

Validation of Rapid Antibody (IgM – IgG) Test Kit for SARS-CoV-2 Infection in Surabaya, Indonesia

Museyaroh¹, Puspa Wardani², Aryati², Evy Diah Woelansari¹

¹Health Polytechnic Ministry of Health Surabaya, Surabaya, East Java, Indonesia

²Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Correspondence:
Museyaroh, Jl. Karangmenjangan
18 A, Surabaya, East Java,
Indonesia
Zip Code: 60286

Email: museyaroh21@gmail.com

Received: May 31, 2022
Revised: September 18, 2022
Accepted: October 6, 2022
Published: October 30, 2022

DOI: 10.33086/ijmlst.v4i2.3027



Abstract

At the beginning of the Corona Virus Disease 2019 (COVID-19) pandemic, rapid test examinations were widely used as a screening for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection. The purpose of this examination was to detect SARS-CoV-2 IgM/IgG antibodies in the patient's body. One of these tests uses the immunochromatographic method. This study aims to determine the validity of immunochromatography. The study was conducted from August to September 2020. The sample used in this study was 100 patients. The research was conducted at Husada Utama Hospital Surabaya, Indonesia. According to the study's findings, the Zybio brand reagent kit has an accuracy of 85%, a sensitivity of 82%, a specificity of 88%, a positive predictive value of 87%, and a negative predictive value of 83%. In the group of patients who experienced clinical symptoms, < 7 had a sensitivity of 50%, specificity of 88%, positive predictive value of 60%, negative predictive value of 83%, and accuracy of 77.94% while the group of patients experiencing clinical symptoms > 7 days, had a sensitivity value of 100 %, specificity of 88%, positive predictive value of 84%, negative predictive value of 100%, and accuracy of 92.68%. Based on these results, the conclusion is that the Zybio brand reagent kit has a relatively high sensitivity, specificity, positive predictive value, negative value, and sample accuracy. In the group with clinical sensitivity < 7 days, the positive predictive value and accuracy are lower than the sample group with clinical symptoms > 7 days but have the same specificity.

Keywords

IgG, IgM, Immunochromatography, SARS-CoV-2, Validation.



This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. ©2021 by author.

INTRODUCTION

In December 2019 the world was shocked by the outbreak of an acute respiratory disease that occurred in Wuhan, China (1). This outbreak was initially thought to be transmission from animals to humans (zoonosis), but recently it was discovered that transmission of this virus occurs between humans through droplets (2). According to data as of April 13, 2022, in Indonesia the number of confirmed cases of Corona Virus Disease 2019 (COVID-19) was 6,036,909 with recovery cases of 5,814,688 (96.3%) and the death rate of 155,746 people (2.6%) (3).

The clinical symptoms of COVID-19 are very wide ranging, from asymptomatic, fever, dry cough, anosmia, sore throat, fatigue, conjunctivitis, nausea, vomiting, diarrhea, shortness of breath, and sepsis (4). Clinical manifestations of COVID-19 can progress to pneumonia, respiratory failure and even death (5). About 80% of cases were classified as mild or moderate and 13.8% were serious illness, and 6.1% of patients fell into a critical condition (6). Deterioration and death generally occur in older people with congenital disease (50-75%) (5).

Diagnostic speed and accuracy are very important for the diagnosis and control of the COVID-19 outbreak. The examination recommended by World Health Organization (WHO) is molecular examination using nucleic acid amplification or Real-Time

Polymerase Chain Reaction (RT-PCR) because PCR has high sensitivity and specificity, but has drawbacks. One of the drawbacks of the PCR method is that this examination requires a relatively long time, the process is quite complicated, expensive, and requires experts. Therefore, this examination cannot be carried out in all health care facilities, especially in first-level health services such as health centers and hospitals in remote areas. Currently, many antibody-based examinations are used to detect the presence of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies against the SARS-CoV-2 (Severe acute respiratory syndrome coronavirus-2) virus. It is widely known that IgM was the body's first line of defense during viral infections before the appearance of IgG (7). According to Li Z et al., (8) IgM can be detected in the blood of a person infected with the SARS-CoV2 virus for 3-6 days after the onset of clinical symptoms and IgG can be detected 8-14 days after infection with the SARS-CoV-2 virus.

