

Seroprevalence of Anti-SARS-CoV- 2 Antibodies among Health Care Workers: Kasr Al Ainy Screening Study

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Abstract

Background: Egypt is affected by the COVID-19 pandemic in all aspects of life: Health, economy and socially. Serological survey for SARS-CoV-2 antibodies is a valuable method to assess the extent of spread of the pandemic especially in healthcare workers (HCW), and to detect asymptomatic cases.

Aim of Study: This research aims at proving the usefulness of SARS-CoV-2 antibody detection to identify and isolate infected individuals among HCW. Results may be employed as a surrogate to economize the use of RT-PCR evaluation and to make executive decision limiting viral spread among medical personnel in Kasr Al Ainy hospitals.

Material and Methods: This cross-sectional survey study has included 897 HCW from multiple frontline and susceptible services within Kasr Al Ainy, Cairo University Hospitals. HCW were subjected to wide screening to study the presence of SARS-CoV-2 specific antibody responses (IgG and IgM) by Electro-chemiluminescence immunoassay tests and Lateral Flow Immunochromatographic assay (Rapid detection test) kits.

Results: Our screening program has revealed 105 positive cases which accounts for 11.7% of the screened group. Of those, 33 (31.4%) were symptomatic and 72 (68.6%) were asymptomatic.

Conclusion: The use of COVID-19 antibody testing for HCW can provide crucial information that might prevent further propagation of infection among HCW and their patients. Further research is warranted to provide evidence related to wide implementation of screening programs for HCW and to provide clear guidelines related to specifics of such programs.

Key Words: SARS-CoV-2 antibody – Healthcare workers – Electro-chemiluminescence immunoassay – Rapid detection test – RT-PCR – Egypt.

Introduction

SINCE December 2019, Corona virus disease 2019 (Covid-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly escalated into a world pandemic affecting more than 88 million persons and claiming the lives of more than 1.9 million victims globally [1]. SARS-CoV-2 was first detected in Egypt in February 2020, spreading to reach 146,809 confirmed cases and 8,029 deaths by January 2021.

Health care workers (HCW) are especially vulnerable to being infected in their working environment, with the fact that access to Personal Protective equipment differs significantly on national and international scales. The infection of HCW is troubling because they can spread the infection among patients in clinical settings. In addition, loss of work force during this health crisis can lead to reduction of the healthcare system capacity [2].

The molecular testing methods are considered one of the standard methods for diagnosing Covid-19 [3]. However, molecular testing is not perfect, requiring certified laboratories, expensive equipment, and trained personnel. More important, the results have the possibility of being false negative; with 93% positivity rate in bronchoalveolar lavage, 72% in sputum, 63% in nasal swab, 46% in bronchoscope brush biopsy, and 32% in pharyngeal swab [3,4].

Antibody testing can be considered as an important strategy in the diagnostic toolbox for Covid-19 [5-9], being simple, fast, easy in sampling and

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cost-effective thus reducing the pressure on the more expensive molecular testing reserving it to critical patients [3]. Moreover, antibody testing complements molecular testing for the diagnosis of suspected cases with negative molecular testing results. It is also important in surveying for asymptomatic infection in close contacts [10].

Gaining experience in managing resources and protecting HCW would be extremely valuable not only in epidemiological context but for potential use of antibody testing on larger scales [11,12].

Our work aimed at proving the usefulness of SARS COV2 antibody detection to identify and isolate infected individuals among HCW and to use results as surrogate to economize the use of RT-PCR evaluation and to make executive decision to limit the viral spread among medical personnel working in an academic center of excellence.

Material and Methods

Study design:

This cross-sectional study has included 897 HCW in multiple facilities of Kasr Al Ainy Cairo University Hospitals, Egypt. The study protocol was approved by the institutional ethical committee (according to the WMA Declaration of Helsinki).

All HCW recruited signed an informed consent form. They also answered a questionnaire to provide demographic data; clinical information related to known risk factors as well as multiple health indices and certain key symptoms and signs. A single blood sample of 5ml was drawn in sterile vacutainer. All HCW were tested using both Electro-chemiluminescence immunoassay and Lateral Flow Immunochromatographic assay (Rapid detection test) (RDT) kits and tests were performed under strict biosafety conditions.

