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Sars-CoV-2 in the second half of pregnancy: Maternal and perinatal outcomes

SARS-CoV-2 en la segunda mitad del embarazo: resultados materno – perinatales

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ABSTRACT

Introduction: The COVID-19 pandemic is a global health and social emergency. Knowledge is still limited about its effect on pregnant women. **Objective:** To describe maternal-perinatal outcomes of COVID-19 according to severity classification in women hospitalized in the second half of pregnancy. **Methods:** Retrospective, descriptive, observational study from March to July 2020 at Edgardo Rebagliati Martins National Hospital. All hospitalized pregnant women with RT-PCR and/or rapid positive test for SARS-CoV-2 were included. Pregnancies less than 20 weeks and epidemiological discharges were excluded. Maternal characteristics at admission and maternal-perinatal outcomes were grouped according to the clinical classification of the disease. The qualitative variables are presented in counts and percentages; and quantitative ones, in medians and ranges. **Results:** 247 pregnant women were studied. Most of them were in the third trimester (76%). The most frequent presentation of the disease was asymptomatic (83%), and cases of severe pneumonia were few (3.2%). The cesarean section rate was high (60%), although vaginal deliveries doubled over time (0-24 a 44%). Severe cases had a higher rate of cesarean section (100%) and iatrogenic preterm delivery (75%). No maternal deaths were reported. There were 9 stillbirths and 5 positive neonates for SARS-CoV-2, both among asymptomatic and mild patients. 9 stillbirths and 5 positive neonates for SARS-CoV-2, both among asymptomatic and mild cases. **Conclusions:** The possibility of cesarean section and iatrogenic preterm delivery is greater in severe cases. The vaginal delivery rate increased in recent months. No perinatal complications related to COVID-19 were identified.

Key words: Coronavirus infections, COVID-19, SARS-CoV-2, Pregnancy, Pregnancy complications, infectious, Pregnancy outcome, Perinatal death, Lima, Peru.

RESUMEN

Introducción. La pandemia por COVID-19 es una emergencia sanitaria y social mundial. El conocimiento sobre su efecto en las gestantes es todavía limitado. **Objetivo.** Describir los resultados materno-perinatales de COVID-19 según clasificación de severidad en mujeres hospitalizadas en la segunda mitad del embarazo. **Métodos.** Estudio observacional, descriptivo, retrospectivo, desde marzo hasta julio del 2020, en el Hospital Nacional Edgardo Rebagliati Martins, EsSalud, Lima, Perú. Se incluyeron a todas las gestantes hospitalizadas con RT-PCR y/o prueba rápida positiva para SARS-CoV-2. Se excluyeron los embarazos menores a 20 semanas y las altas epidemiológicas. Las características maternas al ingreso y los resultados materno-perinatales fueron agrupados según la clasificación clínica de la enfermedad. Las variables cualitativas son presentadas en recuentos y porcentajes; y las cuantitativas, en medianas y rangos. **Resultados.** Se estudiaron 247 gestantes. La mayoría correspondía al tercer trimestre (76%). La presentación más frecuente de la virosis fue asintomática (83%) y los casos de neumonía severa fueron pocos (3,2%). La tasa de cesárea fue alta (60%), aunque los partos vaginales se duplicaron en el tiempo (0-24% a 44%). Los casos severos tuvieron mayor tasa de cesárea (100%) y parto prematuro iatrogénico (100%). No se reportaron muertes maternas. Se registraron 9 óbitos fetales y 5 neonatos positivos para SARS-CoV-2, ambos entre las asintomáticas y leves. **Conclusiones.** En nuestra institución, la posibilidad de cesárea y de parto prematuro iatrogénico fue mayor en los casos severos. La tasa de parto vaginal aumentó en los últimos meses. No se identificaron complicaciones perinatales relacionadas al COVID-19.

Palabras clave. Infecciones por coronavirus, COVID-19, SARS-CoV-2, Embarazo, Complicaciones infecciosas del embarazo, Resultado del embarazo, Muerte perinatal, Lima, Perú.



INTRODUCTION

The World Health Organization (WHO) reported the novel coronavirus SARS-CoV-2 for the first time on December 31, 2019, in Wuhan, China. In a few weeks, the virus has spread throughout China, and in less than a month, it had affected several countries. Later on, this disease has been named COVID-19, and its rapid expansion has covered all continents, being declared a pandemic on March 11, 2020⁽¹⁾.