Many methods are currently widely used to detect anti-SARS-CoV-2 IgM and IgG antibodies. One of them is the immunochromatography method. This method is relatively fast, low cost, and does not require experts (8). There are many brands of rapid diagnostic tests for IgM and IgG SARS-CoV-2 antibodies available. One of the rapid test brands that are widely used in health

care centers, both hospitals and clinical laboratories, is the Zybio brand rapid test. This rapid test has a Limit of Detection (LOD) IgM: 0.25 g/mL and IgG: 0.23 g/mL. The purpose of this study was to determine the validity of the Zybio brand rapid test including sensitivity, specificity, positive predictive value, and negative predictive value.

MATERIALS AND METHODS

Study setting

The study is of the descriptive diagnostic test kind and has a prospective cross-sectional study design.

Study population

The population used in this study were inpatients or outpatients with symptoms of COVID-19 or without symptoms of COVID-19. PCR is the method recommended by WHO to detect the SARS-CoV-2 virus, which is based on the principle of nucleic acid amplification. Positive samples, if at least two genomic targets are detected, namely N (nucleocapsid), E (envelope), S (spike), or RdRP (RNA-dependent RNA Polymerase) gene specific to the SARSCoV-2 virus (3). PCR test and Samples were taken from inpatients or outpatients who had performed a positive or negative PCR swab examination at Husada Utama Hospital Surabaya, East Java-Indonesia.

Sample size and sampling technique

Sampling in the study was conducted from August 2020 to October 2020 at Husada Utama Hospital Surabaya. There are 100 samples total, 50 of which are COVID-19 positive patients who were verified by a positive PCR test and 50 of which are non-COVID-19 positive patients who were verified by a negative PCR test. Consecutive sampling was used to collect the samples.

Data management and analysis

The analysis of the data was descriptive. Analysis of the diagnostic value of commercial SARS-CoV-2 rapid immunochromatographic test kits was done by immunochromatography principle. When a patient's sample contains anti-SARS-CoV-2 IgM/IgG antibody, it will bind to an antigen labeled Colloidal Gold (SARS-CoV-2 recombinant antigen). A color band will be formed. The performance of Rapid Diagnostic Test (RDT) by ZyBio brand was expressed by determining diagnostic sensitivity, diagnostic specificity, positive predictive value, and negative predictive value, diagnostic efficiency.

Ethical considerations

The study obtained ethical approval from the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia with No 273/EC/KEPK/FKUA/2020.

RESULTS

Characteristics of COVID-19 and Non-COVID-19 Patients

Gender distribution in patients with confirmed COVID-19, male patients

amounted to 30 patients (60%) and female patients amounted to 20 patients (40%) while in healthy patients or non-COVID-29 patients, gender patients 23 patients (46%) male and 27 female patients (56%).

Table 1. Reactivity of Anti-SARS-CoV-2 IgM or IgG Antibodies

Anti-SARS-CoV-2 IgM and IgG antibody reactivity		
Antibody reactivity	COVID-19 Patient	Non COVID-19 Patient
IgM/IgG and IgM+IgG reactive	41	6
IgM/IgG and IgM+IgG non-reactive	9	44
Number of samples	50	50

Table 2. Analysis of Anti-SARS-CoV-2 IgM and IgG Antibody Diagnostic Tests

Anti-SARS-CoV-2 IgM and IgG antibody diagnostic test			
Diagnostic value	IgM/IgG and IgM + IgG	IgM	IgG
Diagnostic sensitivity	82%	62%	72%
Diagnostic specificity	88%	94%	88%
Positive predictive value	87%	91.1 %	85.7 %
Negative predictive value	83%	71.2 %	75.8 %
Accuracy	85%	78%	80%

