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Screening of severe acute respiratory syndrome coronavirus-2 infection during labor and delivery using polymerase chain reaction and immunoglobulin testing

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ABSTRACT

Aims: To assess severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection during labor and delivery with polymerase chain reaction (PCR) and using immunoglobulin G and M testing to correlate with maternal and perinatal outcomes.

Main methods: Pregnant women admitted for labor and delivery at two Spanish hospitals were screened for SARS-CoV-2 infection by PCR test and by detection of serum immunoglobulins G and M. Maternal and perinatal outcomes were compared in women with laboratory evidence of SARS-CoV-2 infection with those with negative tests.

Key findings: Between March 31st and September 30th, 2020, 1211 pregnant women were screened for SARS-CoV-2 infection. The prevalence of laboratory evidence of SARS-CoV-2 infections was 5.4% ($n = 65$), corresponding to (i) 22 ongoing infections at admission, including two with mild clinical symptoms and 20 asymptomatic women; (ii) 43 cases of previous SARS-CoV-2 exposure; (iii) and 1146 women who were negative for both SARS-CoV-2 PCR and serological test. None of the screened mothers required hospital admission for coronavirus disease before or after delivery, nor were any of the newborns admitted to the intensive care unit. All newborns from mothers with positive PCR on admission were PCR negative. There were no significant differences in maternal or perinatal outcomes among the three studied groups.

Significance: Ongoing or previous SARS-CoV-2 infection with asymptomatic or mild clinical symptoms detected during screening in pregnant women at labor and delivery do not have a higher rate of adverse maternal or perinatal outcomes.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the most rapid epidemic in the history of humankind. At the end of December 2020, the World Health Organization reported over 79.2 million cases and over 1.7 million deaths since the start of the pandemic [1]. In pregnant women the viral infection has been

associated with adverse outcomes [2] and the risk of vertical transmission is a matter of debate [3,4]. The first reported cases of this infection in pregnant women from Wuhan (China) presented with pneumonia, confirmed by chest computed tomography. They were treated between December 2019 and March 2020, and presented a positive polymerase chain reaction (PCR) [5]. However, a large proportion of pregnant women had less severe or asymptomatic forms of the

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infection during the same period. The review of Pettiroso et al. [6] provided information from 1287 confirmed infections in pregnant women, including 19 infected neonates. When universal screening is undertaken, the maternal asymptomatic infection rates range from 43.5 to 92% of cases. It seems that the variable number of severe clinical cases in gravids could be related to differences in viral prevalence among their respective communities.

The systematic review by Huntley et al. [7] of 13 studies (including at least 10 pregnant women with SARS-CoV-2 infection) pointed out the low rate of severe cases, reporting intensive care unit admission at 3.0%, maternal critical disease at 1.4%, and no maternal deaths. However, preterm birth and cesarean delivery rates are increased and influenced by different critical practices. The recent meta-analysis by Yee et al. [8] concluded that during pregnancy, SARS-CoV-2 infection displays relatively mild symptoms, more frequent laboratory parameter alterations than in non-pregnant women, a fetal SARS-CoV-2 affection of around 2%, and a neonatal death rate of 0.4%. However, new alarming data have been reported from macro-studies on the severity of the SARS-CoV-2 infection and mortality in pregnant women, such as the Mexican National study [9,10].

SARS-CoV-2 screening of pregnant women during labor and delivery has been a widespread clinical practice since the beginning of the pandemic [11,12]. The prevalence of SARS-CoV-2 among this population ranges from 0.43 to 19.9%, depending on the point along the pandemic curve (first wave, second wave, or interwave period), and where the study was carried out [12–15]. In comparison to non-pregnant adults, half of gravids with SARS-CoV-2 pneumonia display a normal initial body temperature with leukocytosis and lymphopenia. Moreover, mixed consolidation and complete consolidation were common among laboratory-confirmed cases [3]. High asymptomatic rates (43–88%) have also been demonstrated among pregnant women admitted for labor and delivery [11,14–17], resembling rates in the non-pregnant population (86%) [18]. The main diagnostic tool for the detection of ongoing infection with SARS-CoV-2 has been polymerase chain reaction (PCR).

