Assessment of Rapid SARS-CoV-2 Testing with Lateral Flow Immunoassay among Asymptomatic Healthcare Workers in Makati Medical Center

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Authors' contributions

This work was carried out in collaboration among all authors. Authors CLMB and EHBS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author JPON managed the analyses of the study. Author DMS managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aims: Corona Virus Disease-19 (COVID-19) is a global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). While the gold standard for diagnosis is still reverse transcription Polymerase Chain Reaction (RT-PCR), it is not readily available. Serologic testing is considered to be a faster method of identifying individuals who may have been exposed and developed antibodies against SARS-CoV-2.

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Methodology: This was an ambirectional observational study aimed to determine the prevalence of exposure to COVID-19 infection among asymptomatic healthcare workers in Makati Medical Center, a tertiary hospital in the Philippines, using rapid antibody testing (lateral flow immunoassay) in May 2020.

Results: A total of 1557 asymptomatic healthcare workers were included in the study. Majority belonged to the paramedical group (52%). Twenty (1.3%) healthcare workers were IgM positive while 17 (1.1%) tested positive for IgG. Three healthcare workers (0.2%) tested positive for both antibodies. Participants with history of being quarantined who tested positive for either IgM or IgG were significantly higher compared to those who tested negative for both antibodies (55%, 33.3%, 41.2% vs 28.5%, p = 0.036). Those with diabetes had 6.8 times higher risk of being IgM positive and IgG negative (p=0.001). In addition, those with diabetes were more likely (13.6 times) to be positive in both tests (p=0.034).

Conclusion: There was a low prevalence (2.6%) of COVID-19 infection among healthcare workers of Makati Medical Center. Among those with positive serologic test, diabetes mellitus, history of exposure and history of quarantine were risk factors associated with COVID-19 infection.

Keywords: COVID 19; asymptomatic healthcare workers; serologic testing; immunoassay.

ABBREVIATIONS

Corona Virus Disease-19 (COVID-19); rapid antibody test; asymptomatic healthcare workers; lateral flow immunoassay; prevalence.

1. INTRODUCTION

Corona Virus Disease-19 (COVID-19) is a global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Laboratory diagnosis of COVID-19 involves detection of viral nucleic acid using reverse transcription Polymerase Chain Reaction (RT-PCR) or identification of viral antibody using serologic/antibody test. While the gold standard for diagnosis is still RT-PCR, it is not readily available and has a turnaround time of 12-48 hours [1]. Commercially manufactured antibody tests vary in specificity and sensitivity but have the advantage of ease of performing the test, being readily available and can deliver results in 15-20 minutes. This allows faster identification of large numbers of infected patients or asymptomatic carriers thus supporting containment efforts for COVID-19 [2].

Antibodies, also known as immunoglobulins, are proteins produced by the body to neutralize pathogens, such as bacteria and viruses. Antibodies function by agglutinating and precipitating pathogens to promote phagocytosis and complement activation leading to eventual lysis of foreign pathogens [3]. Antibodies are usually produced one to three weeks after infection [4]. Some people, however, may take a longer period of time before developing antibodies.

Serologic tests detect antibodies present in the blood in response to a specific infection. These tests are utilized for diagnosis of previous infection in patients without symptoms. People with active infection usually have no circulating antibodies, thus antibody testing usually is not recommended in this subset of patients [5].

There are several immunodiagnostic methods used for detection of antibodies, usually utilizing antigen-antibody complex. Examples of these methods are ELISA, immunofluorescence, Western blot, immunodiffusion, immunoelectrophoresis, and magnetic immunoassay. With the harsh and severe impact of COVID-19 on global economies and populations, several serologic tests have developed for rapid detection of recent or previous COVID-19 infection. These rapid point-of-care test kits usually utilize lateral flow assays [6]. However, not all test kits are the same and have varying degrees of sensitivity and specificity [7]. Nonetheless, serologic tests play a critical role in the fight against COVID-19 infection by identifying individuals who may have been exposed and developed antibodies against SARS-CoV-2.

The Food and Drug Administration of the Philippines has approved several commercially manufactured antibody test kits for detection of SARS-CoV-2. One of these one step rapid antibody test is the Innovita 2019-nCoV Antibody test which is manufactured by Innovita (Tangshan) Biological Technology Co., Ltd. in China [8]. It is a lateral flow 15-minute immunoassay that detects both IgM and IgG antibodies against SARS-CoV-2 in the blood [9].

