

# Diagnosis Challenges, Management, and Outcome of Infants Born to Mothers With COVID 19

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## Research

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# Abstract

**Background:** Severe acute respiratory distress syndrome with Coronavirus 2 (SARS-CoV-2) infection affected the pregnant women during the pandemics. Immunological particularity of this population and the increased need for medical assistance put this population in a high-risk category for SARS-Cov-2 infection.

Because of high contamination risk and limited studies about vertical transmission, the labor and delivery of positive women require special conditions. Cesarean section is probably the best option for delivery of infants to reduce the risk of infection during birth.

**Aim:** Our study aims to present the management and outcome of infants born to mothers confirmed with coronavirus disease 2019 (COVID19) before delivery.

**Material and methods:** This is longitudinal, retrospective study, analyzing demographics, laboratory data and management of neonates born of mothers with diagnosis of SARS-Cov -2 infection.

**Results:** 5 neonates were born of SARS-Cov-2 positive mothers , all by C- section and had negative real time –PCR ( RT-PCR) test. None of them was breastfed during hospital stay. The negative RT-PCR test allowed us to reduce the hospital stay of infants and care them in non –isolated area.

**Conclusion:** In our study, vertical or perinatal transmission of the infection was not present. The testing of the pregnant women, their isolation and delivery in safe conditions for the medical staff were possible, using adequate protection equipment to limit their infection and the risk for the newborns.

## Introduction

SARS-CoV-2 infection can determine various forms of respiratory insufficiency (ARDS) with clinical and radiological features of pneumonia [1]. Similarly, to general population, SARS-Cov2 infection has also affected the population of pregnant women during the pandemics. At present, the predominant symptoms, the rate of morbidity and mortality among pregnant women are not known.

The immunological particularity of this population is represented by its high susceptibility to infections due to hormonal changes during pregnancy. It is well accepted that, due to the increased need for medical assistance and pregnancy monitoring, this population presents a high contamination risk. There are few data regarding the incidence of pneumonia caused by SARS-CoV-2 in the period of pregnancy. The majority of the pregnant women who contracted the infection were asymptomatic or presented mild symptoms [2]–[5].

The vertical transmission of the infection to the newborn, even in the case when the mother is symptomatic, has been described in few cases [1], [6]. The risk of contamination of the newborn seems higher in the immediate postnatal period, from the infected symptomatic or healthy carrier mother, if strict hygienic measures are not respected during skin-to-skin care. Due to COVID – 19 high contagion,

obstetricians, neonatologists and infectionists have focused on the implementation of preventive measures in all areas (from the delivery room, to the neonatal, maternity ward and intensive care unit) to limit the risk of viral transmission [3], [7]–[9].

Breast feeding in the immediate postpartum period remains a problem in certain situations. Although breast feeding is recommended, this is not always possible, since the mother may require isolation and treatment in a different hospital service than that in which delivery occurs. This limits the breast feeding of the newborn, with the loss of the important benefits of this type of feeding, including the protective benefit against infections [3], [10].

## Material And Method

Between April 1st and May 15th, 229 pregnant women were admitted for delivery in the Clinic of Obstetrics and Gynecology I<sup>st</sup>, County Emergency Hospital, Cluj-Napoca, Romania, a tertiary level hospital. Among them, five tested positive for SARS-Cov 2 infection. The newborns were admitted to the Neonatology Department of Clinic of Obstetrics and Gynecology I<sup>st</sup>.

Institutional review board and COVID – 19 specific research committee approval was obtained for this study. All charts of newborns from positive women were retrospectively reviewed.

All neonates of mothers with SARS-CoV-2 infection, were delivered by cesarean section, in the dedicated operating room for cases with SARS-CoV-2 infection. After delivery, the newborns were admitted to the quarantine ward according to the local protocol. An umbilical venous catheter was placed, and prophylactic antibiotic therapy was administered. Vital functions were assessed: temperature, respiratory rate, heart rate, blood pressure, oxygen saturation. Laboratory parameters were monitored: central blood count (CBC), inflammatory markers: C-reactive protein and procalcitonin, glycemia, creatine kinase, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase.

All newborns underwent SARS-CoV-2 testing using the real-time PCR technique from upper airway specimens (nasopharyngeal and pharyngeal swabs). The testing was carried out on the first day and 5th day of life. Sampling was performed by a physician wearing appropriate personal protection equipment (PPE), in the quarantine room. Each nasopharyngeal swab was collected in the Nasopharyngeal Sample Collection Kit for Viruses and transferred to the laboratory. Within the negative-pressure fume hood 30 mL of viral culture media from the collection kit was extracted. Nucleic acids isolation was done with STARlet IVD (Hamilton), automat extractor. Cartridge was placed in Biorad CFX96 equipment for polymerase chain reaction, by Real Time PCR. The result was scored as “positive” or “negative.” Data were collected from the infant’s charts and centralized in tables. Results were presented as absolute frequency.

