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1. Instituto Nacional Materno Perinatal (National Maternal Perinatal Institute) Lima, Perú
2. Universidad Nacional Mayor de San Marcos, School of Human Medicine, Lima, Perú
  - a. Obstetrician and Gynecologist
  - b. Professor Gynecology and Obstetrics
  - c. Surgeon, MSc Clinical Investigation
  - d. Maternal-Perinatal Research Unit
  - e. Clinical Pathologist
  - f. Graduate in Statistics
  - g. Health Administrator Physician

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### Correspondence:

Marcos Espinola Sánchez, MD

📍 Research Unit, National Maternal Perinatal Institute, Jr. Santa Rosa 941, Cercado de Lima, Lima, Peru

✉ marcosespinola.es@gmail.com

ORCID: <https://orcid.org/0000-0002-1005-5158>

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# SARS-COVID-19 antibodies in pregnant women at a level III hospital in Peru

## Anticuerpos anti-SARS-CoV-2 en gestantes en un hospital nivel III de Perú

Enrique Guevara-Ríos<sup>1,2,a,b</sup>, Marcos Espinola-Sánchez<sup>1,c,d</sup>, César Carranza-Asmat<sup>1,2,a,b</sup>, Félix Ayala-Peralta<sup>1,2,a,b</sup>, Ricardo Álvarez-Carrasco<sup>1,e</sup>, Antonio Luna-Figueroa<sup>1,2,a,b</sup>, Luis Meza-Santibáñez<sup>1,a</sup>, Carlos Pérez-Aliaga<sup>1,a</sup>, Kelly Zevallos-Espinoza<sup>1,a</sup>, Augusto Racchumi-Vela<sup>1,d,f</sup>, Jorge Segundo-Paredes<sup>1,d,g</sup>, Pedro Arango-Ochante<sup>1,a,d,c</sup>

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### ABSTRACT

**Introduction:** COVID-19 disease spreads rapidly. Seroprevalence in pregnant women entering for hospitalization and clinical characteristics in this type of population in Peru is not known. **Objective:** To determine the prevalence and clinical-epidemiological characteristics of pregnant women with anti-SARS-CoV-2 antibodies at a level III hospital in Peru. **Methods:** Observational and cross-sectional study performed at the National Maternal Perinatal Institute of Peru. Pregnant women admitted for hospitalization were screened for COVID-19 infection. Results of anti-SARS-CoV-2 serological tests and information on maternal and perinatal characteristics were obtained. Data analysis was performed using descriptive statistics and 95% confidence intervals. **Results:** In 2 419 pregnant women screened we identified a prevalence of 7.0% of anti-SARS-CoV-2 antibodies (95% IC: 6.1% to 8.1%), including IgM in 10% (95% IC: 6.1% to 15.8%), IgM / IgG in 78.8% (95% IC: 71.8% to 84.6%), IgG in 11.2% (95% IC: 7.0% to 17.1%). 89.4% of the seropositive pregnant women were asymptomatic. Most frequent complications were premature rupture of membranes (11.8%) and preeclampsia (6.5%). No association was found between clinical and epidemiologic characteristics and type of serological response to SARS-CoV-2 ( $p > 0.05$ ). **Conclusions:** Pregnant women had prevalence of anti-SARS-CoV-2 antibodies of 7.0% on admission to the hospital; most of them were asymptomatic. There was no association between clinical-epidemiological characteristics analyzed and type of anti-SARS-CoV-2 antibody response.

