LETTER TO THE EDITOR

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Interpretation of tests for COVID-19 in the pregnant woman
Pruebas para el COVID-19 en la gestante y su interpretación

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In the publication of Lorena Campodónico Olcese et al. 'Management of eutocic delivery in a patient with COVID-19 in Lima, Peru'[1], we read in the case report the following comment on the test results for for COVID-19: "... since there is a percentage of asymptomatic carriers, ... universal screening with both tests is performed at the clinic on all patients admitted for vaginal delivery or C-section. Requesting both tests benefits the diagnosis of patients in whom the molecular RT-PCR test may be unnoticeable by low viral load, which happens about two weeks after the onset of symptoms. On the other hand, IgM and IgG antibodies reach or start their peaks in the second or third week of symptoms onset and decline around the fifth to seventh week." "In the labor room, a rapid blood test (CELLEX SARS-CoV–2 IgG/IgM Rapid Test) and a nasopharyngeal swab molecular test (RT–PCR SARS-CoV–2) for COVID-19 were taken. The rapid test result was IgM (+) IgG (-). A week after delivery, the results were IgM (+) IgG (-) and negative molecular test, and a chest CT was reported as normal."

The consideration of this case as positive to COVID-19 despite negative molecular evidence has drawn attention. In the literature it is pointed out that RT-PCR results suggest that viral loads may be detected soon after the onset of the disease, even in minimally symptomatic people[2]. One or more negative results do not rule out the possibility of infection[3]. And a percentage of negative tests may be due to inappropriate sampling[4].

These concepts are supported by various publications by laboratory experts such as Sethraman (Figure 1)[5] and Pineda (Figure 2)[6], and the Peruvian Ministry of Health Health Directive flowchart (Figure 3)[7].

On the other hand, in the World Association of Perinatal Medicine's 9 May 2020 webinar on COVID-19 in pregnancy, Gabriele Saccone of Italy reported that two consecutive negative qRT-PCR tests are considered to rule out that the pregnant woman has COVID-19[8].

As curves and opinions currently diverge in publications, it is important to emphasize, especially in times of the rising epidemic curve, that the approach should be to consider everyone positive or infected until proven otherwise.

Symptoms, anamnesis, adequate interpretation of the results of diagnostic tests (molecular or serological), the time of the disease when the tests are taken, the correct sampling, among others, should be factors to consider by the attending physician to reach an adequate diagnosis, management and treatment.

FIGURE 1. BEGINNING AND VARIATION OF THE POSITIVITY OF THE TESTS FOR THE DIAGNOSIS OF **SARS-CoV-2**, IN RELATION TO THE ONSET OF SYMPTOMS[5].
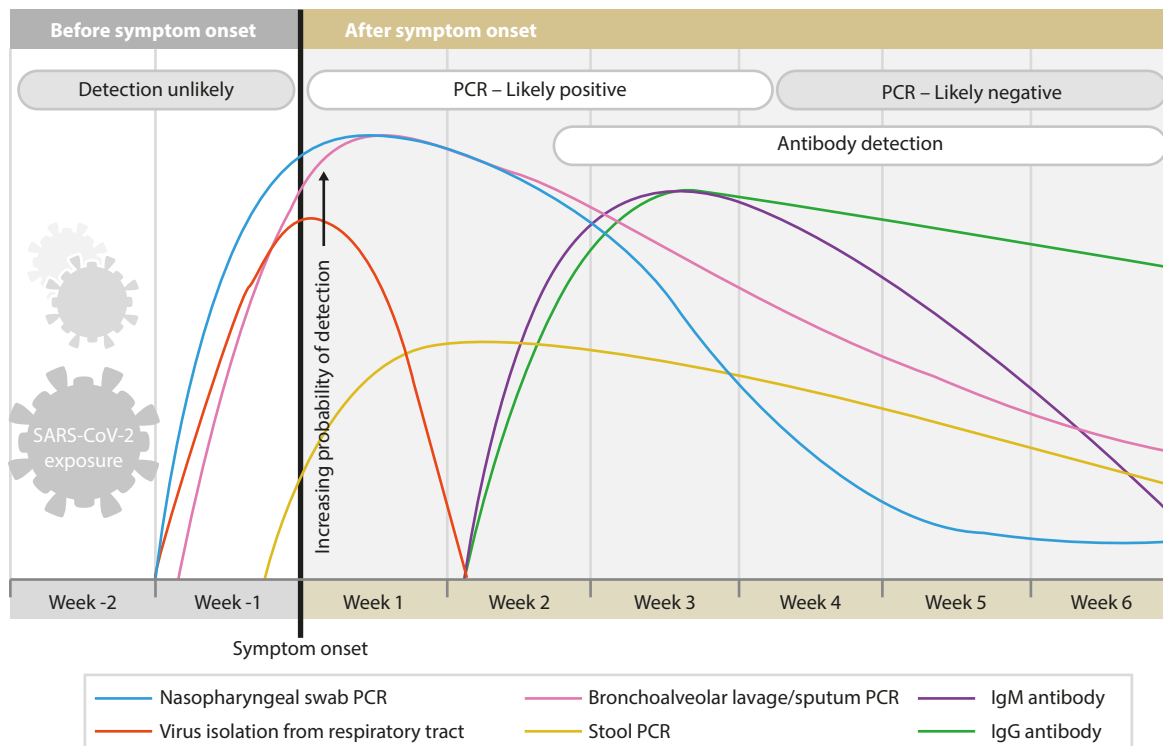

FIGURE 2. RESULTS OF COVID-19 TESTS AND PROBABLE CLINICAL SIGNIFICANCE[6].

