Evaluation of a Rapid Antigen Test for the Diagnosis of SARS-CoV-2 during the COVID-19 Pandemic

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Abstract

Objectives: Reverse transcriptase-polymerase chain reaction (RT-PCR), the reference laboratory method of confirmed SARS-CoV-2 diagnosis, though requiring equipment, is time-consuming. There is a crucial demand for rapid techniques such as antigen detection test during the pandemic. This study assessed whether a rapid antigen detection (RAD) test was an effective and essential method for the early diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the COVID-19 pandemic. The probability of public screening at home and the application of RAD during the novel SARS-CoV-2 outbreak were also topics of interest. Methods: A retrospective analysis based on the systemic screening for COVID-19 was conducted at Taipei City Hospital (TCH) from May 28 to June 06, 2021, the first week of outbreak in Taiwan. The results of the RAD and RT-PCR tests were collected from 5 major branches of the TCH. Results: We collected a total number of 6368 cases. We found that the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy ranged from 60.5% to 78.6% (mean 66.0%), 98.2% to 99.9% (mean 99.0%), 74.4% to 97.8% (mean 82.8%), 94.0% to 98.4% (mean 97.5%), and 93.8% to 98.3% (mean 94.2%), respectively. Although the sensitivity score was not high (up to 95% or higher), the other results were satisfactory, with an accuracy of more than 93% in all branches. Furthermore, it had high specificity, PPV, NPV, and accuracy. Conclusion: We concluded that RAD could be a quick and feasible method to identify individuals infected with SARS-CoV-2 from non-contagious individuals during the COVID-19 outbreak. A RAD test was an effective and essential method for the early diagnosis of SARS-CoV-2 during the COVID-19 pandemic.

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What do we Already Know about this Topic?
It can be used as a quick sharp tool to identify infected persons in high-risk areas during outbreaks or pandemics. Conversely, antibody testing is usually used for the subsequent understanding of the prevalence of the virus, not as a diagnostic proof of infection. Reverse transcriptase-polymerase chain reaction (RT-PCR) has been used as a confirmatory diagnostic screening tool worldwide.

How does your Research Contribute to the Field?
This study assessed whether a rapid antigen detection (RAD) test was an effective and essential method for the early diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the COVID-19 pandemic. The probability of public screening at home and the application of RAD during the novel SARS-CoV-2 outbreak were also topics of interest.

What are your Research's Implications towards Theory, Practice, or Policy?
We concluded that RAD could be a quick and feasible method to identify individuals infected with SARS-CoV-2 from non-contagious individuals during the COVID-19 outbreak. Furthermore, it had high specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. In addition, regarding self-screening at home as a novel method for early detection, RAD was convenient, cost-effective, and comfortable.

Introduction

Since its outbreak in December 2019, the coronavirus disease 2019, also known as SARS-CoV-2, has been prevalent in over 200 countries and regions worldwide. Most infected people have mild disease with non-severe symptoms, and only approximately 5% become critically ill with respiratory failure, septic shock, and multiple organ failure.[1] Even with good personal protective habits such as wearing masks, washing hands, and social distancing, it is difficult to completely prevent the transmission of SARS-CoV-2 during the pandemic.[2] Approximately 43% to 46% of all people diagnosed with SARS-CoV-2 are asymptomatic.[3]

In 2021, following the first wave of the SARS-CoV-2 pandemic, there was an outbreak for 3 months (May to July) in Taiwan. Subsequently, the curve flattened due to proactive measures of border restrictions and public self-protection awareness. However, due to the novel SARS-CoV-2 variant Omicron, a new outbreak began in early January 2022. Hence, the government implemented the self-screening policy again.

There are 3 methods to detect and diagnose SARS-CoV-2, all with their special characteristics, advantages, and disadvantages (Table 1). In addition, their application methods are different.[4] Rapid antigen detection (RAD) rapidly discovers the viral infection and guides the medical staff to further action. It can be used as a quick, sharp tool to identify infected persons in high-risk areas during outbreaks or pandemics. Conversely, antibody testing is usually used for the subsequent understanding of the prevalence of the virus, rather than as a diagnostic proof of infection. Reverse transcriptase-polymerase chain reaction (RT-PCR) has been used as a confirmatory diagnostic screening tool worldwide.