Based on Table 2, the results of the analysis of the diagnostic test for anti-SARS-CoV-2 IgM and IgG antibodies are: the sensitivity of IgM/IgG and IgM + IgG is greater than the sensitivity of IgM or IgG alone, the specificity of IgM/IgG and IgM + IgG is equal to specificity of IgG alone and

smaller than IgM alone, positive predictive value of IgM/IgG and IgM + IgG is greater than IgG but lower than IgM, negative predictive value of IgM/IgG and IgM + IgG is greater than IgM or IgG, accuracy of IgM /IgG and IgM + IgG is greater than IgM or IgG.

Table 3. Analysis of Anti-SARS-CoV-2 IgM and IgG Antibody Diagnostic Tests Based On The Patient's Day Of Illness

Analysis of anti-SARS-CoV-2 IgM and IgG antibody diagnostic tests		
Diagnostic value	< days after the onset of symptoms > days after the onset of symptoms	> days after the onset of symptoms > days after the onset of symptoms
Diagnostic sensitivity	50 %	100%
Diagnostic specificity	88%	88%

Diagnostic value	< days after the onset of symptoms > days after the onset of symptoms	> days after the onset of symptoms > days after the onset of symptoms
Positive predictive value	60%	84 %
Negative predictive value	83 %	100%
Accuracy	77.94%	92.68 %

Based on Table 3 the results in the sample group < days after the onset of symptoms: rapid diagnostic tests for anti-SARS-CoV-2 IgM and IgG antibodies have

lower sensitivity, positive values, negative predictive values, and accuracy than the sample group > days after the onset of symptoms but have the same specificity.

Table 4. Cross-reaction of IgM and IgG SARS-CoV-2 with Non-SARS-CoV-2 Antibody Antibodies

Non COVID -19 patient			
Other antibody tests	Other antibody test results	SARS-CoV-2 antibody results	Number
IgM Salmonella	Positive	Negative	10
IgG dengue	Positive	Negative	7
IgM dan IgG dengue	Positive	Negative	1
Anti HCV	Positive	Negative	2
Total			20

Of the 50 samples of non-COVID-19 patients known through negative PCR examination results, there were 20 samples that were positive for antibodies other than anti-SARS-CoV-2 IgM and IgG antibodies, namely 10 samples of positive IgM salmonella patients through TUBEX-TF and ICT Salmonella examinations, 7 positive Dengue IgG patients through the dengue virus ICT examination, and 1 positive patient for dengue IgM and IgG through the dengue virus ICT examination, and 2 positive patients with anti-hepatitis C virus (HCV)

antibodies through the anti-HCV ICT examination.

DISCUSSION

Characteristics of COVID-19 Patients and Non-COVID-19 Patients

The results of the analysis based on the sex distribution of confirmed COVID-19 patients showed that there were more males than females, namely 30 male patients (60%) and 20 female patients (40%). According to Hidayati (9) which states that men dominate the population of confirmed positive for

COVID-19 in Indonesia, the positive male population accounts for more than half of the total confirmed COVID-19 patients. Clinical manifestations in male patients are much worse than in female patients. The percentage of men who die is much higher than that of women. This may be related to the habit of men who smoke more often, therefore respiratory tract diseases in men are often worse than women (9).

Reactivity of SARS-CoV-2 IgM and IgG antibodies in COVID-19 patients

Based on the of the anti-SARS-CoV-2 antibody reactivity analysis, the results were obtained, namely in COVID-19 patients, IgM/IgG or IgM+IgG reactive were 41 patients, and IgM/IgG or non-reactive IgM+IgG were 9 patients. In healthy or non-COVID-19 patients, the results were IgM/IgG or IgM+IgG reactive as many as 6 patients and IgM/IgG or non-reactive IgM+IgG as many as 44 patients.

