ORIGINAL ARTICLE

EVALUATION UNDER FIELD CONDITIONS OF A RAPID TEST FOR DETECTION OF IgM AND IgG ANTIBODIES AGAINST SARS-CoV-2

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ABSTRACT

Objective: To determine the additional diagnostic performance of a rapid serological test for detection of IgM and IgG antibodies compared to the real-time polymerase chain reaction (RT-PCR) test; for detection of SARS-CoV-2. **Materials and methods:** A cross-sectional study was carried out including patients hospitalized for COVID-19 in 3 hospitals, health workers exposed to the infection and outpatients who met suspicious case criteria, all of which underwent the molecular test (RT-PCR) and the rapid serological test. The additional diagnostic performance of rapid serological test was evaluated in comparison to molecular tests. Likewise, an approximation was made to the sensitivity and specificity of the rapid serological test. **Results:** 144 people were included. With the rapid test, 19.4% of positive results were obtained compared to 11.1% in the molecular test (p = 0.03). The rapid serological test detected 21 cases that had been negative by the initial (RT-PCR), providing an additional diagnostic performance of 56.8% compared to the RT-PCR. The additional diagnostic performance was 50.0% during the first week, 70.0% during the second week and 50.0% during the third week of symptom onset. The sensitivity of the rapid serological test was 43.8% and the specificity of 98.9%. **Conclusions:** The rapid serological test was able to detect a greater number of cases than those detected by the molecular test especially after the second week of onset of symptoms. It also showed high specificity. It is therefore useful as a complementary test to RT-PCR, especially during the second and third week of illness.

Keywords: Coronavirus; Validation Studies; Serologic Test; SARS-CoV-2; COVID-19 (source: MeSH NLM).

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INTRODUCTION

As of April 7, 2020, the World Health Organization (WHO) reported a total of 417,416 confirmed cases and 12,597 deaths from SARS-CoV-2 virus infection (COVID-19) in the Americas, from which 2,954 confirmed cases and 107 deaths were reported from Peru [1].

The diagnosis of SARS-CoV-2 infection is made using the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test, which detects the presence of viral RNA. This molecular test (RT-PCR) is useful in the first three weeks of infection and is currently the WHO recommended reference standard [2]. However, the test has some drawbacks such as: high cost; difficulty to implement in limited-resource settings; variable sensitivity depending on the sample type (93% in bronchoalveolar lavage, 72% in sputum, 63% in nasal swabs and 32% in pharyngeal swabs) [3]; and its low sensitivity beyond the third week of symptom onset [4]

For epidemiological surveillance, the immunological tests can be a complementary diagnostic aid and an important support. These tests are based on the detection of immunoglobulins IgM and IgG against SARS-CoV-2, which appear during the second week of infection [5]. There are tests based on the detection of antibodies found in venous and capillary blood, these are called rapid serological tests and deliver results in a few minutes. However, sensitivity seems to depend on the timing on which the sample was taken and can be > 90% since the second week of symptom onset [6]. Using these tests would contribute significantly to improve the accuracy of clinical diagnosis, particularly, in hospitalized patients with negative molecular test results and in patients yet to undergo RT-PCR [6].

In Peru, until March 2020, COVID-19 diagnosis was carried out only with the molecular tests (approximately 800 daily tests). In a possible scenario of an increase in the number of cases, under-recording could happen. In this context, the Peruvian government acquired more than one million rapid serological tests. However, before being implemented on a large scale, the utility of the tests had to be evaluated and thus, compared to the molecular tests.

The objective of the study was to evaluate, under field conditions, the rapid serological test for detection of IgM and IgG antibodies, by means of comparing its additional diagnostic performance with the one of the RT-PCR, for detecting SARS-CoV-2 infections.

KEY MESSAGES

Motivation for the study: In Peru, the diagnosis of COVID-19 is based on the real-time reverse transcriptase polymerase chain reaction (RT-PCR) test; however, rapid serological tests can support the diagnosis, taking into account the simplicity of its application and that the result is obtained in just ten minutes. However, the performance of such tests under field conditions needs to be evaluated.

Main findings: Rapid serological tests give an additional diagnostic performance of 56.8% compared to the molecular test, and its sensitivity increases as the time of illness also increases.