Result			Probable clinical significance
PCR	IgM	IgG	
-	-	-	Negative
+	-	-	Window period
+	+	-	Early stage of infection
+	+	+	Active phase of infection
+	-	+	Final stage or recurrent infection
-	+	-	Early stage with false negative PCR
-	-	+	Past infection
-	+	+	Recovery phase

The error of antibody tests is a current concern around the world. Depending on the test, it may have a sensitivity of 100% and a specificity of 99.8%, so only 0.2% of people without antibodies are considered as if they had the virus. Pre-exposure to other coronaviruses does not affect results[9]. Therefore, the criterion that a negative test does not negate and a positive affirms it, must be valid, especially in these times of epidemic.

One of the authors (AGC) of this letter considers that, in Campodónico's case report, 4 weeks symptomatic (although it was just cough), perhaps the molecular test taken at the beginning was no longer diagnostic (if it had been COVID-19, viral load would have already dropped) and whether the diagnosis with rapid tests was more useful. However, it turned out IgM was positive - which AGC believes is not specific - and not IgG, which at that time it should be positive or a week later. AGC's opinion is that it was not a COVID-19 patient, but he considers this case report is valid because it explains the ideal protocol in an obstetric setting.

In the U.S. National Institute of Health first quick review series publication, based on two studies developed in China published in 2020, the combined IgG and IgM antibody screening test showed good sensitivity (87-88%) and specificity (90-100%) for diagnosis for SARS-CoV-2 compared to RT-PCR. Diagnosis accuracy was higher when IgG and IgM were detected simultaneously. The utility of the positive and negative predictive value calculated by the studies (96-100% and 72-81%, respectively) is limited, considering that at this time the disease prevalence in our country is significantly lower than reported in other studies (>60%), as we are at an early stage of the epidemic[10].

FIGURE 3. PERUVIAN MINISTRY OF HEALTH: COVID-19 POSITIVE CASES CLASSIFICATION FLOWCHART[7].
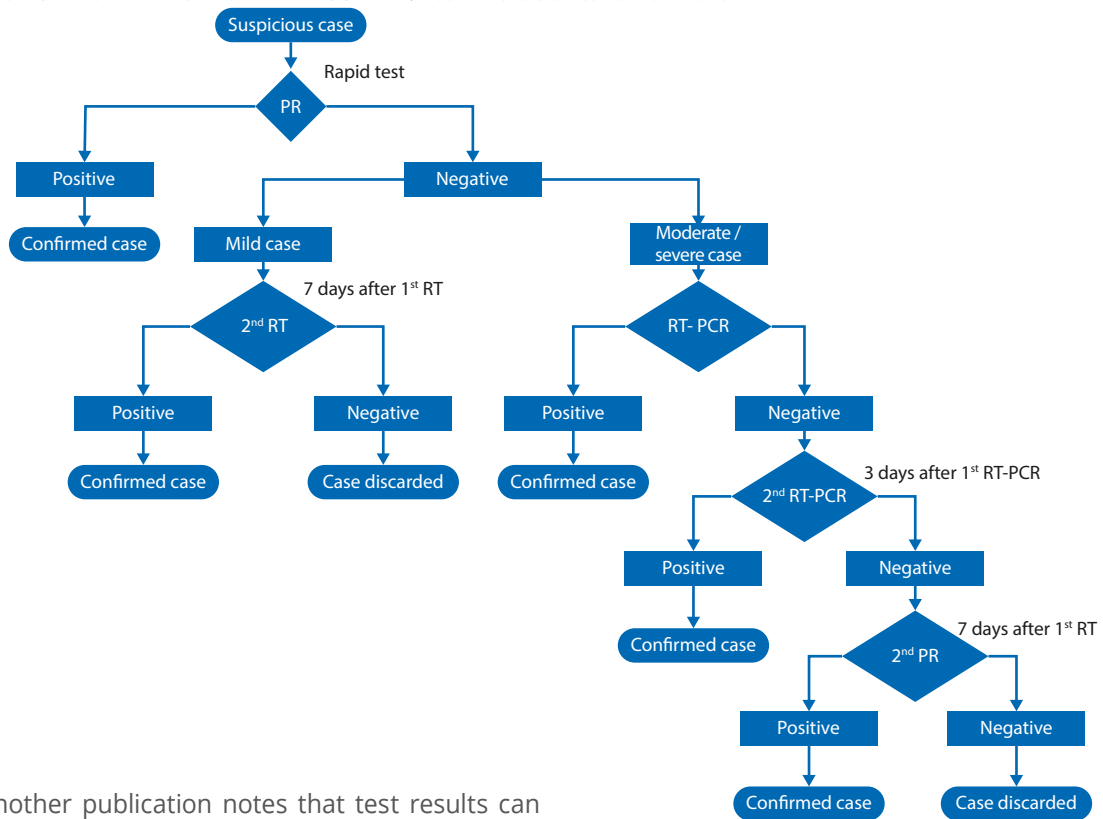
Another publication notes that test results can be false positive, false negative, or ambiguous, causing great confusion for diagnosis and follow-up[11]. About 60 different tests for RNA or antibodies are available in the U.S. after authorization by the U.S. Food and Drug Administration for use during the emergency.

On the other hand, variation can be due to virus variants or genetic variants of people and their response to the virus.

As curves diverge in publications, we suggest that in any asymptomatic or symptomatic pregnant woman in labor, a good anamnesis should be performed for COVID-19 symptoms and SARS-CoV-2 TR-PCR molecular tests and IgM and IgG antibodies be requested. A negative test does not deny and a positive test affirms the probability of occurrence of the disease, and the pregnant woman should be managed as such.

For the final diagnosis, consideration will be given to the clinical evolution of the puerperal woman and her baby and the results of the new tests in both, with special care when taking the sample for molecular testing to be analyzed in quality laboratories. With more experience, this controversy will be clarified.

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