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# Comparison of Two SARS-CoV-2 Rapid Antigen Test

**Stefany Boroh[1], Irda Handayani[1], Nursin Abdul Kadir[1,2], Uleng Bahrun[1]**

[1] Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia
E-mail: stefany_boroh.86@yahoo.com
[2] Clinical Pathology Laboratory, Labuang Baji Hospital, Makassar, Indonesia

## ABSTRACT

The Coronavirus Disease 2019 (COVID-19) pandemic continues to spread worldwide. A quick, simple, and accurate test to diagnose COVID-19 is essential for this situation. This study aims to evaluate and compare the rapid antigen examination of SARS-CoV-2 with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) in detecting SARS-CoV-2. A retrospective study with a cross-sectional approach using medical record data from suspected, controlled, and confirmed COVID-19 patients whose samples were taken simultaneously for rapid antigen examination of SARS-CoV-2 (SD-Biosensor and Lungene) and RT-PCR at Labuang Baji Hospital, Makassar from September 2020-September 2021. Each instrument's sensitivity, specificity, negative predictive value, and positive predictive value were analyzed with the Receiver Operating Characteristics (ROC) curve method. This study obtained data from 312 rapid antigen tests for SARS-CoV-2, divided into two categories, 98 using Lungene and 214 using SD-Biosensor. Rapid antigen Lungene had a sensitivity of 71.4%, specificity of 71.4%, an accuracy of 71.4%, and a 31 reactive result in CT value. The SD-Biosensor Rapid antigen had a sensitivity of 62.6%, a specificity of 99.1%, an accuracy of 82.2%, and a 26 reactive result in CT value. In summary, the sensitivity of rapid antigen Lungene is higher than SD-Biosensor. Specificity and accuracy of rapid antigen SD-Biosensor higher than Lungene. Rapid test antigen SARS-CoV-2 has the potential to be a screening test for COVID-19 as long as the sampling time is right.

**Keywords:** COVID-19, rapid antigen, RT-PCR, SARS-CoV-2

## INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a highly contagious infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 is transmitted quickly through droplets, both directly and indirectly, through contact with surfaces contaminated with droplets from people infected with SARS-CoV-2. This mechanism causes COVID-19 to spread very quickly throughout the world and has become the cause of a global pandemic. The morbidity and mortality of COVID-19 are high, as shown by the number of infected people. On August 2, 2021, 3,496,700 confirmed cases were reported in Indonesia, and 98,889 died with a Case Fatality Rate (CFR) of 2.8%.[1-5]

The general signs and symptoms of COVID-19 infection vary widely, ranging from typical acute respiratory symptoms such as fever, cough, and shortness of breath to atypical non-respiratory symptoms. More severe symptoms are found in patients who are older and have comorbidities.[1-4]

Various parties have attempted infection control efforts. The Emergency Committee has stated that the spread of COVID-19 can be stopped by providing protection, early detection, isolation, and immediate treatment to create a robust system implementation. Based on this, one way to overcome the spread is early detection through screening tests, contact tracing, and immediate confirmation tests for COVID-19. The World Health Organization (WHO) has recommended a standard test for confirmation of COVID-19 using the Reverse Transcription Polymerase Chain Reaction (RT-PCR) examination method, using the RdRp gene and E gene, and the Center for Disease Control and Prevention (CDC) added the N gene to confirmation.[1,2,6,7]

The RT-PCR method can be carried out conventionally or automatically to detect the genetic material of the SARS-CoV-2 virus present in patient samples. Samples can be in the form of nasopharyngeal swabs, oropharyngeal swabs, sputum, saliva, gastric lavage, feces, and blood/serum. However, the sampling technique that is widely used in nasopharyngeal and oropharyngeal swabs to increase the positivity of patient samples examined is based on the Decree of the Minister of Health of the Republic of Indonesia regarding guidelines for preventing and controlling COVID-19. The virus is usually found in high levels during the

pre-symptomatic phase (1-3 days before the appearance of symptoms) and early symptomatic phase (within the first 5-7 days of the course of the disease). It will survive up to 20 days on average.[7-13]

RT-PCR is a microbial detection method with very high sensitivity and specificity. However, PCR examinations require money, and trained personnel, and are very long to conduct, and not all health facilities have a PCR laboratory breaking the chain of transmission requires accurate results that can be obtained quickly and can run a large number of samples simultaneously to expand the inspection scope. The presence of the SARS-CoV-2 rapid antigen test gives hope for this solution, at least for fast, inexpensive, and easy screening or the diagnosis of COVID-19 in PCR-limited areas.[7-12]