Serological testing for SARS-Cov-2 specific antibodies by:

1- Elecsys® (Roche diagnostics, Switzerland) Anti SARS CoV 2 immunoassay intended for qualitative detection of antibodies to SARS CoV 2 in human serum and plasma (according to manufacturer's instructions). This technique is associated with sensitivity of 65.5% (0-6 days); of 88.1% (7-13 days); 100%, and 99.81% specificity (14 days onwards) [13].

2- Artron® Laboratories Inc. (BC, Canada) one step Covid-19 IgM/IgG antibody test: (According to manufacturer's instructions). Detection of IgM and IgG antibodies for SARS-CoV2 was performed using the One Step Novel Coronavirus (Covid-19) IgM/IgG Antibody Test (Artron, Burnaby, Canada).

The test is associated with 93.4% sensitivity and 97.7% specificity [13].

Statistical analysis:

Continuous variables were expressed as the mean \pm standard deviation (SD) categorical variables were described as the count (%). All analyses were done with SPSS Statistics software (version 23.0). A two-sided *p*-value of less than 0.05 was considered statistically significant. Comparison of numerical variables was done using unpaired *t*-test. For comparing categorical data, chi square test was performed.

Results

Demographic data, risk factors and clinical manifestations of the study group are shown in Table (1).

The screening program of serological testing of 897 HCW has revealed that 105 (11.7%) HCW were positive for virus-specific antibodies while the remaining 792 (88.3%) were negative. Comparison between the positive and negative SARS-CoV-2 specific antibodies HCW groups regarding demographic data, risk factors and clinical manifestations revealed statistically significant difference concerning; age (*p*-value=0.045), fever (*p*-value=0.011), dyspnea (*p*-value <0.001), cough (*p*-value=0.009), and diabetes (*p*-value=0.035) (Table 2). The vast majority of the positive group were asymptomatic 72 (68.6%) while the rest 33 (31.4%) reported at least one of the following symptoms, namely dyspnea, cough or fever.

Among the positive 105 HCW; 64 (61%) were positive for virus specific antibodies by both Electro-chemiluminescence immunoassay and RDT techniques, 39 (37.1%) cases had positive virus specific antibodies with RDT only while testing negative with Electro-chemiluminescence immunoassay. Only two cases (1.9%) tested positive with Electro-chemiluminescence immunoassay while providing negative results with RDT. Regarding the positive HCW screened by RDT, 52 (50.5%) had positive IgM antibodies only, 13 (12.6%) had positive IgG antibodies only while 38 (36.9%) tested positive for both IgG and IgM.

Patients who tested positive with serological tests were referred to the infection control unit. They were advised to self-isolate and RT-PCR testing was proposed. 85 subjects out of the 105 who tested positive accepted to undergo RT-PCR. Among those 85 SARS Cov2 specific antibodies positive cases; 44 (51.8%) tested positive and 41 (48.2%) tested negative with RT-PCR.

Table (1): Demographic data, risk factors and clinical manifestations.

Characteristics	Study group (n 897)
Age (years)	38.7±11.3
Males	387 (43.14%)
Diabetes	81 (9.0%)
Hypertension	118 (13.1%)
Obesity	100 (11.1%)
Asthma	57 (6.3%)
Fever	80 (8.9%)
Cough	140 (15.6%)
Dyspnea	85 (9.4%)

Table (2): Comparison of the demographic data, risk factors and clinical manifestations between the positive and negative SARS-CoV-2 specific antibodies HCW groups.

	Positive group (n 105)	Negative group (n 792)	p-value
<i>Sex:</i>			
Male	40 (38.1%)	347 (43.8%)	0.223
Female	65 (61.9%)	445 (56.2%)	
Age (Mean ± SD)	41.01 ± 11.02	38.57 ± 10.95	0.045
Diabetes	17 (16.2%)	72 (9.1%)	0.035
Hypertension	19 (18.1%)	110 (13.9%)	0.271
Obesity	19 (18.1%)	90 (11.4%)	0.06
Fever	18 (17.1%)	70 (8.8%)	0.011
Sore throat	32 (30.5%)	215 (27.1%)	0.139
Cough	28 (26.7%)	125 (15.8%)	0.009
Dyspnea	23 (21.9%)	71 (8.9%)	<0.001

p<0.05 is statistically significant.

