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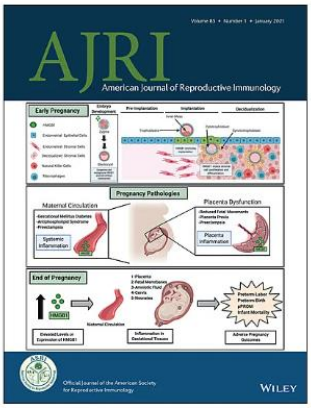

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ORIGINAL ARTICLE

Epidemiological and clinical characteristics of pregnant women and neonates with COVID-19 in Northwest Mexico

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Abstract

Introduction: The SARS-CoV-2 virus, which causes COVID-19, has spread quickly worldwide, causing millions of cases and thousands of deaths. Some risk factors in the general population are related to the development of severe COVID-19 or death, but in pregnant women and neonates, the information is limited.

Objective: To determine the epidemiological and clinical characteristics of pregnant women and neonates diagnosed with COVID-19 by RT–PCR and serological tests, and analyze the relationship between the influenza vaccination and COVID-19 symptoms in infected pregnant women in Sinaloa state.

Methods: We collected samples from 116 pregnant women and 84 neonates from the Woment's Hospital of Sinaloa. They were diagnosed with COVID-19 by RT–PCR and serological tests (IgG), and sociodemographic, clinical and laboratory parameters were recorded.

Results: A total of 11.2% (13/116) of the pregnant women were RT–PCR+, 25% (29/116) were IgG+ and 4.3% (5/116) were positive for both tests. Symptoms such as rhinorrhea (P = .04), cough (P = .02) and polypnea (P = .04) in pregnant women were related to COVID-19, also leukocyte index was higher in pregnant women with COVID-19 (P = .03), but the associations were lost after the Bonferroni correction. No laboratory parameters or underlying diseases were associated with COVID-19, and most infected pregnant women had mild cases. We found an association between the influenza vaccine and less common COVID-19 symptoms in pregnant women who were infected (P = .01). A total of 7.2% (6/84) of neonates were RT–PCR+, 35.7%

(30/84) were IgG+, and there were no symptoms or underlying diseases associated with neonates who were infected. In conclusion, this work demonstrated that some symptoms were related to COVID-19, most pregnant women and neonates had mild cases, and the influenza vaccine could decrease the severity of COVID-19 cases in pregnant women.

KEYWORDS
COVID-19, IgG, neonates, pregnant women, RT–PCR

1 | INTRODUCTION

The emerging novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified by the International Committee on Taxonomy of Viruses.[1] SARS-CoV-2 was identified in Wuhan, China, in December 2019 and is the etiological virus responsible for the current pandemic. SARS-CoV-2 has rapidly expanded to become one of the most significant public health threats in recent years.[2] This virus has caused more than 527 211 631 coronavirus disease 2019 (COVID-19) cases and 6 289 371 deaths worldwide[3] (Accessed June 01, 2022). Studies have demonstrated symptoms or risk factors related to severe cases of COVID-19, such as sex, age, and underlying diseases, but due to physiological changes during pregnancy, such as reduced functional residual volumes, diaphragm elevation, and altered cell immunity, unfortunately, the impact of COVID-19 on pregnant women is still poorly understood.[4] Few studies have demonstrated that pregnant women infected with SARS-CoV-2 could be asymptomatic patients or symptomatic patients with respiratory complications, such as requiring mechanical ventilation, and these alterations could occur until the pregnant woman's death.[5]

Pregnant women not only develop alterations in their body such as preeclampsia, but fetuses also can present alterations by COVID-19. COVID-19 is related to the risk of preterm birth, low birth weight, and the need for neonatal hospitalization in a neonatal intensive care unit, as well as the risk of fetal malformations, and intrauterine growth restriction [6,7] The changes that neonates can present from COVID-19 could be related to the vertical transmission of the virus from the mother to neonate. Some studies showed that neonates became RT–PCR positive for SARS-CoV-2 from their mothers with COVID-19 in their first hours of life, a phenomenon that suggests possible vertical transmission, which could represent a significant public health issue.[8] On the other hand, mothers infected with SARS-CoV-2 can also protect the fetus due to vertical transmission of IgG from the mother to fetus.[9]

To avoid complications of COVID-19, the timely diagnosis of this virus is important, and there are some tests than can achieve it. The gold standard is RT–PCR, which performs the direct detection of virus-specific nucleic acids. This virus is isolated from the nasopharynx of infected patients. RT–PCR had high sensitivity (95%) to identify SARS-CoV-2 in the acute stage of infection [10]. Other techniques to diagnose infection by SARS-CoV-2 are serological tests, which are indirect methods for the detection of infections because antibodies against SARS-CoV-2, such as IgM and IgG, are identified from peripheral blood, and serological tests present high sensitivity in the late states of infection.[10,11]

On the other hand, before of apparition of vaccines anti-COVID-19 to prevent this disease, options to help to combat the ravages caused by the SARS-CoV-2 were needed, and different research have demonstrated that influenza virus and coronavirus share some features,[12] due to similarities between viruses the vaccination against influenza confers some level of protection against SARS-CoV-2 due to epitopes cross-reactivity or common immunological pathways involved and some works demonstrated it, because influenza vaccine have reduced risk of SARS-CoV-2 infection, also it has increased the survival rate of infected patients.[4,13]

Mexico is one of the countries that has been more affected by COVID-19, and Sinaloa is within the 10 states with the most cases in Mexico. Additionally, in Sinaloa, a large proportion of the population suffers from chronic diseases, such as obesity, type 2 diabetes or hypertension, which can cause pregnant women to suffer severe COVID-19.[14,15] The vertical transmission mechanism(s)of COVID-19 in pregnant women and neonates is still unclear. In this comprehensive study, we investigated the prevalence of SARS-CoV-2 in pregnant women and neonates who tested positive by RT–PCR and serological tests in Sinaloa state, located in Northwest Mexico. We also analyzed the associations between the symptoms and underlying diseases of pregnant women and neonates with COVID-19. Finally, we analyzed the relationship between influenza vaccination and COVID-19 symptoms in infected pregnant women.