Diagnostic tests for rapid antigen detection are designed to directly detect the SARS-CoV-2 protein produced by the virus replicating in secretions of the respiratory tract. This antigen test is specific for COVID-19, but the sensitivity could be better, particularly in samples with low virus counts. WHO declared good concordance with a CT value ≤ 25 (on tests with a maximum CT value of 40) or > $10^6$ viral genomic copies/mL. Therefore, a negative result does not rule out COVID-19 infection, so confirmation by RT-PCR is still needed.[8-14]

Various studies continue to be developed to see the Rapid Diagnostic Test (RDT) performance against RT-PCR SARS-CoV-2. The results of these studies showed varied results. Among them is a study by Chaimayo *et al.* in Thailand, which stated that a rapid test for the detection of SARS-CoV-2 antigen showed sensitivity and specificity comparable to the RT-PCR test with a sensitivity of 98.33% and a specificity of 98.73%. Pena *et al.* in Chile conducted a rapid antigen performance test for SARS-CoV-2 by RT-PCR in asymptomatic individuals showing lower sensitivity (69.86%) and higher specificity (99.61%).[15-19]

The SARS-CoV-2 rapid antigen test is increasingly being used under various brands in Indonesia for initial screening. It is necessary to evaluate the performance of the rapid antigen test brand in detecting SARS-CoV-2. Therefore, based on the reasons above, the performance of the two most widely used SARS-CoV-2 antigen RDT instruments in Makassar (Lungene and SD-Biosensor) for initial screening and contact tracing of patients with or without symptoms of COVID-19, who were examined at the Labuang Baji Hospital, were compared. The method mentioned above has a similar antigen target but different methods of mixing the buffer solution. Research on SARS-CoV-2 antigen RDT compared to RT-PCR is still limited, with varying results. This research has never been conducted in Makassar. Furthermore, a recent study has yet to be established comparing the diagnostic accuracy of the SARS-Cov-2 rapid antigen test. Rapid antigen is expected to be used as an initial screening method and can be used for diagnostics in areas where the RT-PCR is not available.

## METHODS

This research is a retrospective study with a cross-sectional approach using secondary data from patient medical records at Labuang Baji Hospital from September 2020 to September 2021. All protocols in this study have been reviewed and approved by the Health Research Ethics Commission, Faculty of Medicine, Hasanuddin University/University Hospital Hasanuddin Central General Hospital Dr. Wahidin Sudirohusodo, Makassar (KEPK-FKUH RSUH-RSWS) with article number: 663 /UN4.6.4.5.31/PP36 /2021.

The research samples were all individuals who took the SARS-CoV-2 rapid antigen test and RT PCR at Labuang Baji Hospital, who met the inclusion criteria: the sample for the RT-PCR test was taken at the same time or less than 24 hours after taking the sample for the SARS-CoV rapid antigen test, the rapid tests used were the Lungene antigen rapid test (Hangzhou Clongene Biotect.co Ltd, China) and the Standard F COVID-19 Ag FIA (SD-Biosensor, Republic of Korea), and the RT-PCR examination was carried out at the Labuang Baji Hospital and Makassar Health Laboratory Center (BBLK). Incomplete medical record data (ID card number) and inclusive RT-PCR results were excluded from this study.

Data were processed by statistical tests using SPSS software version 25.0. Receiver Operating Characteristics (ROC) curve analysis was used to measure the sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of each of the rapid antigen instruments studied. The cut-off value of each instrument was determined by using the RT-PCR examination results as a standard for comparison.

## RESULTS AND DISCUSSIONS

This study involved 312 subjects with the characteristics shown in Table 1. The majority of the samples were female (192 subjects, 61.5%), ages 26-35 years and <25 years (75 subjects, 24% each), and had no complaints (2014 subjects, 65.4%). The proportion of rapid antigen tests used was

SD-Biosensor with 214 subjects (68.6%) and Lungene with 98 subjects (31.4%).

**Table 1.** Subject characteristics

| Characteristics | Patients, n=312 (%) |
|---|---|
| **Gender** | |
| Male | 120 (38.5) |
| Female | 192 (61.5) |
| **Age** | |
| = 25 years | 75 (24.0) |
| 26-35 years | 75 (24.0) |
| 36-45 years | 68 (21.8) |
| 46-55 years | 58 (18.6) |
| > 55 years | 36 (11.5) |
| **Clinical manifestation** | |
| Present | 108 (34.6) |
| Absent | 204 (65.4) |
| **Brand of rapid test** | |
| Lungene | 98 (31.4) |
| SD-Biosensor | 204 (65.4) |

The diagnostic value of the rapid antigen test of the brands studied in this study can be seen in Table 2. The Lungene brand rapid antigen test had a sensitivity of 71.4%, a specificity of 71.4%, a PPV of 86.2%, and NPV of 50%. The SD-Biosensor rapid antigen test had a sensitivity of 62.6%, a specificity of 99.1%, a PPV of 98.4%, and NPV of 75.5%.