Studies have proposed the screening of SARS-CoV-2 of pregnant women during labor and delivery, including both the PCR and plasma enzyme-linked immunosorbent assay (ELISA) plasma SARS-CoV-2 G and M immunoglobulin (Ig) testing [19,20]. This approach has been postulated to provide a much more accurate prevalence than PCR alone. The main objective of the present study was to assess the value of combined PCR and IgG and M detection by serological tests performed during labor and delivery, and to correlate results with adverse maternal (AMOs) and perinatal (APOs) outcomes in three groups of pregnant women: (i) ongoing SARS-CoV-2 infection (positive PCR), (ii) previous viral infection (negative PCR with positive IgG regardless of IgM), and (iii) no evidence of infection (asymptomatic woman with both negative PCR and negative IgM and IgG tests).

2. Methods

This cohort study was conducted between the 31st of March and 31st of September 2020, at the *Villalba General University Hospital*, Madrid, and the *Miguel Servet University Hospital*, Zaragoza, Spain. The research protocol was approved by the Fundación Jiménez Díaz Clinical Research Ethics Committee, Madrid, Spain (Protocol EO194-20 HGV), and the Clinical Research Ethics Committee of Aragon (PI 20/508). The STROBE statement for observational studies was followed during study [21]. A total of 1211 pregnant women admitted for labor and delivery or scheduled for labor induction or cesarean delivery were screened by PCR using nasopharyngeal swabs and testing IgG and IgM class antibodies. The inclusion criterion considered pregnancies over 23 weeks in gestations with spontaneous or induced labor. Exclusion criteria corresponded to non-pregnant women, twin pregnancies, and neonatal or intrauterine deaths due to fetal malformations. Three patients with negative PCR, positive IgM and negative IgG were considered as possible

false-positive cases and were excluded following the recommendations of the Spanish Ministry of Health Guidelines [22].

We recorded the following maternal characteristics: age, parity, hypertensive disorders, and pregestational and gestational diabetes mellitus. Adverse maternal outcomes included intrapartum fever, and hemorrhage or postpartum uterine atony. Other symptoms such as cough, rhinorrhea, dyspnea, chest pain, diarrhea, myalgia, new anosmia, or ageusia were recorded, but with no incidence. Obstetric and perinatal data recorded for each delivery corresponded to newborn sex, delivery (vaginal, instrumental, or cesarean delivery), gestational age at birth, birth weight, percentile of the birth weight, and arterial cord blood pH. We also recorded the following adverse perinatal outcomes: small for gestational age (birth weight less than 3rd percentile), 5 min Apgar score < 7, arterial cord blood < 7.10, instrumental delivery for non-reassuring fetal status (NRFS), cesarean delivery for NRFS, still-birth, and neonatal Intensive Care Unit (ICU) admission rates.

All the women were classified into one of the three SARS-CoV-2 categories: (i) ongoing infection (positive PCR); (ii) previous infection (negative PCR with positive IgG regardless of IgM), following the recommendations of the Spanish Ministry of Health Guidelines [12]; and (iii) women with no evidence of SARS-CoV-2 infection (negative PCR and negative IgG and IgM tests).

2.1. Laboratory tests

At the *Villalba General University Hospital*, ELISA serological IgG and IgM testing were carried out in pregnant women with positive PCR or positive rapid antibody test. The rapid antibody test is a lateral flow immunochromatographic assay that uses the Biozek coronavirus 2019 IgG/IgM Rapid Test Cassette. The ELISA serological presence of antibodies was determined for G type with Abbott reagent, and for M type with Vircell reagent. At the *Miguel Servet University Hospital*, PCR reagents corresponded to the Xpert Xpress SARS-CoV-2, Liaison® SARS-CoV-2 solutions, and the Viasure SARS-CoV-2 real-time PCR detection kit. The ELISA serological presence of IgM and IgG was determined using the Liaison Diasorin reagent.

2.2. Statistical analysis

As continuous variables did not follow a normal distribution, median and interquartile ranges were calculated, and for categorical variables, absolute or relative frequencies were reported. Comparisons among the three SARS-CoV-2 patient categories (ongoing infection, previous infection, and women with no evidence of ongoing or previous SARS-CoV-2 infection) were performed by Kruskal-Wallis or chi-square tests for continuous and categorical variables. Moreover, we performed a two-by-two comparison between the groups: positive PCR, negative PCR with positive IgG regardless of IgM, and negative PCR with negative results for IgG and IgM antibodies using Mann-Whitney or chi-squared tests. Analyses were performed using R version 3.6.2 language programming (R Foundation for Statistical Computing, Vienna, Austria), and *p*-values < 0.05 were considered significant.

