

# Neonatal outcomes in pregnant women infected with COVID-19 in Babol, North of Iran: retrospective study with short-term follow-up

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## Research Article

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# Abstract

During the Coronavirus disease 2019 (COVID-19) pandemic, the number of pregnant women and neonates suffering from COVID-19 increased. However, there is a lack of evidence on clinical characteristics and neonatal outcomes in pregnant women with COVID-19. We evaluated short-term outcomes (4 weeks post-discharge) and symptoms in neonates born to mothers infected with COVID-19. In this retrospective cohort study, we included all neonates born to pregnant women with COVID-19 who were admitted to Ayatollah Rohani Hospital, Babol, Iran, from February 10 to May 20, 2020. Clinical features, treatments, and neonatal outcomes were measured. Eight neonates were included in the current study. The mean gestational age and birth weight of newborns were  $37 \pm 3.19$  weeks (30<sup>0/6</sup> – 40) and  $3077.50 \pm 697.64$  gr (1720–3900) respectively. Apgar score of the first and fifth minutes in all neonates was  $\geq 8$  and  $\geq 9$  out of 10 respectively. The most clinical presentations in symptomatic neonates were respiratory distress, tachypnea, vomiting, and feeding intolerance. This manifestation and high levels of serum C-reactive protein (CRP), in three infants, are common in neonatal sepsis. The blood culture in all of them was negative. They have been successfully treated with our standard treatment. Our pregnant women showed a pattern of clinical characteristics and laboratory results almost similar to those described for non-pregnant COVID-19 infection. This study found no evidence of intrauterine or peripartum transmission of COVID-19 from mother to her child. Furthermore, the long-term outcomes of neonates need more study.

## 1. Introduction

Coronavirus disease 2019 (COVID-19) pandemic is known to have originated from Wuhan, China in December 2019 (1-3). This unique viral infection, officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is known to commonly cause serious symptoms in humans. By August 30, 2020 there have been 24,854,140 confirmed cases of COVID-19, including 838,924 deaths, that have been reported to the World Health Organization (WHO) (4). The pandemic has spread to 188 countries around the world. Along with the rapid spread of infection, the number of pregnant women and neonates with COVID-19 is also on the rise (5-7). Though, information is lacking on clinical features and neonatal outcomes in pregnant women with COVID-19. We assessed short-term outcomes (4 weeks after discharge) and symptoms among neonates born to mothers infected with COVID-19 at the end of the first regional peak of the outbreak.

## 2. Materials And Methods

### *2.1. Study design, ethical considerations, and participants*

In the current retrospective cohort study, all pregnant women suspected of contracting COVID-19 were admitted to Ayatollah Rohani Hospital, Babol, Iran, for delivery between February 10 and May 20, 2020. This study protocol was approved by the Ethics Committee of Babol University of Medical Sciences, Babol, Iran (Code: IR.MUBABOL.REC.1399.092). Also, written informed consent was obtained from the patients. All women with COVID-19 enrolled in the recent research were diagnosed and managed according to WHO interim guidance for 2019 novel coronavirus (8). In another word, all women with laboratory-confirmed (positive in nasopharyngeal/ throat swab specimens by reverse transcription- polymerase chain reaction (RT-PCR)) COVID-19 infection or suggestive findings on high-resolution computed tomography (HRCT) of the chest were included, while suspected patients with similar symptoms were excluded from the study. According to the instructions at the time, a cesarean section was recommended unless vaginal delivery progressed rapidly. Due to insufficient evidence, a cesarean section was recommended to minimize the presence of the mother suspected of having COVID-19 in labor and reduce the risk of infection acquisition. Newborns have also undergone neonatal surveillance in neonatal accordance with national guidelines. Nasopharyngeal swabs for RT-PCR were taken in the neonates 24 and 72 hours after birth. Clinical signs such as respiratory distress, milk intolerance, and decreased reflexes were also recorded. If there were no contraindications to breastfeeding, the infant was fed with her or his breast milk. After 72 hours, if the baby has stabilized clinical condition

and does not require hospitalization, she/ he would be discharged. An outpatient visit was made to infants within the first week of discharge. The neonate clinical outcomes were followed for 4 weeks. Furthermore, at the end of the first month, the general condition and weight of newborns were requested over the phone. Infants who needed serum and antibiotics for any reason (e.g., prematurity, treatment of respiratory distress, clinical sepsis) were visited twice in the first month following discharge.

