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Original research article

Performance of Rapid, Antigen-Detecting Point-of-Care Test for Suspected SARS-CoV-2 Patients Presented to the Emergency Department

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ABSTRACT

Patients who present to the emergency department (ED) with SARS-CoV-2 are highly contagious. Early diagnosis is necessary to reduce the transmission of this disease. We aimed to determine the performance of a rapid, antigen-detecting point-of-care test in symptomatic patients with suspected SARS-CoV-2 infection, using rt-PCR as the reference standard. A single- centered, cross-sectional retrospective study from data registry was conducted in the ED. Patients who were 18 years or older and had symptoms that were compatible with COVID-19 infection were eligible for inclusion. All patients were tested with rapid, antigen-detecting point-of-care tests and rt-PCR in the same visit. The diagnostic performances of the test were demonstrated with sensitivity, specificity, and predictive value, including positive predictive value (PPV) and negative predictive value (NPV). In total, 703 eligible patients were included in the analysis. Of these, 120 patients infected with SARS-CoV-2 were confirmed by rt-PCR. Total prevalence was 17.07%. The rapid antigen test demonstrated high sensitivity (87.5%), very high specificity (99.8%), PPV (99.1%), and NPV (97.5%). The test demonstrated high performance in patients with high viral loads (sensitivity of 94.2 - 100% in Ct values ≤ 25). However, the test showed a decline performance in patients with higher Ct values (sensitivity of 40 – 85.7% in Ct values > 25). In conclusion, the rapid, antigen-detecting point-of-care test showed high sensitivity and very high specificity in symptomatic ED patients, as compared to rt-PCR. This test can be

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used as an initial screening tool to detect and guide clinical decisions for suspected COVID-19 patients who present to the ED.

Keywords: Antigen-detecting point-of-care test; COVID-19; Rapid; SARS-CoV-2 infection

1. Introduction

Since 2020, there has an outbreak of 2019 Corona Virus Disease (COVID-19) in Thailand. There are approximately 15,000 new cases reported per day (data of April 2022) [1], and approximately 15 new patients present every day at Thammasat University Hospital (TUH) with COVID-19. COVID-19 is caused by infection of the SARS-CoV-2 virus. Infected patients can develop respiratory symptoms or pneumonia. Many COVID-19 patients have had symptoms so severe that they had to present and be triaged to the emergency department (ED).

Patients who have COVID-19 are highly contagious, either through droplet or aerosol spreading, especially in severely ill patients who need invasive procedures. Many patients need an aerosol generating procedure (AGP) in the ED, which allows the infection to spread either through contact or air to healthcare workers and other nearby patients [2]. The current standard method for diagnosis of COVID-19 is the reverse transcriptase polymerase chain reaction (rt-PCR) test [3, 4]. However, the rt-PCR test takes approximately 4-6 hours to obtain results. Therefore, congestion problems in the ED can result in an increased risk of disease spread.

The rapid, antigen-detecting point-of-care test has a shorter testing duration (15-20 minutes). It can also be performed bedside [5]. In previous clinical studies, diagnostic accuracy was high (sensitivity 86.8%, specificity 99.9%) compared to rt-PCR test [5-8]. Its diagnostic performance varies by the areas and patients at risk (Positive predictive value [PPV] of 55%-94.7% and Negative predictive value [NPV] of 89.2%-96.2%) [5-8]. However, there is very little information on patients who present to the ED.

The ED of TUH has introduced a rapid, antigen-detecting point-of-care test as part of the COVID-19 screening process since July 2021, used alongside patient history, symptoms, and initial radiology results. This study aimed to determine the performance of the rapid, antigen-detecting point-of-care test for screening of symptomatic ED patients with suspected SARS-CoV-2 infection as compared to rt-PCR as the reference. The results of this study will be used to help organize the ED, to reduce the spread of the disease to medical personnel and other patients.

