

## Report of a series of healthy term newborns from convalescent mothers with COVID-19

Serafina Perrone<sup>1</sup>, Michela Deolmi<sup>1,2</sup>, Maurizio Giordano<sup>1</sup>, Tiziana D'Alvano<sup>1,2</sup>, Lucia Gambini<sup>1</sup>, Mara Corradi<sup>1</sup>, Tiziana Frusca<sup>3</sup>, Tullio Ghi<sup>3</sup>, Susanna Esposito<sup>2</sup>

<sup>1</sup>Neonatology Unit, Department of Medicine and Surgery, University of Parma, Parma, Italy; <sup>2</sup>Pediatric Clinic, Department of Medicine and Surgery, University of Parma, Parma, Italy; <sup>3</sup>Unit of Obstetrics and Gynecology, Department of Medicine and Surgery, University of Parma, Parma, Italy

**Abstract.** *Background:* The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly transmittable virus associated with a significantly increased risk of complications among the infected population. Few data are available for the outcome of pregnancy complicated by serious respiratory disease due to SARS-CoV-2 infection. *Aim:* We herein report a series of four neonates whose mothers had recovered from new coronavirus 2019 disease (COVID-19) diagnosed in the third trimester of pregnancy. *Methods:* pregnant women with documented COVID-19 infection during their pregnancy, who gave birth in Parma Hospital, University of Parma, Italy, in March and April 2020, during the peak of incidence of COVID-19 in Italy. Clinical records and laboratory tests were retrospectively reviewed. *Results:* All neonates were delivered at term in good conditions without congenital COVID-19 infection. *Conclusions:* Findings from our series of cases indicated that adverse effects on foetuses from pregnancies complicated by COVID-19 infection in late pregnancy are unlikely.

**Key words:** newborn infants, covid19, pregnancy, viral recovery

### Introduction

Human infection with the novel 2019 coronavirus has been reported worldwide following the initial identification of the virus in December 2019, in Wuhan, the capital of Hubei Province, China. Pregnant women are expected to be at high risk for new coronavirus 2019 disease (COVID-19)-related complications because of their increased immune tolerance and their physiological changes in cardiovascular and respiratory system (1). There is little evidence for vertical transmission in pregnancy, but early neonatal acquisition has been reported. In China, 33 women with COVID-19 infection delivered a neonate by caesarean section at term of pregnancy. Out of 33 newborns only 3 acquired COVID-19, but a postnatal transmission was postulated since amniotic fluid, cord blood and breast

milk PCR assays were all clear from virus (2). A further case series described 7 women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), all of whom required oxygen therapy and received Caesarean section at term; only 3 neonates were tested, of whom one was positive. Again, this baby seems to have acquired the infection postnatally as placental and cord blood samples were negative for viral nucleic acid (3). Another report of 10 babies born to mothers with COVID-19 infection described one death in a baby born at 34+5 weeks, however none of the babies tested were positive for SARS-CoV-2 (4). More recently, two severe clinical presentation of COVID-19 during pregnancy, leading to respiratory failure, mechanical ventilation, and preterm delivery were reported (5,6). The two premature babies resulted SARS-CoV-2 positive in their first day of life. In the first case

**Table 1.** Clinical characteristics of pregnant women

	Case 1	Case 2	Case 3	Case 4
Age (years)	36	35	32	26
Nationality	Italy	Italy	Moldova	Italy
Positive Swabs (data)	09-03	03-03	13-03	NO
Swabs became negative	27-03, 30-03	18-03, 19-03	20-03, 23-03	NA
CT	NA	NA	bilateral interstitial pneumonia (visual score: 20%)	bilateral ground glass areas, suggestive for interstitial pneumonia (visual score 15%)
Symptoms	Fever, Cough, Vomit, diarrhea, loss of smell, asthenia	Fever, Cough, malaise	Fever, acute respiratory distress syndrome	Fever, cough, dispnea
Infected relatives	Husband	Husband	NO	NO
Linkage to risk area	YES	YES	YES	YES
Maternal comorbidity	Hypothyroidism	Hypothyroidism	Gestational diabetes	NO
Treatment	NO	NO	Non-invasive ventilation (CPAP)	NO
Drugs	NO	NO	Azytromicyn Ceftriaxone, Lopinavir+ritonavir Enoxaparin	Levofloxacin, Azytromicyn Enoxaparin
Placental swab for SARS-CoV2	NA	Negative	NA	NA