2 | METHODS

2.1 | Population of study and procedures

In this study, pregnant women and neonates from the Women's Hospital located in Sinaloa state, Northwest Mexico, were collected from August to December 2020. Women who were not pregnant or those with previous SARS-CoV-2 infection were excluded, and a representative sample of pregnant women was chosen for this study using the formula for a proportion: $Z\alpha^2$ (p)(q)/d2 in base of prevalence of pregnant women with COVID-19 during the third trimester until December 2020 in Mexico. The Supplementary Figure 1 show the steps to choose

the study subjects. Clinical history, symptoms, underlying diseases, and vaccination history (all those vaccinated less than 1 year ago were taken as positive for the influenza vaccine) were collected from the electronic medical records of all pregnant women and neonates. Additionally, throat swab samples were taken to diagnose SARS-CoV-2, and blood samples were taken for serological testing. The blood samples from pregnant women were taken to measure hemoglobin levels, hematocrit levels, leucocyte levels, neutrophil count, lymphocyte count, monocyte levels, eosinophil levels, platelet levels, blood urea nitrogen levels, prothrombin time, prothrombin partial time, and oxaloacetic transaminase levels. Additionally, weight, body mass index, oxygen saturation, heart rate, breathing frequency, blood pressure and temperature of the pregnant women were measured, and all the procedures were carried out by trained medical staff of the Women's Hospital following official Mexican standards.

The clinical severity of COVID-19 in pregnant women was classified as *i) mild grade*, which included patients who exhibited a variety of signs and symptoms, but they did not have shortness of breath, dyspnea on exertion, or abnormal imaging; *ii) moderate grade*, which included patients who had lower respiratory disease during clinical assessment or imaging, with an SpO_2 level ≥94% on room air at sea level; and *iii) severe grade*, which included patients who had an SpO_2 level < 94% on room air at sea level, a respiratory rate > 30 breaths/min, a PaO_2/FiO_2 ratio < 300 mmHg, or lung infiltrates > 50%.[16]

2.2 | RT–PCR and serological tests

To identify SARS-CoV-2 from throat swab samples of the pregnant women and neonates, RNA extractions and RT–PCR were performed on all samples in the Sinaloa State Public Health Laboratory following the guidelines of the Institute of Epidemiological Diagnosis and Reference (Instituto de Diagnóstico y Referencia Epidemiológicos, InDRE) and World Health Organization standards.[17] For serological tests, peripheral blood samples of the pregnant women and neonates were collected and analyzed for anti-SARS-CoV-2 antibodies by electrochemiluminescence immunoassay (ECLIA) using a qualitative Elecsys Anti-SARS-CoV-2 probe (Roche Diagnostics, USA), which detects IgG antibodies. Sample processing and interpretation results (positive: COI ≥ 1, negative: COI < 1) were performed according to the manufacturer's instructions using the module Cobas e602 (Roche Diagnostics, USA).

2.3 | Ethical approval

The subjects were informed about the investigation and signed informed consent forms agreeing to participate in the study. The study was approved by the Ethics Committee of the Women's Hospital, Secretariat of Health (No. 202008-06) and was conducted following the ethical principles of the World Medical Association Declaration of Helsinki.

2.4 | Statistical analyses

Fisher's exact test was used to assess differences between the groups and categories (symptoms, clinical outcome, comorbidities, clinical severity, laboratory parameters and vaccination history). A P value ≤.05 was considered to indicate statistical significance, moreover Bonferroni correction was applied to avoid alpha error 1. The data were analyzed using the statistical package SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

3.1 | Concomitant diagnosis for SARS-CoV-2 by RT–PCR and serological tests in pregnant women

From August 2020 to December 2020, a total of 116 pregnant women who attended the prenatal care outpatient clinic, and the obstetric emergency department were analyzed to identify those who were positive for SARS-CoV-2 by RT–PCR or by detecting IgG antibodies; of the pregnant women, 11.2% (13/116) were positive for SARS-CoV-2 by PCR, while 25% (29/116) of them were positive for IgG antibodies, as shown in Table 1. Moreover, 4.3% (5/116) of the pregnant women were positive for both the RT–PCR and IgG tests.

The sociodemographic and clinical characteristics of the pregnant women who were positive for SARS-CoV-2 or IgG antibodies are shown in Table 1. Most of them were housewives, living in free union, aged between 21 and 25 years, and had completed secondary school. The higher prevalence of women positive for RT–PCR or IgG tests was in urban areas compared with rural areas. All of the women were obstetric hospitalized, and none were treated with intensive therapy (Table 1). SARS-CoV-2 and IgG positivity were more prevalent in women with multiple pregnancies, as well as women with only one product, than in those with multiple pregnancies or abortions (Table 1).

3.2 | Clinical characteristics and laboratory parameters of pregnant woman who had positive RT–PCR and IgG tests for SARS-CoV-2

Pregnant women who were positive for COVID-19 or IgG antibodies reported many symptoms, which are shown in Table 2. The most prevalent symptoms that were reported, regardless of whether the women were positive by RT–PCR or IgG tests, were abdominal pain, headache, vomiting, rhinorrhea, cough, and dyspnea, among others (Table 2). No symptoms were related to the 13 women who were positive according to the RT–PCR test, while rhinorrhea (P: .04), cough (P: .02) and polypnea (P: .04) were associated with pregnant women who were positive for IgG antibodies compared with those who were negative, but the association was lost after to apply the Bonferroni correction (Table 2).