The results of the analysis of anti-SARS-CoV-2 antibody reactivity based on the type of antibody, namely in COVID-19 patients, reactive IgM in 31 patients, non-reactive IgM in 19 patients, and reactive IgG in 36 patients, non-reactive IgG in 14 patients while in healthy patients, or non-COVID-19 patients, 3 patients has reactive IgM, 47 patients with non-reactive IgG and 6 reactive IgG, 44 patients with non-reactive IgG.

According to the Indonesian Association of Clinical Pathology Doctors, negative

results on rapid diagnostic tests of anti-SARS-CoV-2 IgM and IgG antibodies (rapid tests) occur: (a) when someone is not infected with the SARS-CoV-2 virus, (b) in the window period where the patient infected with the SARS-CoV-2 virus but antibodies have not been formed so that the antibody is not detected by the device, (c) in immunocompromised patients whose immune function is impaired so that they cannot produce enough antibodies to be detected by the device or because the patient's antibody levels are below the device's detection level, while positive results on rapid diagnostic tests of anti-SARS-CoV-2 IgM and IgG antibodies can be caused by (a) exposure/infection with the SARS-CoV-2 virus, (b) cross-reaction with other coronavirus antibodies or other viruses that resemble the SARS-CoV-2 virus and rheumatic factors (10).

According to Spicuzza et al., (11) in their research, two cases of confirmed COVID-19 patients had negative IgM/IgG antibody test results. This could be due to seroconversion from COVID-19 patients and related to inappropriate timing of sampling, such as in the first week of infection when the body has not yet formed antibodies so that the results of the IgM and IgG examine analysis of IgM and IgG Antibody Diagnostic Tests -SARS-CoV-2.

Based on the analysis of the anti-SARS-CoV-2 antibody validation test, this reagent

kit has a sensitivity of 82%, specificity of 88%, positive predictive value of 87%, negative predictive value of 83% and accuracy of 85%.

In the analysis of the anti-SARS-CoV-2 antibody diagnostic test, based on the type of antibody, the results obtained are IgM has a sensitivity of 62%, specificity of 94%, positive predictive value of 91.1%, negative predictive value of 71.2% and diagnostic accuracy of 78%, while IgG antibody has a sensitivity of 72%, specificity of 88%, positive predictive value of 85.7%, negative predictive value of 75.8%, and accuracy of 80%.

The above results are slightly different from the research of Liu et al., (12) which states that the IgM/IgG RDT has a sensitivity of 85.6%, specificity 91%, positive predictive value 95.1%, negative predictive value 82.7%, and accuracy of 88.3%. The reasons underlying the discrepancy in the results are still not known with certainty but may be due to the analytical differences between the tests. In addition, the difference in the results may also be caused by differences in immune responses between patients in population groups and differences in sampling time. The exact timing for detecting IgM and IgG responses after infection with SARS-Cov-2 is so far unclear as few studies are available with differing results nations become negative. If this result is confirmed in a larger sample, the test may

be considered a potential tool for measuring population immunization.

According to Barbosa et al., (13) the rate of increase in SARS-CoV-2 antibodies is different for each individual. In patients with mild clinical symptoms, specific antibodies appear earlier, usually on day 7 when IgM is lower and IgG continues to increase. In patients with severe clinical symptoms of SARS-CoV-2, antibody seroconversion appeared longer, usually on day 12 and IgM continues to increase.

Diagnostic sensitivity is the ability to diagnose a patient with a disease that is correctly identified as a positive result through screening tests. In this study, the sensitivity value of this reagent kit was 82%. These results indicate that the sensitivity of this reagent kit is relatively low, so it is hoped that manufacturers can increase the sensitivity of the detection of this SARS-CoV-2 IgM and IgG test reagent kit, because the lower the sensitivity, the falser negative cases, and this will result in increased transmission of the SARS-CoV-2 virus in people who are in close contact with patients infected with the SARS-CoV-2 virus. For the specificity of this reagent kit, it has a relatively high value of 88%. This result shows that the reagent kit is likely to correctly identify people who are not sick with screening tests / screening for 88%. With regard to the positive predictive value of 87%, this result shows that the proportion of

people with positive test results who actually have the disease is 87%. With regard to the negative predictive value of 83%, this result shows that the proportion of patients with negative results who do not suffer from COVID-19 is 83%. With regard to the diagnostic accuracy of 85%, this result shows that the proportion of true test results (true value) among all those examined is 85%. However, according to several studies, PCR as a reference examination in research has a sensitivity of around 75%. Therefore, this rapid diagnostic test still has the possibility of having higher sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

