

# The Clinical Features and Outcomes of Four Neonates Born to Mothers with a Severe Form of COVID-19 and a Positive RT-PCR for SARS Co-V2 in Douala Gynaeco-Obstetric and Pediatric Hospital in Cameroon

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## Abstract

**Background:** A novel viral respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is responsible for a worldwide pandemic. The effects of this new disease in pregnant women and newborns are actually not well known. **Methods:** We investigated the clinical features and outcomes of four neonates born to mothers with a severe form of COVID-19 and a positive RT-PCR for SARS Co-V2 in Douala Gynaeco-Obstetric and Pediatric Hospital (Cameroon) from April 20 to June 5, 2020. **Results:** All four mothers were symptomatic and had a positive RT-PCR for SARS CoV-2 from nasopharyngeal swab on admission. All of them delivered prematurely through cesarean section because of severe respiratory distress and one died shortly after delivery. The four premature male infants were born between 30 weeks and 35 weeks 2 days of gestation and had birth weights ranging from 1090 g to 2950 g. All infants had 1-minute Apgar scores that ranged from 7 to 8 and 5-minute Apgar scores varying between 8 and 9. They were isolated from their mothers immediately after birth and re-



ceived formula feeding. Three of the four infants were tested using nasopharyngeal swab specimens for RT-PCR 24 to 48 hours after birth and were negative for COVID-19. All the infants were treated in a dedicated area at the neonatal care unit and presented with mild respiratory distress on admission with a Silverman score that varied between 2 and 4/10. During their hospitalization, all the infants also presented with jaundice and underwent phototherapy. Three of them had anemia with hemoglobin levels ranging from 105 to 123 g/L requiring for blood transfusion. The hospital stay varied between 3 and 48 days. Three infants were discharged healthy and one died. **Conclusion:** This case series suggests the possibility of poor maternal and neonatal outcomes in case of severe COVID-19 in mothers. It also suggests that severe COVID-19 in pregnant women may be a risk factor for prematurity for the newborns. It is crucial to screen pregnant women, to implement infection prevention, control measures and to provide close monitoring of neonates born to mothers with a severe form of COVID-19.

## Keywords

COVID-19 Infected Mothers, Premature Newborns, Severe Respiratory Distress, Outcome, Cameroon

## 1. Introduction

In December 2019, an increasing number of cases of pneumonia outbreak in Wuhan, a city in central China with a novel coronavirus (2019-nCoV) rapidly identified as the causative agent [1] [2] [3]. Human coronaviruses belong to the order Nidovirales, family Coronaviridae, and genus *Alphacoronavirus* or *Betacoronavirus* [3]. The emerging SARS-CoV-2, a beta coronavirus, can cause COVID-19 (Corona Virus Disease) as officially named by the World Health Organization (WHO) on February 11, 2020 [4]. The SARS-CoV-2 is highly infectious. The entire population is generally susceptible, and respiratory droplets and contact being the main routes of transmission. To date, there is not consistent evidence on mother-to-newborn transmission given the paucity of studies on COVID-19 and pregnant women [5]. In Cameroon, data on clinical features and outcome of infants born to mothers with COVID-19 are scarce. In this article, we retrospectively analyzed data of four infants born to four mothers with confirmed 2019-nCoV severe infection at the Douala Gynaeco-Obstetric and Pediatric Hospital from April 20 to June 5, 2020, in order to describe the clinical features and short-term outcomes of these neonates.

## 2. Methods

### 2.1. Subjects and Conditions of the Study

All neonates born to mothers with positive RT-PCR for 2019-nCoV RNA and hospitalized in the neonatal care unit from April 20 to June 5, 2020, were in-

cluded. In accordance with the flow of patients infected with COVID-19, all pregnant women admitted at the maternity during the study period benefited from a Reverse-Transcriptase PCR test for the detection of 2019-nCov on nasopharyngeal swabs. Once the positive result was obtained and depending on the clinical condition of the patients, a multidisciplinary staff with gynecologists, pediatricians and anesthesiologists decided on the treatment which included rapid child delivery in case of severe maternal acute respiratory distress syndrome. The patients were isolated in all cases, either in intensive care unit or in maternity ward. All the newborns were managed by a team including a nurse and a pediatrician, wearing full personal protective equipments. After neonatal evaluation and primary care in the delivery room, neonates were admitted and treated in neonatal care unit in a dedicated area. If their clinical condition permitted, they were given an antiseptic bath using CYTEAL® (hexamidine diisetonate, chlorhexidine gluconate and chlorocresol) before installation in an incubator. Routine care was then administered by the nursing staff with the usual infection preventive measures in the neonatal unit. Since the mothers were usually still in isolation, visits to newborns were only permitted through the window of the isolation area. Due to the clinical condition of the mothers, but also because of the difficulty to ensure expression and transport of breast milk under ideal aseptic conditions, all the newborns in our series received infant formula during their hospital stay.