3. Results

During the study period study, 1211 pregnant women were admitted for labor and delivery and subjected to SARS-CoV-2 screening using PCR and serological examination for anti-SARS-CoV-2 antibodies (IgG and IgM; Fig. 1). None of the gravids were affected by SARS-CoV-2 pneumonia or any other severe clinical symptom during the study period. The prevalence of SARS-CoV-2 infection was 5.4%, corresponding to 43 previous SARS-CoV-2 exposures and 22 ongoing infections, two of them had coronavirus disease 2019 (COVID-19) symptoms at the time of admission, and 10 were asymptomatic cases without antibodies. Both PCR and antibodies for SARS-CoV-2 were negative in 1146 women. None of the screened mothers were admitted for COVID-19 before or

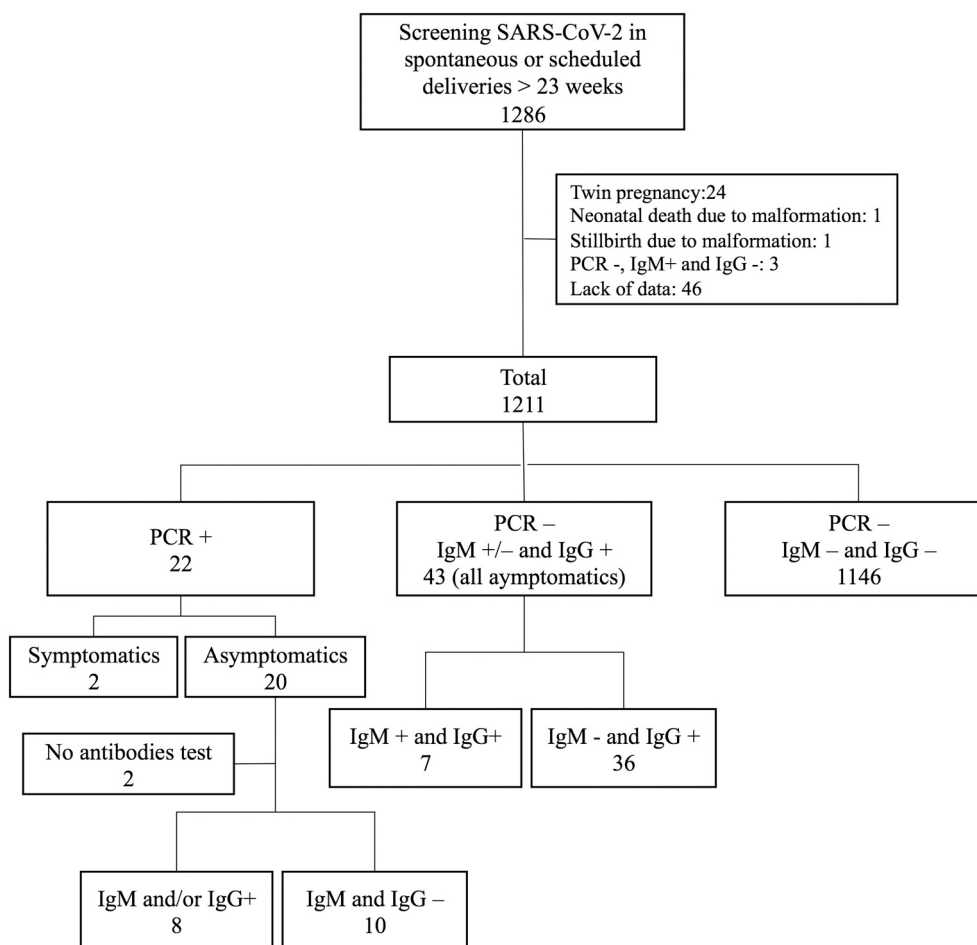


Fig. 1. Flowchart of universal screening with polymerase chain reaction (PCR) and immunoglobulins G and M in spontaneous or planned deliveries (labor induction or cesarean delivery).

after delivery, nor were any of the newborns required to stay in the neonatal ICU. All newborns of 22 mothers with positive PCR on admission were PCR negative. During the study period, there were no pregnant women admitted to the Department of Infectious Diseases or the Intensive Care Units (ICUs).