**Key words:** Pandemic coronavirus infections, 2019-nCoV, prevalence, Pregnancy, Pregnancy complications, Peru.

### RESUMEN

**Introducción.** La enfermedad de COVID-19 se propaga rápidamente. Se desconoce la seroprevalencia en mujeres embarazadas que ingresan a hospitalización y sus características propias en este tipo de población en Perú. **Objetivo.** Determinar la prevalencia y características clínico-epidemiológicas de gestantes con anticuerpos anti-SARS-CoV-2 en un hospital nivel III de Perú. **Métodos.** Estudio observacional de tipo transversal, realizado en el Instituto Nacional Materno Perinatal de Perú, entre el 15 de abril y 15 de mayo de 2020. Participaron todas las gestantes que ingresaron a hospitalización y fueron tamizadas para la infección por SARS-CoV-2 mediante pruebas serológicas, cuyos resultados fueron analizados conjuntamente con sus características clínicas y epidemiológicas, utilizando estadígrafos descriptivos e intervalos de confianza al 95%, y mediante la prueba de independencia de chi cuadrado con una significancia de 0,05. **Resultados.** Se tamizaron 2 419 embarazadas, identificando una prevalencia de 7,0% con resultados positivos a los anticuerpos anti-SARS-CoV-2 (IC95%: 6,1% a 8,1%). Se observó IgM en 10% (IC95%: 6,1% a 15,8%), IgM/IgG en 78,8% (IC95%: 71,8% a 84,6%), IgG en 11,2% (IC95%: 7% a 17,1%). El 89,4% de gestantes seropositivas fueron asintomáticas. Se observó como complicaciones obstétricas más frecuentes la rotura prematura de membranas (11,8%) y la preeclampsia (6,5%). No se halló asociación de las características clínico epidemiológicas y el tipo de respuesta serológica para el virus SARS-CoV-2 ( $p > 0,05$ ). **Conclusiones.** Las gestantes con ingreso hospitalario en el periodo estudiado presentaron prevalencia de anticuerpos anti-SARS-CoV-2 de 7,0%, siendo mayormente asintomáticas. No se evidenció asociación entre las características clínico-epidemiológicas analizadas y el tipo de respuesta de los anticuerpos anti-SARS-CoV-2.

**Palabras clave.** Pandemia, Infección por coronavirus 2019-nCoV, prevalencia, Anticuerpos, Gestación, Complicaciones del embarazo, Perú.



## INTRODUCTION

COVID-19 disease spreads rapidly in the world's population, from asymptomatic forms to severe cases<sup>(1)</sup>, resulting in an overall mortality rate of 5.98%, which varies by region<sup>(2)</sup>. In the context of the health emergency in Peru and the world, it is important to know vulnerable groups, with pregnant women being a particularly susceptible group<sup>(3,4)</sup>. In previous coronavirus studies, adverse maternal results<sup>(5)</sup> have been reported; however, it is not yet clear what effect the new SARS-CoV-2 coronavirus can have on pregnancy and the fetus<sup>(6,7)</sup>. Most pregnant women are asymptomatic, but when they have symptoms, the most common are fever, cough and dyspnea, similar to non-pregnant patients<sup>(3)</sup>.

The disease clinic is divided into three periods: viremia phase, acute phase and recovery phase. Diagnostic tests, both molecular RT-PCR and serological detection of immunoglobulins, may be applied, according to specific indications<sup>(8)</sup>. Although the RT-PCR molecular test is recommended for diagnosis, it is limited in scenarios where resources are limited for development and implementation. Meanwhile, serological testing contributes to clinical diagnosis and epidemiological surveillance<sup>(9,10)</sup>. Serological tests may be useful for the identification of asymptomatic infections, and contribute to clinical diagnosis in patients who have not had molecular tests<sup>(11,12)</sup>. Moreover, in a context where the infection curve is increasing and resources are limited<sup>(10)</sup>.

The objective of this study was to determine the prevalence and clinical-epidemiological characteristics of pregnant women with anti-SARS-CoV-2 antibodies attended at the National Perinatal Maternal Institute.

## METHODS

This an observational, transversal, descriptive and associative study accomplished at the National Maternal-Perinatal Institute (as of now, INMP), a third level of attention establishment of the Health Ministry of Peru, category III-2 and a national reference center. Due to the declaration of state of national sanitary emergency caused by the COVID-19 pandemic, the establishment is now attending only emergencies and provides SARS-CoV-2 antibodies serological testing to every pregnant woman fulfilling criteria for hospitalization, as determined by the medical specialist due to labor or pregnancy morbidity.

All pregnant women hospitalized between April 15 and May 15, 2020 participated in the study if they fulfilled the following inclusion criteria: a) hospital admission indicated by the specialist; b) SARS-CoV-2 antibodies serological on admittance; c) having the SARS-CoV-2 antibodies serological test results. Exclusion criteria were: a) under-registration of the study variables in the medical record; b) not having the results of the serological tests requested for admission.

The serological test used in the institution is the One Step Test Kit Covid-19, a rapid test certified and authorized by the European Community, which is required for consumable goods produced in Asia and commercialized in the Schengen territory. The test required samples of serum/plasma and immunochromatography to simultaneously detect IgM and IgG immunoglobulins; test efficiency is described in the insert specifications. Sensitivity for IgM immunoglobulin detection is 94% and specificity 100% with total coincidence of 97.1%. Sensitivity for IgG immunoglobulin detection is 94% and specificity 100% with a total coincidence of 97.1%. Overall sensitivity for the detection of both immunoglobulins is 97.6%, joint specificity 100% and total coincidence 98.8%.