## Results

### 1. Maternal cohort

Between April 1st and May 15th, 2020, 229 pregnant women were admitted for delivery. All of them were tested for Covid-19 infection, using throat swab specimens and infection was confirmed by RT-PCR. Five (2.18%) of these 229 patients had a positive real-time PCR test: four of them were diagnosed COVID 19 + at the time of admission for delivery, while one patient was transferred for delivery from the infectious diseases department after a hospitalization period of 20 days; at the time of the transfer, she presented positive real-time PCR test.

Three of the five COVID 19 + women were asymptomatic at the time of admission. One of them presented gestational diabetes; this could be a risk factor for severe form of infection. None of them have contact with SARS CoV 2 positive person of travel history to an epidemic area. Another woman presented symptoms of acute respiratory infection (fever, sore throat and cough) one week before delivery; she received symptomatic treatment (paracetamol) and vitamin C.

All positive mothers underwent C-section. They were admitted postoperatively to separate wards, maternal quarantine wards, and were transferred to the infectious disease department 72 hours later.

## 2. Demographic and general characteristics of infants

Out of the 229 deliveries, 108 were by vaginal route and 121 by cesarean section. There were 186 neonates at term, and 43 preterm neonates. The demographic characteristics and the general data of the newborns are shown in Table 1.

Table 1  
Demographic and general characteristics of infants

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gestational age (weeks)	38	39	36	38	38
Birth weight (g)	3370	3210	2350	3070	3200
Length (cm)	53	52	50	53	53
Head circumference (cm)	34	33	32	34	34
Apgar score (1' and 5')	10/10	10/10	9/9	10/10	10/10
Gender (male/female)	F	F	F	M	F
Gravida (parity)	II	III	I	I	I

One newborn born to a COVID 19 + mother was preterm. The pregnant woman was admitted for minimal hemorrhage, and the test for SARS-CoV-2 at admission was positive. Delivery by cesarean section was decided.

## 3. Laboratory data

In all newborns of the studied group, the evolution of CBC, of inflammatory markers (protein C reactive) and procalcitonin were dynamically monitored, on the first and third day of life. The variation of the monitored laboratory parameters is shown in Table 2.

Table 2  
Laboratory parameters evolution

Parameter	Day of life	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
HGB(g/dl)	1	18.4	14	14.9	18.4	15.70
HCT(%)		51.8	39.8	43.6	52.2	44.40
PLT(10 <sup>9</sup> /L)		369	318	268	159	291
WBC(10 <sup>9</sup> /L)		26.50	26.94	21.57	7.45	26.20
Ne(/10 <sup>9</sup> /L)		70.9/18.8	69.3%/18.65	69.2%/14.94	45%/3.35	60.9%/15.96
Ly(/10 <sup>9</sup> /L)		21.1%/5.6	21.8%/5.86	24.4%/5.27	37.1%/2.77	31.7%/8.3
ASAT	1	49	117	93	55	47
(*NV 25–75 U/L)	3	34	29	65	51	44
ALAT	1	29	22	13	21	12
(*NV 13–45 U/L)	3	32	20	20	24	14
CK	1	848	1225	1316	525	NA
(*NV < 712U/L)	3	306	204	303	468	NA
LDH	1	529	904	790	467	NA
(*NV 290–775 U/L)	3	49	117	93	55	47
Protein C reaction (mg%)	1	1.27	0.14	0.17	0.12	0.1
	3	0.46	0.06	0.24	0.10	0.18
PCT(ng/ml)	1	20.13	NA	NA	NA	1.96
	3	4.39	NA	NA	NA	0.4

\*NV = normal value, NA = not available

HGB = hemoglobin, HCT = hematocrit, PLT = platelets, WBC = white blood cells, Ne = neutrophils (% and absolute no), Ly = lymphocytes, PCT = procalcitonin, ASAT = aspartate amino transferase, ALAT = alanine amino transpherase, LDH = lactate dehydrogenase, CK = creatin kinase

In four newborns, white blood cells ( WBC), platelets were within the normal range.

In one of five newborns (patient 1), inflammatory markers were reacted on the first day of life, and neutrophilia with mild lymphopenia was present. He received antibiotic therapy for 7 days, with laboratory tests returning to normal values. There were no clinical symptoms suggestive of neonatal sepsis. This patient had a symptomatic mother one week before delivery. The mother's therapeutic response was slow and first SARS-CoV-2 negative test was obtained 5 weeks after delivery.

#### **4. Management**

All newborns had an umbilical venous catheter inserted immediately after delivery. The umbilical venous catheter was maintained until the second negative real -time PCR was obtained. For all newborns, the real-time PCR tests performed on the first day and on the 5th day of life were negative.

Enteral feeding with formula was administered. Feeding with breast milk during admission to the maternity ward was not possible for any of the newborns with SARS-CoV-2 positive mothers. They received breast milk only after the mother's discharge from the infectious disease service.