In Peru, its rapid advance has resulted in a health and social emergency, leading to institutional changes in the care of COVID-19 patients, including pregnant women.

In a previous publication, it has been reported that universal screening with serological tests identified most of the cases in asymptomatic patients (68.3%), and among those who presented symptoms, cough (84.6%) and fever (76.9%) were the most frequent. Furthermore, the cesarean section rate was high (76.5%)⁽²⁾.

This study describes the maternal and perinatal outcomes according to the clinical classification of COVID-19, from March to July in the Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru.

METHODS

This is a descriptive, observational, retrospective study that included pregnant women attended from March to July 2020 at the HNERM. The inclusion criteria were: 1) Pregnant women who required hospital admission; 2) Diagnosis of SARS-CoV-2 infection confirmed by RT-PCR and/or rapid serological test according to guidelines of the Ministry of Health (MINSA)⁽³⁾. The exclusion criteria were: 1) Pregnancies less than 20 weeks; 2) Patients with epidemiological discharge according to MINSA resolution⁽⁴⁾.

The maternal clinical and laboratory characteristics are described upon admission due to emergency, as well as the maternal and perinatal results. The pregnant women, in turn, were grouped according to the clinical classification of the disease based on the resolution of the MINSA⁽⁵⁾.

During the study period, the rapid serological test SARS-CoV-2 Detection Kit (Zhejiang Orient Gene BioTech) was used first, with sensitivity

43.8% and specificity 98.9%.⁽⁶⁾ Later, the Standard™ Q COVID-19 IgM/IgG Combo Test (SD Biosensor) was available with a sensitivity of 88.5% and specificity 98.8%.⁽⁷⁾

The information was entered into an electronic filling form, and the data obtained were processed in the SPSS version 23 program. The values of the qualitative variables are presented using counts and percentages, whereas those of the quantitative variables, in medians and ranges.

RESULTS

247 pregnant women with SARS-CoV-2 infection were analyzed and hospitalized for obstetric causes and/or pneumonia. Asymptomatic cases corresponded to 83.0% and mild cases to 10.5% of the population studied. Only 3.2% of the cases had severe COVID-19 pneumonia.

Of the asymptomatic patients, 80.5% were hospitalized with a full-term pregnancy. 75% of severe cases occurred in the third trimester, and 87.5% of these were premature. The most common symptoms were fever in 81.3% and cough in 84.4%. The most common laboratory findings in moderate and severe cases were elevated CRP, lymphopenia, and increased transaminases by 70%, 62.5%, and 56.3%, respectively.

It was observed that 4.8% required admission to critical care in all severe cases, although in moderate ones, half remained in the obstetric service. No maternal deaths were reported.

Of the 227 patients, three delivered twins: one from the asymptomatic group, one from the mild symptomatic group, and one from a patient with severe pneumonia. Conversely, 19 were discharged pregnant, and one remained hospitalized until the end of the study. No patient with moderate or severe clinical presentation had vaginal delivery. The preterm birth rate was 18.5% and, within these, the medically indicated preterm birth rate was 83.3%, being 100% for moderate and severe cases.

The overall cesarean section rate was 59.9%. A variation in time was observed: in March and April, there was a high rate (100%–76.5%) of cesarean sections, and from May it decreased significantly, reaching 56.3% in the month of July.



TABLE 1. MATERNAL CHARACTERISTICS AT ADMISSION ACCORDING TO SEVERITY CLASSIFICATION.