2. Materials and Methods

2.1 Setting

From July 2021 to December 2021, a cross-sectional, single-centered, retrospective study using prospectively collected registry data was conducted by the Emergency medicine research group in TUH at Pathum Thani, Thailand. The TUH is an 800-bed, tertiary, academic teaching hospital. Around 60,000 patients visit the ED of TUH annually.

2.2 Participants

Patients who were 18 years or older and were at risk of SARS-CoV-2 infection or who had suspicious symptoms of COVID-19 were eligible for inclusion. The symptoms included fever, respiratory symptoms, loss of smell or taste, altered mentation, gastro-intestinal symptoms, or radiological signs of viral pneumonia. All eligible patients were immediately tested

for the SARS-CoV-2 virus with the rapid, antigen-detecting point-of-care test in the ED and had undergone rt-PCR testing during the same visit. Patients who were not tested with rt-PCR on the same day were excluded from the study.

2.3 Ethics approval

This study was approved by the Human Research Ethics Committee of Thammasat University, Faculty of Medicine. The informed consent was waived due to the retrospective nature of the study.

2.4 Data collection

Naso/oropharyngeal swab samples, or endotracheal tube washed samples were obtained from each eligible patient by a trained nurse or doctor in the ED. The samples used for the rapid, antigen-detecting point-of-care test and the rt-PCR test may not have necessarily came from the same sample, however, the results always came from the same patient, during the same visit.

The only rapid, antigen-detecting point-of-care test evaluated in this study was the PanBio™ COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostics, Jena, Germany) [9]. All patients were tested with the same rapid test band. The result was interpreted 15 to 20 minutes after a nurse or doctor instilled the solution and the results were considered invalid if the test was interpreted more than 20 minutes after the test began. The sampling, testing, and interpretation were performed according to the manufacturer's instructions. The results were then interpreted by trained emergency personnel who were not involved in this study.

2.5 Statistical analyses

Sample size calculations estimated that a minimum of 610 cases were needed to demonstrate statistically significant results according to the rate of positive COVID-19 diagnoses (25%), test sensitivity value of 90%, and specificity value of 95%, using a statistical significance level of $p \leq 0.05$ [10].

Using rt-PCR test results as the reference standard, the diagnostic performance of the rapid, antigen-detecting point-of-care test were demonstrated with sensitivity, specificity, and predictive value including PPV, and NPV with their respective 95% confidence intervals (CI). The patients with positive rt-PCR test results had been categorized and analyzed according to their level of Ct-value. The rapid, antigen-detecting point-of-care test diagnostic performance measures were calculated across Ct-value categories.

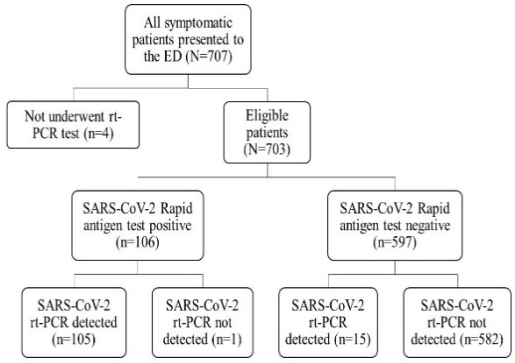

Fig. 1. Flow chart of the study. ED; emergency department, rt-PCR; reverse transcriptase polymerase chain reaction.

3. Results and Discussion

3.1 Results

During the 6-month study period, there were 707 patients who presented to the TUH ED with signs or symptoms suggestive of COVID-19 and who then underwent rapid, antigen-detecting point-of-care testing in the ED (Fig.1). Four patients were excluded because they were not tested with rt-PCR. The remaining 703 eligible patients were included in the analysis. Of these 703 patients, 120 were

infected with SARS-CoV-2, confirmed by rt-PCR. During the study period, SARS-CoV-2 infection prevalence in symptomatic ED patients was 17.07%.