The Lungene and SD-Biosensor rapid antigen tests use a sandwich immunodetection method that uses an easy-to-use lateral flow test format. The target analyte often used for the SARS-CoV-2 rapid antigen is viral nucleocapsid protein due to its relatively large number.[7,14,20,21] This is quite different from the chemiluminescent immunoassay (CLIA) serological test, which is based on detecting IgM/IgG antibodies against SARS-Cov-2. This examination has relatively better sensitivity and specificity values  compared to those obtained in this study.[22]

The Lungene brand rapid antigen test has a sensitivity of 71.4%, a specificity of 71.4%, a PPV of 86.2%, an NPV of 50%, and an accuracy of 71.4%. The SD-Biosensor brand rapid antigen test has a sensitivity of 62.6%, a specificity of 99.1%, a PPV of 98.4%, an NPV of 75.5%, and an accuracy of 82.2%. From these results, it can be interpreted that if the results of the Lungene and SD-Biosensor rapid antigen tests show non-reactive results, it is not sure whether or not there was SARS-CoV-2 infection in the patient, so an RT-PCR examination must be carried out. Clinical manifestations may be a factor influencing the RDT results. If the results of the Lungene rapid antigen test were reactive, it is not sure whether the patient was infected with SARS-CoV-2 or not, so it is necessary to proceed with an RT-PCR examination. Meanwhile, if the SD-Biosensor rapid antigen test results were reactive, it was almost certain that the person was infected with SARS-CoV-2. This study's sensitivity results differ from that of Chaimayo *et al*. who tested rapid antigen against RT-PCR. In his research, obtained a sensitivity of 98.33% and a specificity of 98.73%. The sensitivity results were different because, in his study, 88.3% of the samples were patients accompanied by symptoms. In this study, out of 20 false negatives of the Lungene rapid antigen, 16 were asymptomatic patients. Likewise, with the rapid test using the SD-Biosensor, out of 37 false negatives, 29 people were asymptomatic patients. Pena *et al*. in Chile conducted a performance test for the SARS-CoV-2 rapid antigen compared to RT-PCR on asymptomatic individuals. The results obtained a sensitivity of 69.86% and a specificity of 99.61%. The results of the specificity of the two studies that also used the SD-Biosensor rapid antigen test in their study were comparable to the specificity results of the SD-Biosensor in this study. In contrast, the specificity of the Lungene rapid antigen was 71.4%. False positives can result from cross-reactions from the Lungene rapid antigen test and contamination during sample handling. This was based on the data obtained. Out of 8 false positives, there were 4 with complaints of headaches and flu. In addition, the processing of samples using the Lungene rapid antigen test could lead to environmental contamination because the extraction buffer is separated from the extraction tube. Unlike the SD Biosensor rapid antigen test, where the extraction buffer is already in the extraction tube.[16,17,20,21]

**Table 2.** Diagnostic value of rapid antigen test of SARS-Cov-2

| Rapid Antigen | RT-PCR (+) | RT-PCR (-) | Total | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|---|---|
| **Lungene** | | | | | | | |
| Reactive | 50 | 8 | 58 | 71.4 | 71.4 | 86.2 | 50 |
| Non-reactive | 20 | 20 | 40 | | | | |
| **SD-Biosensor** | | | | | | | |
| Reactive | 62 | 1 | 63 | 62.6 | 99.1 | 98.4 | 75.5 |
| Non-reactive | 37 | 114 | 151 | | | | |

**Table 3.** Comparison of CT value by brand of rapid antigen test

| Rapid Antigen | n | RT-PCR | | | p-value |
|---|---|---|---|---|---|
| | | Minimum | Maximum | Mean±SD | |
| **Lungene** | | | | | |
| Reactive | 50 | 11.76 | 38.73 | 26.12±6.59 | <0.01 |
| Non-reactive | 20 | 17.56 | 38.73 | 32.03±4.71 | |
| **SD-Biosensor** | | | | | |
| Reactive | 62 | 5.92 | 36.39 | 21.40±6.28 | <0.01 |
| Non-reactive | 37 | 14.35 | 38.98 | 30.31±6.54 | |