Maternal characteristics	Asymptomatic (205)	Mild (26)	Moderate (8)	Severe (8)
Maternal age				
Median (range)	31 (15-45)	33 (15-43)	32 (26-42)	35 (22-37)
Gestational age, n (%)				
20 - 27 ⁶ weeks	3 (1.5)	3 (11.5)	2 (25.0)	2 (25.0)
28 - 33 ⁶ weeks	14 (6.8)	5 (19.2)	2 (25.0)	5 (62.5)
34 - 36 ⁶ weeks	23 (11.2)	4 (15.4)	0	0
≥ 37 weeks	165 (80.5)	14 (53.9)	4 (50.0)	1 (12.5)
Parity, n (%)				
Nulliparous	96 (46.8)	11 (42.3)	1 (12.5)	3 (37.5)
Multiparous	109 (53.2)	15 (57.7)	7 (87.5)	5 (62.5)
Symptoms, n (%)				
Fever	0	15 (57.7)	4 (50.0)	7 (87.5)
Cough	0	12 (46.2)	7 (87.5)	8 (100.0)
Sore throat	0	9 (34.6)	4 (50.0)	6 (75.0)
Dyspnea	0	0	6 (75%)	8 (100.0)
Headache	0	4 (15.4)	2 (25.0)	4 (50.0)
Myalgia	0	1 (3.8)	0	4 (50.0)
Laboratory findings, n/N (%)				
Leukocytosis (>11.0 *10 ⁹ /L)	77/205 (37.6)	5/26 (19.2)	1/8 (12.5)	1/8 (12.5)
Lymphopenia (<1.0 *10 ⁹ /L)	17/205 (8.3)	1/26 (3.8)	3/8 (37.5)	7/8 (87.5)
Elevated CRP (≥ 10 mg/dL)	5/64 (7.8)	2/12 (16.7)	1/4 (25.0)	6/6 (100.0)
Elevated transaminases (TGO≥35/TGP≥45)	41/171 (24.0)	14/24 (58.3)	4/8 (50.0)	5/8 (62.5)

Median birth weight was 1 175 g in the offspring of patients classified as severe. In the asymptomatic group, 7.7% had infants weighting less than the 10th percentile, with 12% of the mild symptomatic group. There were 5 cases of perinatal transmission of SARS-CoV-2 confirmed by nasopharyngeal swab, as well as 9 cases of stillbirth, 8 of which occurred in the last two months of study.

DISCUSSION

The form of presentation of the disease was mostly asymptomatic or mild in 231 cases, coinciding with what was described in the general population

and pregnant women⁽⁸⁻¹⁰⁾. In a systematic review, Capobianco G. et al. described that the mean age of pregnant women was 30.2 years⁽¹¹⁾, similar to that of the women in the present study.

Most of the admitted patients were in the third trimester of pregnancy, corresponding mainly to asymptomatic/mild cases. Crovetto et al. found in 874 women that hospital admission was significantly more prevalent in the last trimester⁽¹²⁾. Khalil et al. also describe in a systematic review, which included 2 567 pregnant women, that 75% were in the third trimester⁽¹³⁾.

In the present study, the parameters most frequently associated with moderate/severe cases were lymphopenia and elevated CRP. This coincides with what Pereira A. et al. correlated with severe pneumonia⁽¹⁴⁾.

The overall rate of cesarean sections was higher than that reported in a systematic review by Khalil et al., where it was 48.3%⁽¹³⁾. However, the HNERM is a referral center; most of its pregnant women have obstetric risk factors. It should be noted the decrease in the rate of cesarean sections as of May, with the consequent increase in vaginal deliveries.

GRAPHIC 1. EVOLUTION OF THE MODE OF DELIVERY BY MONTHS

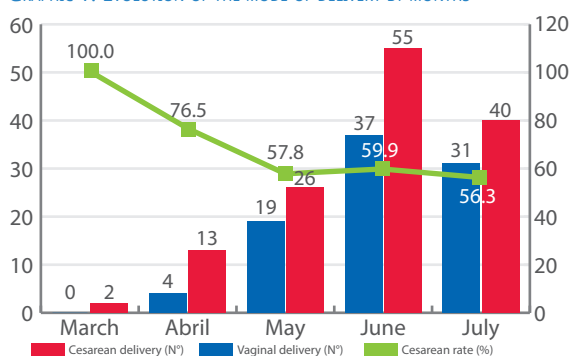




TABLE 2. MATERNAL AND PERINATAL OUTCOMES ACCORDING TO SEVERITY CLASSIFICATION.