Implications: Rapid serological tests are useful as complementary tests to RT-PCR in the diagnosis of COVID-19, their usefulness increasing as the time of illness increases.

MATERIALS AND METHODS

Participants, sample size and sampling

A cross-sectional operative study was carried out. It included three types of subjects: a) hospitalized patients with a clinical and radiological diagnosis of viral pneumonia compatible with COVID-19 at Hipólito Unanue National Hospital, Cayetano Heredia National Hospital and Dos de Mayo National Hospital; b) health workers in permanent exposure to people with confirmed diagnosis of COVID-19 who had undergone molecular testing in the days prior to the study; and c) people who met the criteria for being a suspect case according to Peru's National Epidemiology, Prevention and Disease Control Center (a symptomatic person with direct contact with a confirmed case of COVID-19 within 14 days prior to the onset of symptoms), assessed at home by alert and response teams.

To evaluate the possibility of false positive cases having other type of acute febrile condition, the rapid serological test was carried out in 90 serum samples stored in the Biomedicine serum bank of the National Health institute (INS) from patients with confirmed diagnosis of chikingunya, dengue, leptospira and zika (15 from each one), from brucella, HBAsAG (+), hepatitis c(+), HIV (+), Oropuche (5 from each one), hypertriglyceridemia (n=3) and hypercholesterolemia (n=2), all of which gave consent for their serum to be used in the context of an investigation.

In the suspect case group, samples were obtained simultaneously for the molecular and serological test evaluation. In hospitalized and healthcare personnel, who already had a nasopharyngeal swab sample taken in the days previous to the rapid test sampling, resampling was not possible because of ethical aspects.

Sample size was calculated with the infinite population proportion formula, considering a confidence level of 95% and an additional diagnostic performance of 50% (the most conservative estimate when a proportion is unknown) of the serological test compared to the RT-PCR. A precision of 10% was considered. The required sample was of 97 patients. Assuming 10% of incomplete or lost data, the final sample size was of 108. The calculation was carried out using the free software OpenEpi (http://www.openepi.com/SampleSize/SSPropor.htm). For convenience, non-probabilistic sampling was used.

RT-PCR procedure

RT-PCR sample processing was carried out following recommendations from the Pan American Health Organization (PAHO) [2], which allows detection of two genes: gene E (whose presence shows it is part of the beta-coronavirus family) and RdRp (whose presence is specific to SARS-CoV-2 and is used as confirmation).

Likewise, the RnaseP gene was used as an inhibition control. The RT-PCR test was carried out in samples from nasal and pharyngeal swabs with the standard technique in a viral

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culture medium and taken to the cold chain of the National Respiratory Viruses Laboratory (LNVR) from the National Health Institute (INS).

Rapid serological testing procedure

Identification of IgG and IgM was carried out according to recommendations from the manufacturer. (COVID -19 IgG/IgM Rapid Test Cassette (wholeblood/serum/Plasma. Zhejang Orient Gene, Biotech Co LTD, China) [7]. Sample lecture requires only 10 minutes and the appearance of a first band (control) indicates that the test has been carried out properly. The capillary blood used for the rapid serological test was obtained by finger puncture according to the standard method [8].

Statistical Analysis

The data analysis was carried out with the statistical program Stata v15.1 (Stata Corporation, College Station, Texas, USA) which was used to evaluate the composition of the sample by group, using the Pearson chi-square test to identify gender differences. Student's T-Test was used for independent variables (with or without equal variances) and the Mann-Whitney U test was used to identify differences in the descriptive measures of age in males and females in each study group. These calculations were carried out for the total sample, and for the patients with registered time of disease. For each method, a percentage of positive tests was obtained. The additional diagnostic performance was calculated by dividing the number of cases additionally diagnosed with the rapid tests, by the total number of cases detected by both tests, expressed in percentage [9]. Likewise, the sensibility estimation for the rapid serological test was carried out using RT-PCR as a reference standard. For the specificity estimation, the percentage of negative serological tests was evaluated regarding the total number of samples obtained from serum samples which were positive for other pathogens. All the point estimators were obtained with a 95% confidence interval (95%CI).

Ethical Aspects

In the context of the current health emergency, the study has been approved by the "Review of protocols in the context of epidemics, outbreaks or emergency situations" procedure established by the Ethics Committee of the National Institute of Health as stipulated in the RD N°112-2020-OGITT-INS.