Independent T-test

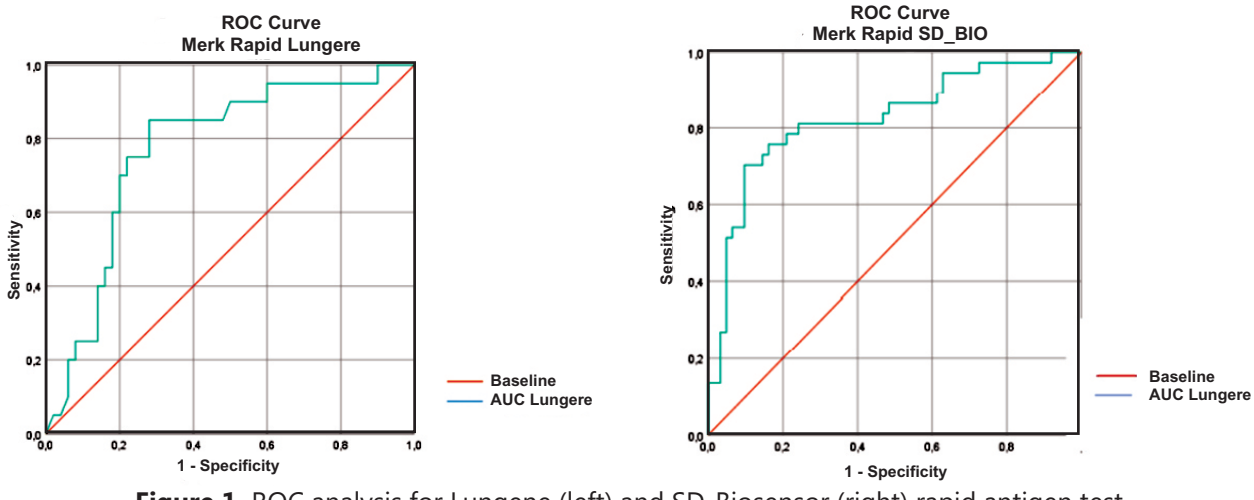


**Figure 1.** ROC analysis for Lungene (left) and SD-Biosensor (right) rapid antigen test

A comparison of CT values according to the brand of rapid antigen test in this study can be seen in Table 3. Reactive results on the rapid antigen test using Lungene had a mean CT value of 26.12±6.59, and non-reactive results had a mean CT value of 32.03±4.71. Reactive results on the rapid antigen test using SD-Biosensor had a mean CT value of 21.4±6.28, and non-reactive results had a mean CT value of 30.31±6.54.

Figure 1 shows the ROC curve analysis for the rapid antigen test for the two brands analyzed. The ROC curve analysis results obtained the Area Under the Curve (AUC) CT value for the Lungene rapid antigen test of 0.773. The optimal cut-off value for the CT value against the Lungene rapid antigen test is the optimal cut-off for the sensitivity and specificity of the Lungene rapid antigen test against the CT value with a CT cut-off value of 31. The results of the ROC curve analysis for the SD rapid antigen test -Biosensor obtained a CT AUC value of 0.825. The optimal cut-off value for the CT value against the SD-Biosensor rapid antigen test is the optimal cut-off for the sensitivity and specificity of the SD-Biosensor rapid antigen test against the CT value with a CT cut-off value of 26.

The CT cut-off value for the Lungene rapid antigen test was 31. This finding means that if the CT value of RT-PCR was ≤ 31, it would give a reactive result on the rapid antigen test. In addition, if the CT value of RT-PCR > 31 it would give non-reactive results on the rapid antigen test. The CT cut-off value for the SD-Biosensor brand rapid antigen test was 26. This finding means that if the CT value of RT-PCR was ≤ 26, it would give reactive results on the rapid antigen test examination. In addition, a CT value of RT-PCR > 26 would give non-reactive results on the rapid antigen test.

The results of the rapid antigen test were not affected by the sex and age of the person conducting the examination. From the data obtained, it was found that there was no significant difference in the distribution of gender according to the type of rapid test.

The main limitation of this study was the memory bias of the study participants. The majority of subjects did not know for certain when they had contact with COVID-19 patients and some were asymptomatic. In addition, the relatively large amount of data between those using the rapid ag SD biosensor and Lungene could be a bias in conducting comparative analysis.

## CONCLUSIONS AND SUGGESTIONS

The sensitivity of the Lungene brand rapid antigen test was higher than the SD Biosensor brand.

Meanwhile, the SD-Biosensor rapid antigen test's specificity and accuracy were higher than the Lungene brand. In addition, the Lungene and SD-Biosensor rapid antigen tests showed reactive results on a CT RT-PCR value ≤ 31.4 and a CT RT-PCR value ≤ 26, respectively. The SD-Biosensor and Lungene RDT had a good diagnostic accuracy for screening purposes of COVID-19 patients.

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