CT: computerized tomography; CPAP: continuous positive pressure airway; NA: not available

the presence of the virus in amniotic fluid, cord blood, or placental tissue was not tested; in the second one amniotic fluid PCR test was positive for COVID-19 infection, raising the suspicion of vertical transmission. Here we report a series of cases of healthy term newborns whose mother developed COVID-19 infection during the third trimester of pregnancy and were convalescent with negative test at the time of delivery.

## Materials and methods

Our case series include all the pregnant women with documented COVID-19 infection during their pregnancy, who gave birth in Parma Hospital, University of Parma, Italy, in March and April 2020, during the peak of incidence of COVID-19 in Italy. Clinical records and laboratory tests were retrospectively reviewed.

### Data Collection

Demographic data, age, swab results, computerized tomography (CT) scan, symptoms, epidemiologi-

cal information, morbidity and treatment of the pregnant mothers were collected. Moreover, birth date, mode of delivery, gestational age, birth weight (g), anthropometric data, Apgar score 1'-5', amniotic fluid, mother-child contact, clinical signs or symptoms and swab results was collected by newborns.

### Diagnosis

The infection status of the mother was accessed by RT-PCR for SARS-CoV-2 nucleic acid (as per Corman protocol) (7) of nasopharyngeal swabs and, when their hospital admission was necessary, by CT. Related samples were collected from neonates at birth. The study was conducted in accordance with the Declaration of Helsinki.

## Results

*Case 1.* A pregnant woman, affected by hypothyroidism, during the third trimester of pregnancy (36 weeks + 2 days) presented fever and asthenia, associated with respiratory (cough, anosmia) and gastrointes-

**Table 2.** Clinical characteristics of newborns at birth

	<b>Case 1</b>	<b>Case 2</b>	<b>Case 3</b>	<b>Case 4</b>
<b>Birth date</b>	05-04	18-04	22-04	23-04
<b>Mode of delivery</b>	VD	VD	ECS	VD
<b>Gestational age (weeks)</b>	40+4	38+5	38+2	39+6
<b>Birth weight (g)</b>	3790	3535	2290	3720
<b>Head circumference (cm)</b>	35	36	35	36
<b>Length (cm)</b>	52	53	50	49
<b>Apgar score 1'-5'</b>	9-9	9-9	9-10	9-9
<b>Amniotic fluid</b>	Clear	Clear	Clear	Stained
<b>Exclusively breastfeeding</b>	YES	YES	YES	YES
<b>Clinical signs or symptoms of infection</b>	NO	NO	NO	NO
<b>Nasopharyngeal swab for SARS-CoV-2</b>	Negative	NA	Negative	Negative
<b>White Blood Cells count/ul</b>	17.170	NA	17.110	20.590
<b>Red Blood Cells count/ul</b>	4.960.000	NA	6.120.000	5.070.000
<b>Hemoglobin (g/dl)</b>	17,8	NA	20	18,8
<b>Hematocrit (%)</b>	52	NA	60,9	55,4
<b>Platelets/ul</b>	403.000	NA	328.000	335.000

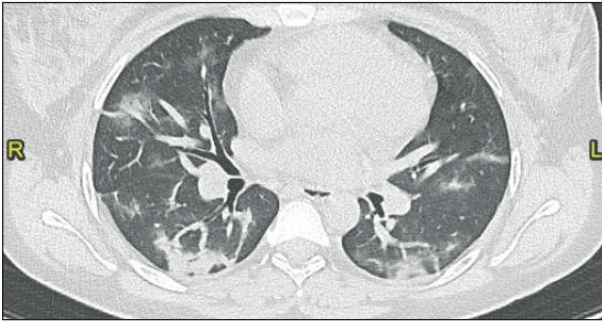
VD: vaginal delivery; ECS: elective caesarean section

tinal (vomit, diarrhoea) symptoms. Her husband suffered from COVID-19 infection and RT-PCR assay on her nasopharyngeal swab was positive for SARS-CoV-2. There was no need for any treatment. Eighteen and twenty days later, RT-PCR assays on nasopharyngeal swabs were negative. She gave birth to a term and healthy newborn aged 40 weeks + 4 days, by vaginal delivery. She presented metrorrhagia minor and her cervical swab positive for *Gardnerella vaginalis*. Amniotic fluid was clear. The puerperant breastfed the neonate. Newborn nasopharyngeal swab performed in the first day of life was negative and his blood tests showed normal values.

