Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 81 (2020) e53–e54

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Reliability and usefulness of a rapid IgM-IgG antibody test for the diagnosis of SARS-CoV-2 infection: A preliminary report.

Sir,

Since December 2019 the novel coronavirus SARS-CoV-2 has emerged as the cause of a pandemic disease known as coronavirus disease 19 (COVID-19).[1] On February 21th 2020 the outbreak began in Italy, presently the world's worst affected country.[2] The diagnosis of Covid 19 is based on a molecular test, aimed to detect the virus RNA in respiratory samples such as nasopharyngeal swabs (NS) or bronchial aspirate (BA).[3] This is an imperfect gold standard, which can give false negatives if the amount of viral genoma is insufficient or if the correct time-window of viral replication is missed.[4] Testing the IgM and IgG production in response to viral infection might be a simple method to enhance the detection sensitivity and accuracy of the molecular test.[5] In addition, it may be used for screening purpose to assess antibody profiles in a large population. Large-scale screening programs using antibody tests are currently under evaluation by different governments. Recently, a test for the rapid detection of combined IgG and IgM antibodies to SARS-CoV-2 in human blood, serum/plasma has become available.[6] As soon as the kits were commercially available, we assessed the reliability and usefulness of the 2019-nCoV IgG/IgM Antibody Rapid Test Kit (Beijing Diagreat Biotechnologies Co., Ltd) in patients with confirmed Covid 19 and in a small sample of patients with suspected disease, who were screened to be admitted to either a Covid 19 Unit or to a non Covid 19 ward.

We enrolled a total of 30 patients admitted to the Infectious Disease Covid 19 Unit or to the Pneumology Unit (Azienda UO Policlinico-San Marco, Catania) and 7 healthy controls. The study population was divided in three groups:

(1) 23 patients with confirmed Covid 19 who had, according to the WHO definition, consistent radiological/clinical findings and positive molecular tests for SARS-Cov-2;[3]
(2) 7 patients with suspected Covid 19 who had suggestive radiological/clinical findings but negative molecular tests;
(3) 7 asymptomatic controls with negative molecular tests.

All patients had molecular testing using NS or BA as they arrived to our emergency room with Covid 19 symptoms. SARS-Cov-2 RNA in the samples was detected by real-time reverse transcriptase quantitative PCR (RT-PCR) assay, according to guidelines.[3]

Qualitative assessment of IgG and IgM was performed using the rapid immunochromatographic assay during hospital stay (confirmed cases) or upon admission to the emergency room (suspicious cases). Following the manufacture's instruction, the response was obtained within 15 minutes using 200µl of blood. The test allowed detection of a single antibody or combinations of both. The presence or absence of each antibody was expressed as + or –, respectively.

Table 1
Number of patients with positive or negative molecular test and concordance with the antibody test.

		Antibody test	
		Positive	Negative
RT-PCR	Positive	19	4
	Negative	1	13

Overall concordance 86.4%
Cohen's K: 0.72 (substantial agreement).

In the group with confirmed Covid 19 (mean age 57±17 yrs), two patients were intubated for severe disease and 10 were treated with non invasive ventilation and/or O_2-therapy. The time from symptoms onset to antibody testing ranged from 3 to 34 days. Overall, the seroconversion rate for both IgM and IgG was 82.6% (19/23). Four confirmed cases had both negative IgM and IgG (IgM-/IgG-). Among these, two patients were tested at day 3 and 5 from symptoms onset. Since a recent report showed that the median time for IgM and IgG detection from symptoms onset was 11 and 12 days, respectively,[3] we reasoned that these two were likely early tests. Excluding these two, in the remaining patients, after a median time of 18 days from symptoms onset the conversion rate was 90.4%.

In the group with suspected Covid 19 (mean age 67±15 yrs), only a 40 yrs old man, considered a "highly probable case" had IgM+/ IgG+ after 12 days from symptoms onset and two negative molecular tests. Based on consistent clinical/radiological and antibody test findings he was admitted and properly treated for Covid 19. All the remaining 6 patients with suspected Covid 19 had two to three negative molecular testis on NA, confirmed by negative tests on bronchial aspirate. Consistently, they all had IgM-/IgG-. All healthy controls had IgM-/IgG-. Overall, including 37 tests, the concordance between RT-PCR and antibody test was 86.4% (Table 1), Cohen's K: 0.72 (substantial agreement). Considering the molecular test the gold standard for diagnosis, the sensitivity and specificity of the antibody test were 83% and 93%, respectively.

The reason why two patients with confirmed Covid 19 had negative IgG/IgM, at a time when seroconversion was already expected, remains unclear. One was a 93 yrs old woman, so that immunesenescence can explain the finding. However, the other patient was young and immunocompetent, so that we must consider an issue related to the test performance, e.g the lower limit of detection.

The correct timing to detect IgM and IgG response after infection with SARS-Cov-2 is so far unclear as few studies are available with divergent results.[5,7] Our preliminary data suggest that the rapid IgG/IgM test is reliable in evidencing seroconversion as

https://doi.org/10.1016/j.jinf.2020.04.022

long as the testing is not performed <6 days before symptoms onset. If this finding will be confirmed in a larger sample, the test could be a putative mean by which assessing population immunization.

In the group with suspected Covid 19, which was anyway very small, we found mainly a consistency between negative molecular and negative antibody test. However, the antibody test was performed earlier, compared to the group with confirmed disease (median 9 days vs 18 days) and this may have biased these results, so that we will further test these patients.

To our opinion this antibody test is quite reliable and useful, since it has the advantage to be a point-of-care test that gives a response within minutes. In those patients presenting with a discrepancy between the clinical/radiological feature and the molecular test, the rapid antibody detection might be an additional element helping the clinician to make a correct diagnosis. This is true, as long as the test is not performed within the first days of symptoms onset. Indeed, further studies are granted to investigate both the diagnostic and the screening value of this test.

Conflict of interest

None.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020. doi:10.1016/S0140-6736(20)30183-5.
2. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA* 2020. doi:10.1001/jama.2020.4344.
3. WHO. Global surveillance for COVID-19 caused by human infection with COVID-19 virus. Interim guidance 20 March 2020
4. Zou LR, Ruan F, Huang MX, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020 doi.org/. doi:10.1056/NEJMc2001737.
5. Guo L, Ren L, Yang S, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). *Clin Infect Dis* 2020. doi:10.1093/cid/ciaa310.
6. Li Z, Yi Y, Luo X, et al. Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. *J Med Virol* 2020. doi:10.1002/jmv.25727.
7. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis* 2020. doi:10.1093/cid/ciaa344.

Lucia Spicuzza*
Dipartimento di Medicina Clinica e Sperimentale, University of Catania, Italy

Arturo Montineri, Rosa Manuele
UO Malattie Infettive e Tropicali, Azienda OU Policlinico-San Marco, Catania, Italy

Claudia Crimi, Maria P Pistorio, Raffaele Campisi, Carlo Vancheri, Nunzio Crimi
Dipartimento di Medicina Clinica e Sperimentale, University of Catania, Italy

*Author for correspondence: Prof. Lucia Spicuzza, MD, PhD, UO Pneumologia, Az Policlinico-San Marco, Via S. Sofia, 95123, Catania, Italy.
E-mail address: luciaspicuzza@tiscali.it (L. Spicuzza)