The procedure was conducted by laboratory personnel trained on the application of said test, following the indications on the insert. The interpretation of results was according to the presence and/or lack of IgM or IgG, according to the test insert indications. For negative IgM / negative IgG, there is no infection, or it is in a very precocious stage. For positive IgM / negative IgG, acute infection in early stage. For positive IgM / positive IgG, acute infection in more evolved stage. For negative IgG / positive IgG, infection in stage of resolution.

Variables considered in the study were: maternal age indicated in years previous to the pregnancy - adolescent (younger than 19 years), adult (from 19 to 34 years) and advanced maternal age (35 years old or more)-; trimester of pregnancy considered by date of last menstruation or by ultrasound in the first trimester; parity, indicated as nulliparous when there was no previous labor, primiparous when there was one previous labor and multiparous when there were two or more labors; results of the rapid test, either for IgM, IgG, or both; prenatal controls, considering 6 or



more an adequate number of controls; education level: primary (middle school), secondary (high school) or superior; civil status: married, cohabiting, divorced, single or widowed; respiratory symptoms present or absent (considering cough, sore throat, headaches, fever, chills and/or nasal congestion) at hospital admission; type of pregnancy complication (abortion, threatened preterm birth, ectopic pregnancy, bleeding in the second half of pregnancy, hyperemesis gravidarum, placental insufficiency, preeclampsia, premature rupture of membranes, dysfunctional labor, pneumonia, urinary tract infection); type of labor: C-section or vaginal delivery.

Results of the rapid tests conducted on each pregnant woman were obtained from the standardized cards for serological tests of the Epidemiology and Environmental Health Office of the INMP, and recollection of maternal information from every pregnant woman's clinical record. Measurement biases when collecting information in retrospective studies were reduced by comparing the information on each standardized serological test card, performed by one investigator, with the respective information in the clinical chart from patient's admission to discharge with the definitive diagnoses, performed by a different investigator.

Bivariate descriptive statistics using contingency tables with absolute and relative frequency summaries were used to describe the results. Inferential analysis consisted of the estimation of 95% confidence intervals. Cross-association measurements between variables were performed using Fisher's exact test, with a significance level of 0.05. Processing of data and graph used the R statistical software version 4.0.

Regarding ethical considerations, the research had approval of the Research Ethics Committee of the National Maternal Perinatal Institute, and from the corresponding institutional permit. The data were collected retrospectively and safeguarding the participants identity.

## RESULTS

During the study period, 2 427 pregnant women admitted to the hospital were screened. Eight patients were excluded because they did not have a medical history at the time of the study. Finally, the study was conducted with 2 419 patients who met the selection criteria. Of these, 170 screened preg-

nant women had anti-SARS-CoV-2 antibodies, with seroprevalence of 7% (IC95%: 6.1% to 8.1%). Among the cases of positive seroprevalence, IgM was observed in 10% (IC95%: 6.1% to 15.8%), IgM / IgG in 78.8% (IC95%: 71.8% to 84.6%) and IgG in 11.2% cases (IC95%: 7.0% to 17.1%) (Table 1). The daily number of new cases with anti-SARS-CoV-2 antibodies remained erratic, not showing a definite trend. But, the number of cumulative cases per day was on the rise during the study period (Figure 1).

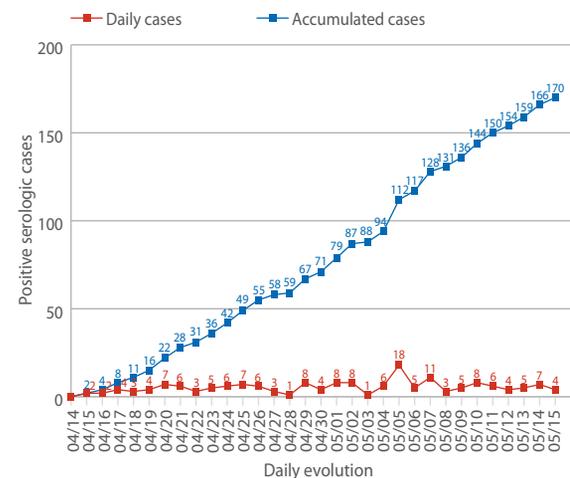
Among pregnant women who tested positive to the serological test, the IgM / IgG type was most frequently observed, mainly in adulthood or at an advanced maternal age. It occurred more frequently in pregnant women during the third trimester of pregnancy with inadequate prenatal control, in primiparous and multiparous women, cohabitants, with secondary education and housewives. No association was found between these characteristics and the type of anti-SARS-CoV-2 antibody response (Table 2).