The result of this antibody test kit is interpreted as follows:

A) 2019 NCoV-IgM Positive: presence of two purple bands (T and C) within the IgM result window.
B) 2019 NCoV-IgG Positive: presence of two purple bands (T and C) within the IgG result window.
C) Negative: appearance of only one purple band at the control line (C).
D) Invalid: if control line (C) fails to appear whether the purple band is visible or not.

Timely identification of COVID-19 is especially important for healthcare workers who are asymptomatic and run the risk of being carriers of infection. This study aimed to determine the prevalence of exposure to COVID-19 infection among asymptomatic healthcare workers of Makati Medical Center using rapid antibody testing by lateral flow immunoassay. The results of this investigation could provide a useful surveillance strategy for assessing exposure of this population to COVID-19 and should be essential in policy formulations and recommendations regarding screening for COVID-19 infection.

2. METHODOLOGY

This was an observational and ambidirectional study that included all asymptomatic medical staff, trainees (residents and fellows), employees and outsourced personnel who underwent rapid antibody testing with lateral flow immunoassay in Makati Medical Center, a tertiary hospital in the Philippines, from May 12, 2020 to May 31, 2020.

All healthcare workers who underwent rapid antibody testing were invited to participate in the study. All participants who gave informed consent were included in the study and were asked to fill-up a short questionnaire. Participants were categorized into three groups, namely: Medical (consultants, fellows, and residents), Paramedical (nurses, medical technologist, nursing aides, pharmacist, radiology technician, and clerks) and Ancillary (physician's assistants or secretaries, corporate personnel, security guards, office clerks, orderly, facilities and engineering crew).
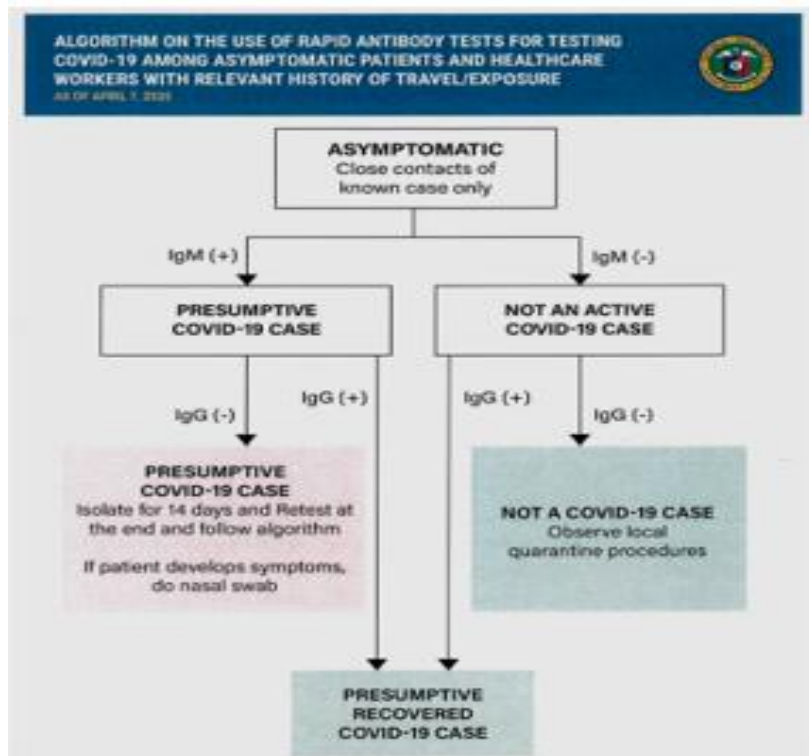

Fig. 1. Algorithm on the use of rapid antibody tests for testing COVID-19 among asymptomatic patients and healthcare workers with relevant history of travel/exposure

This study utilized convenience sampling method [minimum sample size of 423 will give 95% confidence interval with margin of error of 5%]. Study participants were grouped based on the following serologic results: Group A – IgM positive, IgG negative; Group B – IgM positive, IgG positive; Group C – IgM negative, IgG positive: Group D – IgM negative, IgG negative. Those who tested positive for the rapid antibody assay were coordinated with the Infection Prevention and Control Unit (IPCU) for further management and diagnostics. As part of the hospital policy, those who tested positive for antibodies were required to undergo RT-PCR testing.

The disposition of the study participants were based on Administrative Order of the Department of Health 2020-0174 (April 9, 2020) which provided the framework for the use of antibody testing among asymptomatic patients and healthcare workers (Fig. 1).