Table 1 shows the data on the baseline characteristics of the study participants. Most patients older than 60 years (66.7%), were triaged in the emergency category (72.1%), had a history of traveling, living, or working in a high-risk area (88.1%), or had respiratory symptoms (68.8%). Most patients did not had infiltration on chest radiograph (41.3%) or had only interstitial infiltration (25.9%). The rapid, antigen-detecting point-of-care test came back positive in 106 cases (15.1%), the overall true positive rate for the rapid, antigen-detecting point-of-care test was 87.5%.

Table 1. Baseline characteristic of participants.

Characteristic	No. of patients (N=703)	% of patients
Male	361	51.35
Age (year) mean (SD)	65.12 (18.34)	
18 - 40	79	11.24
41 – 60	155	22.05
>60	469	66.71
Triage category		
critical	88	12.52
emergency	507	72.12
urgency	108	15.36
History risk		
travel, live, or work in a risk area	619	88.05
contact with a confirmed case of COVID-19	72	10.24
go to a gathering place where has confirmed COVID-19 case	28	3.98
history associated with 5 or more clusters	3	0.43
Symptom associated with COVID-19		
fever at least 37.5 °C or history of fever	315	44.94
respiratory symptom	483	68.80
gastro-intestinal symptom	110	15.67
alteration of consciousness	59	8.40
no symptom	59	8.40
Radiological sign		
only interstitial infiltration	182	25.89
only alveolar infiltration	128	18.21
ground grass appearance	103	14.65
no infiltration	290	41.25
Duration of symptom (day) median (IQR)	2 (1. 3)	
Rapid antigen test positive for COVID-19	106	15.08
Rt-PCR test detected for COVID-19	120	17.07
Ct value mean (SD)	23.43 (5.26)	

Table 2 shows the diagnostic performance of the rapid, antigen-detecting point-of-care test. The test demonstrated high sensitivity (87.5%), very high specificity (99.8%), very high PPV (99.1%), and very high NPV (97.5%).

Table 3 shows the sensitivity of the rapid, antigen-detecting point-of-care test according to patients rt-PCR Ct-value categories. The test demonstrated high performance in patients with high viral loads (sensitivity of 94.2 - 100% in rt-PCR Ct values ≤25). However, it showed a decline in performance for patients with higher Ct values (sensitivity of 40 – 85.7% in rt-PCR Ct values over 25).

3.2 Discussions

Rapid identification and separation of patients at risk of, or infected with, COVID-19 in the ED is very important, in order to minimize spread of the disease to healthcare personnel and other patients. This observational study demonstrated the diagnostic performance of the rapid, antigen-detecting point-of-care test for screening of symptomatic, ED-presenting patients with suspected COVID-19, by using rt-PCR as the reference. The use of the rapid test in the ED showed high sensitivity (87.5%) and very high

specificity (99.8%). The rapid test in the ED also showed very high predictive performance, with a PPV of 99.1% and an NPV of 97.5%.

Table 2. Diagnostic performance of rapid, antigen-detecting point-of-care test for screening of symptomatic patients with suspected SARS-CoV-2 infection, using rt-PCR test as the reference.

Diagnostic performance	Value (N=703)	95% confidence interval
Cases (prevalence)	120 (17.07)	
Sensitivity (%)	87.5	80.2 – 92.8
Specificity (%)	99.8	99.0 – 100
Positive predictive value (%)	99.1	94.9 - 100
Negative predictive value (%)	97.5	95.9 – 98.6

Table 3. Sensitivity of rapid, antigen-detecting point-of-care test according to patients' level of Ct-value from rt-PCR test.

