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Assessment on COVID-19 Antibody and Antigen Rapid Test Devices as Screening Tools for SARS-CoV-2 Infection at the Academic Premises

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Abstract Since early 2020, a novel coronavirus named SARS-CoV-2 is causing COVID-19 pandemic. This novel virus is very contagious as it spreads quickly, primarily via droplets during person-to-person contact. The gold standard method to confirm SARS-CoV-2 infection is the reverse transcriptase-quantitative polymerase chain reaction (RT-qPCR) assay, but this technology is labor-intensive and time-consuming. An effective, point-of-care assay will be required to screen the general population for SARS-CoV-2 infection, hence RT-qPCR assay could be used mainly to confirm suspected cases with COVID-19. In this cross-sectional study, we described our experiences in using the antibody and antigen rapid test devices to screen for SARS-CoV-2 infection among staff and students at Universitas Pelita Harapan, respectively. Firstly, we found that the participating staff who worked regularly at the academic premises were not infected by SARS-CoV-2 during November and December 2020, suggested by seronegative results (0 out of 55). Secondly, we observed that among seropositive students who were living at the dormitory, the antigen rapid testing did not detect any positive subject (0 out 26), despite some among those exhibited the positive results when tested with RT-qPCR (8 out 26). The calculated sensitivity was 0%, while the specificity was 100%. Taken together, our findings indicated the weakness of using the antibody and antigen rapid test devices as a screening tool for SARS-CoV-2 infection among our cohorts.

Keywords: COVID-19, SARS-CoV-2, screening, antibody rapid test, antigen rapid test.
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Introduction

The year of 2020 saw a novel pandemic, causing a major disruption in daily-life activities, including in Indonesia. This worldwide outbreak was due to a new human coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), causing a primarily respiratory disease named Coronavirus Disease 2019 (COVID-19) [1]. Transmission of SARS-CoV-2 is mainly through respiratory droplets during face-to-face interaction with infected subjects. However, contracting the virus after touching a surface covered by the virus (i.e., fomites) is also possible. Intriguingly, infected patients could be asymptomatic or exhibit myriad symptoms, ranging from anosmia, dry cough, fever to respiratory distress [2]. Self-isolation theoretically must be strictly imposed, especially among the unvaccinated population, to suppress the viral spreading. However, a dire necessity to drive the national economy pressured the Indonesian government to allow the workforces to resume their jobs from their respective workplaces or to combine it with a mode of working-from-home. This decision has been implemented for staff at Universitas Pelita Harapan as well since July 2020. The decision to permit the workforces to congregate at their workplaces might contribute to new cases of COVID-19.

Accumulating evidence had shown that the confirmed cases through detection of viral nucleic acid, presumably represent a part of true cases only, as many infected subjects do not aware that they are infected (due to mild or no symptom) and many as infected subjects do not get tested (because they do not seek for medical care or are not suspected to contract from COVID-19). Hence it was a challenge to accurately diagnose the patient solely based on clinical observation. Additional examination methods, including chest radiology (showing ground-glass opacity) and blood work-up (exhibiting lymphopenia and elevated inflammatory markers), would boost clinicians' confidence to suspect a patient contracting COVID-19 [2]. These asymptomatic or mild patients can be confirmed by assessing their respective antibodies.

The current gold-standard laboratory method to confirm an infection of SARS-CoV-2 is the reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay [2]. Briefly, this molecular biology assay utilizes a method of reverse-transcription

polymerase chain reaction and enables to detect, and measure amplified genetic material products (*i.e.*, the viral RNA collected from nasopharyngeal or oropharyngeal swabs) during each cycle of PCR [2]. This assay has both high sensitivity and specificity rates. However, the mass deployment of this assay is hindered due to several factors, including limited numbers of RT-qPCR machines, high cost and complexity of conducting a RT-qPCR assay, a requirement of a prior extraction step of genetic materials, a relatively long turn-over time of each round of RT-qPCR (~2 hours, excluding the extraction step), as well as a continuous shortage of reagents [3]. Taken together, this method could not be used as a widespread, point-of-care assay to detect SARS-COV-2 infection among the otherwise healthy general population.