RESULTS

Evaluation was carried out from March 30 to 31, 2020. From the 144 people included in the study, there was 1 missing data regarding gender. Distribution by groups showed statistically significant differences between male and female (n=143) (Table 1).

Data for age evaluation was gathered from 139 patients, because there were 5 missing data belonging to the suspect group. The average age was 41.2 ± 13.5 years. From the three groups, hospitalized patients were found to be the oldest, followed by suspect cases and finally healthcare workers, who were found to be the youngest. No statistically significant differences were found regarding age between males and females from the entire population of the study (p>0.05) (table 2).

From the group of the evaluated people (n=144), the rapid serological test identified 28 (19.4%) positive subjects, and the molecular test found 16 (11.1%) (p=0.03). The rapid serological test detected 21 cases that had been registered as negative by the molecular test, providing an additional diagnostic performance of 56.8%. From these 21 cases, 13 were patients hospitalized with clinical and radiological criteria for viral pneumonia compatible with COVID-19 and 8 were suspect cases with more than 7 days since the onset of symtptoms (except for 1, from whom there was no data), both groups had risk factors (Table 3.)

Evaluation by time of the disease

From the 144 included subjects, 109 had data collected since the symptom onset (75.7%), it was established with this information that the average duration of the disease until the day of diagnostic evaluation was 17.59 ± 4.1 days. For subjects who had provided samples for the molecular test in previous days, the date in which the rapid serological test was taken, was considered as the evaluation date. With this

Table 1. Demographic characteristics from the study sample.

Study group	Female n (%)	Male n (%)	Total n	p Value [b]
Total sample				
Hospitalized patients	6 (25.0)	18 (75.0)	24	0.005
Healthcare workers	14 (53.9)	12 (46.1)	26	
Suspect cases [a]	58 (62.4)	35 (37.6)	93	
Total	78 (54.6)	65 (45.5)	143	

[a] There was one missing data due to the absence of information collected by the brigades.
[b] Pearson's Chi Square test..

Table 2. Age distribution in the study sample, according to sex and group evaluated.

Study group	Total			Female			Male			p Value
	n	Mean (SD)	Median (IQR)	n	Mean (SD)	Median (IQR)	n	Mean (SD)	Median (IQR)	
Total sample										
Hospitalized patients	24	48.5 (13.1)	44,5 (41,0-59,0)	6	45.7 (21.2)	38.0 (28.0-66.0)	18	49.5 (9.7)	47.0 (41.0-56.0)	0.684[b]
Healthcare workers	26	38.4 (9.0)	36,5 (32,0-46,0)	14	37.9 (9.3)	36.0 (32.0-42.0)	12	39.1 (9.1)	40.0 (30.5-48.0)	0.738[c]
Suspect cases[a]	89	40.0 (14.1)	36,0 (29,0-47,0)	55	40.4 (13.9)	36.0 (29.0-47.0)	34	39.2 (14.6)	35.0 (28.0-49.0)	0.667[d]
Total	139	41.2 (13.5)	39,0 (31,0-49,0)	75	40.4 (13.8)	36.0 (29.0-46.0)	64	42.1 (13.2)	42.0 (31.5-50.0)	0.266[d]

[a] There were five missing data due to the absence of information collected by the brigades.
[b] Student's T-test for independent samples with different variances
[c] Student's T-test for independent samples with equal variances.
[d] Mann-Whitney U test.
SD: Standard Deviation, IQR = Interquartile Range.

data, the duration of the disease was categorized according to the week of clinical manifestations. This way, it was identified that 60 (55.1%) were on the second week of the disease, 28 (25.7%) on the first week and 21(19.3%) had over 2 weeks since the onset of symptoms (Table 3.) Figure 1 shows the positive tests according to both tests since the day of symptom onset.

During the first week of symptom onset, the additional diagnostic performance of the rapid serological test was 50% compared to that of the RT-PCR, during the second week it was 70% and after the second week, the additional diagnostic performance was of 50% compared to that of the RT-PCR (Table 3, Figure 2).

Table 3. Comparison between the results from the serological and molecular tests, according to the time of illness.

