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Evaluation of Swab Diagnostic Performance for Suspected Covid-19 Patients Using ID NOW

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Abstract: Molecular rapid test may provides an alternative to time-consuming PCR tests. There is a continuing need for reliable molecular rapid test detection methods to be quick and easy applied to individuals with acute SARS-CoV-2 infection. Features ability of molecular rapid test should be considered and compared with the gold standard Real-time-Polymerase Chain Reaction (RT-PCR) test for diagnosis of COVID-19 cases. In this research, the goal was to analyze the ability of ID Now. Molecular rapid test (ID Now) was compared with the real-time RT-PCR test for diagnosis of SARS-CoV-2 in nasopharyngeal. ID NOW works with isothermal nucleic acid amplification for the qualitative detection of the Rdrp gene. Otherwise, RT-PCR detects gene N, gene E, and Orf1ab from SARS-CoV-2 for virus identification or quantification of viral load. One hundred thirty six (from nasopharyngeal swabs) were get from COVID-19 suspected cases and exposed individuals in three hospitals: Universitas Brawijaya Hospital Malang, Baptis Hospital, and Regional Hospital Lawang, east Java, Indonesia, during May 2021. A total of 136 samples, 66 samples were positive, and 70 sampels were negative for SARS-CoV-2 RNA by ID Now. Comprehensively, sensitivity and specificity were 98.4% (95% confidence interval 91 – 100%) and 92% (95% confidence interval 85-92%), respectively, PPV 90,9% NPV 98,6% with a diagnostic accuracy of 94% and Kappa coefficient of 0.89. Molecular rapid test (ID Now) showed good sensitivity and specificity. This test can be used for the early detection and rapid diagnosis of SARS CoV-2.

Keywords: *Covid-19, ID Now, PCR, TCM*

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I. INTRODUCTION

COVID-19 is a breathing system disease caused by SARS-CoV-2, which was detected in 2019. The virus is estimated to infect mainly from person to person through respiratory droplets produced from an infected person coughs, sneezes, or talks [1]. The number of confirmed cases and death rates are currently increasing. The COVID-19 confirmed cases in Indonesia as of May 16, 2021, was 1,739,750, with a Case Fatality Rate (CFR) of 2,8%. Meanwhile, Indonesia's CFR was above the global CFR of 2,1%. The data shows no signs that the pandemic will end.

Accurate and rapid diagnostic tests are important to stop the spreading of SARS-CoV-2, the virus that causes COVID-19. Testing for SARS-CoV-2 infection is part of a wholistic goal to reduce transmission, symptom screening, and contact tracing, which is also a strategy for identifying people with SARS-CoV-2. Hence, some measures can be done to decelerate and stop the COVID-19 pandemic [1].

RT-PCR detects the presence of viral genetic material or viral load quantification from SARS-CoV-2. Some primers and probes have been used in several countries worldwide to detect the SARS-CoV-2 gene. But instead, it can take hours to detect nucleic acids and viruses. In addition, special instruments and expertise are required for the rapid diagnosis of SARS-CoV-2 infection. The use of rapid test kits allows earlier detection and better isolation of coronavirus confirmed cases [2, 3].

Indonesia currently has several rapid molecular test kits. Some of those tools are Gene Xpress, Pockit Central, and ID Now. Gene Xpert is an automated in vitro diagnostic test for the qualitative detection of nucleic acids from SARS-CoV-2. A particular cartridge device for COVID-19 is required to be able to carry out the examination. The name of the particular cartridge is Xpert Xpress SARS-CoV-2 [4]. This test also requires equipment, computers, and software that must be prepared in advance to run the test and see the results [5]. Although this tool is widely spread in Indonesia, it still requires a particular cartridge device and training for laboratory personnel who will operate it. Therefore, not all medical personnel can handle it. Another rapid molecular test is Pockit Central. This tool is qualitative PCR amplification and detection system based on Insulated Isothermal technology, which applied the concept of Rayleigh-Benard convection to drive PCR by a single heating source at the bottom of capillary tubes by targeting the target Orf1ab gene. This tool takes less than an hour and a half to process until the results are read [6]. ID Now has the fastest time to detect the Sars CoV-2 gene, which is less than 13 minutes compared to the two previous tools [7].