In 2020, Indonesia relied on COVID-19 antibody rapid testing to screen for suspected SARS-COV-2 infection. The antibody rapid testing provides seroprevalence data, i.e., whether a particular individual has specific antibodies to SARS-CoV-2 structural proteins. As the specific antibodies were produced and detected in the late phase of the infection, the serological assays for COVID-19 (such as antibody rapid test device) inherit a notable weakness as a seropositive case indicates a past infection. Nonetheless, measuring specific antibodies toward SARS-CoV-2 would be useful to provide a more thorough information of COVID-19 epidemiology. One subgroup of the population that might warrant a seroprevalence data was a group of staff in the academic setting. This group of people are generally considered having a lower risk to get infected as well as to transmit the virus (hence a lower seroprevalence rate) than health-care workers. However, as this pandemic continuously demonstrates that many groups considered as low-risk people, *e.g.*, office workers, could become the next cluster of infection, it is prudent to investigate a group of academic staff as they are and would interact closely with students.

In 2021, an alternative screening method was widely used in Indonesia, i.e., the antigen rapid testing. The currently available antigen rapid test devices in the market are designed to detect nucleocapsid antigen of SARS-CoV-2. Interestingly, this assay was developed as a point-of-care test, as it was easy to be used and it was cheaper than the RT-qPCR as well as it generated a result in 10-15 minutes after the start of assay [3]. Its samples were mainly derived from nasopharyngeal swabs. However, the limitations of this assay need to be properly acknowledged, such as lacking a control mechanism to ensure the samples have been taken properly and having a lower sensitivity (but a similar level of specificity) as compared to RT-qPCR. By balancing its strengths and weaknesses, the COVID-19 antigen rapid testing could be used as an alternative method to screen for the current infection of SARS-CoV-2 [3].

We hereby reported our experiences in using the antibody rapid test devices (in November-December 2020) and the antigen rapid test devices (in February-May 2021) to screen for possible SARS-CoV-2-infected cases at the academic premises. The first part of the study was using the antibody rapid test device to screen academic staff at the Faculty of Science and Technology, Universitas Pelita Harapan (FaST-UPH), who were regularly working at the office, for COVID-19. The first cohort comprised lower-risk individuals to get infected by SARS-CoV-2 as they did not interact with patients and as they did not work in the hospital. The subsequent part was using the antigen rapid test device to screen seropositive students of the Faculty of Nursing, Universitas Pelita Harapan (FoN-UPH). This second cohort comprised higher-risk individuals as they lived in a dormitory within the UPH premises and as they regularly interacted with patients in the hospital. In addition, the second cohort consisted of seropositive FoN-UPH students (tested with the same antibody rapid test device utilized in the first project), who went for confirmation testing of SARS-CoV-2 infection with the RT-qPCR and the antigen rapid test assays. Our findings suggested that both antibody and antigen rapid testing were not effective in screening for SARS-CoV-2 infection in our cohorts.

Materials and methods

Subjects

This cross-sectional study was approved by the Mochtar Riady Institute for Nanotechnology Ethics Committee (026/MRIN-EC/ECL/XI/2020 and 018/MRIN-EC/ECL/V/2021 for the first and second part of the study, respectively). In the first part of the study, fifty-five (n=55) eligible staff of FaST-UPH were recruited. The first cohort was generally considered having a lower risk to get infected as well as to transmit the virus (hence a lower seroprevalence rate) than health-care workers. In the second part of the study, twenty-six (n=26) seroreactive students of FoN-UPH were recruited. The second cohort was considered having a higher risk to contract COVID-19 than the general population due to several risk factors, such as living together in a dormitory and interacting with patients at the hospital. All subjects were consented to participate in this study.

Devices

The first cohort was qualitatively tested with the Abbott Panbio™ Covid-19 IgG/IgM Rapid Test Device, to detect the presence of anti-SARS-CoV-2 IgG and/or IgM. This device was claimed by its manufacturer to have a sensitivity and specificity of 96.2% and 100%, respectively, when using fingerstick blood. The second cohort was qualitatively tested with the Abbott Panbio™ COVID-19 Antigen Rapid Test Device. This device was claimed by its manufacturer to have a sensitivity of 91.4% (94.1% for samples with Ct values ≤33) dan specificity of 99.8%, when using nasopharyngeal swab sample.