2.1 Data Analysis

Continuous data were summarized and presented as medians and range. Distribution of categorical data was expressed in frequency and percentages. Fisher-Freeman-Halton analysis (Fisher's Exact for contingency tables larger than 2x2) was used to examine significant association between categorical variables. For variables with significant association, a univariate multinomial logistic regression was used to measure the strength of its association. A p-value of <0.05 was considered statistically significant.

3. RESULTS

A total of 1557 participants were included in the study. The median age was 30 years. Majority of the participants, 1507 (96.8%) were 18-59 years old with only 32 (2.1%) participants aged 60 and above. Participants were mostly females (1084, 69.6%). More than half of the participants belonged to the paramedical group (811, 52.1%), followed by ancillary group (503, 32.3%) and medical group (243, 15.6%). Nearly 56% had known exposure to either suspected or confirmed COVID-19 positive patients. Four hundred fifty-one (29%) participants had a history of being quarantined while only 24 [1.5%] had history of travel. Among the participants, 112 (7.2%) were smokers and 381 (24.5%) were alcohol drinkers. The most common comorbidity was hypertension (144, 9.3%), followed by bronchial asthma (117, 7.5%), diabetes mellitus type 2 (59, 3.8%).

Overall, majority of the healthcare workers (1517, 97.4%) tested negative for IgM and IgG [Group D]. There were 40 (2.6%) participants who tested positive for either IgM or IgG. Twenty (1.3%) participants were IgM positive [Group A] while 17 (1.1%) were IgG positive [Group C]. Three participants (0.2%) were positive for both IgM and IgG [Group B]. The association between type of work and seroprevalence was not statistically significant (p value = 0.844) (Table 2). Only two of 40, tested positive for Sars-CoV-2 RT - PCR (one for Group A and one for Group B).

Table 3 shows the demographic and clinical profile of patients distributed among groups based on seropositivity. Among the demographic data and clinical profiles obtained, only history of being quarantined (p value = 0.036) and diabetes mellitus (p value = 0.003) were significantly associated with seroprevalence. Majority of the participants (1085, 71.5%) who tested negative for both IgM and IgG [Group D] had no history of quarantine. Participants with history of being quarantined who tested positive for either IgM or IgG were significantly higher compared to those who tested negative for both antibodies (55%, 33.3%, 41.2% vs 28.5%, p value = 0.036). Furthermore, diabetic participants who tested positive for IgM alone [Group A] (4, 20%); and those who tested positive for both IgM and IgG [Group B] (91, 33%) were significantly higher compared to participants who tested negative for both IgM and IgG [Group D] (54, 3.6%).

Table 4 shows that among the participants who tested positive with rapid antibody test (n=40), 17 (42.5%) had both history of being quarantined and history of exposure to suspected or confirmed COVID-19 positive patients while 14 (35%) denied any history of both.

Since diabetes and history of being quarantined were associated with serologic results, the strength of association was evaluated using the univariate multinomial regression (Table 5). Those with diabetes mellitus had 6.8 times higher risk of being IgM positive and IgG negative than being negative in both tests (p=0.001). In addition, those with diabetes were more likely (13.6 times) to be positive in both tests (p=0.034). For those with history of quarantine relative to those who did not have history, the relative risk of being IgM positive and IgG negative compared to being negative to both tests was 3.1 times higher (p=0.013).

4. DISCUSSION

Antibodies have different functions namely: neutralization, opsonization and complement system activation. The two antibodies commonly utilized in serologic tests are IgM and IgG; and having either of these would indicate acute response to infection and long-term immunity, respectively. Of the 1557 participants, 40 (2.6%) were positive to either COVID 19 IgM or IgG antibody. Most of these were from the paramedical (50%) and ancillary group (32.5%). In the United States, 19% of the reported cases from February 12 to April 9, 2020 were identified as healthcare workers [10]. Compared to the US data, the prevalence of exposure to COVID-19 infection in Makati Medical Center is low (2%), presumably due to the hospital's early implementation of strategies to minimize or control healthcare workers' exposure to infected patients.