Table 1 shows the baseline characteristics of the three groups studied: (i) pregnant women with ongoing SARS-CoV-2 infection, (ii) previous viral infection, and (iii) no evidence of infection. We found statistically significant differences in maternal age ($p = 0.028$), parity ($p = 0.023$), and pregestational diabetes mellitus ($p = 0.022$) rates. Other clinical variables studied (chronic hypertension, gestational diabetes mellitus, and obstetric outcomes) did not show significant differences. Table 2 displays the maternal and perinatal adverse outcomes, with no significant differences among the three predefined groups for maternal intrapartum fever, postpartum uterine hemorrhage or atony, hypertensive disorders of pregnancy, fetal growth restriction, 5-min Apgar score < 7 , arterial cord blood pH < 7.10 , instrumental delivery for NRFS, cesarean delivery for NRFS, stillbirth and neonatal ICU admission. The Hospital protocols did not include repetition of serological testing.

There were similar results in the two-by-two comparisons among the three studied groups (Table 3), with statistically significant differences in mode of delivery ($p = 0.03$) in the comparison of (i) SARS-CoV-2 PCR negative/IgG positive versus; (ii) SARS-CoV-2 PCR negative/IgG negative; and maternal age ($p = 0.015$), parity ($p = 0.02$), and pregestational diabetes mellitus ($p = 0.008$) in the comparison of (iii) SARS-CoV-2 PCR positive versus (iv) SARS-CoV-2 PCR negative/IgG negative. As shown in Table 3, there were no significant differences among the studied groups for other variables: maternal age, parity, chronic hypertension,

hypertensive disorders of pregnancy, pregestational diabetes mellitus, gestational diabetes mellitus, fever, hemorrhage or postpartum uterine atony, newborn sex, mode of delivery, gestational age at birth, birth and percentile birth weight, arterial cord blood pH, fetal growth restriction, 5-min Apgar score < 7 , arterial cord blood pH < 7.10 , instrumental and cesarean delivery for NRFS, stillbirth and neonatal ICU admission.

4. Discussion

Of the 1211 pregnant women screened for SARS-CoV-2 exposure, 43 had a previous viral exposure with positive IgG test, and 1146 women were negative for both PCR and immunoglobulin G and M tests. The prevalence of SARS-CoV-2 infection in pregnant women was 5.4%. During the study period, none of the women or the newborns had pneumonia or any other symptoms that required their admission to the intensive care unit. There were no differences in maternal or neonatal outcomes across the three groups of pregnant women (ongoing infection, previous infection, and women with no evidence of SARS-CoV-2 infection).

A large number of publications during the first wave of the SARS-CoV-2 epidemic were based on severe forms of the infection. However, the viral infection can display only mild symptoms or even be asymptomatic. Several reports have described screening with PCR in pregnant women admitted for labor and delivery since the beginning of the pandemic situation, with results ranging from less than 1% [13,17] to 15–20% [11,12]. This variability may be due to several factors, including differences among the studied populations, lifestyle, health-care systems, and recruitment of studied women in different phases of

Table 1

Maternal characteristics and obstetric outcomes in three groups of pregnant women studied during labor and delivery: (i) pregnant women with ongoing SARS-CoV-2 infection, (ii) previous viral infection, and (iii) no evidence of viral infection. Results expressed as n (percentages) and median (interquartile range).