Reactivity of IgM and IgG antibodies based on the day of onset of symptoms

Based on the results of this study, the SARS-CoV-2 IgM and IgG reagent kit obtained results in the group of patients who experienced clinical symptoms < 7 days having a sensitivity of 50%, specificity of 88%, positive predictive value of 60%, negative predictive value of 83% and an accuracy of 77.94% based on the type of antibody, namely IgM antibody has a sensitivity of 50%, specificity of 94%, positive predictive value of 75%, negative predictive value of 83.9% and accuracy of 82%, while for IgG antibody it has a sensitivity of 27.7%, 88% specificity, 45.45% positive predictive value, 77% negative predictive value and 59.75%

accuracy. Patients in this group may be in the early stages of infection or the window period or because the antibody concentration is too low so that the antibody cannot be detected. (12).

The results above are different from the results in the group of patients who have clinical symptoms > 7 days, where this reagent kit has higher sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, namely sensitivity of 100%, specificity of 88%, positive predictive value of 84%, a negative predictive value of 100%, and an accuracy of 92.68%. Based on the type of antibody, IgM antibody has a sensitivity of 68%, specificity of 94%, positive predictive value of 88%, negative predictive value of 82.45%, and accuracy of 84%, while antibody IgG has a sensitivity of 96.87%, specificity of 88%, a positive predictive value of 83.78%, a negative predictive value of 97.7%, and an accuracy of 91.46%. These results are in line with the research of Liu et al., (12) which is in 16 confirmed COVID-19 patients with symptoms of 0-7 days the SARS-CoV-2 IgG/IgM reagent kit only had a sensitivity of 18.8%, while in group 8 - 15 days the IgM/IgG has a sensitivity of 50%, and in the group of patients with clinical symptoms > 16 days the IgM/IgG sensitivity is 100%.

According to Andrey et al., (14) most of the false negatives in the SARS-CoV-2 IgM/IgG antibody test were in the subgroup

of samples taken 0-6 days after the onset of clinical symptoms. This may be related to seroconversion from COVID-19 patients, but until now seroconversion in COVID-19 patients is still not clearly known, because there are only a few studies and there are differences in the results of some of these studies. According to Hoffman et al., (15) seroconversion in COVID-19 patients occurs between 7-12 days after the onset of symptoms., Generally, IgM is produced first and IgG is produced later. The presence of IgG lasts for a long time in the body. Hsueh et al., (16) added that IgG seroconversion occurs on average 10 days after the onset of clinical symptoms in COVID-19 patients and the peak of this antibody seroconversion is at 15 days. According to Döhla et al., (17) seroconversion occurs sequentially for IgM and then IgG with a median time of 11 and 14 days, respectively. Therefore, if the sample is taken less than that time, it is likely that antibodies have not been formed and the test results will be false negative. According to research by Long et al., (18) mentioning seroconversion in 26 patients who were initially seronegative during the observation period, the results obtained were 3 types of seroconversion, namely synchronous seroconversion of IgG and IgM, IgM seroconversion earlier than IgG, and IgM seroconversion slower than IG. IgM can be detected in the blood of a person infected with the SARS-CoV2 virus for 3-6 days after

the onset of clinical symptoms and IgG can be detected 8-13 days after infection with the SARS-CoV-2 virus (19,20).