COVID-19 Antibody Rapid Testing

Consented subjects were serologically tested (via finger prick) by using the Abbott Panbio™ Covid-19 IgG/IgM Rapid Test Device. They were tested twice with a duration of 14 days between each test. The result of this rapid antibody test was obtained within 15 minutes. If there was an inconclusive result, the assay would be repeated. Each time when their fingers were pricked, the health status of each subject were recorded by using a brief written questionnaire. Basic screening of vital signs, comprising temperature, heart rate and oxyhemoglobin saturation, were performed as well. Temperature were measured non-invasively with an infrared thermometer (DT-8826) with a distance of ~ 3 cm to a subject's forehead. Both heart rate and oxyhemoglobin saturation were measured with a non-invasive pulse oximetry (Fingertip Pulse Oximeter). This device provided a qualitative result whether a tested subject had anti-SARS-CoV-2 antibody (i.e., whether the subject was seroreactive/seropositive). A brief overview on how to use this device and how to interpret the results were depicted below.

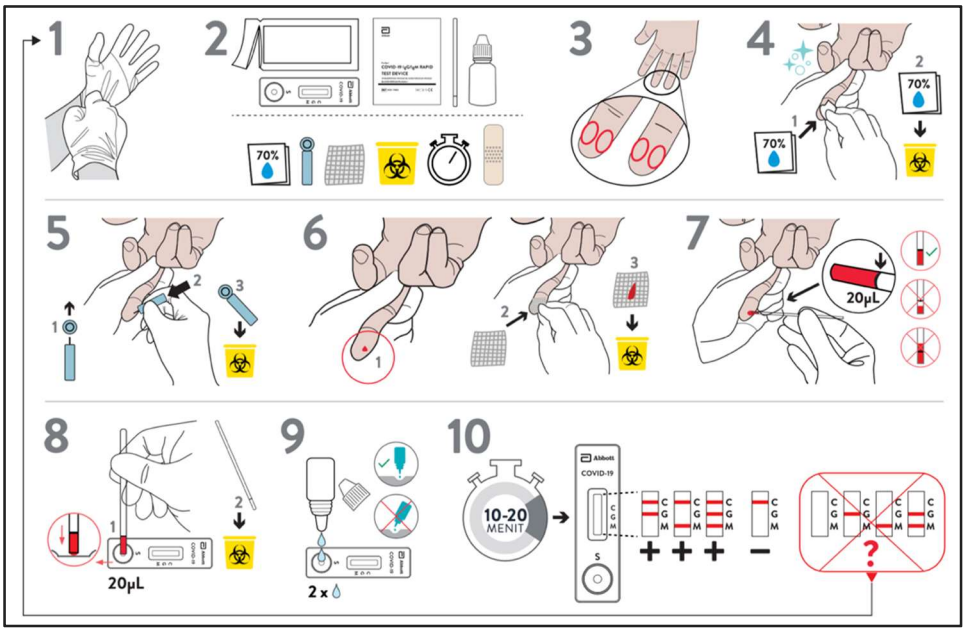

Figure 1. Fingerstick quick manual of the Abbott PanBio™ Covid-19 IgG/IgM Rapid Test Device. The figure was obtained from https://www.globalpointofcare.abbott/en/product-details/panbio-covid-19-igg-igm-antibody-test.html.

COVID-19 Antigen Rapid Testing

Consented subjects were seroreactive FoN-UPH students who went for the RT-qPCR assay and rapid antigen testing. Brief demographical data, current clinical data, date of the serological assay and result of RT-qPCR were collected from each subject. Of note, the RT-qPCR assays were performed at the nearest government health care center. Nasopharyngeal swab of consented subjects were tested by using the Abbott Panbio^{TM} COVID-19 Antigen Rapid Test Device. Results of this rapid antigen test were obtained within 15 minutes. If there was an inconclusive result, the assay would be repeated. Upon obtaining results of RT-qPCR and rapid antigen test from subjects, sensitivity, specificity, negative predictive value, and positive predictive value of Panbio^{TM} COVID-19 Antigen Rapid Test Device were calculated. A brief overview on how to use this device and how to interpret the results were depicted below.