## **2.2. Research Methods**

Demographic data, obstetrical history, disease onset, specific COVID-19 treatment protocols, method of delivery and maternal outcome were collected from the files of mothers with 2019-nCoV infection. Information from the neonates including gender, gestational age, birth weight, clinical presentation, laboratory findings, chest X-ray images, treatment on admission and outcome were also collected.

## **3. Case Report**

### **3.1. Case of the Mothers**

All four mothers were symptomatic with poor general condition, asthenia, fever, cough and severe respiratory distress and had a positive RT-PCR for SARS Co-V2 from nasopharyngeal swab on admission (**Table 1** and **Table 3**). They were aged between 26 and 34 years. The onset of the disease ranged between 7 and 11 days prior to childbirth. All the mothers were managed in the intensive care unit where they received hydroxychloroquine and azithromycin as specific treatment for COVID-19 according to the national therapeutic guidelines (**Table 3**). They all gave birth through cesarean delivery indicated for persistent severe respiratory distress. Four preterm infants were born. Three mothers recovered from their COVID-19 infection and were discharged healthy. One mother died from severe respiratory distress within 24 hours after surgery (**Table 1**).

**Table 1.** Clinical characteristics and outcomes of COVID-19 infected mothers and their newborns.

	Case 1	Case 2	Case 3	Case 4
<b>Mothers clinical features</b>				
Mothers' age (years)	34	26	32	31
Obstetrical history/GxPy	4-2-011	2-1-001	4-3-003	3-1-011
Mother's disease onset/delivery (days)	10	7	10	11
Intensive Care Unit	Yes	Yes	Yes	Yes
Premature rupture of membranes	No	No	No	No
Maternal complications	Dyspnea	APE <sup>1</sup>	SARS <sup>2</sup>	Dyspnea
Maternal outcome	Healthy	Healthy	Dead	Healthy
<b>Infants clinical features at birth</b>				
Mode of delivery	CS <sup>3</sup>	CS	CS	CS
Sex	M	M	M	M
Gestational age (weeks + days)	32 + 4	35 + 2	30	33 + 6
APGAR score (1/5 min)	8/8	7/9	8/9	7/8
Birth weight (g)	1770	2950	1090	2060
Percentile	53.36	87.36	12.75	59.80
<b>Infants clinical features on admission</b>				
Respiratory distress	Yes	Yes	Yes	Yes
Silverman Score /10	4	2	4	2
Temperature (T°)	36.0	36.1	36.4	36.3
<b>Infants clinical course during hospitalization</b>				
Jaundice	Yes	Yes	Yes	Yes
Anemia	No	Yes	Yes	Yes
Severe Sepsis	No	No	Yes	No
<b>Mother-Child dyad</b>				
Immediate separation	Yes	Yes	Yes	Yes
Breastfeeding	No	No	No	No
<b>Infant short term outcome</b>				
Hospital stay (days)	3	7	48	8
Death	Yes	No	No	No

<sup>1</sup>APE: Acute Pulmonary Edema. <sup>2</sup>SARS: Severe Acute Respiratory Syndrome. <sup>3</sup>CS: Cesarean section

### 3.2. Case of the Infants

Four male infants were born prematurely through cesarean section between 30 weeks and 35 weeks 2 days of pregnancy. The birth weight ranged between 1090 g and 2950 g. All infants had a 1-minute Apgar scores between 7 and 8 and 5-minute Apgar scores varying from 8 to 9 (Table 1). They were isolated from their mothers immediately after birth and received formula feeding. Three of the four infants were tested using a nasopharyngeal swab specimen for RT-PCR 24 to 48 hours after birth and were all negative for COVID-19. One of the new-

borns had not been tested due to a shortage of tests. Clinically, all the infants presented with respiratory distress on admission in neonatal care unit with a Silverman score that varied between 2 and 4/10. During their hospitalization, all the infants also presented with jaundice and underwent phototherapy. They all had normal white blood cells and platelets. Three had anemia with hemoglobin levels ranging from 105 to 123 g/L requiring for blood transfusion (Table 2 and Table 3). One of the infants (Case n°3) presented a prolonged oxygen dependence and was maintained under oxygen for one month, suggesting mild bronchopulmonary dysplasia. All infants received supportive care with intra venous fluids and oxygen. The time of initiating enteral feeding was between 2 and 3 days (Table 3). None of our patients received a specific COVID-19 therapy (Table 4). The hospital stay varied from 3 to 48 days. Though presenting a mild respiratory distress, one newborn died unexpectedly 3 days after birth. The three others were discharged healthy.