ID NOW automated assay that utilizes isothermal nucleic acid amplification technology for the qualitative detection of SARS-CoV-2 viral nucleic acids. This tool is designed for amplification of the RdRp segment of SARS CoV-2 RNA. It is hoped that the ID NOW tests can shorten the time of COVID-19 diagnosis.

The performance of ID Now in Indonesia is currently unknown. Therefore, the goal of this research is to analyse the ability of the COVID-19 swab diagnosis using ID Now on COVID-19 patients at Brawijaya University Hospital (RSUB), Baptist Hospital Batu, and Lawang Hospital.

II. METHOD

This cross-sectional diagnostic study was done at Brawijaya University Hospital (RSUB), Baptist Hospital Batu, and Lawang Hospital in May 2021. The research subjects were patients with suspected COVID-19 who visited the COVID Polyclinic at the three hospitals. The research subjects were randomly selected. The inclusion criteria for this study are (1) People with Acute Respiratory Infections (ARIs) and in the last 14 days before the symptoms develop have lived or traveled in a country or area of Indonesia that reports local transmission, (2) People with one of the symptoms of ARI and in the last 14 days before the symptoms develop have contact with infected/probable cases of COVID-19. Patients were examined for SARS – CoV 2 by taking swab in the right and left nasopharyngeal. The first nasopharyngeal swab was examined directly using ID Now.

ID Now comprised of a Sample Receiver containing a buffer, a Test Base comprising two sealed reaction tubes, a Transfer Cartridge for transfer of the eluted sample to the Test Base, and the ID NOW Instrument [8].

The reaction tubes in the Test Base contain the reagents required for amplification of SARS-CoV-2, as well as an internal control. The templates were designed to target SARS-CoV-2 RNA amplify a unique region of the RdRp segment. Fluorescently-labeled molecular beacons are used to identify each of the amplified RNA targets specifically [8].

There are two parts of carrying out the examination, including the Sample Receiver and the Test Base are inserted into the IDNOW Instrument. The sample is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, initiating target amplification. Heating, mixing, and detection are provided by the instrument [8].

The second nasopharyngeal swab was inserted into the vtm and sent to the biomolecular department of the

central laboratory of Saiful Anwar Malang Hospital to be tested by RT-PCR.

A. *Ethical Statement*

Informed consent was taken from all study patients. The Ethics Commission of Universitas Brawijaya, Faculty of Medicine, Malang, reviewed and approved this study.

B. *Statistical Analysis*

Assuming that RT-PCR is the gold standard for the COVID-19 testing, the researchers calculated the sensitivity and specificity with the kappa agreement index that values < 0 poor, 0,00 - 0,21 slight, 0,21 - 0,40 fair, 0,41 - 0,60 moderate, 0,61 - 0,80 substantial, and 0,81 - 1,00 almost perfect. Continuous variables with normal distributions are stated as mean (± Standard Deviation [SD]), and non-normal distributions are stated as medians (Interquartile Range [IQR]) and compared using *t*-test and Man Whitney test for parametric and non-parametric data. Categorical variables are stated as numbers (percentages) and compared with the x^2 test or Fisher's exact test.

RESULTS

A diagnostic test study has been conducted on 136 patients with suspected COVID-19 who were examined using ID Now and the gold standard RT-PCR. The characteristics of the research sample are shown in Table 1.

TABLE 1
SAMPLE CHARACTERISTICS

	Positive	Negative	*p* value
Gender			
Male (n)	34	40	0.510
Female (n)	32	30	
Age			
(Median (IQR))	57(44-63)	42(33-63)	0.000

From the characteristic of the data, it was found that there was no difference between men and women. The age of subjects with positive ID Now results had a significantly higher median age than those with negative ID Now results. Meanwhile, the results of the comparison of ID Now and RT-PCR can be seen in Table 2.

TABLE 2
COMPARISON OF ID NOW AND RT - PCR

		RT - PCR		
		Positive	Negative	Total
ID Now	Positive	60	6	66
	Negative	1	69	70
	Total	61	75	136

From the results, after the analysis, the sensitivity value of the ID Now is 98,4% with (95% confidence interval of 91 - 100%). Specificity is 92% with (95% confidence interval of 85-92%). The value of the kappa agreement index is 0,89%, with a diagnostic accuracy of 94%. Based on Table 2, the positive probability ratio is 90,9%, and the negative probability ratio is 98,6%.

