

Recall of symptoms suggestive of previous COVID-19 over a long time may lead to recall bias. Apart from loss of smell and diarrhea, these symptoms are non-specific. Furthermore, the study did not focus on the source of infection, hospital or community acquired whether for the past one or that discovered during the study. The study revealed significantly lower odds ratio of antibody seroreactivity among current smokers. However, this result could not be generalized due to their small number.

Conflict of interest

The authors declare no conflict of interest.

Funding:

The study was funded by the contributing authors.

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