**Table 2.** Laboratory findings in newborns to COVID-19 positive mothers.

	Case 1	Case 2	Case 3	Case 4
<b>Laboratory findings</b>				
White blood cell count, $\times 10^9/L$	10.8	13.4	6.6	11.9
Lymphocyte count, $\times 10^9/L$	6.8	1.6	3.3	5.1
Neutrophil count, $\times 10^9/L$	3.4	10.9	2.5	5.7
Hemoglobin, g/L	150	114	123	105
Platelet count, $\times 10^9/L$	251	273	245	360
C-Reactive Protein, mg/L	4	3.2	6	5.1
Blood group	NA	B+	A+	B+
Blood glucose (g/L)	0.95	4.3	0.36	3.6
Blood culture	(-)	(-)	(+)	(-)
Total bilirubin (mg/L)	124	205	50.5	121.1
Sodium (mEq/L)	140	140	138	136
Potassium (mEq/L)	5.6	5.8	3.6	3.2
Chloride (mEq/L)	116	111	108	110
Calcium (mg/L)	85.39	93.53	84.74	NA
Chest radiograph	No	No	Yes	No

NA: not available.

**Table 3.** Treatment received by the newborns of COVID-19 infected mothers.

	Case 1	Case 2	Case 3	Case 4
IV fluids	Yes	Yes	Yes	Yes
IV Antibiotics	Yes	Yes	Yes	Yes
Oxygen	Yes	Yes	Yes	Yes
Blood transfusion	No	Yes	Yes	Yes
Phototherapy	Yes	Yes	Yes	Yes
Feeding tube	Yes	Yes	Yes	Yes
Delay to enteral feeding (days)	2	3	3	2

**Table 4.** Results of 2019-nCoV nucleic acid testing (RT-PCR) and antiviral treatment in mothers and neonates.

Case N°	Mothers				Neonates		
	Specimen	Result	Specific COVID-19 Therapy	Delay of specimen collection (days)	Specimen	Result	Specific COVID-19 Therapy
1	Nasopharyngeal swab	(+)	Chloroquine + Azithromycine	Not done	Nasopharyngeal swab	NA	None
2	Nasopharyngeal swab	(+)	Chloroquine + Azithromycine	1	Nasopharyngeal swab	(-)	None
3	Nasopharyngeal swab	(+)	Chloroquine + Azithromycine	2	Nasopharyngeal swab	(-)	None
4	Nasopharyngeal swab	(+)	Chloroquine + Azithromycine	2	Nasopharyngeal swab	(-)	None

NA: not available.

## 4. Discussion

This study describes the clinical features and short term outcome of four premature infants born to mothers with severe COVID-19 infection in a middle income setting. To the best of our knowledge, there is not yet any existing literature in Cameroon on the outcome of premature infants born to 2019-nCoV infected mothers presenting a severe disease.

### 4.1. The Clinical Features of the Mothers with 2019-nCoV Infection

The 4 mothers included in our study were young with ages ranging from 26 to 34 years (average age of 30.75 years). Di Mascio *et al.* in a systematic review on the outcome of coronavirus spectrum infections during pregnancy found an average age of 34.6 years in mothers affected by coronavirus infections [6]. Another systematic review on maternal and perinatal outcomes with COVID-19 in 108 pregnancies found a maternal age ranging between 29 and 32 years which is similar to our findings [7]. The mean time between the onset of symptoms and delivery was 9.5 days in our series, same as 9.4 days found by Liu *et al.* [8]. All our patients presented a severe form of the disease with severe respiratory distress requiring treatment in intensive care unit. Care to positive COVID-19 patients was given in a dedicated ward of the hospital allowing isolation and with adequate monitoring systems. Regarding the mode of delivery, all our patients underwent cesarean delivery indicated for severe acute maternal respiratory distress syndrome. Other studies on COVID-19 during pregnancy reported a higher rate of cesarean delivery compared to general population, with a rate ranging from 91% to 92% [6] [7], and fetal distress was the most frequent indication for cesarean section [7] [9].