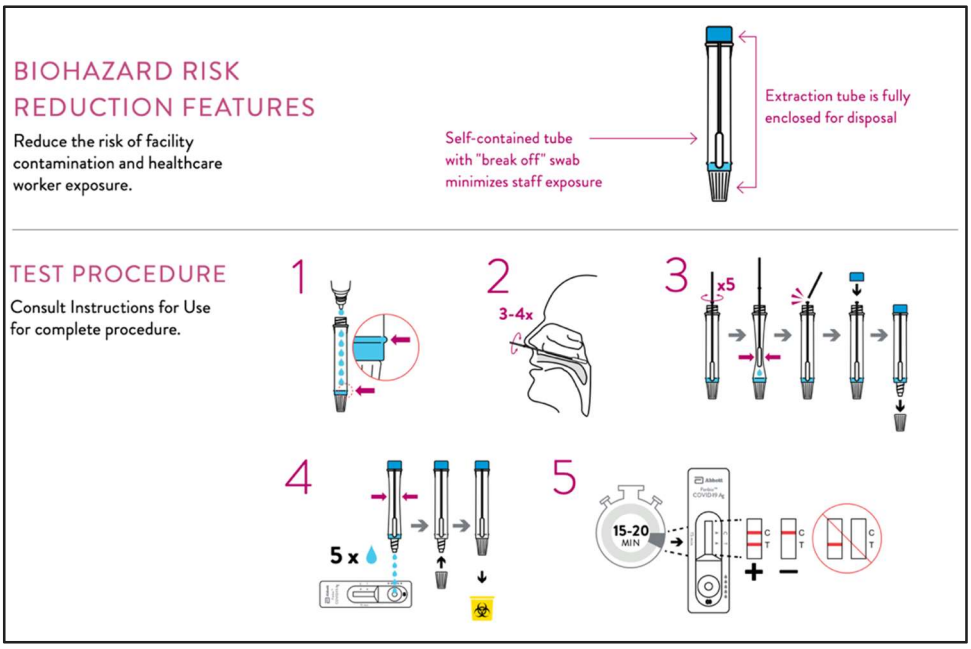

Figure 2. Test procedure of the Abbott PanBio^{TM} Covid-19 Antigen Rapid Test Device. The figure was obtained from https://www.globalpointofcare.abbott/en/product-details/panbio-covid-19-ag-antigen-test.html.

Statistical Analyses

Analyses of data were performed with the software Stata IC version 16. The demographic data of categorical variable was presented as number and percentage and the numerical variable was presented as mean, standard deviation, minimum and maximum values.

Results and discussion

The cross-sectional study to assess the usefulness of various screening tools for SARS-CoV-2 infection was performed from November 2020 until April 2021. In the first part of the study, the seroprevalence of SARS-CoV-2-specific antibodies among staff at the Faculty of Science and Technology, Universitas Pelita Harapan (FaST-UPH) were tested twice in November and December 2020.

Table 1. Physical examination's data of subjects in the first cohort. SpO_2, the percent saturation of oxygen in the blood.

Variable	n	Mean	SD	Min	Max
Temperature-1st (°C)	55	36.5	0.2	35.9	36.7
Temperature-2nd (°C)	48	36.4	0.1	36.2	36.7
Heart rate-1st (beat/minute)	55	82.8	11.7	61	113
Heart rate-2nd (beat/minute)	48	85.5	13.9	57	135
SpO_2-1st (%)	55	98.8	0.5	97	99
SpO_2-2nd (%)	48	98.8	0.5	97	99

There were 55 and 48 participating subjects in the first and second serological screening, respectively (**Table 1**). During the first examination, the mean of the subject's temperature was 36.5°C, with the lowest temperature was 35.9°C and the highest one was 36.7°C **(Table 1)**. Among all subjects, 48 subjects (87.3%) had an average temperature of 36.4°C. A similar observation was observed in the second examination. This indicates all subjects had normal temperatures. Pertaining to heart rate, the measurement in the first screening revealed an average of 82.8 beats per minute, with the lowest and highest values were 61 and 113 beats per minute, respectively. The measurement of heart rate in the second screening revealed an average of 85.5 beats per minute. Regarding the measurement of oxygen saturation (SpO_2), the first and second examination yielded an average of 98.8%.

