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Original Research Article

Diagnostic value of SARS-CoV-2 RDT-Ab with RT-PCR: Secondary data at Diponegoro National Hospital

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Abstract

Background: The SARS-CoV-2 rapid diagnostic test antibody (RDT-Ab) was most often used as an early detection tool for COVID-19 at the beginning of pandemic. Whereas the antibody response was formed in the second week after the onset of symptoms.

Objective: To evaluate the diagnostic value of the SARS-CoV-2 RDT-Ab, including sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR), in patients at Diponegoro National Hospital, Semarang, Indonesia.

Methods: Data subjects have been selected retrospectively using purposive sampling based on inclusion criteria (patients who had shortness of breath, pneumonia, suspected, possible, or confirmed COVID-19, and data on the results of the SARS-CoV-2 RDT-Ab IgM and/or IgG (Leccurate® SARS-CoV-2 Antibody Rapid Test Kit) with a valid RT-PCR as gold standard) and exclusion criteria (patients who only had one of either SARS-CoV-2 RDT-Ab or RT-PCR). Researchers analyzed the diagnostic value of SARS-CoV-2 RDT-Ab with RT-PCR which gave the possibility of true-positive, false-positive, true-negative, and false-negative results arranged in a 2x2 table. According to WHO, the diagnostic value is said to be good at least having a sensitivity value of 80% and specificity of 97%.

Results: The diagnostic value of SARS-CoV-2 RDT-Ab with RT-PCR, which was evaluated from 1142 patients retrospectively, included IgM (Se 65.25%, Sp 89.51%, PPV 46.70%, NPV 94.81%, PLR 6.22, NLR 0.39), IgG (Se 58.16%, Sp 93.01%, PPV 53.95%, NPV 94.04%, PLR 8.32, NLR 0.45), IgM and IgG (Se 53.90%, Sp 94.21%, PPV 56.72%, NPV 93.55%, PLR 9.30, NLR 0.49), IgM and/or IgG (Se 69.50%, Sp 88.31%, PPV 45.58%, NPV 95.36%, PLR 5.95, NLR 0.35).

Conclusion: SARS-CoV-2 RDT-Ab (Leccurate® SARS-CoV-2 Antibody Rapid Test Kit) is not ideal to be used as a rapid diagnostic test for COVID-19.

INTRODUCTION

The COVID-19 pandemic spread rapidly from Wuhan, Hubei Province, China to more than 190 countries in early 2020.[1] This disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2,3] Clinical manifestation of COVID-19 patients varies from asymptomatic, mild to severe. The most frequently seen symptoms are fever, shortness of breath, cough, and myalgia.[4]

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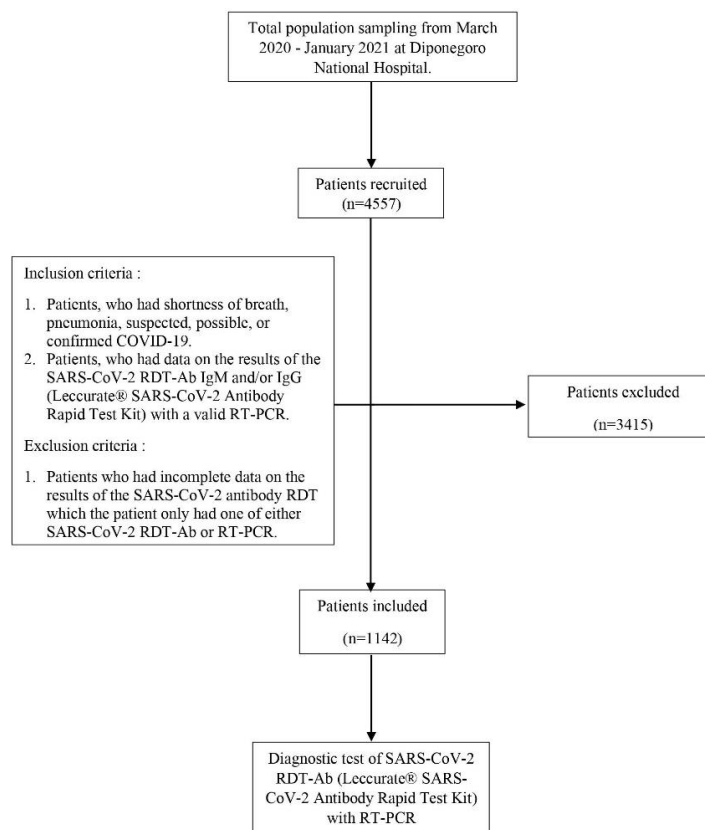cross-reaction with other pathogens such as other types

Figure 1. Patients Flowchart

COVID-19 patients can be detected using molecular assays.[5] The recommended method for the detection of SARS-CoV-2 is nucleic acid amplification by reverse transcription-polymerase chain reaction (RT-PCR).[6] The sample is said to be positive if the RT-PCR is positive at a minimum of two target genes that are specific for SARS-CoV-2 or positive for β-coronavirus.[7] This method takes a minimum of 24 hours to obtain the results, so it is longer than the SARS-CoV-2 antibody-detecting rapid diagnostic test (RDT-Ab).[8] However, not all laboratories in Indonesia have this tool, so RT-PCR is not suitable as a quick and simple diagnostic test.[9]