TABLE 1 Sociodemographic characteristics of pregnant women who tested positive for SARS-CoV-2 with PCR or IgG tests

	RT–PCR test			IgG test		
	Positive n = 13	Negative n = 103	Total PCR test	Positive n = 29	Negative n = 87	Total IgG test
Variables	n (%)	n (%)	n = 116 (%)	n (%)	n (%)	n = 116
Marital status						
Single	2 (15.3)	17 (16.5)	19 (16.3)	4 (13.7)	15 (17.2)	19 (16.4)
Married	3 (23.0)	22 (21.3)	25 (21.5)	7 (24.1)	18 (20.6)	25 (21.5)
Free Union	8 (61.5)	59 (57.2)	67 (57.7)	17 (58.6)	50 (57.4)	67 (57.7)
Divorcee	0 (.0)	4 (3.8)	4 (3.4)	1 (3.4)	3 (3.4)	4 (3.4)
Not know	0 (.0)	1 (.9)	1 (.8)	0 (.0)	1 (1.1)	1 (.8)
Age (years)						
11-15	1 (7.6)	1 (.9)	2 (1.7)	1 (3.4)	2 (2.3)	3 (2.5)
16-20	3 (23.0)	22 (21.3)	25 (21.5)	3 (10.3)	21 (24.1)	24 (20.6)
21-25	3 (23.0)	29 (28.1)	31 (26.7)	10 (34.4)	22 (25.2)	32 (27.5)
26-30	4 (30.7)	26 (25.2)	30 (25.8)	6 (20.6)	24 (27.5)	30 (25.8)
31-35	0 (.0)	13 (12.6)	13 (11.2)	4 (13.7)	9 (10.3)	13 (11.2)
>36	2 (15.3)	12 (11.6)	14 (12.0)	5 (17.2)	9 (10.3)	14 (12.0)
Education						
Illiterate	1 (7.6)	0 (.0)	1 (.8)	1 (3.4)	0 (.0)	1 (.8)
Incomplete Elementary school	1 (7.6)	6 (5.83)	7 (6.0)	2 (6.9)	5 (5.7)	7 (6.0)
Elementary school	3 (23.0)	12 (11.6)	15 (12.9)	3 (10.3)	12 (13.7)	15 (12.9)
Incomplete secondary school	0 (.0)	8 (7.7)	8 (6.8)	2 (6.9)	6 (6.9)	8 (6.9)
Secondary school	4 (30.7)	34 (33.0)	38 (32.7)	10 (34.4)	28 (32.1)	38 (32.7)
Technical school	0 (.0)	2 (1.9)	2 (1.7)	1 (3.4)	1 (1.1)	2 (1.74)
Incomplete high school	2 (15.3)	2 (1.9)	9 (7.7)	1 (3.4)	8 (9.2)	9 (7.7)
High school	1 (7.6)	17 (16.5)	18 (15.5)	5 (17.2)	13 (14.9)	18 (15.5)
Incomplete university	0 (.0)	7 (6.8)	7 (6.0)	1 (3.4)	6 (6.9)	7 (6.0)
University	1 (7.6)	5 (4.8)	6 (5.1)	2 (6.9)	4 (4.6)	6 (5.1)
Postgraduate	0 (.0)	1 (.9)	1 (.8)	0 (.0)	1 (1.1)	1 (.8)
Not know	0 (.0)	4 (3.8)	4 (3.4)	1 (3.4)	3 (3.4)	4 (3.4)
Occupation						
Housewife	13 (100)	98 (95.1)	111 (95.6)	28 (96.5)	83 (95.4)	111 (95.6)
Student	0 (.0)	2 (1.9)	2 (1.	0 (.0)	2 (2.3)	2 (1.7)
Employee	0 (.0)	3 (2.9)	3 (2.5)	1 (3.4)	2 (2.3)	3 (2.5)
Professional	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)
Others	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)
Demography						
Urban	4 (30.7)	42 (40.7)	46 (39.6)	13 (44.8)	33 (37.9)	46 (39.6)
Rural	9 (69.23)	61 (59.2)	70 (60.3)	16 (55.1)	54 (62.0)	70 (60.3)
Hospital situation						
Obstetric hospitalization	13 (100)	103 (100)	116 (100)	29 (100)	87(100)	116 (100)
Intensive therapy	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)
External consultation	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)	0 (.0)
Gestation						
First	5 (38.4)	50 (48.5)	33 (28.4)	8 (27.5)	25 (28.7)	33 (28.4)
Second	2 (15.3)	25 (24.2)	27 (23.2)	4 (13.7)	23 (26.4)	27 (23.2)
Multiple gestations	6 (46.1)	28 (27.1)	56 (48.2)	17 (58.6)	39 (44.8)	56 (48.2)

(Continues)

TABLE 1 (Continued)

Variables	RT–PCR test Positive n = 13 n (%)	RT–PCR test Negative n = 103 n (%)	Total PCR test n = 116 (%)	IgG test Positive n = 29 n (%)	IgG test Negative n = 87 n (%)	Total IgG test n = 116
Pregnancy type						
Singleton pregnancy	12 (92.3)	101 (98.0)	113 (97.4)	29 (100)	84 (96.5)	113 (97.4)
Multiple	0 (.0)	1 (.9)	1 (.8)	0 (.0)	1 (1.1)	1 (.8)
Abortions	1 (7.6)	1 (.9)	2 (1.7)	0 (.0)	2 (2.3)	2 (1.7)

Years of duration by degree of education. Elementary school: 6 years; Secondary school: 3 years; Technical school: 3 years; High school: 3 years; University: 5 years; Postgraduate: Master's degree 2 years, PhD degree: 5 years. Obstetric hospitalization: Women who go to hospital to give birth.