	Positive PCR	Negative PCR Positive IgG	Negative PCR Negative IgG	p- value
Miguel Servet Hospital	13 (73.4)	24 (59.1)	841 (55.8)	0.015
Villalba General Hospital	9 (26.6)	19 (40.9)	305 (44.2)	
Total pregnant women	22 (1.8)	43 (3.6)	1146 (94.6)	
Maternal characteristics				
Median maternal age	29.2 (24.4–35.4)	33.0 (27.8–36.7)	33.5 (29.6–37.3)	0.028
Parity				0.023
0	13 (59.1)	19 (44.2)	587 (51.2)	
1	3 (13.6)	13 (30.2)	381 (33.2)	
2	2 (9.1)	9 (20.9)	120 (10.5)	
≥3	4 (18.2)	2 (4.7)	58 (5.1)	
Chronic hypertension	0 (0)	0 (0)	15 (1.3)	0.483
Pregestational diabetes mellitus	1 (4.5)	0 (0)	5 (0.4)	0.022
Gestational diabetes mellitus	2 (9.1)	7 (16.3)	172 (15.0)	0.720
Obstetrics outcomes				
Newborn sex				
Male	13 (59.1)	17 (39.5)	539 (47.0)	0.324
Female	9 (40.9)	26 (60.5)	607 (53.0)	
Mode of delivery				
Vaginal delivery	16 (72.7)	38 (88.4)	798 (69.6)	0.129
Instrumental delivery	3 (13.6)	3 (7.0)	192 (16.8)	
Cesarean delivery	3 (13.6)	2 (4.7)	156 (13.6)	
Gestational age (weeks)	39.6 (38.6–40.7)	39.7 (38.7–40.6)	39.9 (39.0–40.3)	0.976
Birth weight (grams)	3387 (3032–3700)	3335 (2959–3577)	3260 (2970–3552)	0.484
Birth weight (percentile)	55.0 (29.1–86.6)	54.8 (34.9–75.9)	50.9 (25.9–76.3)	0.493
Arterial cord blood pH	7.28 (7.23–7.33)	7.27 (7.24–7.32)	7.27 (7.22–7.33)	0.977

Ig: immunoglobulin; PCR: polymerase chain reaction.

the SARS-CoV-2 pandemic. In pregnant women during their first trimester, Crovetto et al. [20], in Barcelona (Spain), reported a higher prevalence of SARS-CoV-2 by serological testing (14%) than by PCR (0.78%) in 871 women, attending at first-trimester screening ($n = 372$) or delivery ($n = 502$). Our preliminary study of 266 pregnant women studied during delivery in Zaragoza (Spain) found a prevalence of 6.8% for serological tests and 2.2% for the PCR procedure [23], whereas prevalence for the present sample of 1211 women from Madrid and Zaragoza were 3.6% and 1.8%, respectively. Our seroprevalence of SARS-CoV-2 during labor and delivery is close to the 5.0% reported rate in the main Spanish population [24].

The maternal and neonatal clinical course of our studied population showed similar maternal and perinatal outcomes when comparing women with and without SARS-CoV-2 infection. Previous studies using only PCR testing during labor and delivery, in both symptomatic and asymptomatic COVID-19 patients, reported high rates of cesarean delivery among these women [15,16]. In a series of 675 pregnant women from New York admitted for labor and delivery, Prabhu et al. [15] reported a slight increase in the rate of cesarean delivery in symptomatic COVID-19 women (46.7%) compared to asymptomatic ones (45.5%). Díaz-Corvillón et al. [16] in Chile described another study for SARS-CoV-2 in 583 patients using only PCR during labor and delivery admission. They reported a 43.2% rate of asymptomatic women and no

Table 2

Adverse maternal and perinatal outcomes (percentages) in three groups of pregnant women studied during labor and delivery: (i) gravids with ongoing coronavirus 2019 infection, (ii) previous viral infection, and (iii) no evidence of viral infection.

Outcomes	SARS- CoV-2 positive PCR	SARS-CoV-2 negative PCR and positive IgG	SARS-CoV-2 both negative PCR and IgG	P
Adverse maternal outcomes				
Maternal intrapartum fever	0 (0)	3 (7.1)	141 (12.3)	0.151
Hemorrhage or postpartum uterine atony	1 (5)	0 (0)	27 (2.4)	0.475
Hypertensive disorders of pregnancy	0 (0)	0 (0)	26 (2.3)	0.481
Adverse perinatal outcomes				
Fetal growth restriction (percentile <3)	0 (0)	0 (0)	45 (3.9)	0.271
5-min Apgar score < 7	0 (0)	0 (0)	7 (0.6)	0.818
Arterial cord blood pH < 7.10	0 (0)	1 (2.3)	32 (2.8)	0.718
Instrumental delivery for NRFS	0 (0)	0 (0)	16 (1.4)	0.631
Cesarean delivery for NRFS	0 (0)	0 (0)	23 (2)	0.514
Stillbirth	0 (0)	0 (0)	2 (0.2)	0.944
Neonatal intensive care unit admission	0 (0)	2 (4.7)	35 (3.1)	0.891

Ig: immunoglobulin; NRFS: non reassuring fetal status; PCR: polymerase chain reaction,

significant differences in perinatal outcomes, but a trend towards a higher rate of preterm birth. In our cohort, we had a low rate of cesarean deliveries, and there were no differences in vaginal or cesarean delivery rates among any of the groups. However, our rate of symptomatic SARS-CoV-2 infections was lower than those reported in both the New York and Chilean studies. Therefore, we must exercise caution when interpreting the cesarean section rates and other outcomes of pregnant women included in universal PCR screening, compared to those of symptomatic cases.