SARS-CoV-2 RDT-Ab has been developed as a quick and simple diagnostic tool for COVID-19. The principle of using this tool is a serological test based on lateral flow immunoassay[10] to detect SARS-CoV-2 IgM and/or IgG antibodies.[11] Specimens used include whole blood, serum/plasma, or capillary blood. The advantage of this tool is that the price is affordable and short duration, approximately 15 minutes.[6,12]

The SARS-CoV-2 rapid diagnostic test antibody (RDT-Ab) was most often used as an early detection tool for COVID-19 at the beginning of pandemic because of the lower cost factor and its method simpler than RT-PCR and RDT SARS-CoV-2 antigen.[13] In fact, the new antibody response is formed in the second week after the onset of symptoms.[14,15] This means that the use of SARS-CoV-2 RDT-Ab is possible in the recovery phase. Detection of antibodies also results in the possibility of

of human coronavirus, giving false-positive results.[16,17]

Previous research in Malaysia discussed the diagnostic test for the SARS-CoV-2 RDT-Ab in patients with confirmed COVID-19 without providing information that the patient was inpatient or outpatient.[12] SARS-CoV-2 RDT-Ab also performed at Diponegoro National Hospital, Semarang, Indonesia, as as an early detection tool, even though this test was actually intended for the second week. The objective of this study is to evaluate the diagnostic value of SARS-CoV-2 RDT-Ab performed at Diponegoro National Hospital, Semarang, Indonesia, with RT-PCR as gold standard.

MATERIALS AND METHODS
Study design

This study was a diagnostic test for SARS-CoV-2 RDT-Ab (Leccurate® SARS-CoV-2 Antibody Rapid Test Kit) with RT-PCR as the gold standard.

Study subjects

The target population of this diagnostic study was the patients who were tested for SARS-CoV-2 RDT-Ab and RT-PCR at Diponegoro National Hospital. The sample size used in this study was the total population sampling from March 2020 - January 2021. Data subjects have been selected using purposive sampling through census data based on inclusion and exclusion criteria. The inclusion criteria for this study were patients who had shortness of breath, pneumonia, suspected, possible, or confirmed COVID-19, and data on the results of the SARS-CoV-2 RDT-Ab IgM and/or IgG (Leccurate®

SARS-CoV-2 Antibody Rapid Test Kit) with a valid RT-PCR as gold standard. The exclusion criteria for this study were patients who had incomplete data on the results of the SARS-CoV-2 antibody RDT which the patient only had one of either SARS-CoV-2 RDT-Ab or RT-PCR.

Data analysis

The stages of data management included coding and data tabulation. Researchers analysed the diagnostic value of SARS-CoV-2 RDT-Ab with RT-PCR which gave the possibility of true-positive, false-positive, true-negative, and false-negative results arranged in a 2x2 table (supplementary 1). The results were obtained in the form of sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR). According to WHO, the diagnostic value is said to be good at least having a sensitivity value of 80% and specificity of 97%.

Table 1. Diagnostic value of SARS-CoV-2 RDT-Ab to RT-PCR

	IgM	IgG	IgM and IgG	IgM and/or IgG
Se	65,25%	58,16%	53,90%	69,5%
Sp	89,51%	93,01%	94,21%	88,31%
PPV	46,7%	53,95%	56,72%	45,58%
NPV	94,81%	94,04%	93,55%	95,36%
PLR	6,22	8,32	9,30	5,95
NLR	0,39	0,45	0,49	0,35

Abbreviations: Se: Sensitivity; **Sp**: Specificity; **PPV**: Positive predictive value; **NPV**: Negative predictive value; **PLR**: Positive likelihood ratio; **NLR**: Negative likelihood ratio.

Ethical clearance

This study received ethical clearance no. 136/EC/KEPK/FK-UNDIP/IV/2021 from the Ethics Committee of Faculty of Medicine Universitas Diponegoro/ Dr. Kariadi Hospital.

RESULTS

Researchers searched for the required patient medical data through census data based on information about a diagnosis of shortness of breath, pneumonia, suspected, possible, or confirmed COVID-19. Based on the search, 4557 patients were found. The researchers obtained 1142 patients which met the inclusion criteria, while 3415 patients met the exclusion criteria (figure 1).

SARS-CoV-2 RDT-Ab can be known to be true-positive, false-positive, true-negative, and false-negative by confirming the results of the test with RT-PCR as gold standard. Researchers analyzed the diagnostic value of SARS-CoV-2 RDT-Ab with RT-PCR results arranged in a 2x2 table (supplementary 2).

The sensitivity of RDT-Ab IgM (Se 65.25%) is higher than RDT-Ab IgG (58.16%) and RDT-Ab IgM and IgG (53.90%), but the positive predictive value of RDT-Ab IgM (46.70%) was lower than RDT-Ab IgG (53.95%) and RDT-Ab IgM and IgG (56.72%). This is due to the false-positive value of IgM which is higher than the true-positive.