Anthropometrical and laboratory parameters related to COVID-19, such as weight, BMI, oxygen saturation, breathing frequency, and temperature, were also analyzed (Table 3). The only laboratory parameter related to pregnant women with COVID-19 RT-PCR positivity was the leukocyte index, in comparison with those with test negativity (Table 3). Although pregnant women who were positive for SARS-CoV-2 and IgG antibodies had higher BMIs than those who were negative, no associations were found. Most of the parameters were normal in the pregnant women who were positive for RT-PCR or IgG tests, except leukocyte index which was significant higher in women positive to RT-PCR in comparison with those negative (3.3 vs 1.6, respectively, *P*: .03), but after to Bonferroni correction the association was lost (Table 3).

Regarding the clinical severity of COVID-19 in the pregnant women, most cases were mild grade, with 69.2% of the RT–PCR positive women and 68.9% of the IgG positive women belonging to this classification; 23% and 27.5% had moderate grade and 7.6% and 3.4% had severe grade COVID-19 with RT–PCR and IgG positivity, respectively (Table 4). No associations were found between the women who were positive or negative for the RT–PCR or IgG tests and the clinical severity of COVID-19.

3.3 | The clinical outcomes in pregnant women with COVID-19 (RT–PCR) and IgG positivity

Some underlying diseases, such as hypertension, gestational diabetes, obesity, cardiovascular diseases, cancer and asthma, were detected in the pregnant women with COVID-19 (RT–PCR) or IgG positivity (Table 5). The pregnant women with COVID-19 (RT–PCR positive) presented only hypertension (30.7%) and obesity (23%), while women with IgG antibodies presented most of the diseases except cancer (Table 5). However, the pregnant women who were negative by RT–PCR and IgG tests presented a higher prevalence of underlying diseases than those who were positive. Therefore, no associations were found among the underlying diseases and pregnant women with COVID-19, IgG positivity or both.

3.4 | Influenza vaccination and symptoms in pregnant women who tested positive for COVID-19

The influenza vaccination history and presence of common COVID-19 symptoms in pregnant women were analyzed (Table 6). Twenty-four of the pregnant women with RT–PCR or IgG positive tests were vaccinated, while 18 of them were not; of them, 45.8% (11/24) of those who were vaccinated presented symptoms and 51.4% (13/24) did not, in comparison with the 83.3% (15/18) of nonvaccinated women who had symptoms, and 16.6% who did not (3/18), a fact that was statistically significant (Odds ratio: 5.9, 95% confidence index; 1.4 – 22.2, *P*: .01), as shown in Table 5. This indicates that pregnant women with a previously influenza vaccination had less common COVID-19 symptoms.

3.5 | The RT–PCR and IgG tests of newborns born to mothers diagnosed with or without COVID-19: Symptoms and clinical outcomes

The probability of neonates being infected intrahospital, by their mothers with COVID-19, or the mother transferring antibodies to the neonates is high; therefore, the neonates born in the Women's Hospital were also analyzed. Two groups of neonates were examined in this study: twenty-two neonates from the mothers included in this study and 62 neonates from mothers who were not included in this study (Table S1). In Group 1, three neonates (RT–PCR- and IgG-) from mothers who were RT–PCR+ and IgG-, 4 neonates (one who was RT–PCR- and IgG-, one who was RT–PCR+ and IgG+, and 2 who were RT–PCR- and IgG+) from mothers who were RT–PCR- and IgG+, three neonates (RT–PCR+ and IgG-) from mothers who were RT–PCR- and IgG- and 12 neonates (RT–PCR- and IgG-) from mothers who were also negative for both tests, were included (Table S1). Group 2 included 23 neonates RT–PCR- and IgG+ and 2 who were RT–PCR+ and IgG+, and the rest of the neonates were negative for both tests (Supplementary Table 1). Overall, of the 84 neonates, 7.2% (6/84) were positive for SARS-CoV-2, and 35.7% (30/84) were IgG positive (Table 7).

Symptoms such as phlegm, dyspnea, polypnea, and fatigue, among others, were found in the neonates who were studied. Regarding

TABLE 2 Clinical characteristics related to pregnant women who tested positive for SARS-CoV-2 with PCR or IgG tests