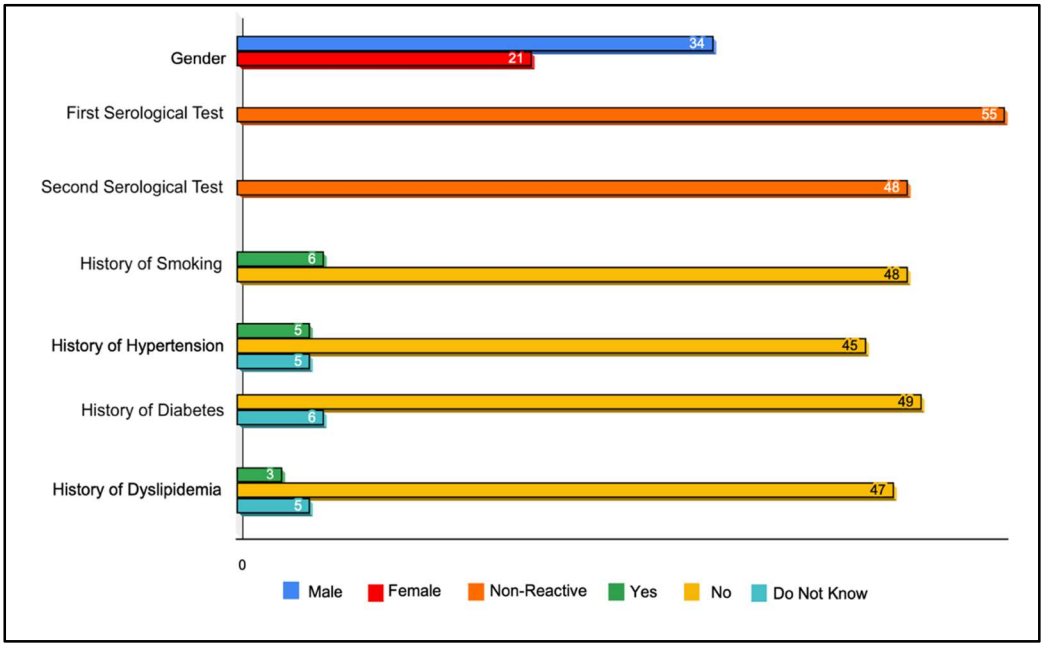

Figure 3. Demographic & Clinical Data and serological results of all respondents. The test was conducted twice, with a duration of 14 days between each test. Absolute number of subjects in each category was displayed within each bar.

As shown in **Figure 3**, there were 34 males and 21 females participating in this survey. Six of them (10.9%) had a history of smoking. Five of them (9.1%) had hypertension and 3 of them (5.5%) had dyslipidemia. All results were conclusive, as the control line emerged in all testing. Both serological tests showed non-reactive results in all subjects. Intriguingly in the second test, there was one subject who exhibited a faint line for IgG at approximately 20 minutes after testing. Due to its late emergence, as advised by the manufacturer, we interpreted this result as negative.

Table 2 displays the latest medical history of 55 respondents during screening. Only 1 respondent (1.8%) admitted having headache during the examination. No other medical histories were found in all subjects. As all recruited subjects displayed non-reactive results in the first and second testing (end of November & mid-December 2020, respectively), our finding suggested that the participating staffs who working regularly at the premises of FAST-UPH were not infected by SARS-CoV-2 during November and December 2020. This finding was corroborated by a fact that most subjects did not report any COVID-19-related symptom during both screening. There were several limitations in the first part of our study. Firstly, our cohort was small (n=55) and mainly comprised mature, well-educated adults (i.e., lecturers) who arguably having a higher discipline to follow rules. The tendency to regularly abide by the rules might not be applicable to other cohorts at the university, such as students. Secondly, the study's duration was short (only 1 month with two observations). A longer observation might capture more seroconversion events. Thirdly, our cohort had a lower risk to contract COVID-19 as they did not interact with patients or patient's biological samples.

Table 2. Current medical history of subjects in the first cohort. Pink colour highlighted the only "yes" answer in this table.