Reactivity of SARS-CoV-2 IgM and IgG with other antibodies

Based on the results of this study, from 20 samples of healthy or non-COVID-19 patients with negative PCR results and patients experiencing clinical symptoms resembling COVID-19 such as fever and diarrhea, there were 10 positive patients with IgM salmonella, 1 patient positive for IgM and IgG dengue virus, 7 patients positive for dengue virus IgG and 2 positive patients with anti-hepatitis C (HCV) antibodies, and the results of the SARS-CoV-2 IgM and IgG examinations were negative. Therefore, from these results the researchers concluded that this reagent kit did not cross-react with salmonella bacteria antibodies, viral antibodies dengue, and hepatitis C virus (HCV) antibodies. These results can be used as additional information, because the reagent insert kit only states that these reagents do not cross-react against antibodies to parainfluenza virus, chlamydia pneumonia, mycoplasma pneumonia, and adenovirus.

WHO does not recommend the SARS-CoV-2 IgM/IgG rapid test as a tool for the diagnosis of COVID-19 because this test is not specific (does not detect the presence of the virus directly) so that if the rapid test results show non-reactivity, it does not rule

out the possibility of not being infected with the SARS-CoV-2 virus because the performance of this test is influenced by many factors such as the time of onset of illness, the patient's immune response, the time of sampling and inter-analytical testing (13). However, this assay can be a reliable option in controlling the prevalence of COVID-19, especially in situations where RT-PCR and ELISA assays are not available, or cannot be used reliably. According to Liu et al., (12) the rapid diagnostic test of IgG/IgM SARS-CoV-2 is reliable if it is not performed < 6 days after the onset of clinical symptoms.

The advantage of the rapid test for anti-SARS-CoV-2 IgM and IgG antibodies is that this test provides a fast response that only takes a few minutes. In patients who come with a discrepancy between the clinical/radiological picture and molecular tests, the detection of these antibodies can be used as an additional element that helps the doctor to make the correct diagnosis.

The limitations of this study were that the researcher could not determine the seroconversion of the anti-SARS-CoV-2 IgM and IgG antibodies, the sampling was limited to < 7 days after the onset of clinical symptoms and > 7 days after the onset of clinical symptoms, so that the researchers could not determine the seroconversion and the best timing in sampling IgM and IgG

antibody tests for SARS-CoV-2. In the negative PCR samples, the researchers were unable to determine other diseases other than COVID-19.

CONCLUSIONS

In patients with Corona Virus Disease-19 (COVID-19) with clinical symptoms > 7 days, rapid diagnostic tests for anti-SARS-CoV-2 IgM and IgG antibodies have greater sensitivity, specificity, positive predictive value, negative predictive value, and accuracy than rapid diagnostic tests in patients with Corona Virus Disease-19 (COVID-19) with clinical symptoms < 7 days.

AUTHOR CONTRIBUTIONS

Muza: conceptualization, methodology, investigation, writing-reviewing editing, software, data curation, and writing-editing, methodology. Puspa Wardani: Validation, Aryati: Validation. Evy Diah Woelansari: Editing – reviewing.