The sensitivity of RDT-Ab IgM and/or IgG (69.50%) was higher than that of RDT-Ab IgM (65.25%), but the positive predictive value (45.58%) was lower than RDT-Ab IgM (46.7 %). This is due to false-positive values of IgM and/or IgG which are higher than true-positives. However, the classification of RDT-Ab IgM and/or IgG causes an increase in the sensitivity value of the diagnostic test results.

DISCUSSION

The SARS-CoV-2 RDT-Ab diagnostic test was performed to assess sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio. Researchers conducted diagnostic tests and classified them into 4 groups which included RDT antibodies IgM only, IgG only, IgM and IgG, and IgM and/or IgG (table 1). The difference between the RDT-Ab IgM and IgG groups and the RDT-Ab IgM and/or IgG groups is the selection of the test results. The RDT-Ab IgM and IgG group consisted of patients who gave both IgM and IgG results at the same time, while the RDT-Ab IgM and/or IgG group consisted of patients who gave IgM only, IgG only, and both IgM and IgG. The purpose of this classification is to increase the sensitivity value of the diagnostic test.

The sensitivity of RDT-Ab IgM and/or IgG SARS-CoV-2 was 69.50% with a positive predictive value of 45.58% and a positive probability ratio of 5.95. Although a strong positive diagnostic test result gives a likelihood ratio value greater than 1, the positive likelihood ratio value obtained is not considered important because the positive likelihood ratio value that is considered important is more than or equal to 10.[18] RDT-Ab IgM specificity and/or The IgG of SARS-CoV-2 was 88.31% with a negative predictive value of 95.36% and a negative likelihood ratio of 0.35. This indicates that the negative test result is strong because the negative likelihood ratio value is close to 0. When compared between groups of SARS-CoV-2 RDT-Ab, RDT-Ab IgM and/or IgG is the best screening method because the high prevalence of COVID-19 requires the highest sensitivity value (Se 69.50%).[18]

The sensitivity of SARS-CoV-2 RDT-Ab IgM and IgG was 53.90% with a positive predictive value of 56.72% and a positive likelihood ratio of 9.30. Although a strong positive diagnostic test result gives a likelihood ratio value greater than 1, the positive likelihood ratio value obtained is not considered important because the positive likelihood ratio value that is considered important is more than or equal to 10.[18] Specificity of RDT-Ab IgM and IgG SARS -CoV-2 is 94.21% with a negative predictive value of 93.55% and a negative probability ratio of 0.49. This indicates that the negative test result is strong because the negative likelihood ratio value is close to 0. When compared between groups of SARS-CoV-2 RDT-Ab, RDT-Ab IgM and IgG are the best diagnostic methods because they have the highest specificity value (Sp 94.21%).[18] This high specificity

value is caused by the number of patients who gave true negative results more than false-negative.

The results showed that the sensitivity and specificity of the SARS-CoV-2 RDT-Ab by the researchers gave a lower value than the value recommended by WHO and previous studies so that it was not supporting the researcher's hypothesis.[9,19] According to Li et al[9], the sensitivity of RDT for SARS-CoV-2 IgM and/or IgG antibodies was 88.66%, while the specificity was 90.63%. According to WHO, the diagnostic value is said to be good at least having a sensitivity value of 80% and specificity of 97%. This indicates that the diagnostic test conducted by the researcher and Li et al is below the recommended value. This study supports WHO's statement that RDT-Ab is not recommended as a screening and diagnostic test for COVID-19.[19]

The difference in the results of the SARS-CoV-2 RDT-Ab can be caused by several factors including the number of samples used, the time of examination in the patient, and the immunity of each patient. The number of samples used by Li et al was 525 patients consisting of 397 confirmed positive patients and 128 negative COVID-19 patients from 8 different health institutions, while the number of samples used by researchers was 1142 patients at Diponegoro National Hospital. This indicates that the number of samples used by researchers was more than in previous studies.

SARS-CoV-2 RDT-Ab detects antibodies as an immune response to the virus. This method may be used between days 8 to 13 after symptom onset.[20] False negatives can occur because the patient's antibodies have not been formed due to the body's weak immune response. This response can be caused by various factors including age, gender, and comorbidities.[21] IgM can be detected on days 5 to 7 and IgG on days 7 to 10 after symptom onset.[22] However, IgG antibodies can also be found in the first week. This could be due to the presence of pre-existing antibodies or cross-reactions originating from coronaviruses other than SARS-CoV-2.[23] Thevarajan et al[24] have shown that IgG antibody was detectable in the patient's blood and peak at 4 months after exposure to a previous infection and persist for 16 months. Moreover, antibodies that bind to SARS-CoV-2 do not determine whether they are neutralizing antibodies or confer protective immunity.

CONCLUSION

SARS-CoV-2 RDT-Ab (Leccurate® SARS-CoV-2 Antibody Rapid Test Kit) is not ideal to be used as a rapid diagnostic test for COVID-19.

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