Table 1. Demographic and clinical profile of the participants included in the study (n=1557)

Characteristic	n (%)
Age, median (range)	30 (18-89)
Age group	
18-59	1507 (96.8)
60 and above	32 (2.1)
Missing	18 (1.2)
Sex	
Male	473 (30.4)
Female	1084 (69.6)
Type of Work	
Medical	243 (15.6)
Paramedical	811 (52.1)
Ancillary	503 (32.3)
History of Exposure	
Travel history	
No	1533 (98.5)
Yes	24 (1.5)
Exposure to a confirmed or suspected case of COVID-19	
No	685 (44)
Yes	872 (56)
History of being quarantined	
No	1106 (71)
Yes	451 (29)
Behavioral risk factors	
Smoker	
No	1445 (92.8)
Yes	112 (7.2)
Alcohol Drinker	
No	1176 (75.5)
Yes	381 (24.5)
Comorbidities	
Hypertension	
No	1413 (90.8)
Yes	144 (9.3)
Diabetes Mellitus	
No	1498 (96.2)
Yes	59 (3.8)
Chronic Kidney Disease	
No	1553 (99.7)
Yes	4 (0.3)

Characteristic	n (%)
Coronary Artery Disease	
No	1550 (99.6)
Yes	7 (0.5)
Bronchial Asthma	
No	1440 (92.5)
Yes	117 (7.5)
Pre-existing Pulmonary Disease	
No	1555 (99.9)
Yes	2 (0.1)
Prior Stroke	
No	1553 (99.7)
Yes	4 (0.3)
Malignancy	
No	1544 (99.2)
Yes	13 (0.8)
Autoimmune Disease	
No	1535 (98.6)
Yes	22 (1.4)

Majority of the participants (97.4%) tested negative for both IgM and IgG. Absence of antibodies against COVID-19 could be due to real absence of exposure or low risk exposure such that their bodies did not mount an immune response. However, a negative result for both IgG and IgM could not be conclusive that these subjects were not exposed to the virus [11].

Results of this study showed that those with diabetes were 13.6 times more likely than those without diabetes to be positive in both IgM and IgG. Previous reports cited diabetes as one risk factor that can be associated with COVID 19 infection. A meta-analysis of 21 clinical studies done in China showed that the prevalence of diabetes in COVID-19 infected individuals is 7.7% and this was associated with increased severity and mortality [12]. A single center study done in China showed a case fatality rate of 7.3% [13]. while a multi-center study done in France has a 10.3% mortality rate [14]. These findings support the data that patients with diabetes are more susceptible to infections. This is attributable to immune dysfunction in diabetics [15,16,17] and increased virulence of some pathogens due to the hyperglycemic state [18].

Those who were quarantined also showed association with positive serologic test results. Subjects who had history of quarantine were presumed to have exposure to suspected or confirmed COVID-19 infected individuals and thus had higher risk of contracting the disease.[13] This supports the World Health Organization' strategy of isolating people who have known exposure in order to prevent the spread of the disease.

Table 2. COVID19 serologic results by health workers' type of work (n=1557)

	Total Participants n(%)	Medical n(%)	Paramedical n(%)	Ancillary n(%)	p-value
Group A (IgM+, IgG-)	20 (1.3)	4 (1.65)	11 (1.36)	5 (0.99)	0.844
Group B (IgM+, IgG+)	3 (0.2)	1 (0.41)	1 (0.12)	1 (0.2)	
Group C (IgM-, IgG+)	17 (1.1)	2 (0.82)	8 (0.99)	7 (1.39)	
Group D (IgM-, IgG-)	1517 (97.4)	236 (97.12)	791 (97.53)	490 (97.42)	
Total	1557	243 (15.6)	811 (52)	503 (32.3)	

Table 3. Demographic and clinical profile of the patients by group (n=1557)