Hence, in this study, we assessed whether RAD was an effective and essential method for the early diagnosis of SARS-CoV-2. Furthermore, the probability of the public screening at home and the application of RAD in the new SARS-CoV-2 outbreak are also topics of interest.

Materials and Methods

Study Period and Study Population

We conducted a retrospective analysis based on the systemic screening for COVID-19 at Taipei City Hospital (TCH) from May 28 to June 06, 2021, the first week of Taiwan's outbreak. The TCH has 7 branches with a total of 3103 beds. Data were collected from the 5 major branches: RenAi, Zhongxiao, Yang-Ming, Zhongxing, and Heping. During the outbreak period, anyone who had COVID-19 related symptoms or close contact with an affected person would come to the city hospital to screen. The screenings (both RAD and PCR) were carried out by physicians to ensure quality assurance at the time. This study was approved by the TCH Research Ethics Committee (Approval number: TCHIRB-111010099-E). The reporting of this study conformed to STROBE guidelines.

Equipment and Facilities

Different Brands of RAD used in (1). YangMing and Zhongxiao, (2). Zhongxing and Heping, and (3). RenAi were (1). TAIDOC TECHNOLOGY CORPORATION®, (2). ENIMMUNE CORPORATION®, and (3). Abbott® Laboratories. The diagnosis was confirmed via an RT-PCR test. (Taipei City Hospital using AIO SP-qPCR System® (AIO48S-144) and the PCR kit (AIOQS3480、AIOLVX500).

Statistical Analyses

The data were presented as percentages. The confidence interval was set at 95%. All analyses were performed using SAS (version 9.4; SAS Institute, Inc., Cary, NC, USA).

Results

Table 2 shows the number of cases in TCH from May 28 to June 06, 2021, the first week of Taiwan's outbreak. The diagnosis was confirmed via an RT-PCR test. The cases we collected in the 5 major branches of TCH ranged from 637 (Zhongxiao branch) to 2100 (Zhongxing branch), constituting a total number of 6368 cases. The samples not published or performed with RT-PCR were 163, accounting for 2.6%. The number of people tested positive in RAD test was 349, with 289 positive in RT-PCR and 60 negative in RT-PCR, respectively, while 5825 people tested negative in RAD test, with 118 positive in RT-PCR and 5707 negative in RT-PCR, respectively.

Table 3 presents the results from all the 5 branches. We found that scores for sensitivity, specificity, PPV, NPV, and accuracy ranged from 62.0% to 78.6% (mean 66.0%), 98.2% to 99.9% (mean 99.0%), 74.4% to 97.8% (mean 82.8%), 94.0% to 98.4% (mean 97.5%), and 93.8% to 98.3% (mean 94.2%), respectively. Although the sensitivity score was not high (up to 95% or higher), the other results were satisfactory, with an accuracy of more than 93% in all branches.

Discussion

Due to the spread of SARS-CoV-2 and its ability to mutate, early detection of the infection is essential. Reverse transcriptase-polymerase chain reaction and rapid antigen tests are important diagnostics for SARS-CoV-2. The advantages of rapid antigen test (RAD) include low cost, rapid turnaround time, and wide availability, making them important screening tests. However, the sensitivity of rapid antigen tests was demonstrably lower than that of RT-PCR.[5]

Table 1. Comparison among the RAD, Testing for Antibodies against SARS-CoV-2, and RT-PCR.

	Rapid Antigen Detection (Screening)	Testing for Antibodies Against SARS-CoV-2 (Screening)	Reverse Transcriptase-Polymerase Chain Reaction
Characteristics	Detect the surface protein of SARS-CoV-2	Detect the production of antibodies after being infected or injected with a vaccine	Detect and amplify the genetic materials of SARS-CoV-2 Used for confirmation
Advantages	1. Rapid (within 20-30 minutes) 2. Convenient (only requires a stick to be inserted 2.5 cm into nose)	1. Can detect the antibody level for post-vaccine and post-infected people	1. High accuracy even in low copies of the virus
Limitation	1. Less accurate than a RT-PCR 2. May result in PPV and NPV	1. Positive only for those post-vaccine and post-infected 2. May result in a false negative 3. Has to be tested at least 2 to 3 weeks after infection or vaccination for high accuracy	1. Expensive 2. Time-consuming 3. Requires to be executed by professionals in bio-safety level 2 and above laboratories

Note: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RAD, rapid antigen detection; RT-PCR, reverse transcriptase-polymerase chain reaction; PPV, positive predictive value; NPV, negative predictive value.