	RT–PCR test					IgG test				
	Positive n = 13	Negative n = 103		*P value non-corrected*	*P value corrected*	Positive n = 29	Negative n = 87		*P value non-corrected*	*P value corrected*
Symptoms	**n (%)**	**n (%)**	***P* value**	***.05***	***.002***	**n (%)**	**n (%)**	***P* value**	***.05***	***.002***
Abdominal pain	5 (38.4)	38 (36.8)	1	–	–	9 (31.0)	34 (39.1)	.43	–	–
Headache	2 (15.3)	20 (19.4)	1	–	–	5 (17.2)	17 (19.5)	.78	–	–
Vomiting	2 (15.3)	16 (15.5)	1	–	–	4 (18.3)	14 (16.1)	.76	–	–
Rhinorrhea	1 (7.6)	8 (7.7)	1	–	–	5 (17.2)	4 (4.6)	.04	*	–
Cough	2 (15.3)	6 (5.8)	.22	–	–	5 (17.5)	3 (3.4)	.02	*	–
Dyspnea	1 (7.6)	7 (6.8)	1	–	–	4 (13.8)	4 (4.6)	.1	–	–
Poor general health	1 (7.6)	7 (6.8)	1	–	–	0 (.0)	3 (3.4)	.57	–	–
Fever	2 (15.3)	5 (4.8)	.17	–	–	0 (.0)	7 (8.0)	.11	–	–
Chills	1 (7.6)	6 (5.8)	.57	–	–	2 (6.9)	5 (5.7)	.82	–	–
Fatigue	0 (.0)	7 (6.8)	1	–	–	3 (10.3)	4 (4.7)	.26	–	–
Diarrhea	0 (.0)	6 (5.8)	1	–	–	3 (10.3)	3 (3.4)	.16	–	–
Sickness	0 (.0)	5 (4.8)	1	–	–	2 (6.9)	3 (3.4)	.59	–	–
Polypnea	0 (.0)	4 (3.8)	1	–	–	3 (10.3)	1 (1.2)	.04	*	–
Myalgia	0 (.0)	4 (3.8)	1	–	–	1 (3.4)	3 (3.5)	1	–	–
Dizziness	0 (.0)	4 (3.8)	1	–	–	1 (3.4	3 (3.4)	1	–	–
Expectoration	0 (.0)	3 (2.9)	1	–	–	1 (3.4)	2 (2.3)	1	–	–
Conjunctivitis	0 (.0)	3 (2.9)	1	–	–	1 (3.4)	2 (2.3)	1	–	–
Irritability	0 (.0)	3 (2.9)	1	–	–	0 (.0)	3 (3.4)	.57	–	–
Odynophagia	0 (.0)	3 (2.9)	1	–	–	0 (.0)	3 (3.4)	.57	–	–
Anosmia	1 (7.6)	2 (1.9)	.3	–	–	1 (3.4)	2 (2.3)	1	–	–
Arthralgia	0 (.0)	2 (1.9)	1	–	–	1 (3.4)	1 (1.1)	.43	–	–
Thoracic pain	0 (.0)	1 (.9)	1	–	–	1 (3.4)	0 (.0)	1	–	–

Fisher's exact test was performed to check for statistical significance. Bonferroni correction was applied to *P* value corrected.

TABLE 3 Anthropometrical and laboratory parameters of pregnant women who tested positive for SARS-CoV-2 with PCR or IgG tests

	RT–PCR test					IgG test				
	Positive n = 13	Negative n = 103		*P value non-corrected*	*P value corrected*	Positive n = 29	Negative n = 87		*P value non-corrected*	*P value corrected*
Traits	**Mean (SD)**	**Mean (SD)**	***P* value**	***.05***	***.002***	**Mean (SD)**	**Mean (SD)**	***P* value**	***.05***	***.002***
Weight (kg)	81.7 (16.2)	78.2 (16.5)	.47	–	–	82.7 (17.4)	77.2 (15.9)	.12	–	–
BMI (kg/m^2)	32.3 (6.5)	30.3 (6)	.29	–	–	32.4 (6.5)	29.9 (5.9)	.06	–	–
Oxygen saturation (%)	98.0 (.7)	97.8 (1.4)	.49	–	–	97.6 (2.2)	97.9 (.9)	.3	–	–
Heart rate (beats per minute)	81.0 (9.7)	80.3 (14.1)	.88	–	–	80.5 (9.1)	80.3 (15.2)	.95	–	–
Breathing frequency (breath per minute)	19.0 (1.2)	19.4 (1.8)	.48	–	–	19.2 (1.6)	19.4 (1.8)	.68	–	–
Diastolic pressure (mmHg)	74.4 (11.3)	74.1 (13.8)	.93	–	–	75.4 (15.4)	73.7 (13)	.57	–	–
Systolic pressure (mmHg)	113.1 (11.6)	115.2 (18.2)	.69	–	–	118.3 (26)	113.9 (13.9)	.25	–	–
Temperature (°C)	36.5 (.43)	36.5 (.36)	.53	–	–	36.5 (.35)	36.5 (.37)	.59	–	–
Haemoglobin (g/dL)	11.7 (1.1)	11.8 (1.7)	.79	–	–	11.9 (1.9)	11.8 (1.6)	.87	–	–
Hematocrit (%)	33.2 (5.3)	35.2 (4.5)	.18	–	–	34.4 (5.9)	35.2 (4.2)	.46	–	–
Leucocyte,/μL	9.4 (2.3)	10.2 (2.7)	.34	–	–	10.2 (2.7)	10.1 (2.6)	.97	–	–
Neutrophil count,/μL	66.8 (22.7)	68.2 (13.7)	.75	–	–	70.4 (8.8)	67.5 (16)	.41	–	–
Lymphocyte count,/μL	18.3 (11.0)	20.7 (8.3)	.4	–	–	20.9 (6.3)	20.2 (9.2)	.75	–	–
leukocyte index	3.3 (5.7)	1.6 (1.6)	.03*	*	–	1.4 (.7)	1.9 (2.6)	.42	–	–
Monocyte count,/μL	5.1 (2.8)	6.8 (2.7)	.06	–	–	6.3 (2.0)	6.7 (3.0)	.54	–	–
Eosinophil count,/μL	.7 (.58)	1.3 (1.7)	.22	–	–	1.3 (2.2)	1.2 (1.4)	.9	–	–
Platelet count,/μL	225.7 (60.4)	233.1 (69)	.74	–	–	232.5 (65.6)	232.3 (69.9)	.99	–	–
Blood urea nitrogen (mg/dL)	6.6 (3.1)	7.4 (2.8)	.37	–	–	8.0 (2.9)	7.1 (2.8)	.17	–	–
Prothrombin time (INR)	11.1 (1.5)	11.0 (.8)	.82	–	–	10.9 (.8)	11.1 (.9)	.47	–	–
Prothrombin partial time (INR)	28.8 (6.3)	27.7 (3.2)	.4	–	–	28.5 (2.7)	27.6 (3.9)	.34	–	–
Oxaloacetic transaminase (UI/l)	27.0 (21.0)	33.3 (25.4)	.74	–	–	–	–		–	–

Abbreviations: cm, centimetres; dL, decilitres, SD, standard deviation. Mean and standard deviation were obtained by means of a frequency analysis. Fisher's exact test was performed to check for statistical significance, Bonferroni correction was applied to p value corrected.; Hg, mercury; kg, kilograms; m, metres; mg, milligrams; mm, millimeters.