TABLE 1. RESULTS OF THE SARS-CoV-2 VIRUS SEROLOGICAL TEST IN PREGNANT WOMEN SCREENED AT HOSPITAL ADMISSION.

Results of the serological test	N=2 419	Percentage (95% CI)
Positive	170	7.0% (6.1% a 8.1%)
Negativo	2 249	92.9% (91.9% a 93.9%)
Type of positive serology	n=170	Percentage (95% CI)
IgM	17	10.0% (6.1% a 15.8%)
IgG/IgM	134	78.8% (71.8% a 84.6%)
IgG	19	11.2% (7.0% a 17.1%)

Source: own elaboration

FIGURE 1. DAILY NUMBER OF NEW CASES AND ACCUMULATED CASES OF PREGNANT WOMEN WITH ANTI-SARS-CoV-2 ANTIBODIES AT HOSPITAL ADMISSION.





Obstetric complications occurred in 35.9% of the patients, with premature rupture of membranes, preeclampsia and spontaneous abortion being more frequent (Table 3). 89.4% of pregnant women were asymptomatic, 39.4% presented some type of clinical complications, and the most frequent type of delivery was vaginal (57.6%); no association was observed between these clinical characteristics and type of anti-SARS-CoV-2 antibody response ( $p>0.05$ ) (Table 4).

## DISCUSSION

In a short time, diagnostic test manufacturers around the world developed molecular and immunological tests for the diagnosis of SARS-CoV-2. The key criterion for the choice of these

tests for procurement and use was validation by one of the world's leading bodies, such as the European Community (EC) and the US Food and Drug Administration (FDA). An EC-validated test was used in this study, ensuring that the parameters were within internationally acceptable standards.

Although serological tests are useful for studies to determine epidemiological variables of public health interest<sup>(13)</sup>, there are still limited reports of their application in the pregnant population.

In the present study, a 7% seroprevalence of anti-SARS-CoV-2 antibodies was observed in pregnant women admitted to the hospital. The rapid test applied met the recommendation of simultaneous detection of IgM and IgG immu-

TABLE 2. ASSOCIATION OF EPIDEMIOLOGICAL AND OBSTETRIC CHARACTERISTICS ACCORDING TO THE ANTI-SARS-CoV-2 ANTIBODIES RESPONSE.

Epidemiological and obstetric characteristics	Positive anti-SARS-CoV-2 antibodies in pregnant women								p*
	Total		IgM		IgG / IgM		IgG		
	N=170	%	n=17	%	n=134	%	n=19	%	
<b>Maternal age</b>									<b>0.79</b>
Adolescent	11	6.5%	1	5.9%	9	6.7%	1	5.3%	
Adult	119	70.0%	10	58.8%	95	70.9%	14	73.7%	
Advanced maternal age	40	23.5%	6	35.3%	30	22.4%	4	21.1%	
<b>Gestational age (trimester)</b>									<b>0.05</b>
First	11	6.5%	3	17.6%	5	3.7%	3	15.8%	
Second	7	4.1%	0	0.0%	7	5.2%	0	0.0%	
Third	152	89.4%	14	82.4%	122	91.0%	16	84.2%	
<b>Prenatal control</b>									<b>0.05</b>
Not adequate	140	82.4%	11	64.7%	115	85.8%	14	73.7%	
Adequate	30	17.6%	6	35.3%	19	14.2%	5	26.3%	
<b>Parity</b>									<b>0.74</b>
Nulliparous	46	27.1%	4	23.5%	39	29.1%	3	15.8%	
Primiparous	62	36.5%	6	35.3%	49	36.6%	7	36.8%	
Multiparous	62	36.5%	7	41.2%	46	34.3%	9	47.4%	
<b>Civil status</b>									<b>0.99</b>
Married	8	4.7%	1	5.9%	6	4.5%	1	5.3%	
Cohabitant	137	80.6%	14	82.4%	108	80.6%	15	78.9%	
Single	25	14.7%	2	11.8%	20	14.9%	3	15.8%	
<b>Level of Education</b>									<b>0.66</b>
Primary	7	4.1%	1	5.9%	6	4.5%	0	0.0%	
Secondary	144	84.7%	13	76.5%	114	85.1%	17	89.5%	
Superior	19	11.2%	3	17.6%	14	10.4%	2	10.5%	
<b>Profession</b>									<b>0.09</b>
Housewife	154	90.6%	15	88.2%	123	91.8%	16	84.2%	
Freelancer	9	5.3%	1	5.9%	6	4.5%	2	10.5%	
Employed	5	2.9%	0	0.0%	5	3.7%	0	0.0%	
Student	2	1.2%	1	5.9%	0	0.0%	1	5.3%	