Table 2. Data analysis of the COVID-19 Systemic Screening in TCH from 28 May to 05 June 2021, the First Week of Taiwan's Outbreak; Using RAD.

	Total Number (n)	Screen (+) PCR (+)	Screen (+) PCR (−)	Screen (−) PCR (+)	Screen (−) PCR (−)	PCR Not Performed & Published
RenAi	1652	44	1	27	1546	34
Zhongxiao	637	52	5	34	533	13
YangMing	864	44	13	12	718	77
Zhongxing	2100	93	32	51	1885	39
Heping	1115	56	9	25	1025	0
Total	6368	289	60	149	5707	163

Note: TCH, Taipei City Hospital; RAD, rapid antigen detection; PCR, polymerase chain reaction. Screen (+): positive finding in RAD test. Screen (−): negative finding in RAD test. RT-PCR (+): positive finding in reverse transcriptase-polymerase chain reaction. RT-PCR (−): negative finding in reverse transcriptase-polymerase chain reaction.

Table 3. The Data and Results from the 5 Major Branches of Taipei City Hospital.

	Sensitivity (%)	95%CI (%)	Specificity (%)	95%CI (%)	Positive Predictive Value (PPV) (%)	95%CI (%)	Negative Predictive Value (NPV) (%)	95%CI (%)	Accuracy (%)
RenAi (n = 1618)	62.0	(61.6, 62.3)	99.9	(99.9, 99.9)	97.8	(97.6, 97.9)	98.3	(98.3, 98.3)	98.3
Zhongxiao (n = 624)	60.5	(60.1, 60.8)	99.1	(99.0, 99.1)	91.2	(91.0, 91.5)	94.0	(93.9, 94.1)	93.8
YangMing (n = 787)	78.6	(78.2, 78.9)	98.2	(98.2, 98.3)	77.2	(76.8, 77.5)	98.4	(98.3, 98.4)	96.8
Zhongxing (n = 2061)	64.6	(64.3, 64.8)	98.3	(98.3, 98.3)	74.4	(74.2, 74.6)	97.4	(97.3, 97.4)	96.0
Heping (n = 1115)	69.1	(68.8, 69.5)	99.1	(99.1, 99.1)	86.2	(85.9, 86.4)	97.6	(97.6, 97.6)	97.0
Total (n = 6205)	66.0	(65.8, 66.1)	99.0	(99.0, 99.0)	82.8	(82.7, 82.9)	97.5	(97.4, 97.5)	94.2

Note: PPV, positive predictive value; NPV, negative predictive value. CI, confidence interval.

In this study, although the sensitivity score (mean 66.0%) of the screening was not extremely high, the specificity (mean 99.0%), PPV (82.8%), NPV (97.5%), and accuracy (94.2%) were satisfactory to an extent. The sensitivity score was also not inferior to that of the commercially available rapid influenza diagnostic tests (RIDTs) often used.[6] Thus, RAD for SARS-CoV-2 screening is a reasonable choice, especially during this critical period.

According to a statistical study in 2017,[7] the predictive values of a screening test were more relevant than sensitivity and specificity values. Also, the positive predictive value (PPV) and negative predictive value (NPV) are influenced by prevalence.[8] As the prevalence increases, the PPV also increases but the NPV decreases. Similarly, as the prevalence decreases the PPV decreases while the NPV increases. Thus, because the epidemic is dynamic, it is crucial for experts and healthcare workers to notice the prevalence of SARS-CoV-2. Furthermore, screening test materials of varied brands and skill variations could influence the accuracy of the results. For the rapid screening of another common and notorious respiratory tract virus,[8] influenza, the commercially available RIDTs provided results in less than 30 min, similar to the screening for SARS-CoV-2. However, they had decreased sensitivity (thought to be only 40%–60% in adults, with a range of 10%–80%). Besides, in studies of respiratory syncytial virus (RSV),[9,10] the sensitivity of rapid antigen test for RSV was from 12% to 65%, which was less than that of COVID-19 in our study. Therefore, there is no reason to deny the use of RAD for SARS-CoV-2 screening.