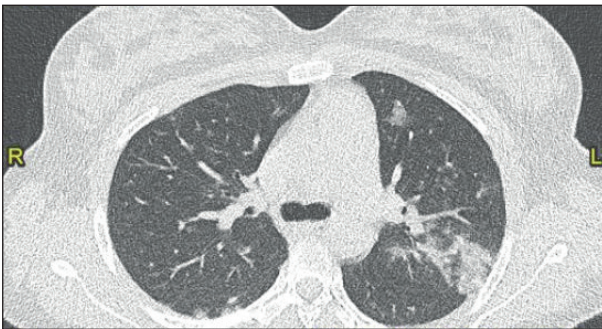
*Case 2.* A pregnant woman, affected by hypothyroidism treated with levothyroxine, during the third trimester of pregnancy (34 weeks + 1 day) presented fever, cough and generalized malaise. Her husband suffered from COVID-19 infection and RT-PCR assay on her nasopharyngeal swab was positive for SARS-CoV-2. There was no need for any treatment. Sixteen and seventeen days later, RT-PCR assays on her nasopharyngeal swab were negative. She gave birth to a term and healthy newborn aged 38 weeks + 5 days, by vaginal delivery, without any complication. Amniotic fluid was clear. The puerperant breastfed the neo-

nate. Moreover, mother placental swab, collected the delivery day, was negative for SARS-CoV-2.

*Case 3.* A pregnant woman, suffering from gestational diabetes, during the third trimester of pregnancy (34 weeks + 2 days) presented with acute respiratory distress syndrome and fever. She was admitted to hospital and CT scan showed bilateral interstitial pneumonia, involving 20% of the lung (Figure 1). RT-PCR assay on her nasopharyngeal swab was positive for SARS-CoV-2. No previous contacts with COVID-19 infected people were reported. During the hospitalization, non-invasive ventilation, continuous positive pressure airway (CPAP), was provided and she was treated with azytromycin, ceftriaxone, lopinavir+ritonavir and enoxaparin. Moreover, the results of feto-maternal surveillance were reassuring during clinical observation and treatment. Seven and ten days later, RT-PCR assays on mother nasopharyngeal swabs were negative, then she was discharged. She gave birth to a term and healthy newborn aged 38 weeks + 2 days, by elective caesarean section due maternal request. Amniotic fluid was clear. The puerperant breastfed the neonate. Newborn nasopharyngeal swab performed in the first day of life was negative and his blood tests showed normal values.



**Figure 1:** Computerized tomography of case number 3 showed interstitial pneumonia



**Figure 2:** Computerized tomography of case number 4 showed interstitial pneumonia

*Case 4.* A pregnant woman, during the third trimester of pregnancy (33 weeks + 4 days) presented fever, cough and dyspnoea. She was admitted to hospital and CT scan showed bilateral ground glass areas, suggestive for interstitial pneumonia due to SARS-CoV-2, involving 15% of the lung (Figure 2). Despite this, RT-PCR assay on her nasopharyngeal swab was negative and no previous contact with COVID-19 infected patients were known. During the hospitalization, there was no need for oxygen supply; azitromycin, levofloxacin and enoxaparin were administered. Moreover, periodic ultrasound scan showed foetus normal vital signs. Three days later she was discharged. Two more nasopharyngeal swabs, repeated twenty days and forty days apart, were negative. She gave birth to a term and healthy newborn aged 39 weeks + 6 days, by vaginal delivery. Amniotic fluid was clear. The puerperant breastfed the neonate. Newborn nasopharyngeal swab performed in the first day of life was negative and his blood tests showed normal values.