\*Fisher's exact test

Source: own elaboration



TABLE 3. CLINICAL CHARACTERISTICS IN PREGNANT WOMEN ADMITTED TO THE HOSPITAL.

Clinical characteristics	Positive anti-SARS-CoV-2 antibodies in pregnant women							
	Total		IgM		IgG/IgM		IgG	
	N=170	%	n=17	%	n=134	%	n=19	%
<b>Complications during pregnancy</b>								
Obstetric complications	61	35.9%	8	47.1%	44	32.8%	9	47.4%
Other complications	6	3.5%	2	11.8%	4	3.0%	0	0.0%
No complications	103	60.6%	7	41.2%	86	64.2%	10	52.6%
<b>Type of complications</b>								
Premature rupture of membranes	20	11.8%	3	17.6%	14	10.4%	3	15.8%
Preeclampsia	11	6.5%	0	0.0%	10	7.5%	1	5.3%
Miscarriage	8	4.7%	2	11.8%	4	3.0%	2	10.5%
Threatened preterm birth	6	3.5%	1	5.9%	4	3.0%	1	5.3%
Urinary tract infection	5	2.9%	1	5.9%	4	3.0%	0	0.0%
Dysfunctional labor	4	2.4%	0	0.0%	4	3.0%	0	0.0%
Acute fetal distress	4	2.4%	0	0.0%	3	2.2%	1	5.3%
Second trimester bleeding	2	1.2%	0	0.0%	2	1.5%	0	0.0%
Hyperemesis gravidarum	2	1.2%	1	5.9%	1	0.7%	0	0.0%
Fetal demise	2	1.2%	0	0.0%	2	1.5%	0	0.0%
Ectopic pregnancy	1	0.6%	0	0.0%	0	0.0%	1	5.3%
Pneumonia	1	0.6%	1	5.9%	0	0.0%	0	0.0%
Intrauterine growth restriction	1	0.6%	1	5.9%	0	0.0%	0	0.0%
No complications	103	60.6%	7	41.2%	86	64.2%	10	52.6%

Source: own elaboration

TABLE 4. ASSOCIATION OF CLINICAL CHARACTERISTICS ACCORDING TO RESPONSE TO ANTI-SARS-CoV-2 ANTIBODIES.

Clinical characteristics	Positive anti-SARS-CoV-2 antibodies in pregnant women								p*
	Total		IgM		IgG/IgM		IgG		
	N=170	%	n=17	%	n=134	%	n=19	%	
<b>Respiratory symptoms</b>									<b>1.00</b>
Yes	18	10.6%	2	11.8%	14	10.4%	2	10.5%	
No	152	89.4%	15	88.2%	120	89.6%	17	89.5%	
<b>Complications during pregnancy</b>									<b>0.14</b>
Yes	67	39.4%	10	58.8%	48	35.8%	9	47.4%	
No	103	60.6%	7	41.2%	86	64.2%	10	52.6%	
<b>Type of delivery</b>									<b>0.67</b>
Cesarean section	43	25.3%	3	17.6%	36	26.9%	4	21.1%	
Vaginal	98	57.6%	9	52.9%	77	57.5%	12	63.2%	
No delivery	29	17.1%	5	29.4%	21	15.7%	3	15.8%	

\*Fisher's exact test

Source: own elaboration

noglobulins<sup>(10,12)</sup>. Among all pregnant women with positive result, positive IgM / IgG was most frequently observed. Studies suggest that most patients seroconvert between 7 and 11 days after exposure to the virus<sup>(10,11)</sup>. Our findings in the studied population would represent a possible infection of pregnant women in the community who attend a specialized center for delivery or for care of morbidities. The health professional should consider these findings when providing the corresponding comprehensive care and management.