Time of illness	RT-PCR		Total n (%)
	Positive n (%)	Negative n (%)	
First week			
Positive	0 (0.0)	2 (7.7)	2 (7.1)
Negative	2 (100)	24 (92.3)	26 (92.9)
Total	2 (100)	26 (100)	28 (100)
Second week			
Positive	2 (33.3)	14 (25.9)	16 (26.7)
Negative	4 (66.7)	40 (74.1)	44 (73.3)
Total	6 (100)	54 (100)	60 (100)
After second week			
Positive	2 (50.0)	4 (23.5)	6 (28.6)
Negative	2 (50.0)	13 (76.5)	15 (71.4)
Total	4 (100)	17 (100)	21 (100)

RT-PCR: Real-time reverse transcriptase polymerase chain reaction test

Evaluation by study group

In the 94 patients who were evaluated at their homes, the additional diagnostic performance was 50% compared to that of the RT-PCR. In the 24 hospitalized patients, the additional diagnostic performance was 65% (Table 4, Figure 2.)

Sensitivity

When comparing results from the rapid test with those from the molecular test, the rapid test was found to have a sensitivity of 43.8% (95%: CI 19.8 - 70.1). According to the time of the disease it was found that the sensitivity increased gradually over time, in this regard sensitivity of 0% was identified in patients during the first week, 33.3% during the second week and 50% beyond the second week. According to the evaluated groups, the test had higher sensitivity among hospitalized patients (71.4%; 95% CI: 29.0-96.3), followed by the group of suspect cases (25.0%; 95% CI: 3.19-65.1) (Table 5).

Specificity

Rapid tests were carried out on 90 serum samples from patients with infections by different pathogens. From these sera, only one turned out to be positive, the one from a patient with HIV infection, resulting in a specificity of 98.9% (95% CI: 94.0 - 100).

DISCUSSION

When comparing the performance of the molecular test with the one of the rapid test, it was found that the latter identified 56.8% additional cases. In the stratification by study group, the rapid test detected 61.9% and 38.1% additional cases in

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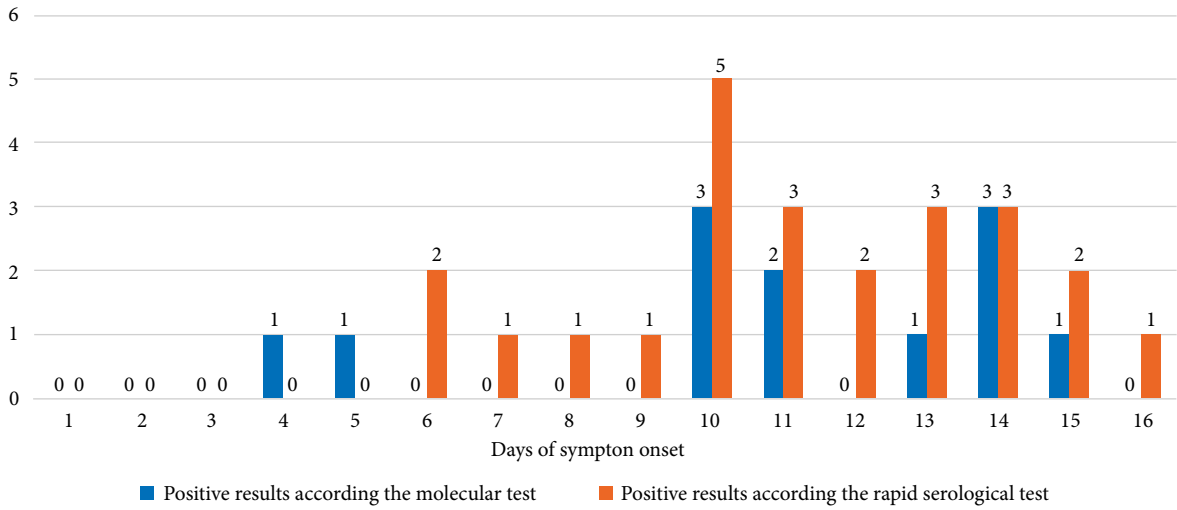

Figure 1. Distribution of positive results obtained per day according to test used.

hospitalized patients and suspect cases evaluated at home, respectively. Likewise, regarding the time of the disease, an increase in the number of positive cases is observed as time progresses.