ACKNOWLEDGEMENTS

Husada Utama Hospital Surabaya 2020 gave this work its support. Clinical Pathology Laboratory was where this work was done.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Adhikari SP, Meng S, Wu Y, Mao Y, Ye R, Wang Q, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of COVID during the early outbreak period. *Infect Dis Poverty*. 2020;9(29):1–12. <https://doi.org/10.1186/s40249-020-00646-x>
2. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. 2020; 215: 108427. <https://doi.org/10.1016/j.clim.2020.108427>
3. World Health Organization. Rational use of personal protective equipment for coronavirus disease (COVID-19). Geneva: World Health Organization. 2020;202 download at [https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-\(covid-19\)-and-considerations-during-severe-shortages](https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-for-coronavirus-disease-(covid-19)-and-considerations-during-severe-shortages)
4. Han Y. The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID - 19): A Chinese perspective. 2020;1–6. DOI: 10.1002/jmv.25749
5. Özdemir Ö. Coronavirus Disease 2019 (COVID-19): Diagnosis and management. 2020;42(3):242–7. <https://doi.org/10.14744/etd.2020.99836>
6. Han Y, Yang H. The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID-19): A Chinese perspective. 2020 *J Med Virol*. <https://doi.org/10.1002/jmv.25749>
7. World Health Organization. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. Geneva: World Health Organization; 2020:78.
8. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, et al. Development and clinical application of a rapid IgM - IgG combined antibody test for SARS - CoV - 2 infection diagnosis. *J Med Virol* [Internet]. 2020: 23-45. <https://doi.org/10.1002/jmv.25727>
9. Hidayati D. the Profile of Population that confirmed positive for Covid-19 and died: Indonesia and DKI Jakarta Cases. *J Kependud Indones*. 2020: 2902: <https://doi.org/10.14203/jki.v0i0.541>
10. PDS. Revisi panduan tatalaksana pemeriksaan antibodi SARS-CoV-2 (PDS PatKLIIn) pemeriksaan antibodi SARS-CoV-2. 2022;(5).
11. Spicuzza L, Montineri A, Manuele R, Crimi C, Pistorio MP, Campisi R, et al. Reliability and usefulness of a rapid IgM-IgG antibody test for the diagnosis of SARS-CoV-2 infection: A preliminary report. *J Infect* [Internet]. 2020;81(2): e53–4. Available from: <https://doi.org/10.1016/j.jinf.2020.04.022>
12. Liu Ying, Liu Yue-ping, a Diao Bo2 Ren Feifei, Wang Yue, Ding Jinya et al. Diagnostic indexes of a rapid IgG/IgM combined antibody test for SARS-CoV-2. 2020: Original Article. medRxiv. <https://doi.org/10.1128/JCM.01224-20>
13. Barbosa VA de F, Gomes JC, de Santana MA, de Lima CL, Calado RB, Bertoldo Junior CR, et al. Covid-19 rapid test by combining a random forest-based web system and blood tests. 2020: Department of Mechanical Engineering, Federal University of Pernambuco, Recife, Brazil. <https://doi.org/10.1080/07391102.2021.1966509>
14. Andrey DO, Cohen P, Meyer B, Torriani G, Yerly S, Mazza L, et al. Diagnostic accuracy of Augurix COVID-19 IgG serology rapid test. *Eur J Clin Invest*. 2020;50(10):1–7. <https://doi.org/10.1111/j.14690691.2004.01009.x>
15. Hoffman T, Nissen K, Krambrich J, Rönnberg B, Esmaeilzadeh M, Salaneck E, et al. Evaluation of a COVID-19 IgM and IgG rapid test: an efficient tool for assessment of past exposure to SARS-CoV-2. *Infect Ecol Epidemiol* [Internet]. 2020;10(1).<https://doi.org/10.1080/20008686.2020.1754538>
16. Hsueh, Huang L, Chen P, Yang CKP. 2004 Chronological evolution of IgM, IgA, IgG and neutralisation antibodies after infection with SARS-associated coronavirus. *Clin Microbiol Infect*. 2004; 10: 1062–1066. original article <https://doi.org/10.1111/j.1469-0691.2004.01009.x>
17. Döhla M, Boesecke C, Schulte B, Diegmann C, Sib E, Richter E, et al. Rapid point-of-care testing for SARS-CoV-2 in a community screening setting shows low sensitivity. *Public Health*. 2020; 182:170–2. <https://doi.org/10.1016/j.puhe.2020.04.009>
18. Long Q-X, Liu B-Z, Deng H-J, Wu G-C, Deng K, Chen Y-K, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med*. 2020;26(6):845–8. <https://doi.org/10.1038/s41591-020-0897-1>
19. Park R, Cancer C. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. 2020:2019–21. <https://doi.org/10.1056/nejmc2001737>
20. Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling early humoral response to diagnose novel Coronavirus Disease (COVID-19). 2020; 71(15):778-785. <https://doi.org/10.1093/cid/ciaa31>