In the group of pregnant women who tested positive for anti-SARS-CoV-2 serology, a higher frequency was observed in adulthood and older women than in adolescence, similar to the national trend<sup>(14)</sup>. In previous studies, it has been identified that the current pandemic is mainly affecting older patients<sup>(15)</sup>, which may also be one of the factors involved in the differences found between older pregnant women and pregnant adolescents. The most frequent positive pregnancies were cohabiting women with low level of education and mainly housewives. This also



reflects the trend in sociocultural characteristics of the pregnant population in Peru<sup>(14)</sup>. The current pandemic is spreading rapidly in the Peruvian population<sup>(16)</sup>, so its distribution would be similar among pregnant women.

Pregnant women presented a higher frequency of positive anti-SARS-CoV-2 serological results during the third trimester, similar to recent studies<sup>(3,6)</sup>. One factor involved may be the current system of prenatal controls, which are more continuous only in the third trimester<sup>(17)</sup>, as well as to morbidities at the end of pregnancy for which pregnant women seek care<sup>(17,18)</sup>. COVID-19 impact on the evolution of pregnancy itself is not clear yet<sup>(7)</sup>.

In the study, 89.6% of the pregnant women with positive serological test were asymptomatic, and the frequency of respiratory symptoms was similar among the types of anti-SARS-CoV-2 antibody response. These findings were similar to those found by Sutton et al<sup>(19)</sup> in New York, but using molecular PCR testing, in which 88% of pregnant women with COVID-19 infection admitted for labor were asymptomatic. Vintzileos et al<sup>(20)</sup> found a lower proportion (66%) of asymptomatic women. On the other hand, we should consider that the performance of the test depends on a factor that is difficult to measure and predict, which is the time of sampling with respect to the time of illness, which can be calculated only in frankly symptomatic cases, but much difficult in asymptomatic or oligoasymptomatic cases, that according to research reaches 80-85% of those infected<sup>(21)</sup>. These results support the screening of all pregnant women admitted to hospitals, regardless of the presence or absence of respiratory symptoms, since most pregnant women do not present characteristic symptoms; this allows facilities to differentiate the respective care and isolation of positive cases.

35.9% of the pregnant women with positive SARS-CoV-2 antibodies had obstetric complications, most often premature rupture of membranes, preeclampsia and miscarriage. These findings were similar to those of studies where molecular PCR tests were used to identify disease cases<sup>(22)</sup>. Other studies have found increased frequency of preterm delivery and intrauterine growth restriction<sup>(3)</sup>. Premature termination of pregnancy has also been identified, although these women also manifested concurrent complications such as

preeclampsia, premature rupture of membrane, irregular contractions and history of fetal death, without being able to prove if these complications were associated with SARS-CoV-2 infection<sup>(6)</sup>.

In the present study, the predominant route of delivery among serologically positive pregnant women was vaginal (57.6%). We observed that the indication for cesarean section was obstetrical. In the period studied, the rate of cesarean section decreased to 25.3%, which is less than our hospital historical rate (43%)<sup>(23)</sup>. This is in accordance with the review by Ashokka et al<sup>(24)</sup> and with the expert consensus<sup>(25)</sup>, that recommend the mode of delivery be based on obstetrical indications, allowing vaginal delivery whenever possible and reserving cesarean section only for obstetrical reasons, not only because of the mother's SARS-CoV-2 infection. However, there are studies in pregnant women with SARS-CoV-2 infection in which cesarean section has increased, not justified by obstetrical causes or illness severity<sup>(26,27)</sup>, and vaginal delivery decreased between 6.8%<sup>(26)</sup> and 9.4%<sup>(27)</sup>.

Although data were collected from a large population of pregnant women, with serological testing used to screen all patients admitted to hospital, there are limitations to the study, such as the retrospective data collection and the use of the test itself. Although serological tests are not the first choice for timely diagnosis, they are used when molecular tests are not available or not easily accessible, as is the case in our population, in face of growing increase of cases that saturate health services. On the other hand, sensitivity and specificity data are variable in the literature, and this will probably depend on the kinetics of antibody production in each patient, and there is still limited literature on their evaluation in the pregnant population.

Based on these results, we conclude that in our study pregnant women with hospitalization for delivery or pregnancy morbidity care presented a seroprevalence of 7%. Most of them did not show clinical evidence of infection and were in a more evolved acute phase, presenting IgM / IgG anti-SARS-CoV-2 antibodies type. The most frequent complications were premature rupture of membranes and preeclampsia. No association was evident between the clinical-epidemiological characteristics analyzed and the type of anti-SARS-CoV-2 antibody response.



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