III. DISCUSSION

In this study, the researchers present data on the characteristics of research subjects which are summarized in Table 1. There is no significant difference in gender. In previous study the prevalence of symptomatic COVID-19 was found to be higher in men than in women. The high prevalence of smoking and alcohol consumption contributed to the high prevalence of COVID-19 among men [9]. However, there is a significant difference between the subjects' ages who have positive and negative results. Data shows that older people are more susceptible to the Sars CoV-2 virus. This is supported by a previous study conducted by Huanyuan Luo et al. that the majority (80%) of COVID-19 cases were among young adult patients aged 19-44 years and patients aged 45-64 years. Older age is also said to be more at risk of experiencing respiratory failure and death [10]. Older adults have been found to be particularly susceptible to this infection. In comparison to younger adults, older patients have shown increased need for Intensive Care Unit (ICU) admission and mechanical ventilation [11].

The ID Now agreement test in the study of Smithgall MC et al. showed a low agreement value. However, in the study of Farfour Eric et al., it was revealed that the agreement test was perfect. The value of the Kappa ID Now agreement index in this study is 0.89. Therefore, it can be interpreted as excellent. The different agreement tests are considered due to preanalytic and analytical factors, such as the use of transport media, frozen samples, or new samples [7, 12].

The sensitivity of ID Now from previous studies is varied from 44% to 94% [2]. In this study, it was found that of the 136 subjects who took part in the study, 60 subjects out of 136 were positive with ID Now and RT-PCR-assuming that RT-PCR is the gold standard. Therefore, from this study, the results of the diagnostic test tool were obtained with a sensitivity of 98,4% with a (95% confidence interval of 91 - 100%). Specificity of 92% with (95% confidence interval of 85-92%). Six subjects from Table 2 data were found to be positive with the ID Now instrument but negative with RT-PCR. The researchers believe that the six subjects are certainly positive when it is seen from the positive probability ratio of 90,9%. Based on previous research conducted by Basu et al., the positive probability ratio value of the ID Now instrument was reported as 94,4%. Thus, it could remove false positives [13]. This study also found one negative subject with the ID Now Abbot test but positive with the RT-PCR test. The researchers suspect this one patient is a false negative. Previous studies reported that ID Now Abbot can only detect specimens with ct $\leq$ 30 and cannot detect specimens with ct $\geq$ 30 [7]. Other studies reported the false negatives of the ID NOW COVID-19 display a median CT value of 21.1 (CT range 6.8–30.3 [12]. Viral load is known to change during the clinical course of COVID-19. A high SARS-CoV-2 viral load was detected soon after the symptoms developed, followed by a gradual decline up to the detection limit around day 21, with no clear difference in viral load by gender, age, and disease severity and before the onset of the symptoms [14]. The limitations of the ID NOW is the lack of strong data to identify its effectiveness in detecting SARS-CoV-2 in clinical settings. The studies used to obtain FDA approval were in vitro. These studies showed that the limit of detection of the Abbott ID NOW is similar to other nucleic acid amplification tests at approximately 125 genome equivalents per millilitre. In addition, many of these studies vary in their research's method such as comparing nasopharyngeal to nasal specimens or having major delays in testing specimens on the ID NOW. Some studies were also conducted prior to Abbott's updated guidance on ID NOW specimen transportation that recommended against using UTM [15]. In the other hand, the benefit of ID- NOW is the shortest turnaround time provided by the ID NOW platform, a much more accurate assay performance is highly expected due to severe clinical manifestations/complications of COVID-19 and the likelihood of further spreading infection by those tested false-negatives. Therefore, our institute generated an ordering algorithm on SARS-CoV-2 testing to make sure clinicians order RT-PCR testing if results from ID NOW do not fit in the clinical indications [16]. Limitations in this study are the researchers did not analyze viral load on ID NOW results, and there was no division of symptomatic and asymptomatic subject groups.

IV. CONCLUSION

ID Now has a sensitivity of 98,4% and a specificity of 92% with a kappa agreement index of 0,89%. ID Now can be used as an instrument to detect patients with suspected COVID-19.

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