Discussion

Healthcare workers always play a critical role not only in the clinical management of patients but also in maintaining adequate infection prevention and control measures in health care facilities [14]. The main way to limit spread of the virus is to rapidly diagnose disease, isolate infected personnel and maintain contact tracing methods [15,16]. Serological assays are now being developed as a screening tool for population based serosurveys and detection of past infection [17].

In this study, 105 (11.7%) of the 897 screened HCW tested positive for SARS-CoV-2 specific antibodies. Of those, 33 (31.4%) were symptomatic and 72 (68.6%) were asymptomatic. This agrees with multiple published reports that have concluded that the numbers of asymptomatic Covid-19 cases are significant and ranges from 51.7% in one report, to 87.9% in another. The advantage of detecting such cases is clear, asymptomatic subjects seem to account for a significant percentage of SARS-CoV-2 infections, approximately half of patients according to published reports [18-28].

On the other hand, in a study by Khalil et al., [29], 266 HCW were tested using RT-PCR and 18% were found to be positive; of these 66% were symptomatic and 34% were asymptomatic. Hunter et al., [2], screened symptomatic HCW in their establishment, also using RT-PCR, and reported 14% positives out of 244 screened subjects. Worthy of note, that in our study we offered our screening program to most frontline subjects without specifically targeting symptomatic cases.

RT-PCR assay is one of the standard methods in diagnosing SARS-CoV-2. The method nevertheless has a relatively high percentage of false-negative results. This can be due to issues inherent to the method, to sample collection and transportation among other things [30].

Testing for antibodies to screen subjects has obvious advantages over RT-PCR [31,32]. The tests do not require highly trained individuals to perform, do not need expertise in reading results, do not require sophisticated and expensive equipment and can be performed in a significantly shorter period [11]. Blood samples for antibody testing are significantly more accessible than nasopharyngeal swabs, which would inherently offer a clear advantage. For all these reasons we have chosen to employ the antibody screening strategy for our HCW.

In addition to such clear advantages, some cases that are detected by antibody screening may test negative with RT-PCR. This could be due to errors related to sampling and transport or could simply be time sensitive, where RT-PCR has been performed in a period within the natural history of the disease that corresponds to high potential of negativity. This in essence denotes that RT-PCR and serological testing can be complementary and that their potential value depends on the period of testing after onset of symptoms.

In this study, 41 out of 85 (48.2%) HCW tested positive for SARS-Cov-2 Abs but showed negative results by RT-PCR this is in accordance with a study by Long et al., [10], where 164 close contacts of patients of Covid-19 were screened, out of those 13 symptomatic individuals were confirmed positive for the disease by RT-PCR. 3 other asymptomatic individuals were confirmed positive by RT-PCR. 148 individuals were both asymptomatic and tested negative with RT-PCR, out of those 7 were found to have virus specific IgG and/or IgM. They thus noted that 4.3% of close contacts were missed with RT-PCR. They concluded that the role of serological testing is important in estimating the extent of the disease pandemic in certain populations.

It is worthy of note that in one published report, RNA detectability decreased from 66.7% in samples collected before day 7 to 45.5% during day 15-39, while the presence of antibodies was <40% among patients within 1-week since onset, and rapidly increased to 100.0% (Total Ab), 94.3% (IgM), and 79.8% (IgG) 15 days after onset of symptoms [3].

In an ideal situation, a screening program should include both RT-PCR and antibody testing. This is because different methodologies are sensitive in different time periods during the disease progression and taking in consideration that screening programs specifically strives to detect asymptomatic cases, it goes without saying that employing multiple screening tools would increase the efficiency of such programs.

Our screening strategy detects the presence of SARS-CoV-2 specific antibody responses (IgG and IgM) by Electro-chemiluminescence immunoassay tests and RDT kits. This goes with the recommendations of the Centers for Disease Control and Prevention (CDC) (the Interim Guidelines for Covid-19 Antibody Testing Updated in Aug. 1, 2020) which suggested that to improve positive predictive value of the testing strategies, persons who initially tested positive are to be tested with a second test, each with unique design characteristics.

In sight of the above mentioned, the attention should be drawn to the pivotal role of screening programs of HCW. Detecting and isolating asymptomatic HCW, the majority of positive cases in our series, should reduce significantly viral spread among HCW and among their highly susceptible patients. This has the potential to maintain more numbers of HCW within the workforce, and potentially reduces the disease severity of infected cases, as care would be offered at an earlier stage, and reduces overall disease burden in the community.