## Discussion

We reported four cases of healthy neonates born from mothers with previous SARS-CoV-2 pneumonia in the third trimester of pregnancy. During previous pandemics, infected pregnant women, particularly those with pneumonia, had remarkably high rates of spontaneous abortion and preterm birth (8,9). Recently, two studies reported preterm delivery in pregnant women affected by COVID-19 during pregnancy complicated by pneumonia (5,6). Furthermore, Breslin et al described two cases of obese and diabetic SARS-CoV-2 positive women, presenting at 37 weeks of gestation for induction of the labor, but at the end, they delivered by caesarean section. In the first case the clinical condition of the patient improved after delivery, while the second patient developed respiratory distress, high fever and she was admitted to ICU due to severe hypertension. These observations raised concerns about severe maternal morbidity during pregnancy complicated by COVID-19 infection (9). In our population, vital signs of the mothers and foetuses remained stable and pregnancy could continue until the term. The symptoms associated with the virus did not determine deleterious effects on the growing foetus. In three cases uneventful vaginal delivery was achieved, one foetus was delivered by elective caesarean section, due to maternal request unrelated to COVID-19. Negative nasopharyngeal swabs of the newborns were obtained immediately at birth, strengthening the hypothesis that vertical transmission is unlikely (10). Babies remained asymptomatic during the hospital stay in rooming-in regimen. They were discharged at 48 hours of life. This is the first case series about healthy neonate born from COVID-19 convalescent mothers. The study is limited by the small number of cases. Moreover, we were not able to determine SARS-CoV-2-specific IgG and IgM in maternal and newborn serum.

## Conclusions

No adverse effects occur in foetus and offspring of mothers who developed a SARS-CoV2 infection in the third trimester of pregnancy, even when com-



plicated by pneumonia. Maternal and neonatal clinical data contribute to fill the lack of knowledge about the perinatal outcome of pregnancy complicated by COVID-19 infection in the third trimester. Data can contribute to guide healthcare professional to formulate the principles of obstetric management for pregnant women with COVID-19. Large, multi-center, national studies are needed with the primary objective of estimate the prevalence of 2019-nCoV infection at birth in infants born to mothers with an infection detected during pregnancy or at the time of delivery.

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

## References

- Schwartz DA. An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. *Arch Pathol Lab Med*. 2020 Mar 17. doi: 10.5858/arpa.2020-0901-SA.
- Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr*. 2020. Mar 26;e200878. doi: 10.1001/jama-pediatrics.2020.0878.
- Yu N, Li W, Kang Q, Xiong Z, Wang S, Lin X, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis*. 2020 Mar 24;S1473-3099(20)30176-6.
- Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020 Feb;9(1):51-60.
- Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. *Am J Perinatol*. 2020 Apr 18. doi: 10.1055/s-0040-1710050.
- Zamaniyan M, Ebadi A, Aghajanjpoor Mir S, Rahmani Z, Haghshenas M, Azizi S. Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. *Prenat Diagn*. 2020 Apr 17. doi: 10.1002/pd.5713
- Nalla AK, Casto AM, Huang MW, Perchetti GA, Sampoleo R, Shrestha L, Wei Y, Zhu H, Jerome KR, Greninger AL. Comparative Performance of SARS-CoV-2 Detection Assays using Seven Different Primer/Probe Sets and One Assay Kit (published online ahead of print, 2020 Apr 8). *J Clin Microbiol*. 2020; JCM.00557-20. doi:10.1128/JCM.00557-20
- Nuzum JW, Pilot I, Stangl FH, Bonar BE. 1918 pandemic influenza and pneumonia in a large civil hospital. *IMJ Ill Med J*. 1976;150(6):612-616
- Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM*. 2020 Apr 9:100118. doi: 10.1016/j.ajogmf.2020.100118.
- Zaigham M, Andersson O. Maternal and Perinatal Outcomes with COVID-19: a systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand*. 2020 Apr 7. doi: 10.1111/aogs.13867

Received: 5 May 2020

Accepted: 7 May 2020

Correspondence:

Prof. Serafina Perrone, MD, PhD.

Associate Professor of Pediatrics

Department of Medicine and Surgery

University of Parma

Via Gramsci

43126 Parma

Tel: 00-0521-703518

E-mail: serafina.perrone@unipr.it