The RAD screening test requires people to insert the stick into their nose 2 to 2.5 cm deep, mix the mucous with the reagent, and wait for 15 to 30 min for the result. In contrast, the PCR test requires people to place the stick deep enough into the nasopharynx, which may cause violent discomfort. Moreover, the price of the PCR test is much higher than that of other screening tests. Considering its convenience, low cost, and prevalence, it is reasonable for hospitals and governments to promote self-screening for SARS-CoV-2. The performance of the different RAD brand did not vary significantly when compared with the different prevalence of PCR-positivity.

Although a rapid screening test is used to identify an infection, a negative result does not imply an uninfected state. In response to the rise in the COVID-19 pandemic, the government of Taiwan combined rapid screening and PCR testing from May 14, 2021. Although rapid screening screens symptomatic patients for infection, false-positive or false-negative results may occur. Therefore, it is necessary to re-confirm the results via an RT-PCR and compile a case number only after the PCR result is positive. Simultaneously, it was repeatedly emphasized that a negative test result did not mean that the virus had not infected the individual. If the viral load was low during the incubation period of the disease, it may not be detected. According to a review,[11] sensitivity was high in those with cycle threshold (Ct) values on PCR $\leq$25 compared to those with Ct values >25. Besides, sensitivity of symptomatic patients was higher than that of asymptomatic patients. During 21 to 26 May 2021, as per the accuracy rate of quick screening, the proportion of those who were positive in the quick screening and then tested positive via a PCR was 73% to 75% in Taipei and New Taipei City. This proportion was different in other counties and cities and ranged from 0% to 71%. If people were in close contact with infected patients or those with a history of activities in Taipei and New Taipei City, the number of people testing positive for COVID-19 infection using the rapid screening test could be high. Thus, the tools should be carefully selected. Conducting screening tests for those who had previous contact and were at high-risk, rather than the general population, was effective. Due to the novel SARS-CoV-2 variant, Omicron, a new outbreak

began in early January 2022, and the government implemented the self-screening policy again.

The COVID-19 Ag Rapid Test Device from varied brands performed well as a point-of-care (POC) test for the early diagnosis of COVID-19. More crucially, the data suggested that patients with RT-PCR-proven COVID-19 negative test via RAD were unlikely to be infected.

Limitations

The overall sensitivity of antigen tests is only 66% in the real-world data, which means that for every ten patients with COVID, 3 patients are missed using the screening test, and some of these missed patients are infectious. To increase the detection rate of rapid antigen screening, we need to detect symptomatic patients with high viral loads as soon as possible after exposure to infection or repeat tests to make increased sensitivity possible.

Clinical implications are as follows: (1). For people with symptoms and a history of exposure, even if the RAD is negative, PCR would be the reference laboratory confirmation method. (2). If large gatherings want to use RAD to control access, it is recommended to conduct 2 or several screenings to reduce the proportion of false negatives. (3). The principle of utilization of emergency department indicates the severity of symptoms, not the negative RAD result. Although the RAD is negative, if the symptoms are serious, patients should be sent to the emergency department for further treatment. On the other hand, even if the RAD is positive and there are no symptoms, patients were directed to the outpatient clinic for treatment.

Conclusion

We conclude that an antigen assay may be quick and feasible for differentiating individuals infected with SARS-CoV-2 from non-contagious individuals, with 66.0% sensitivity and 99.0% specificity. Regarding self-screening at home as a novel method for early detection, the RAD is convenient, cost-effective, and comfortable. It cannot however replace personal protective methods such as washing hands, routine alcohol disinfection, and wearing masks.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Research ethics and patient consent

This study was approved by the relevant Institutional Review Board (TCHIRB-111010099-E).

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