#### 4.2. The Clinical Features and Outcome of the Infants Born to Mothers with Severe 2019-nCoV Infection

Regarding the newborns, all were male and premature. The gestational age ranged from 30 to 33.8 weeks with a mean of 32.9 weeks. In the Di Mascios' *et al.* systematic review, the pooled proportions of preterm birth < 37 and <34 weeks of gestation were 41.1% (14 of 32, 95% CI, 25.6 - 57.6) and 15% (4 of 32, 95% CI, 3.9 - 31.7), respectively [6]. Prematurity with a gestational age of less than 34 weeks of pregnancy seems to represent a low proportion in infants born to COVID-19 positive mothers. In our series, all the children were born prematurely due to the severe clinical condition of the mothers, in whom management of maternal distress required rapid child delivery. The weights of the newborns ranged from 1090 g to 2950 g (12.75 to 87.36 percentile respectively) and one was small-for-gestational age (SGA) [10]. Zhu *et al.* in their series had 2 small infants for gestational age [10] [11]. Being an acute condition occurring during the third trimester of pregnancy, COVID-19 may have little impact on fetal growth and ultimately, the occurrence of intrauterine growth retardation would be more linked to its usual maternal and fetal causes than to COVID-19. None of our patients was born with an APGAR score less than 7 at 5 minutes. All patients presented with respiratory distress at birth although mothers received corticosteroid for fetal lung maturation. One baby presented prolonged respiratory issues related to a mild bronchopulmonary dysplasia which is not an exceptional clinical presentation in a 30 weeks infant. During hospitalization, all infants developed jaundice and were treated with phototherapy and three patients had severe anemia that required packed red blood cells transfusions. We think this evolution is not specific to COVID-19 but it is a common course in premature infants. One newborn died few days after birth. According to *Di Mascio et al.* in their systematic review, the pooled proportion of perinatal death was 7% (2 of 41, 95% CI, 1.4 - 16.3) including 1 stillbirth (2.4%) and 1 neonatal death (2.4%) [6].

#### 4.3. Separation of the Mother-Infant Dyad and Breastfeeding

The four newborns in our series were separated from their mothers immediately after birth and fed with infant formulas. Although strongly supporting breastfeeding, the American Academy of Pediatrics (AAP) and the Center for Disease Control (CDC) recommend temporary separation of newborns from infected mothers, while the World Health Organization (WHO) does not recommend separation of infants from their mothers, but rather encourages skin to skin contact, rooming-in and exclusive breastfeeding [12]. All recommend that mothers who room-in or breastfeed should follow strict hand washing and use of masks. Furthermore, some authors assume that the separation of the mother-infant done at birth and the absence of breastfeeding could be deleterious for the newborn [13]. In our series, considering the severe clinical condition of the mothers, we opted for the separation of the mother-infant dyad at birth and formula feeding of infants born to COVID-19 mothers during their hospital

stay. The mothers were reunited with their infant after discharge from the hospital and breastfeeding was introduced without difficulty at home for two infants, while one was taken care of by the aunt and continued formula feeding since the mother died shortly after cesarean delivery.

#### **4.4. Vertical Transmission of 2019-nCoV**

In order to check whether infants were born infected, we carried out SARS-CoV-2 nucleic acid detection of postnatal throat swab of the newborns. The results showed that all the 3 samples tested were negative, which did not suggest a possible intrauterine transmission. Those results are consistent with other series publications, where no neonates born to COVID-19 mothers were found positive to SARS-CoV-2 at birth [6]. Data suggest that angiotensin-converting enzyme-2 (ACE2) receptors have low expression in the placenta, which makes the chance of SARS-CoV-2 vertical transmission through the placenta unlikely [14]. Some research indicated that SARSCoV-2 nucleic acid in placenta was undetectable [8]. However, it remains unclear if the maternal viral load or timing of SARS-CoV-2 infection may influence the transmission [15].

#### **4.5. Limitations**

The main limitation of this study is the small number of newborns included. Follow-up of a larger sample of infants born to mothers infected with 2019-nCoV is necessary for thorough description and analysis of their clinical evolution and 2019-nCoV transmission.

### **5. Conclusion**

This case series describes the clinical presentation and short-term outcome of four premature neonates born to mothers with severe COVID-19. It suggests the possibility of poor outcome in mothers infected with 2019-nCoV, due to severe respiratory distress and in their newborns, due to induced prematurity. It is crucial to screen pregnant women, to implement infection prevention, apply control measures and to provide close monitoring of neonates born to mothers with a severe form of COVID-19.

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### **Compliance with Ethical Standards**

This study was carried out following the ethics principles of the Helsinki decla-

ration

### Author Contributions

DE, DN and GPN designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. IR, DD, RT, CMT, MB, SW, DK, AN, HN, NE, DM, FLK and SRS designed the data collection instruments, collected the data, and reviewed and revised the manuscript. SPC and ETM designed the study, coordinated, and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

### Declared

No financial aid nor communication or preliminary publication.

### Conflicts of Interest

The authors declare that they have no competing interest.

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