	Asymptomatic (205)	Mild (26)	Moderate (8)	Severe (8)
Maternal outcomes				
Admission to critical care, n (%)	0	0	4	8
Evolution of pregnancy				
Delivery, n (%)	194 (94.6)	24 (92.3)	5 (62.5)	4 (50.0)
Twin pregnancy, n/N (%)	1/194 (0.5)	1/24 (4.2)	0	1/4 (25.0%)
No delivery, n (%)	11 (5.4)	2 (7.7)	3 (37.5)	4 (50.0)
Gestational age at delivery				
Median (range)	39 (24-42)	37 (23-40)	38 (33-39)	33 (28-37)
Preterm birth, n/N (%)				
< 34 weeks	9/194 (4.6)	5/24 (20.8)	1/5 (20.0)	2/4 (50.0)
iatrogenic preterm birth	7/9 (77.8)	5/5 (100.0)	1/1 (100.0)	2/2 (100.0)
34 – 36+6 weeks	17/194 (8.8)	7/24 (29.2)	0	1/4 (25.0)
iatrogenic preterm birth	13/17 (76.5)	6/7 (85.7)	0	1/1 (100.0)
Mode of delivery, n/N (%)				
Vaginal delivery	82/194 (42.2)	9/24 (37.5)	0	0
Cesarean delivery	112/194 (57.8)	15/24 (62.5)	5 (100.0)	4 (100.0)
Indication of cesarean delivery, n (%)				
COVID-19 pneumonia	0	0	2 (40.0)	3 (75.0)
Previous cesarean section	29 (25.9)	7 (46.7)	1 (20.0)	0
Fetal distress	21 (18.7)	3 (20.0)	1 (20.0)	0
Fetal malpresentation/malposition	30 (26.8)	1 (6.7)	0	0
Preeclampsia/Eclampsia	13 (11.6)	1 (6.7)	0	1 (25.0)
HELLP syndrome	1 (0.9)	2 (13.3)	0	0
Fetal macrosomia	6 (5.4)	0	0	0
Placenta previa	0	0	1 (20.0)	0
Placental abruption	3 (2.7)	0	0	0
Abnormal labor/Failed induction	3 (2.7)	1 (6.7)	0	0
Others	6 (5.4)	0	0	0
Maternal mortality	0	0	0	0
Perinatal outcomes				
Birth weight (g)				
Median (range)	3350 (552-4625)	2815 (582-3895)	3130 (1970-3365)	1175 (1080-3444)
< 10th percentile, n/N (%)	15/195 (7.7)	3/25 (12.0)	0	0
Apgar < 7 at 5 min, n/N (%)	3/188 (1.6)	4/23 (17.4)	0	2/4 (50.0)
Premature newborn	1/3 (33.3)	4/4 (100.0)	0	2/2 (100.0)
Stillbirth, n/N (%)	7/195 (3.6)	2	0	0
Positive RT-PCR SARS-CoV-2, n/N (%)	4	1	0	0

Most of the patients admitted to a critical care unit were far from term, and severe cases were associated with high rates of cesarean section and iatrogenic preterm delivery. Only one patient in the severe group underwent surgery for preeclampsia with severe features, and in the immediate puerperium, she developed symptoms of COVID-19 pneumonia. In their cohort study, Martínez-Perez and Vouga found that iatrogenic preterm birth was indicated in all patients with severe CO-

VID-19⁽¹⁵⁾. In a systematic review, Pettiroso found that the preterm birth rate ranged from 10% to 100%⁽¹⁶⁾.

The maternal death rate was zero, coinciding with the low or null mortality described in other studies^(17,18). In systematic reviews, it has been observed that maternal mortality occurred mainly in women with previous comorbidities^(13,19). These variables were not included in the present study.



Knowledge about the possible risk of vertical transmission is very limited. In order to demonstrate this, samples of placenta, amniotic fluid, cord blood and neonate should be collected immediately after delivery⁽²⁰⁾. These requirements were not met in any of the neonates confirmed with SARS-CoV-2 infection, all being diagnosed with a swab taken in the first 24 hours of life. In addition, it is presumed that this occurs in patients with high viremia and severe clinical pictures, such as the case reported in France⁽²¹⁾.

The stillbirth rate increased in the last 2 months. Khalil et al. describe an increase in the incidence of stillbirths during the pandemic⁽²²⁾. These changes could be due to the measures adopted by the pandemic, such as the restriction of care only to emergencies, and not being able to perform prenatal control or ultrasounds, to which is added the fear of patients to go to a health facility due to the risk of acquiring the infection.

In conclusion, the clinical and laboratory characteristics of the women seen during the COVID-19 pandemic were similar to those of non-pregnant women. There is a greater possibility of iatrogenic cesarean section and premature delivery in women who develop a severe infection. Due to institutional measures, the vaginal delivery rate doubled compared to baseline. Perinatal complications, death rate, and infected neonates do not seem to be directly related to COVID-19 during pregnancy. The limitations of the study lie in its retrospective nature, the underreporting, the diagnostic method that went from being combined to being almost exclusive to the rapid serological test, and the uniformity of the time of the neonatal RT-PCR sample collection.

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