Egerup et al. [25] studied a population of 1313 pregnant women, in Copenhagen (Denmark), from April to July 2020, including 28 cases of positive antibodies and one case of positive PCR. The study concluded that SARS-CoV-2 infection was not associated with obstetric complications in pregnant women who had had the disease. In our study with 43 IgG positive women, we also found no differences in adverse perinatal effects between the 22 cases with positive PCR, as compared with women not exposed to the SARS-CoV-2 infection. Some authors have described higher preterm birth rates associated with COVID-19 in pregnant women [26,27]. We did not find a higher rate of preterm birth in ongoing or previous SARS-CoV-2 infections probably due to the mild clinical course in our patients, whereas findings may differ in symptomatic cohorts. Our results fit well with the Flannery et al. study [28] performed in two centers of Philadelphia (Pennsylvania, US), using both the PCR and serological tests. They reported 80 positive serological tests in a population of 1293 women of different ethnicities during labor and delivery, including 6.2% positive IgG and/or IgM SARS-CoV-2 women. This American study, and our results, point out the convenience of studying IgG and IgM to obtain more precise information than only using PCR in parturients at risk of infection by SARS-CoV-2.

The Elshafeey et al. [29] review reported 95.6% of mild cases in pregnant women with SARS-CoV-2 infection, but a 4.41% rate of admission to maternal ICU with 1.67% requiring mechanical

Table 3

Statistical significance (*p* value) for different comparisons of pregnant women SARS-CoV-2 according to polymerase chain reaction (PCR) positive/negative and immunoglobulin (Ig) G positive/negative in three groups of pregnant women during labor and delivery reported by *p*-values of Wilcoxon test comparisons.

	SARS-CoV-2 PCR positive versus both negative PCR and IgG	SARS-CoV-2 PCR negative and IgG positive versus PCR negative and IgG negative	SARS-CoV-2 PCR positive versus PCR negative and IgG positive
Maternal outcomes			
Maternal age (years)	0.015	0.245	0.254
Parity	0.020	0.194	0.094
Comorbidities			
Chronic hypertension	0.589	0.450	0.999
Hypertensive disorders of pregnancy	0.475	0.318	0.999
Pregestational diabetes mellitus	0.008	0.664	0.156
Gestational diabetes mellitus	0.440	0.819	0.427
Fever	0.079	0.293	0.204
Hemorrhage or postpartum uterine atony	0.506	0.308	0.158
Obstetric outcomes			
Newborn sex	0.364	0.417	0.217
Mode of delivery	0.925	0.030	0.265
Gestational age at birth (weeks)	0.892	0.877	0.708
Birth weight (grams)	0.329	0.465	0.713
Percentile birth weight	0.356	0.439	0.731
Arterial cord blood pH	0.828	0.992	0.906
Pathological findings			
Fetal growth restriction (percentile <3)	<i>p</i> -value 0.343	<i>p</i> -value 0.185	<i>p</i> -value 0.999
5-min Apgar score < 7	0.713	0.611	0.999
Arterial cord blood pH < 7.10	0.426	0.872	0.487
Instrumental delivery for NRFS	0.402	0.247	0.999
Cesarean delivery for NRFS	0.502	0.353	0.999
Stillbirth	0.844	0.786	0.999
Neonatal ICU admission	0.404	0.533	0.298

NRFS: non reassuring fetal status.

ventilation. According to this review, the situation may not be as favorable as it initially seemed for pregnant women with COVID-19, although included reports focused on studying women with symptomatic COVID-19. In studies on universal screening for women admitted for labor and delivery, the figures are much more reassuring. Thus, Prabhu et al. [15], in New York, described a mild course of COVID-19 disease among their cohort of 675 pregnant women, with only one case of admission to the maternal ICU. In Chile, Díaz-Corvillón et al. [16] reported a 0.51% admission rate to the maternal ICU and mechanical ventilation. In our study, we did not have severe COVID-19 cases. All of our cases had mild symptoms, and none required admission to the ICU, according to the Wu et al. disease severity characteristics [30]. It seems that SARS-CoV-2 infection during pregnancy is less severe than other coronavirus respiratory infections due to the reduced pro-inflammatory response that is associated with a lower level cytokine storm during pregnancy [31], and the low SARS-CoV-2 titers in cord blood plasma [32]. However, the recent National Mexican Prospective Cohort of