Reducing transmission is of paramount importance in situations where necessary equipment might be in dire need. Multiple studies have also mentioned that such screening programs provide psychological and moral support to HCW, who feel that their leadership is taking their welfare seriously.

Refining the understanding of how to employ antibody screening for HCW, would also potentially offer us a pragmatic tool by which HCW would be repeatedly screened during the peak period of the pandemic, to give us a better measure of our success in employing infection control strategies [33].

Conclusion:

We should not ignore the fact that we are facing a pandemic that gripped the world vigorously. Our work draws the attention to the importance of screening programs for HCW as an indispensable tool in limiting viral propagation. To perfect screening programs and refine tools to augment their value, further longitudinal trials seem to be essential. Researchers around the world are developing vaccines against SARS-CoV-2 but many concerns have emerged concerning antibody testing regarding the recommendation to get antibody test before and/or after receiving the vaccine and the necessity of vaccination in presence of a high antibody titer. All these inquiries are opening the field to many upcoming research involving antibody testing.

Declarations:

- *Ethics approval and consent to participate:*

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Cairo University, Cairo, Egypt. All participants signed a written informed consent.

- *Competing interests:*

The authors declare that they have no competing interests.

- *Authors' contributions:*

HF provided administrative and supervisory support, participated in the design and revision of the manuscript; MMS participated in the design, in the acquisition, analysis and interpretation of the data; MSH participated in the acquisition, analysis and interpretation of the data; HS and AAT provided administrative support; RJF, RHK, MOFH, HMS and FHA participated in the acquisition, analysis and interpretation of the data; DMRB, RMHS, EEK and NMR participated in the acquisition, analysis, interpretation of the data and in revision of the manuscript; HHT participated in the acquisition, analysis, interpretation of the data and is the corresponding author; HEM provided administrative support; NMHS participated in the design, in the acquisition, analysis, interpretation of the data, wrote and revised the manuscript. All authors read and approved the final manuscript.

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الانتشار المصلي للأجسام المضادة لـ SARS-CoV-2 بين العاملين في مجال الرعاية الصحية : دراسة فحص بالقصر العيني

تتأثر مصر بوباء COVID-19 في جميع جوانب الحياة : الصحة والاقتصاد والمجتمع يعد المسح المصلي للأجسام المضادة لـ CoV-2-SARS طريقة قيمة لتقييم مدى انتشار الوباء خاصة في العاملين في مجال الرعاية الصحية، واكتشاف الحالات التي لا تظهر عليها أعراض.

يهدف هذا البحث إلى إثبات فائدة اكتشاف الأجسام المضادة لـ SARS-CoV-2 لتحديد وعزل الأفراد المصابين بين العاملين في مجال الرعاية الصحية. يمكن استخدام النتائج كبديل لأقتصاد استخدام تقييم RT-PCR ولاتخاذ قرار تنفيذي يحد من الانتشار الفيروسي بين العاملين الطبيين في مستشفيات قصر العيني. اشتملت هذه الدراسة الاستقصائية المقطعية على 897 عاملين في مجال الرعاية الصحية من خدمات متعددة في الخطوط الأمامية وحساسة للمخاطر داخل قصر العيني، مستشفيات جامعة القاهرة. خضع المشاركون لفحص واسع لدراسة وجود استجابات الأجسام المضادة المحددة لـ SARS-CoV-2 (IgM و IgG) عن طريق اختبارات المقاييس المناعية للتلاؤل الكيمياء الكهربية ومجموعات مقاييس مناعة عن طريق التدفق الجانبي اختبار الكشف السريع. كشف برنامج الفحص لدينا عن 105 حالة إيجابية تمثل 11.7٪ من المجموعة التي تم فحصها. من بين هؤلاء، كان 33 (31.4٪) يعانون من الأعراض و 72 (68.6٪) بدون أعراض. يمكن أن يوفر استخدام اختبار الأجسام المضادة لـ COVID-19 للعاملين في مجال الرعاية الصحية معلومات مهمة قد تمنع المزيد من انتشار العدوى بينهم وبين مرضاهم. نوصي بإجراء مزيد من البحث لتقديم أدلة تتعلق بالتنفيذ الواسع لبرامج الفحص الخاصة للعاملين في مجال الرعاية الصحية ولتوفير إرشادات واضحة تتعلق بتفاصيل هذه البرامج.