Vaginal delivery in COVID-19 pregnancies: experience from a referral center in a high-prevalence area

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Abstract

Objective: We aimed to describe mode of delivery and perinatal results among COVID-19 confirmed infected women. Design: Prospective cohort of consecutive pregnant women with confirmed SARS-CoV-2 infection, and comparison of perinatal outcome with expected values on an historical cohort. Setting: A tertiary referral center in Barcelona, Spain. Population: Pregnant women with SARS-CoV-2 confirmed infection. Methods: SARS-CoV-2 infected women managed under a standard protocol who delivered during the period March 13th - April 25th, were evaluated. Data on baseline maternal characteristics, COVID-19 disease parameters, clinical management, mode of delivery, and perinatal outcome were collected. Relevant perinatal data were compared with the expected values observed in an historical control of our center. Main Outcome and Measure: Rate of vaginal delivery among COVID-19 pregnancies. Secondary outcomes were maternal or neonatal complications, and vertical transmission of SARS-CoV-2. Results: A total of 21 women with COVID-19 delivered at our center during the study period: 42.9% had moderate or severe respiratory infection. 14 out of 21 (66.7%) delivered vaginally. Three out of 7 caesarean sections were maternal indicated because of maternal worsening secondary to COVID infection. Preterm delivery occurred in 4 cases (19%), half of them related to COVID-19. There were no differences between the observed and the expected perinatal outcomes. Conclusions: In the absence of severe maternal complications, vaginal delivery among pregnant women with COVID-19 infection is a safe option, both for the mother and the baby, with similar perinatal outcomes than expected in a non-infected cohort and with no evidence of vertical transmission.

Introduction

COVID-19 disease was first described in December 2019 in Wuhan (Hubei, China), caused by a novel coronavirus named SARS-Cov-2. The virus spread worldwide and the WHO declared COVID-19 a pandemic infection on March 11th, with more than 4 million infections and 283 153 deaths reported (May 12th)[(1)]. Spain is the third country in number of cases, with more than 227 000 infections[(1)].

Most patients have mild symptoms, but approximately 20% develop a severe disease, including pneumonia and acute respiratory distress syndrome (ARDS)[(2–4)]. Although the existing data is still limited, pregnant women do not appear to be more susceptible to infection or to experience more serious complications[(5)].

Therefore, most pregnant women present with mild disease, and no relevant implications in mode of delivery should be expected. However, regarding perinatal outcome, it is of note that in most series published from Asian countries, a high rate of caesarean section has been described[6,7].

Another aspect of uncertainty and clinical concern is the risk of vertical transmission. This mode of transmission of SARS-CoV-2 has not been clearly demonstrated to date, although the evidence against this route is still limited[7–11]. However, there is no evidence of the presence of the virus in genital fluids, amniotic fluid, urine or breast milk[7,9,12,13]. As a mainly respiratory virus, with small passage to blood[12], the possibility of placental seeding and transmission seems highly unlikely.

In the present study we aimed to describe mode of delivery and perinatal results among COVID-19 confirmed deliveries.

Methods

Study design and setting

We constructed a prospective cohort of consecutive pregnant women with confirmed SARS-CoV-2 infection (positive RT-PCR on nasopharyngeal swab) who delivered in BCNatal (Hospital Clínic and Hospital Sant Joan de Déu), Barcelona, Spain between March 13th and April 25th, 2020.

Clinical management and follow-up of these patients was made from admission until hospital discharge according an established protocol[14]. Moderate or severe cases started treatment for COVID with lopinavir/ritonavir, hydroxychloroquine and azithromycin. Maternal monitoring during admission or labor included hourly monitoring of blood pressure, heart rate, temperature, respiratory rate and oxygen saturation. Labor was managed by attending professionals adhering to personal protection equipment protocols, in a dedicated delivery room under continuous fetal cardiotocographic monitoring. The mode of delivery in women with COVID-19 with no criteria of severe disease was guided by standard obstetric indications. After hospital discharge, telephone follow-up was performed to detect postpartum complications.

Outcomes and variables

Clinical information was obtained from electronic medical reports. Epidemiological data, clinical details of COVID-19 infection, diagnostic tests, management and treatment were collected. Low educational level was considered when less than 8 years of studies had been completed. Co-morbidity was defined as the presence of preexisting hypertension, pre-existing diabetes, obesity (defined as body mass index [?] 30 kg/m^2), obstructive lung diseases or immunosuppression.