Variable	n	Percentage
Fever		
No	55	100
Dyspnea		
No	55	100
Pain		
No	55	100
Headache		
Yes	1	1.8
No	54	98.2
Dry cough		
No	55	100
Running nose		
No	55	100
Anosmia		
No	55	100
Dysgeusia		
No	55	100
Dysphagia		
No	55	100
Nausea		
No	55	100
Diarrhea		
No	55	100

In the second part of our study, we assessed sensitivity and specificity of the Panbio^{TM} COVID-19 Antigen Rapid Test Device in the population of nursing students at the Faculty of Nursing, Universitas Pelita Harapan (FoN-UPH) who were seroreactive from February 2021 to May 2021. The reason for choosing seroreactive students at FoN-UPH was that they had several risk factors to contract COVID-19, such as living together in a dormitory and interacting with patients at the hospital. Of note, the seroreactivity indicates detection of specific antibodies in the blood sera, which among hospitalized patients with COVID-19, the seroconversion (i.e., the starting time of producing specific antibodies) was typically detected between 5-14 days post symptom onset [4,12]. According to the health protocol, students at FoN-UPH who becoming seroreactive will go for the RT-qPCR assay. We therefore recruited the consented students to be swabbed (using nasopharyngeal swab samples) and tested with commercialized COVID-19 antigen rapid test device as well.

As shown in **Figure 4**, there were 19 female and 7 male seroreactive students recruited into this study (total=26 subjects). By using the RT-qPCR assay, there were 8 subjects confirmed to be infected by SARS-CoV-2 (30.8%). However, there was no positive case identified using the antigen rapid testing. **Figure 5** showed that the time duration between RT-qPCR and antigen rapid test assays were between 0 (both done in the same day) and 4 days (RT-qPCR performed 4 days earlier than antigen rapid testing), with the largest proportion underwent both assays on the same day (n=11; 42.3%).

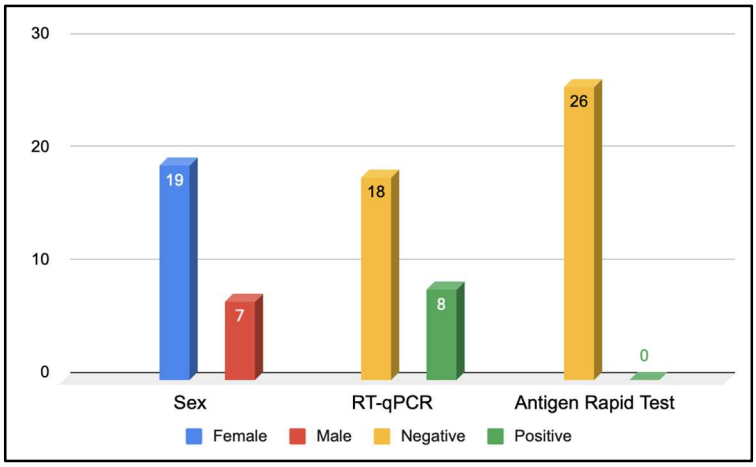

Figure 4. Characteristic and testing results of subjects. Absolute number of subjects in each category was displayed within each bar.

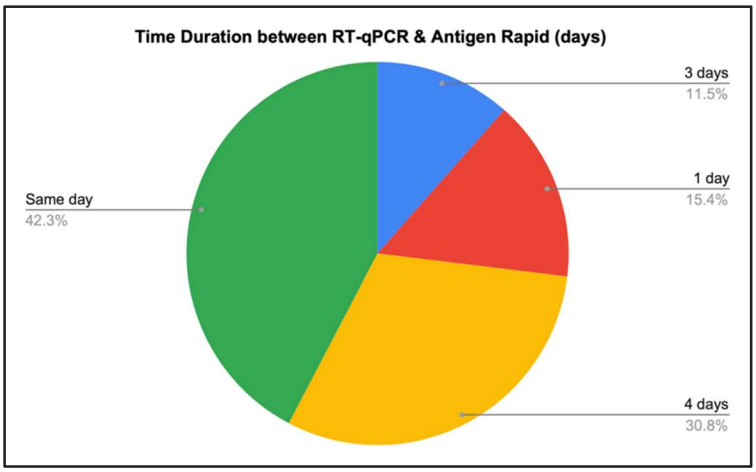

Figure 5. Time duration between RT-qPCR and antigen rapid assays.

Table 3 was created to compare results of COVID-19-specific RT-qPCR and antigen rapid testing in a format of 2x2. As shown, there was a value of zero in two cells (i.e., in the categories of "positive by antigen rapid & positive by RT-qPCR" and "positive by antigen rapid and negative by RT-qPCR. Sensitivity, specificity, prevalence of disease, positive-predictive value and negative-predictive value of the Panbio™ COVID-19 Antigen Rapid Test Device in screening for SARS-CoV-2 infection were calculated accordingly.