TABLE 4 Clinical severity of pregnant women who tested positive for SARS-CoV-2 with PCR or IgG tests

	RT–PCR test					IgG test				
Clinical severity	Positive n = 13 n (%)	Negative n = 103 n (%)	*P* value	*P value non-corrected* .05	*P value corrected* .01	Positive n = 29 n (%)	Negative n = 87 n (%)	*P* value	*P value non-corrected* .05	*P value corrected* .01
Mild	9 (69.2)	81 (78.6)	.49	–	–	20 (68.9)	70 (80.4)	.09	–	–
Moderate	3 (23.0)	19 (18.4)	.71	–	–	8 (27.5)	14 (16.0)	.17	–	–
Severe	1 (7.6)	3 (2.9)	.38	–	–	1 (3.4)	3 (3.4)	1	–	–

Fisher's exact test was performed to check for statistical significance. Bonferroni correction was applied to p value corrected. Mild: patients may exhibit a variety of signs and symptoms, but they do not have shortness of breath, dyspnea on exertion, or abnormal imaging. Moderate: patients may have lower respiratory disease during clinical assessment or imaging, with an SpO2 level ≥94% on room air at sea level. Severe: patients with an SpO_2 level < 94% on room air at sea level, a respiratory rate > 30 breaths/min, a PaO_2/FiO_2 ratio < 300 mmHg, or lung infiltrates > 50% (only to COVID-19 positive were performed imaging studies).

TABLE 5 Underlying diseases related to pregnant women who tested positive for SARS-CoV-2 with PCR or IgG tests

	RT–PCR test					IgG test				
Underlying diseases	Positive n = 13 n (%)	Negative n = 103 n (%)	*P* value	*P value non-corrected* .05	*P value corrected* .008	Positive n = 29 n (%)	Negative n = 87 n (%)	*P* value	*P value non-corrected* .05	*P value corrected* .008
Hypertension	4 (30.7)	12 (11.6)	.08	–	–	6 (20.6)	10 (11.4)	.22	–	–
Gestational diabetes	0 (.0)	4 (3.8)	1	–	–	1 (3.4)	3 (3.4)	1	–	–
Obesity	3 (23.0)	27 (26.2)	.25	–	–	9 (31.0)	20 (22.9)	.66	–	–
Cardiovascular diseases	0 (.0)	1 (.9)	1	–	–	1 (3.4)	1 (1.1)	1	–	–
Cancer	0 (.0)	1 (.9)	1	–	–	0 (.0)	1 (1.1)	1	–	–
Asthma	0 (.0)	1 (.9)	1	–	–	1 (3.4)	0 (.0)	.25	–	–

Fisher's exact test was performed to check for statistical significance. Bonferroni correction was applied to p value corrected.

TABLE 6 Relationship between pregnant women who tested positive for COVID-19 and influenza vaccination and symptoms

	Patients with influenza vaccine *n* (%)			*P value non-corrected*	*P value corrected*
Symptoms	Positive n = 24	Negative n = 18	*P* value	*.05*	*.025*
Yes	11 (45.8)	15 (83.3)	.01	*	*
No	13 (51.4)	3 (16.6)			

Fisher's exact test was performed to check for statistical significance. Bonferroni correction was applied to p value corrected.

neonates who were RT–PCR positive, none presented any symptoms related to COVID-19 (Table 6). Regarding IgG positivity, symptoms such as dyspnea, polypnea, conjunctivitis and poor general health were found, but neonates who were negative for the IgG test presented a higher prevalence of symptoms (Table 6). Therefore, no associations were found.

Finally, associations among the underlying diseases with neonates who were RT–PCR and IgG positive were examined. Respiratory distress syndrome, sepsis, congenital malformations, heart diseases and jaundice were the underlying diseases that were found in neonates, but as for symptoms, PCR-positive neonates did not have any underlying diseases (Table 6). Respiratory distress syndrome, sepsis and congenital malformations were found in IgG-positive neonates, but the prevalence was similar to that in IgG-negative neonates.

4 | DISCUSSION

Since 2019, SARS-CoV-2 has spread around the world and has caused many deaths, but currently, we know that some characteristics in subjects, such as age, sex, and underlying diseases, are important to whether patients develop severe COVID-19 [4], but the information available for pregnant women and their neonates with COVID-19 is very scarce. In this study, we showed that 11.2% of the pregnant women were diagnosed with SARS-CoV-2 by RT–PCR tests and 25% were diagnosed by serological tests (IgG). Most of the women had non-severe cases without alterations in most clinical parameters. However, rhinorrhea, cough and polypnea were symptoms that were related to IgG positivity in pregnant women, also leukocyte index was higher in pregnant women RT-PCR positive. Moreover, influenza vaccination was related to a decrease in COVID-19 symptoms in comparison with not being vaccinated. Finally, 7.2% of the neonates were infected (RT–PCR positive), and 35.7% of the neonates had immunity against SARS-CoV-2 through IgG antibody transfer from mothers who were infected.