Maternal infection was classified as mild, moderate or severe. Moderate maternal infections were considered in cases of pneumonia confirmed by chest X-Ray, without presenting severity signs (basal oxygen saturation >90%; no need for vasopressors or ventilatory assistance). Maternal severe infections were defined when presented severe pneumonia, respiratory distress, sepsis or septic shock. Severe pneumonia criteria followed the American Thoracic Society and Infectious Diseases Society of America recommendations[15]. Adult respiratory distress syndrome (ARDS) was considered in cases with suggestive clinical findings or radiological evidence of bilateral infiltrates plus oxygenation deficit (Sat O_2/Fi O_2ratio [?]315 or Pa O_2/Fi O_2 ratio [?]300). Sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, and septic shock as a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality, according to The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) recommendations[16]. Maternal worsening was considered when maternal transfer to intermediate or intensive care unit was needed for severe pneumonia, ARDS, sepsis or other major complications. Venous thrombosis or pulmonary thromboembolism were recorded as thrombotic complications. Cardiac complications included acute cardiac failure, arrythmias or ischemic disease.

Information about pregnancy and perinatal outcomes were obtained. Gestational age at delivery, mode of delivery, indication for delivery, neonatal weight, Apgar score, need of neonatal intensive care unit admission

and neonatal SARS-CoV-2 infection were analyzed. When maternal conditions were favorable breastfeeding was allowed following the established protective measures. Neonatal SARS-CoV-2 nasopharyngeal PCR was obtained from all neonates within the first 48 hours.

Perinatal outcome results were compared with expected results from an historical cohort in the same institution.

The main outcome was the rate of vaginal delivery among COVID-19 pregnancies. Secondary outcomes were maternal or neonatal complications, and vertical transmission of SARS-CoV-2.

Statistical analysis

Continuous variables were expressed as median, interquartile range (IQR) and range (min-max) and categorical variables as proportions [n(%)].

For the main perinatal outcomes [gestational age at delivery, prematurity rate (<37 weeks), birthweight, birthweight centile, SGA (birthweight centile<$10^{th(17)}$), caesarean section rate, fetal distress requiring emergent delivery and need to neonatal unit admission] one-sample non-parametric tests were performed to compare the observed medians (Wilconox signed-rank test) or proportions (chi-squared test) against the expected values as observed in an historical cohort of deliveries attended in the same institution between March 13^{th} and April 25^{th}, 2019.

Statistically significant differences were considered if $p<0.05$. Data was analyzed using R studio version 1.1.442.

Results

A total of 21 women were included. Table 1 shows the baseline characteristics and the clinical outcomes. Of note, 15 (71.4%) women were admitted for an obstetrical condition and 6 (28.6%) for lower-respiratory signs or symptoms. The median (IQR)[range] gestational age at admission of the respiratory cases was 36.5 (4.8)[32.4-40], while it was 40.0 (1)[33-42] among those women admitted for obstetric conditions. A total of 3 women (14.3%) had co-morbidities (one case of obesity and 2 women with asthma). Regarding disease severity, 19% of women remained asymptomatic, 38.1% presented a mild disease, 28.6% had a moderate infection and 14.3% a severe maternal disease. Radiological abnormalities were present in 47.6% of cases. Eleven women (52.4) received specific treatment for COVID-19, and oxygen therapy was needed in 6 of them (28.6). One third of women presented clinical deterioration, at a median of 7.4 days after symptoms onset, and 3 of them required transfer to critical care unit. There were no cases of sepsis, septic shock, thrombotic or cardiac complications. No maternal deaths occurred.

Table 2 shows the perinatal outcomes, and Figure 1 depicts the gestational age and birthweight centile distribution. Vaginal delivery was achieved in two thirds of cases (12 spontaneous and 2 operative vaginal delivery for fetal indications), with good neonatal outcome. Caesarean section was performed for maternal compromise related to COVID-19 in 3 cases (14.3%), and no indications for fetal distress were reported. Among the cases without respiratory compromise, the global caesarean section rate was 22% (4 cases out of 18). Preterm delivery occurred in 4 cases (19%), half of them related to COVID-19. Table 3 compares the observed main perinatal outcomes to those expected in the same population: of note, the observed outcome did not significantly differ from the expected. All newborns tested negative for SARS-CoV-2 in the first 48h of life.

In 4 cases hospital postpartum readmission was needed, in two due to postpartum fever and two related to COVID-19 disease, with no need for critical care support in any case.

Discussion

Main findings

The findings among this cohort of deliveries in COVID-19 infected pregnant women from a high prevalence area in Spain suggest that in the absence of maternal severe complications, vaginal delivery is a safe option,

both for the mother and the baby; and that perinatal outcomes in these pregnancies do not differ from the expected in the baseline population.