	Group A (IgM+, IgG-) n (%)	Group B (IgM+, IgG+) n (%)	Group C (IgM-, IgG+) n (%)	Group D (IgM-, IgG-) n (%)	p-value
Age group					0.573
18-59	19 (95)	3 (100)	17 (100)	1468 (96.8)	
60 and above	1 (5)	0	0	31 (2)	
Missing	0	0	0	18 (1.2)	
Sex					0.417
Male	5 (25)	1 (33.3)	8 (47.1)	459 (30.3)	
Female	15 (75)	2 (66.7)	9 (52.9)	1058 (69.7)	
Type of Work					0.844
Medical	4 (20)	1 (33.3)	2 (11.8)	236 (15.6)	
Paramedical	11 (55)	1 (33.3)	8 (47.1)	791 (52.1)	
Ancillary	5 (25)	1 (33.3)	7 (41.2)	490 (32.3)	
History of Exposure					
Travel history					1
No	20 (100)	3 (100)	17 (100)	1493 (98.4)	
Yes	0	0	0	24 (1.6)	
Exposure to a confirmed or suspected case of COVID-19					0.219
No	5 (25)	2 (66.7)	9 (52.9)	669 (44.1)	
Yes	15 (75)	1 (33.3)	8 (47.1)	848 (55.9)	
History of being quarantined					0.036
No	9 (45)	2 (66.7)	10 (58.8)	1085 (71.5)	
Yes	11 (55)	1 (33.3)	7 (41.2)	432 (28.5)	
Behavioral risk factors					
Smoker					0.328
No	19 (95)	2 (66.7)	16 (94.1)	1408 (92.8)	
Yes	1 (5)	1 (33.3)	1 (5.9)	109 (7.2)	
Alcohol Drinker					0.168
No	17 (85)	1 (33.3)	11 (64.7)	1147 (75.6)	
Yes	3 (15)	2 (66.7)	6 (35.3)	370 (24.4)	
Comorbidities					
Hypertension					0.738
No	17 (85)	3 (100)	16 (94.1)	1377 (90.8)	
Yes	3 (15)	0	1 (5.9)	140 (9.2)	
Diabetes Mellitus					0.003
No	16 (80)	2 (66.7)	17 (100)	1463 (96.4)	
Yes	4 (20)	1 (33.3)	0	54 (3.6)	
Chronic Kidney Disease					1
No	20 (100)	3 (100)	17 (100)	1513 (99.7)	
Yes	0	0	0	4 (0.3)	
Coronary Artery Disease					1
No	20 (100)	3 (100)	17 (100)	1510 (99.5)	
Yes	0	0	0	7 (0.5)	
BA					0.281
No	18 (90)	2 (66.7)	16 (94.1)	1404 (92.6)	
Yes	2 (10)	1 (33.3)	1 (5.9)	113 (7.5)	
Pre-existing Pulmonary Disease					1
No	20 (100)	3 (100)	17 (100)	1515 (99.9)	
Yes	0	0	0	2 (0.1)	
Prior Stroke					1
No	20 (100)	3 (100)	17 (100)	1513 (99.7)	
Yes	0	0	0	4 (0.3)	

	Group A (IgM+, IgG-) n (%)	Group B (IgM+, IgG+) n (%)	Group C (IgM-, IgG+) n (%)	Group D (IgM-, IgG-) n (%)	p-value
Malignancy					1
No	20 (100)	3 (100)	17 (100)	1504 (99.1)	
Yes	0	0	0	13 (0.9)	
Autoimmune Disease					1
No	20 (100)	3 (100)	17 (100)	1495 (98.6)	
Yes	0	0	0	22 (1.5)	

Table 4. Seropositive profile (Group A to C) based on history of being quarantined and history of exposure

Exposure to a confirmed or suspected case of COVID-19	History of being quarantined		Total	p-value
	No	Yes		
No	14 (35%)	2 (5%)	16	<0.001
Yes	7 (17.5%)	17 (42.5%)	24	
Total	21	19	40	

Table 5. Results of univariate multinomial logistic regression

	Group A (IgM+, IgG-) RR (CI)	p-value	Group B (IgM+, IgG+) RR (CI)	p-value	Group C (IgM-, IgG+) RR (CI)	p-value	Group D (IgM-, IgG-)
with Diabetes Mellitus	6.8 (2.2-20.9)	0.001	13.6 (1.2-151.7)	0.034	0.0000004	0.984	reference category
with History of Quarantine	3.1 (1.3-7.5)	0.013	1.3 (0.1-13.9)	0.853	1.8 (0.7- 4.6)	0.255	reference category

5. CONCLUSION

There was a low prevalence (2.6%) of COVID-19 infection among healthcare workers of Makati Medical Center. Among these healthcare workers, diabetes mellitus, history of exposure and history of quarantine were factors associated with exposure to COVID-19 infection. Early and stringent implementation of and adherence to infection control by the hospital is presumed to be an important factor that has led to a low infection rate among healthcare workers of Makati Medical Center.

6. LIMITATIONS OF THE STUDY

This is a single-center study; thus, it does not reflect the prevalence of COVID-19 infection among healthcare workers in other institutions. The study also did not determine any correlation of test positivity with time interval from exposure, travel or quarantine.

CONSENT AND ETHICAL APPROVAL

This study was undertaken only after review and approval of the protocol by the Makati Medical Center Institutional Review Board. It was conducted in accordance with the ethical principles based on the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use-Good Clinical Practice, Declaration of Helsinki and the National Guidelines for Biomedical Research of the National Ethics Committee (NEC) of the Philippines. The privacy and confidentiality of data was ensured by the researchers in full compliance with the Data Privacy Act of 2012. The authors did not disclose any conflict of interest in the study.

All participants who gave informed and written consent were included in the study and were asked to fill-up a short questionnaire.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62465