Pregnant Women confirms that the SARS-CoV-2 infection is associated with a higher risk of death, intubation, and ICU admissions in pregnant women [10]. These heterogeneous results may be related to the variability in SARS-CoV-2 prevalence in different world regions, and also in healthcare access and quality, lifestyle, and other factors [33–35].

Regarding the relationship between SARS-CoV-2 and perinatal morbidity, cases described in symptomatic cohorts of premature deliveries have been mainly associated with iatrogenesis, ending the pregnancy early to maintain maternal well-being [5,36,37]. Prabhu et al. [15] and Díaz-Corvillón et al. [16] showed no increase in adverse perinatal outcomes in maternal PCR positive cases in universal screening at labor and delivery. Lingkong Zeng et al. [38] described a case of pneumonia in a SARS-CoV-2 infected neonate, although they pointed out that the symptoms could have been due to prematurity, asphyxia, or sepsis, rather than to SARS-CoV-2 infection. In our study population, the maternal and perinatal outcomes were not significantly different between pregnant women with and those without SARS-CoV-2 infection although, as previously mentioned, none of these women had pneumonia or other clinical symptoms.

The risk of vertical transmission of SARS-CoV2 during labor and delivery is still not clear [6]. Some results sustain that there is little evidence for the SARS-CoV-2 vertical transmission [39]. However, there are also some reports of asymptomatic positive SARS-COV-2 PCRs in the newborns of infected mothers [16,38,40]. Yee et al. [8] reported five neonates with positive swab tests that could have become infected during vaginal or cesarean delivery. A recent meta-analysis calculated a 5.3% rate of vertical transmission and a positive SARS-CoV-2 test rate of 8% in neonates from mothers with COVID-19 [41]. However, Algarroba et al. [42] recently reported the presence of SARS-CoV-2 in the placenta, using electron microscopy, in a gravid with pneumonia treated with corticosteroids for fetal lung maturity before a preterm cesarean delivery.

Perinatal results are reassuring, and no neonatal complications were associated with maternal SARS-COV-2 infection in previous studies [15,16]. Egerup et al. [25] also found no differences between patients with positive versus negative antibodies in neonatal complications. We found no significant differences in APOs among our three groups, and none of the neonatal infections were by SARS-CoV-2. Our study is a large cohort studied over several months at two institutions of the Spanish National Health System that provide healthcare to the entire population.

We acknowledge that our study has some limitations. Firstly, some women may have omitted reporting symptoms because of their fear of the implications of having a coronavirus infection. Another limitation is the small number of infected women to report representative results of both maternal and perinatal adverse outcomes, although our results are in line with similar data. Regarding the pregnant women with a previous infection, we were unable to determine when the infection might have occurred, and we did not know if this influenced the outcomes of the pregnancy. Moreover, the detection kits used in both hospitals were from different brands, so could have had different sensitivities and specificities. Finally, our study is an observational clinical research, and we acknowledge that both false positive and negative results may be possible.

5. Conclusion

Pregnant women with asymptomatic SARS-CoV-2 infection or with mild clinical symptoms detected at labor and delivery do not have higher rates of adverse maternal or perinatal outcomes than women with negative PCR and immunoglobulin tests. The key to maternal or perinatal adverse effects is the clinical severity of SARS-CoV-2 infection in the pregnant woman. We provide evidence that the studied neonates were not infected in the uterus or during delivery.

CRediT authorship contribution statement

RSC, AV, LME and FRPL contributed to the conception of the study. RSC, LME, FRPL and BCL contributed to the design of the clinical work. RSC, AV, MT, BRS, MAG, JZ and SR carried out data acquisition. LME and FRPL performed statistical analyses. All authors were involved in the interpretation of the study results, as well as the drafting and revision of the manuscript. All approved the final version to be published.

Declaration of competing interest

This research did not receive a specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors declare that there are no conflicts of interest.

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