It is estimated that in the USA, more than 208, 937 COVID-19 cases have been reported in pregnant women [18]. The prevalence of COVID-19 in pregnant women varies depending on the country. In northern California, a COVID-19 prevalence of 2.5% was found in pregnant women.[19] In Brazil, of 195 pregnant women, 1.02% of them were diagnosed with COVID-19 by RT–PCR tests, and 8.7% were diagnosed with serological tests.[20] These studies are in contrast with our results because we found a higher prevalence, but the pregnant number analyzed in this study was lower in comparison with other study in Mexico City.[21,22] More studies are needed to determine the prevalence of COVID-19 in pregnant women, because there are only few reports which show the pregnant women prevalence with SARS-CoV-2.[23,24]

In this work, RT–PCR and serological tests were used to diagnose the study subjects. RT–PCR has been considered the gold standard to diagnose SARS-CoV-2; however, the sensitivity of RT–PCR as a serological test can change depending on the infection time period. RT–PCR is the gold standard in acute infection with specificity of > 99%,[25] but a previous study demonstrated that after five days of infection, the sensitivity of RT–PCR could decrease to 82%, and as the days after infection increase, the sensitivity decreases to 38%. This is in comparison with serological tests, which, in acute infection, present a low sensitivity of approximately 34%, but as the days after infection increase, the sensitivity increases; after 10 days post-infection, the sensitivity increases from 75% to 95% after 17 days.[10] It is very important to correctly use and interpret both tests to diagnose patients, provide ideal strategies and avoid severe COVID-19.

In the general population, some symptoms have been associated with COVID-19, such as cough, fever, myalgias, poor general health, and dyspnea [4]. In this study, cough, rhinorrhea and polypnea were related to IgG positivity in pregnancy women, but these associations were lost after Bonferroni correction, nevertheless other studies are match with our results. Chen L et al (2020) showed that fever, cough and chest tightness were the symptoms more prevalent in pregnant women infected.[26] A systematic review reported cough and fever more frequent symptoms in pregnant women who were COVID-19 positive.[27] Figueiro-Filho et al. (2020) reported that the main symptoms of 10,996 cases described in 15 countries were fever, cough, dyspnea, and polypnea, among others.[28] On the other hand, no underlying diseases were related to COVID-19 positivity in pregnant women; this result contrasts with other studies, in which authors associated obesity, hypertension or diabetes with COVID-19 in pregnant women.[29,30] The lack of associations in this study between these underlying diseases could be due to the sample size, and a larger sample size could help to find associations.

Regarding the severity of COVID-19 in pregnant women, most cases were mild, with non-alterations in laboratory parameters. These results are similar to those of other studies, including a study of Cardona-Pérez et al. (2021), which showed near of 90% of total pregnant women infected analyzed in Mexico City were asymptomatic [22]. Chen et al. (2020) found that the 9 of 109 pregnant analyzed in Wuhan, China presented severe COVID-19 infection.[26] A systematic

TABLE 7 Symptoms and underlying diseases of neonates who tested positive for SARS-CoV-2 with RT–PCR or IgG tests

	RT–PCR test					IgG test				
	Positive n = 6	Negative n = 78		*P value non-corrected*	*P value corrected*	Positive n = 30	Negative n = 54		*P value non-corrected*	*P value corrected*
Symptoms	**n (%)**	**n (%)**	***P* value**	***.05***	***.003***	**n (%)**	**n (%)**	***P* value**	***.05***	***.003***
Phlegm	0 (.0)	1 (1.2)	1	–	–	0 (.0)	1 (1.8)	1	–	–
Dyspnea	0 (.0)	6 (7.6)	1	–	–	2 (6.6)	4 (7.4)	1	–	–
Polypnea	0 (.0)	7 (8.9)	1	–	–	3 (10.0)	4 (7.4)	.69	–	–
Fatigue	0 (.0)	1 (1.2)	1	–	–	0 (.0)	1 (1.8)	1	–	–
Conjunctivitis	0 (.0)	1 (1.2)	1	–	–	1 (3.3)	0 (.0)	.35	–	–
Cyanosis	0 (.0)	1 (1.2)	1	–	–	0 (.0)	1 (1.8)	1	–	–
Rash	0 (.0)	1 (1.2)	1	–	–	0 (.0)	1 (1.8)	1	–	–
Poor general health	0 (.0)	4 (5.1)	1	–	–	2 (6.6)	2 (3.7)	.61	–	–
Underlying diseases										
Respiratory distress syndrome	8 (10.2)	1	–	–	5 (16.6)	3 (5.5)	.12	–	–	
Sepsis	5 (6.4)	1	–	–	3 (10.0)	2 (3.7)	.34	–	–	
Congenital malformations	2 (2.5)	1	–	–	1 (3.3)	1 (1.8)	1	–	–	
Heart diseases	0 (.0)	–	–	–	0 (.0)	0 (.0)	–	–	–	
Jaundice	1 (1.2)	1	–	–	0 (.0)	1 (1.8)	1	–	–	

Fisher's exact test was performed to check for statistical significance. Bonferroni correction was applied to p value corrected.

review of 31 016 pregnant women from 62 studies demonstrated that only 16.4% of the women developed severe cases.[31] A meta-analysis in which 60 studies were included reported that 11% of infected pregnant women suffered from severe COVID-19.[32] Vouga et al. (2021) reported that 9.9% of a total of 926 pregnant women presented severe COVID-19.[29]However, if we compare pregnant women with COVID-19 with pregnant women without COVID-19, infected pregnant women have a higher probability of death, of suffering pneumonia or being admitted to the intensive care unit.[33] Apparently, the SARS-CoV-2 cause some alterations in placenta of pregnant infected, Verma et al. (2021) demonstrated that SARS-CoV-2 colonize cells that express angiotensin-converting enzyme 2 (ACE2) in placenta, after to colonization, this virus reduced the expression of ACE2 in those cells, as consequence of it the renin angiotensin system was altered, and this alteration could cause adverse hemodynamic in pregnant women as pre-eclampsia.[34] Other studies also have showed alteration in placenta by SARS-CoV-2 infection as vascular malperfusion consisting of infarctions, increased intervillous fibrin, and intervillous thrombosis or inflammation by infiltrate in the intervillous space consisted of histiocytes and neutrophils.[35–37]