The diagnostic performance of the rapid test was superior to that of the molecular test from the second week of symptom onset onwards. This is consistent with data reported by Xie *et al.* [10] who found that the rapid test identified five positive cases that had an initially tested negative for the RT-PCR in hospitalized patients with clinical and radiological pneumonia compatible with COVID-19 who had positive contacts, and who ultimately had a positive RT-PCR after multiple samples. Similarly, as reported by Zhao and Gao, who observed that the presence of antibodies increases as the duration of the disease increases, from 18.8% to 53.8% in the first week and from 87.5% to 89.6% in the second week. According to Liu the presence of antibodies increases from 91.3% to 100% after 15 days of disease [4, 6, 10, 11].

Table 4. Comparison between the results from the serological and molecular tests, according to the study group.

Study group	RT-PCR		Total n (%)
	Positive n (%)	Negative n (%)	
Hospitalized patients			
Positive	5 (71.4)	13 (76.5)	18 (75.0)
Negative	2 (28.6)	4 (23.5)	6 (25.0)
Total	7 (100)	17 (100)	24 (100)
Healthcare workers			
Positive	0 (0.00)	0 (0.0)	0 (0.0)
Negative	1 (100)	25 (100)	26 (100)
Total	1 (100)	25 (100)	26 (100)
Suspect cases			
Positive	2 (25.0)	8 (9.3)	10 (10.6)
Negative	6 (75.0)	78 (90.7)	84 (89.4)
Total	8 (10)	86 (100)	94 (100)
Sera			
Positive	0 (0.0)	1 (1.1)	1 (1.1)
Negative	0 (0.0)	89 (98.9)	89 (98.9)
Total	0 (0.0)	90 (100)	90 (100)

RT-PCR: Real-time reverse transcriptase polymerase chain reaction test

The molecular test may be negative in a person infected with SARS-CoV-2 when: a) the sample extraction, handling, transport or storage was not carried out properly; b) RT-PCR inhibitors are present in the extracted RNA sample; and c) when the amount of virus is insufficient to be detected, which occurs in the earliest or latest stages of infection. The viral load varies depending on the stage of the infection, so that when the immune system produces the antibodies, the virus decreases and may not be detectable by the molecular test [2, 12].

The evaluation of specificity was performed with 90 samples from a collection of sera obtained before the beginning of the COVID-19 epidemic in China, so they were considered as negative references. When applying the rapid test to these sera, only one patient with HIV infection tested positive, resulting in a specificity of 98.9%. This form of evaluation was also performed by Zang *et al.* who performed the rapid test in a group of patients with diseases other than COVID-19 and found 99.1% specificity [13].

Results suggest that the two tests are complementary in their diagnostic ability depending on the on the time of the disease. If there is a positive result using either methodology, the diagnosis is defined.

These findings are consistent with those of Gao Yaung *et al.* who reported that in the first seven days the sensitivity of RT-PCR was 69.2%, decreasing to 25.0% in the second week, and reaching 13.0% after the second week, finding in counterpart an ascending diagnostic performance of the serological test [4].

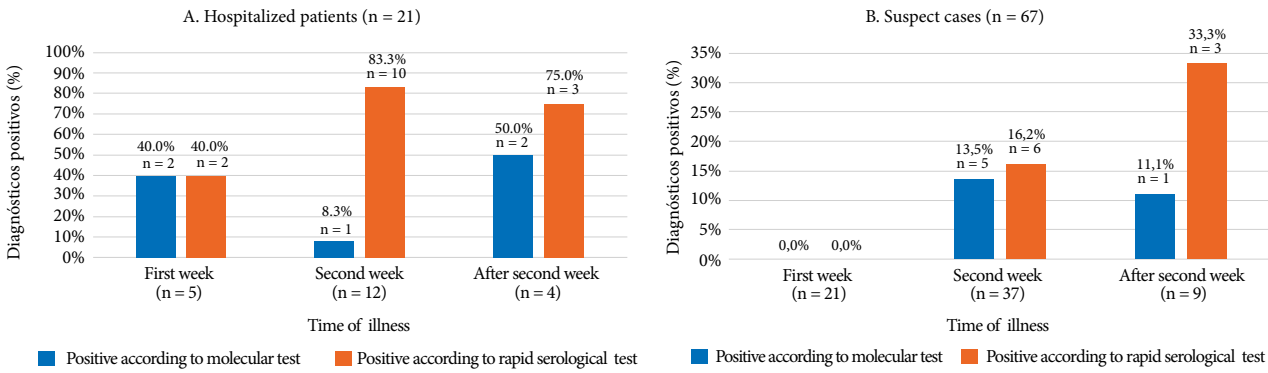

Figure 2. Distribution of positive results obtained by group evaluated and time of illness according to each test.