Interpretation

Our findings are not in concordance with what has been reported in the early series of deliveries among COVID-19 infected women. Indeed, caesarean section rate ranges from 86% to 91% in the earlier series of cases[6,11]. In a multicentre study[11] from China including 99 deliveries, the caesarean section rate was 86%, mostly for maternal pneumonia (39%), although only in 7% of them it was severe. In a systematic review[6] including 86 births mainly from China, but also from USA, Sweden and Corea, a caesarean section was performed in 91% of the deliveries, and fetal distress was found a main contributor to this exceedingly high rate. We found an overall caesarean section rate of 34%, which is in keeping with the one reported in two more recent retrospective multicentre studies, one in New-York involving 18 deliveries[18] and the other in Northern Italy with 42[19] (caesarean section rate of 42% and 43%, respectively). Also in agreement with our results, both studies found overall good maternal and neonatal outcomes. In fact, the caesarean rate observed in our cohort after excluding those women who were delivered preterm because of worsening of maternal respiratory status, was similar (4/18, 22.2%) to our baseline caesarean rate expected as a tertiary center (25.8%). Therefore, our findings support current recommendations on that the mode of delivery in respiratory stable women should be taken depending on obstetric conditions.

It could also be argued that concerns on the risk of vertical transmission during vaginal delivery may have contributed to these initially reported increased rates of caesarean section. However, in previous epidemics of other coronavirus diseases, SARS and MERS, vertical transmission was not confirmed although the evidence against relies on a limited number of small series[20]. It is well known that vaginal route increases the risk of transmission through cervical and vaginal contaminated secretions, as in the case of herpes simplex or HIV viruses. However, SARS-CoV-2 is a respiratory virus that mainly replicates in the respiratory tract and it has not been detected in genital secretions[21] . Another potential way of intrapartum transmission could be through contaminated stool since SARS-CoV-19 RNA has been isolated from feces, but those are probably not infectious forms of the virus[22]. Bloodstream transplacental transmission during uterine life or through placental disruption at the time of delivery is also very unlikely, given that viremia is uncommon. A single positive RNA-PCR reported case in amniotic fluid in a 32 weeks preterm newborn delivered by caesarean section at the time of very severe maternal infection could correspond to a true vertical transmission secondary to a high maternal viremia or inflammatory placental abnormality in this critically ill mother. However, since amniotic fluid was collected for testing during the caesarean section, maternal contamination could not be excluded[10]. Early-onset symptoms in the newborn, and negative PCR at birth, but positive some days after, also suggests a true vertical transmission, although horizontal or iatrogenic transmission could not be discarded. Moreover, 2 articles reporting 3 neonates from mothers with COVID-19 and positive IgM antibodies[23][24] is also of concern, given that IgM antibodies do not cross the placenta and are of fetal origin. However, IgM antibodies assays have false positives, and the tests performed in these studies lacked standardization[25].

In our study, in which newborns were swabbed in the first 48 hours of life, we did not observe any positive RT-PCR in nasopharyngeal samples irrespectively of the way of delivery. Likewise, Yan et al. in the largest series reported so far described negative results of neonatal SARS-CoV-2 PCR in all 86 tested cases[11]. In the ten samples of amniotic fluid and cord blood tested, they could not demonstrate the presence of SARS-CoV-2. As far as we know there are no reported positive newborns after vaginal deliveries. These findings suggest that vaginal delivery is associated with a low risk of intrapartum SARS-Cov-2 transmission to the newborn.

Strengths and limitations

One of the strengths of the study is that it shows the outcomes of the first consecutive COVID-19 positive women managed and delivered under a standardized clinical protocol[14] in a referral fetal-maternal hospital in Barcelona, a high-prevalence area of the infection. In addition, showing reassuring results of vaginal

delivery for both the mother and the offspring may help to define future less interventionist obstetrical attitudes among infected pregnant women. Among the limitations we should underline a limited follow-up of the newborns and a relatively small sample size.

Conclusion

The results of our cohort show that, in the absence of maternal severe complications, vaginal delivery among pregnant women with COVID-19 infection is a safe option, both for the mother and the baby, with similar perinatal outcomes than expected in a non-infected cohort and with no evidence of vertical transmission.

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Contribution to authorship:

ML, AG, FF and MP contributed to the conception, design and coordination of the research. MV, LR and PF recruited the participants. ML, AG, FF and MP contributed to the analysis of data. ML, AG, FF and MP contributed to writing the manuscript. EV, SH, PF and LG-R contributed to the revision of the manuscript and the final version was approved by all the authors.

Details of Ethics Approval:

This study was reviewed and approved by Hospital Clinic and Hospital Sant Joan de Deu Ethical Committee (reference HCB/2020/0393), date April 2nd, 2020. Oral or written Informed consent was obtained according to exceptional measures adopted for COVID-19 protection and research needs.

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