Table 3. Two x two table between COVID-19 RT-qPCR and antigen rapid results.

	Positive by RT-qPCR	Negative by RT-qPCR	Total
Positive by Antigen Rapid	0	0	0
Negative by Antigen Rapid	8	18	26
	8	18	26

Based on values in **Table 3**, the following calculation was performed:
Sensitivity = 0 / (0+8) x 100% = **0%**
Specificity = 18 / (0+18) x 100% = **100%**
Prevalence of Disease = 8 / 26 x 100% = **30.8%**
Positive-Predictive Value = 0 / (0+0) x 100% = **cannot be calculated**
Negative-Predictive Value = 18 / (18+8) x 100% = **69.2%**

Upon comparison to several published studies on the Panbio™ COVID-19 antigen rapid device [5,6], our study did not show a sensitivity value (0% against ~74% on average). Of note, the World Health Organization recommends using antigen rapid devices with sensitivity ≥80% and specificity ≥97% as well as to use the device in strict accordance with the manufacturer's instructions and within the first 5-7 days post symptom onset [5]. Our findings could be due to timing of testing with the antigen rapid testing, asymptomatic/mild condition in all subjects (data not shown), or relatively lower viral load in those subjects with positive RT-qPCR results. Indeed, it has been reported that among subjects who had high viral load and who were highly contagious, the antigen rapid testing had a comparable sensitivity to RT-qPCR assay [6]. In contrast, the specificity of the Panbio™ COVID-19 Antigen Rapid Test Device in our study was similar to published finding [7,8,9,10] (around 95%), suggesting that false-positive result was unlikely if the test was done according to the manufacturer's instructions. We also calculated the prevalence of disease, positive-predictive value and negative-predictive value in our cohort. We observed that the prevalence of COVID-19 was 30.8%. The positive-predictive value could not be calculated, while the negative-predictive value was 69.2%.

There were several limitations of our study. Firstly, the cohort was small (n=26). Despite the interesting characteristics of our cohort (nursing students living in the dorm and interacting with patients at the hospital), the small number did not permit us to draw any reasonable conclusion for that particular cohort. Secondly, there were value of zero within two cells (in the categories of "positive by antigen rapid, positive by RT-qPCR" and "positive by antigen rapid, negative by RT-qPCR"). Thirdly, all subjects underwent for the RT-qPCR assay at the government-operated clinics, in which we did not have any info regarding the brand as well as the CT value of the RT-qPCR assay. Different brands of RT-qPCR assay would have different sensitivity and specificity results. In addition, patients with relatively low CT values (i.e., higher viral load) had a higher chance to exhibit positive result upon antigen rapid testing [11,13]. Finally, all consented subjects had been seroreactive for 3-7 days (data not shown), before went for both RT-qPCR and antigen rapid assays. This means, arguably, that all subjects were beyond 7 days post symptom onset, outside of the window period when antigen rapid device has the highest sensitivity to detect SARS-CoV-2 infection [5]. This suggests a very limited usefulness to deploy antigen rapid device among seroreactive subjects with no/mild symptom to confirm the current state of infection. This hypothesis was partly supported by only 8 out of 26 subjects in our cohort (30.8%) were positively confirmed by the RT-qPCR assay (**Figure 4**), suggesting the majority of those seroreactive subjects were already at the stage of non-infectious or even no infection. Hence, using the antigen rapid device in this situation would not be beneficial.

Conclusions

Our findings suggested that both antibody and antigen rapid testing were not effective in screening for SARS-CoV-2 infection in our cohorts. For the first part of the study, it could partly be due to the low-risk nature of our first cohort. For the second part of the study, it could partly be due to the experimental setting (i.e., testing seroreactive subjects for positivity of SARS-CoV-2 infection). This indicates that in order to utilize rapid testing assay effectively in screening for COVID-19 cases, in particular for antigen rapid test device, nature of the cohort (low risk versus high risk) as well as purpose (screening versus confirming diagnosis) and timeline (in the early phase or late phase of infection) of using the rapid testing would be several important consideration factors.

Conflicts of interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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