## ***2.2.Data collection***

The epidemiological, clinical presentations such as respiratory distress, milk intolerance, and decreased reflexes, laboratory, and radiological findings, medications, and outcomes data were collected with a data collection checklist from electronic medical records. All data were reviewed by two trained nurses.

## ***2.3.RT-PCR assay for SARS-CoV-2 detection***

Mother and neonatal nasopharyngeal/ throat swabs were collected and analyzed to detect SARS-CoV-2 RNA using RT-PCR. Also, viral RNA was freshly extracted using the Ribospin vRD plus Kit (GeneAll, Seoul, South Korea) according to the manufacturer's instructions. Isolated RNA was analyzed by LightMix® SarbecoV E-gene kit (TIB Molbiol, Berlin, Germany) with LightCycler Multiplex RNA Virus Master (Roche). Specimen collection and laboratory testing followed WHO guidance (9, 10).

## ***2.4.Statistical analysis***

Data were analyzed using SPSS version 16. Continuous variables were expressed as the range. Also, categorical variables were expressed as number (%).

# **3. Results**

In this study eleven neonates born to mothers strongly probable or confirmed COVID-19, three of them were transferred to another center after delivery due to the request of their parents, and finally, 8 neonates were identified and included in the current study. The mean gestational age and birth weight of newborns were  $37 \pm 3.19$  weeks ( $30^{06} - 40$ ) and  $3077.50 \pm 697.64$  gr (1720-3900) respectively (Table 1). None of the newborns required resuscitation in the delivery room and only one preterm infant was supported by continuous positive airway pressure (CPAP). Apgar score of the first and fifth minute in all neonates was  $\geq 8$  and  $\geq 9$  out of 10 respectively. Three infants required antibiotic therapy (Ampicillin and amikacine) due to respiratory distress in two cases and vomiting and feeding intolerance in one. One of the two cases with respiratory distress was a preterm infant who also received surfactant (Curosurf) , another case was a neonate with 38 weeks gestational with a diagnosis of transient tachypnea of the newborn (TTN) (Figure1 and 2). In these three cases, a high concentration of C-reactive protein (CRP) (35, 16, and 48 mg / dL) was reported but routine blood culture was negative in these three babies. In the follow-up of infants at age 4 weeks all babies, except in one case, showed that optimal growth ( $3968.75 \pm 843.58$  gr.) The infant, who did not weigh properly, was born to a positive PCR and HRCT mother and did not have successful breast feeding. All babies were breastfed except for two cases. All cases were in an acceptable sensory-motor condition with normal auditory otoacoustic emissions (OAE) at 4 weeks of age.

It is important to note that 23 mothers were admitted with fever and labor pains and also, 11 of whom had a highly probable or confirmed diagnosis of COVID-19. All of these mothers were singleton pregnancies and three of them were preterm and others more than 37 weeks of gestation. Six women tested positive for SARS-CoV-2 PCR, and the remaining five showed suggestive lung HRCT results. A mother had dyspnea and lymphopenia with pulmonary involvement in HRCT in spite of negative RT-PCR testing. Due to this, the pregnancy was terminated at 36 weeks of gestational age. Six mothers had CRP levels greater than 15 mg / dL (two cases with more than 100 mg / dL). Only in 3 cases were amniotic

fluid samples successfully sent for PCR analysis and all were negative. It is noteworthy that, these three cases were only compatible with HRCT for COVID-19.