Interestingly, we found that influenza vaccination confers protection to pregnant women with COVID-19 and they presented fewer symptoms than nonvaccinated pregnant women. Other studies have also demonstrated the protective activity of influenza vaccines against COVID-19. Angulo-Zamudio et al. (2021) showed that influenza vaccination was associated with low mortality due to COVID-19 [4]. Jehi et al. (2020) demonstrated in a cohort study that COVID-19 risk was reduced in patients who had pneumococcal polysaccharide or influenza vaccination.[38] In another study in which 53 752 COVID-19 patients were included, one-third of the patients received influenza vaccinations, and they had 8% lower odds of intensive care unit admission, 18% lower odds of requiring mechanical ventilation and 17% lower odds of death.[39] The influenza vaccine can act as a stimulator of the immune system in COVID-19 patients to attack SARS-CoV-2 because the hemagglutinin esterase protein is very similar in both viruses. Furthermore, the spike protein of coronavirus has similar features to the class 1 viral membrane fusion protein of the influenza virus.[40–42] Moreover, the influenza vaccine activates the immune system through Toll-like receptor 7, which is important in defense against single-stranded RNA respiratory viruses such as SARS-CoV-2.[43] The evidence is very clear that the influenza vaccine can induce protection against SARS-CoV-2; therefore, vaccination against influenza should be promoted, not only because of the aforementioned protection but also to avoid coinfections with influenza and SARS-CoV-2, given that influenza infection upregulates pulmonary ACE2 receptors and allows an increased likelihood of SARS-CoV-2 infection.[44]

Finally, we observed a possible vertical transmission of SARS-CoV-2 and IgG antibodies from infected mothers to neonates. However, the presence of both in neonates is controversial, and there are two possible hypotheses to explain it. One possible explanation of neonates with IgG antibodies is the transplacental transmission of this immunoglobulin from infected mothers to neonates, and there is evidence that IgG antibodies can be transported through the placenta [45]. Fenizia et al. (2020) reported the presence of anti-SARS-CoV-2 IgG antibodies in umbilical cord blood.[8] Sileo et al. (2020) also detected IgG antibodies in cord blood in a pregnant woman infected with SARS-CoV-2.[9] On the other hand, the second hypothesis is that the vertical transmission of SARS-CoV-2 infections is intrauterine. Alzamora et al. (2020), reported a case of a 41-year-old COVID-19 positive pregnant woman with respiratory failure who required mechanical ventilation; the neonate was tested to identify SARS-CoV-2 infection by RT–PCR and he was positive.[46] Another study demonstrated the presence of the SARS-CoV-2 genome in umbilical cord blood and in at-term placentas, suggesting the vertical transmission of the infection.[8] However, there are studies that declared no association between vertical transmission and SARS-CoV-2 infection from mothers to neonates.[47,48]

In this study, neonates with IgG antibodies and/or SARS-CoV-2 infections were found, and both could probably transfer from mothers to neonates, as previously mentioned. However, three SARS-CoV-2-positive neonates were identified from mothers who were negative by RT–PCR and IgG tests, and there was a high probability that these neonates could have been infected in the hospital because limiting transmission of this virus is an essential component of care for patients in a hospital environment.

Regarding neonates born to infected mothers, there is limited information about SARS-CoV-2. There are some case reports in which neonates needed to enter the intensive care unit due to hypoglycemia, hypothermia, fetal distress or multiorgan failure.[49–51] These studies are in contrast with our results because we identified few symptoms and underlying diseases in neonates with RT–PCR and IgG positivity. It is very important to increase the number of studies of neonates from mothers with SARS-CoV-2 to understand the behavior of this virus in this population and avoid complications from this disease.

To the best of our knowledge, this is the first study to have identified the main epidemiological and clinical characteristics of pregnant women and neonates with COVID-19 diagnosed by RT–PCR and serological tests in Mexico. In addition, we also highlighted the protective effects of the influenza vaccine against SARS-CoV-2 in pregnant women. Finally, we observed a possible vertical transmission of the infection or protection from mothers with SARS-CoV-2 to their neonates.

A limitation of this study is the sample size; a larger sample could find more associations. Another limitation was not having analyzed all the neonates from mothers with COVID-19. Both facts could give us important information. Also, the statistical power of the analysis and potential confounding factors not covered in the study are limitations of this work.

5 | CONCLUSION

This study provides evidence that pregnant women from northwestern Mexico suffer mild to moderate COVID-19 disease, and some symptoms are associated with this population. In addition, we found possible protection of the influenza vaccine in pregnant women, decreasing the symptoms of this disease. Finally, a possible vertical transmission of

infection or protection from mothers with SARS-CoV-2 to neonates was observed. Although we found few severe COVID-19 cases in this study, more studies are needed to monitor the behavior of SARS-CoV-2 in pregnant women and neonates, and new variants of this virus are emerging, such as the beta, delta or gamma variants, which could have a larger impact in this population. Continuous monitoring could help to detect factors that affect pregnant women and neonates; in this way, we could create strategies to avoid severe cases and deaths caused by SARS-CoV-2.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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