Ct interval	N (N=120)	True positive (N)	Sensitivity% (95% CI)
≤ 20	32	32	100 (89.1, 100)
>20 - ≤ 25	52	49	94.2 (84.1, 98.8)
> 25 - ≤ 30	21	18	85.7 (63.7, 97.0)
> 30	15	6	40.0 (16.3, 67.7)

A study by Alejandro Fernandez-Montero et al [6] used an antigen-detecting test kit (ATK) in asymptomatic subjects (incidence of COVID-19 was 1.93%) and used rt-PCR as reference standard. They found that the ability to differentiate patients with real disease was low (PPV of 53.3% and NPV of 99.7%). However, when screened with ATK in higher a prevalence population (those at risk or with symptoms), they found that the performance of the test was higher (PPV of 96.4% and NPV of 96.9%). Another study by Lisa J. Krüger et al [5] investigated the use of the PanbioTM (Abbott Rapid Diagnostics) ATK in Germany. Participants were patients who were at risk or who had symptoms; the results indicated high predictive performance (PPV of 98.7% and NPV of 98.1%), with the highest values seen in those with symptoms for less than 7 days. In our study, the test performance measures in symptomatic patients were consistent with the findings of these other studies.

Previous research in an ED located in Germany [7] studied patients with a high prevalence of COVID-19 infection (prevalence of 32.8%) using ATK in symptomatic patients admitted to the ED and used rt-PCR as the reference standard. It was found that the ability to isolate patients with disease was very high (PPV of 100%), while the ability to distinguish patients who did not have disease was acceptable (NPV 89.2%). Although our population prevalence was lower (17.1%), the test's predictive performance was still high for both positive and negative results.

Our study showed a rate of 12.5% for false negative results (15 patients who were determined negative from rapid antigen test, but SARS-CoV-2 was detected by rt-PCR). However, when subgrouping all patients detected with rt-PCR by Ct interval, the rapid antigen test demonstrated a high capacity to detect positive infection in patients with higher viral loads (sensitivity of 94.2 - 100% in Ct values ≤ 25) but there was a decline

performance in patients with higher Ct values (sensitivity of 40 - 85.7% in Ct values over 25). This finding is comparable with previous studies in which it was found that performance of the rapid antigen test was related to the level of viral load [11, 12].

The 28-year-old male patient showed a false positive result from ATK testing. The patient came to the ED with cardiac arrest presumed from cardiac cause. He was tested for SARS-CoV-2 during ED cardiopulmonary resuscitation because he had a history of contact with a confirmed case of COVID-19. He died in the ED after unsuccessful resuscitation. A post-mortem chest radiograph showed alveolar infiltration in both lungs. He was not autopsied because the forensic doctor wanted to limit the spread of disease. However, the rt-PCR result was negative. There are many causes of false positives for ATK, such as alternate viral infections, poor sample collection, or poor sample management. The false positive ATK testing might lead to unnecessary resource use. However, only a 0.9% false positive rate was found; this finding is comparable with that of a systematic review conducted by the Cochrane Collaboration [13]. The rapid test might still be the most useful test in EDs.

Our study had some limitations. First, it was conducted only in one tertiary, academic, teaching hospital, therefore these results might not represent the pandemic at large. Second, this was a retrospective study, patients' characteristics, clinical data, and outcomes were only derived from prospectively collected data, thus the data might be susceptible to selection or information bias. However, to avoid selection bias, this study included all patients in the study period into the analysis. To reduce information bias, all data were extracted from the prospectively collected data registry of the COVID-19 ED of TUH. The results of the rt-PCR test and Ct values were reported officially via hospital data system. Third, this study only included adult patients who were at risk of getting disease and presented to the ED with symptoms suggestive of COVID-19. The study's results cannot be generalized to the asymptomatic population or children.

4. Conclusion

This study found that the rapid, antigen-detecting point-of-care test has a high sensitivity and a very high specificity for symptomatic patients who present to the ED, as compared to rt-PCR as the reference. The test shows high sensitivity in patients with high viral load, but a high rate of false negatives was observed in patients with lower viral load.

The rapid test can be used as an initial screening tool to detect and guide the physicians to make clinical decisions for suspected COVID-19 patients who present to the ED. Further research should focus on creating decision-making guidelines based on patient history, risk level, symptoms, and rapid test results, to be able to effectively separate patients with COVID-19 from those who do not have the disease.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there have no competing interests.

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