## 4. Discussion

Currently, some cases of neonates born to mothers with COVID-19 have been reported. This is a retrospective cohort study of neonatal outcomes in pregnant women suffering from COVID-19. The current study is the first report neonatal outcomes of pregnant women infected with COVID-19 in Babol, North of Iran at the end of the first regional peak of the virus. We have described eight neonates of mothers affected by COVID-19. Like other studies that were reported to date, our neonates were asymptomatic or had mild to moderate clinical signs (11, 12). Common clinical presentations of symptomatic neonates were respiratory distress, tachypnea, vomiting, and feeding intolerance. This manifestation and high serum CRP level, in three infants are common in neonatal sepsis. On the other hand, routine blood cultures were all negative. They have been successfully treated with our standard treatment.

As shown, early antibiotic therapy to prevent secondary bacterial infections may decrease complications and mortality. Zeng et al reported that neonates born to mothers with COVID-19 were suspected of having sepsis that improved with antibiotic treatment (13). These neonates had a pattern of clinical characteristics somewhat similar to other reports and also they had favorable outcomes.

The most common symptoms in the mothers participating in the study were fever and dyspnea. Laboratory findings indicated that the level of CRP and lymphopenia increased. In other words, our pregnant women presented with clinical characteristics and laboratory results almost similar to those described in non-pregnant women infected with COVID-19 (14). Unfortunately, we were successful in testing amniotic fluid samples only in 3 cases that were negative in PCR.

Our findings consisted of some studies that have presented that there were no special clinical symptoms suggestive of COVID-19 infection in these neonates, and also samples such as amniotic fluid were negative for SARS-CoV-2 (11, 15). However, with these findings, we cannot rule out or prove the possibility of vertical transmission of the infection, and this requires further research. To our best knowledge, by August 13, 2020 there have been 16,798 confirmed cases of pregnant women in the U.S. with COVID-19 including 37 deaths, have been reported to the centers for disease control and prevention (CDC).

In our study, there were not maternal and neonatal deaths due to COVID-19 infection. It could be associated with quick delivery or a small sample size. The limitations of this study were the small sample size and some limitations of the clinical data. Furthermore, due to the relatively short time that has passed since the occurrence of this pandemic, the long-term outcomes of the neonates need more study.

## 5. Conclusions

Based on the recent study, there is no evidence of intrauterine or peripartum transmission of COVID-19 from mother to her child.

## Declarations

### Conflicts of interests

There are no conflicts of interest.

### Abbreviations

C/s, caesarean section; NVD, normal vaginal delivery; CPAP, continuous positive airway pressure; BMF, breast milk fortifier

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## Table

**Table 1:** Baseline characteristics of 8 newborns with mothers with COVID-19

	Neonate1	Neonate2	Neonate3	Neonate4	Neonate5	Neonate6	Neonate7	Neonate8
<b>Gestational age at delivery</b>	40 weeks	34 weeks	36 <sup>+1</sup> weeks	40 weeks	39 weeks	38 weeks	38 weeks	30 <sup>+6</sup> weeks
<b>Birth weight (grams)</b>	3830	2850	2660	3340	39	3240	3080	1720
<b>Root of delivery</b>	C/s	C/s	C/s	C/s	NVD	C/s	NVD	C/s
<b>Apgar score</b>	10/10	9/10	9/10	9/10	9/10	8/10	9/10	8/9
<b>Need for resuscitation at birth</b>	no	no	no	no	no	no	no	Only needs CPAP
<b>Respiratory distress</b>	no	no	no	no	no	no	yes	yes
<b>feeding problem</b>	no	no	no	no	no	yes	no	yes
<b>Poor reflexes</b>	no	no	no	no	no	yes	yes	no
<b>Weight at age 4 weeks</b>	4200	3670	4850	4150	3900	4650	4230	2100
<b>Nutrition during 4 weeks</b>	BMF	formula	BMF	BMF	BMF + formula	BMF	BMF	BMF + formula

**Abbreviations:** C/s, caesarean section; NVD, normal vaginal delivery; CPAP, continuous positive airway pressure; BMF, breast milk fortifier

## Figures



**Figure 1**

Chest radiograph of preterm infant with respiratory distress syndrome (RDS)



**Figure 2**

Chest radiograph of the newborn with diagnosis of transient tachypnea of the newborn (TTN)