One of the limitations of the study is the small sample size, although it allowed us to evaluate the additional diagnostic performance of the rapid test it was insufficient to reach conclusions in the specific subgroups, and therefore, we have very wide confidence intervals in the estimates and even in some cases they could not be calculated. In addition, it should be noted that our estimates of sensitivity and specificity represent preliminary data and should be corroborated in larger sample size studies. Another important limitation is the lack of clinical information, some patients did not even have information about the number of days with symptoms. Furthermore, considering that the rapid test gave an additional diagnosis by identifying positive cases that had not been identified by the initial molecular test, we are assuming that the additional cases identified by the rapid test correspond to patients actually infected. This assumption is based on the fact that hospitalized patients and outpatients who met the case definition, had clinical and radiological criteria for pneumonia suggestive of COVID-19 infection.

Table 5. Sensitivity of the rapid serological test compared to the reference test (RT-PCR).

Study group	Prevalence		Sensitivity	
	n	% (95%CI)	n	% (95%CI)
Total sample (n=234) [a]	16	6.8 (4.0 - 10.9)	7	43.8 (19.8 - 70.1)
Hospitalized patients	7	29.2 (13.0 - 51.1)	5	71,4 (29.0 - 96.3)
Healthcare workers	1	3.8[b]	0	0.0[b]
Suspect cases	8	8.5 (3.7 - 16.1)	2	25.0 (3.2 - 65.1)
Samples with data regarding time of disease (n=109	12	11.0 (5.8 - 18.4)	4	33.3 (9.9 - 65.1)
First week	2	7.1 (0.9 - 23.5)	0	0.0 (0.0 - 84.2)
Second week	6	10.0 (3.8 - 20.5)	2	33,3 (4.3 - 77.7)
Over 2 weeks	4	19.0 (5.4 - 41.9)	2	50.0 (6.8 - 93.2)

[a] Considers subjects with and without data regarding their time of disease.
[b] No estimator or confidence interval could be calculated due to the small number of cases.
95% CI = 95% Confidence Interval, RT-PCR: Real-time reverse transcriptase polymerase chain reaction test

Ideally, these patients should have a longitudinal follow-up to assess when both the molecular test and the rapid test become or cease to be positive. Another important factor is the low number of positives among health workers, which prevents drawing conclusions from this particular group. Finally, we have not delved into the differences between IgM and IgG bands since, in this evaluation, only three patients had isolated IgG bands, all other positive cases had both bands. In the future, with more rapid tests carried out, it will be possible to establish the importance of the difference between these bands [12].

Moreover, this evaluation constitutes a first approach to the usefulness of rapid tests for the diagnosis of SARS-CoV-2 infection. In the midst of medical controversy and despite the lack of recommendations for their use by international agencies, our results provide scientific evidence in favor of their use under field conditions, in order to strengthen the diagnosis of both hospitalized patients and suspect ambulatory cases. Such implementation would be relevant for social containment of the epidemic by identifying new affected areas, as well as in the recording of severe cases and deaths.

In conclusion, rapid serological tests provide additional diagnostic performance to molecular tests particularly from the second week of symptom onset and in hospitalized patients. In the context of the current epidemic, its use as a complementary test to the molecular one is recommended, especially after the second week. It is recommended that studies should be carried out on larger samples, and to be able to adequately assess the diagnostic performance of both tests in specific subgroups.

Author's contribution: MV, GS and LS have participated in the creation and design of the article. MV, GS, GM, BA, JA and AL participated in the compilation of data. NR, FC and AJ participated

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in the processing of the samples, MV, GS, LS and AS participated in the statistical analysis of data. All authors participated in the interpretation of the data, writing of the manuscript, critical review of the manuscript, approved the final version and are responsible for the content of the article.

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Conflicts of interest: All the authors except Alonso Soto are workers for the National Institute of Health. Margot Vidal Anzardo is Executive Director of the Executive Directorate of Non-Communicable Diseases/ National Center for Public Health. Lely Solari is General Director of the National Center for Public Health and a member of the Editorial Committee of the Peruvian Journal of Experimental Medicine and Public Health. John Astete Cornejo is Executive Director of the Medical Directorate of Medicine and Occupational Psychology/ National Health of Occupational Health. Ana Jorge is Coordinator of the National Reference Laboratory for Sexually Transmitted Bacteria. Nancy Rojas is Coordinator of the Respiratory Virus Laboratory. Fanny Cárdenas is Coordinator of the Sexually Transmitted Virus and HIV/ AIDS Laboratory. Alonso Soto is a member of the Editorial Committee of the Peruvian Journal of Experimental Medicine and Public Health.

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REFERENCES

1. Pan American Health Organization. Cumulative COVID-19 cases reported by countries and territories [Internet]. Washington DC: PAHO/WHO; 2020 [cited on April 8, 2020]. Available at: https://who.maps.arcgis.com/apps/webappviewer/index.html?id=2203b04c3a5f486685a15482a0d97a87&extent=-17277700.8881%2C-1043174.5225%2C-1770156.5897%2C6979655.9663%2C10210.
2. Pan American World Health Organization. Laboratory Guidelines for the Detection and Diagnosis of COVID-19 Virus Infection [Internet]. Washington DC: PAHO/WHO; 2020 [cited on April 8, 2020]. Available at: www.paho.org/En/Documents/Laboratory-Guidelines-Detection-And-Diagnosis-Covid-19-Virus-Infection.
3. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, *et al*. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. Published online March 11, 2020. doi: 10.1001/jama .2020.3786 [Epub ahead of print].
4. Gao Y, Yuan Y, Li TT, Wang WX, Li YX, Li A, *et al.* Evaluation the auxiliary diagnosis value of antibodies assays for detection of novel coronavirus (SARS-Cov-2) causing an outbreak of pneumonia (COVID-19). medRxiv [Internet]. 2020 Jan 1 [cited on March 1, 2020]. Available at: https://www.medrxiv.org/content/10.1101/2020.03.26.20042044v1.full.pdf doi: 10.1101/2020.03.26.20042044.
5. Swee Saw Hock School of Public Health. Research on COVID-19 [Internet]. Singapore: SSHSPH COVID-19 Science Reports. 2020 [cited on March 1, 2020]. Available at: https://sph.nus.edu.sg/covid-19/research/.
6. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, *et al.* Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis. 2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa 344. [Epub ahead of print].
7. Healgen®. COVID-19 [Internet]. Zhejiang Orient Gene Biotech Co.,LTD; 2020 [cited on April 8, 2020]. Available at: http://www.orientgene.com/asp-en/product/ list.aspx?category_id=1094&product_id=8398.
8. Instituto Nacional de Salud. Prueba Rápida de coronavirus COVID-19 [Internet]. Lima: INS; 2020 [cited on April 8, 2020]. Available at: https://web.ins.gob.pe/es/pr.
9. Soto A, Acurio V, Solari L, Der Stuyft P Van. Incremental yield of bronchial washing for diagnosing smear-negative pulmonary tuberculosis. Rev Saude Publica. 2013;47(4):813–6. doi: 10.1590/S0034-8910.2013047004548.
10. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019- nCoV Pneumonia Relationship to negativa RT-PCR testing. Radiology. 2020. doi: 10.1148/radiol .2020200343.
11. Liu Y, Liu Y, Diao B, Ren F, Wang Y, Ding J, *et al.* Diagnostic Indexes of a Rapid IgG/IgM Combined Antibody Test for SARS-CoV-2. medRxiv [Internet]. 2020 Jan 1 [cited on March 1, 2020]. Available at: https://www.medrxiv.org/content/10.1101/2020.03.26.20044883v1.full.pdf doi: 10.1101/2020.03.26.20044883.
12. 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; [cited on March 1, 2020]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32104917 doi: 10.1002/jmv.25727.
13. Zhang J, Liu J, Li N, Liu Y, Ye R, Qin X, *et al*. Serological detection of 2019-nCoV respond to the epidemic: A useful complement to nucleic acid testing. medRxiv [Internet]. 2020 Jan 1 [cited on March 1, 2020]; Available at: https://www.medrxiv.org/content/10.1101/2020.03.04.20030916v2.full.pdf doi: 10.1101/2020.03.04.20030916.