No patient required oxygen supplement or respiratory support. There were no complications during hospital stay in any of the patients.

The mean length of hospital stay was 12.2 days (6–22 days). The longest hospital stay was determined by the long hospital stay of the mother, until mothers negative SARS-CoV-2 test was obtained.

The hospitalization period of the newborn was marked by no pathological event.

## **Discussions**

SARS-CoV-2 infection present in the pregnant woman involves risks for the newborn. We had no case of vertical transmission in our unit during the mentioned period. To prevent perinatal transmission and to prevent contamination of the medical staff, in the period of onset of the pandemics, our national guidelines for obstetrics and neonatology recommended delivery by cesarean section in pregnant women positive for SARS-CoV-2, as well as for pregnant women suspected to be infected (those with travel history, contacts of SARS -Cov-2 positive persons or presenting respiratory symptoms) [2], [3], [10], [11].

The exact rate of vertical transmission of the infection is not known. Currently, only a limited number of cases with vertical transmission are reported. Seven independent studies, report the outcomes 70 newborns of mothers with confirmed SARS-CoV-2 infection: 65 neonates (92.9% of cases) were negative following RT-PCR analysis of oropharyngeal or nasopharyngeal swab performed in the first hours or days of life; in four patients (5.7% of cases), early infection was diagnosed on the second day of life; thus, vertical transmission cannot be excluded; finally, one patient had a negative throat swab but positive immunoglobulin M( IgM) and immunoglobulin G( IgG )count, and was considered as potentially infected in utero. Consequently, in 5 out of 70 cases (7.1% of neonates), vertical transmission could not be excluded or was considered possible [4], [12], [13].

In our group, all five neonates of SARS-CoV-2 positive mothers were born by cesarean section. In the majority of the reported cases, the delivery of the newborns of mothers with SARS-CoV-2 infection was

performed by cesarean section. The aim of this mode of delivery is to limit the perinatal transmission of the infection from the mother to the neonate, as well as to limit the contamination of the medical staff by assisting the infected pregnant woman during labor and expulsion, which can last few hours [13].

The neonates of our study group had a good clinical outcome, without events during hospitalization. They had no changes in the values of lymphocytes, neutrophils or leukocytes. Inflammatory syndrome was negative, except for one patient. (Table 2) Early inflammatory syndrome present in one neonate had a favorable evolution following antibiotic treatment. This patient had no clinical elements suggestive of neonatal sepsis and had negative blood culture. One week before delivery, the mother had symptoms suggestive of SARS-CoV-2 infection (fever, cough, sore throat). There were no other maternal risk factors explaining inflammatory syndrome of newborn. No analysis of the placenta was performed. The creatine kinase value was out of normal range in three patients on first day of life, but the third day value was in normal range. The aspartate aminotransferase and lactate dehydrogenase had the same behavior in two of the patients. We could not find any explanations for this finding. It is known that SARS-Cov-2 infection can associate liver function abnormalities. We did not expect to have infants with this type of abnormal laboratory data as there RT –PCR tests were negative, and infection wasn't confirmed.

The analysis of the oropharyngeal or nasopharyngeal swab was negative in all newborns of the study group, on the first day as well as on the fifth day of life. Umbilical vein catheterization was carried out in all patients to facilitate their laboratory tests collection, to limit the length of time spent for blood sample collection and to allow a safe venous approach for an eventual medication. After obtaining the second negative test, the venous catheter was removed in all patients.

Enteral nutrition was given in accordance to the local national guidelines. In all neonates of mothers with positive RT-PCR, enteral nutrition was initiated with formula. Although there are studies showing that the breast milk of women with SARS-CoV-2 infection was negative, we chose to give formula to the neonates [3], [14]. The mothers were placed in a dedicated area of maternity wards in the first 72 hours after cesarean section, after which they were transferred to the contagious disease unit.

Feeding with breast milk has a number of benefits for both the mother and the newborn, the immunological benefit playing an important role in the protection of the newborn from infections through the transfer of immunoglobulin with a protective role for the neonate. The recommendation for breast feeding in the case of mothers infected with SARS-CoV-2 is to maintain rigorous hygiene conditions, to wash and disinfect hands, to wear a mask during breastfeeding. If the mother cannot breastfeed the newborn, expressed breast milk can be used, while respecting the same rigorous hygiene conditions for expressing breast milk. If the mother is separated from the neonate, it is recommended to help the mother maintain lactation by manual or mechanical expression. Also, counseling of the mother and the family in case of separation from the newborn should be taken into consideration, and permanent communication with the family and their information about the health of the neonate should be ensured. Whenever it is possible, feeding the neonate with breast milk is recommended if the mother's condition allows it and if she wishes to breastfeed in the current health conditions [2], [9], [15].

The strengths of this study include the timely nature of our findings as the COVID-19 pandemic ensues, the evaluation of the incidence of infection among the pregnant women in our region. The weakness of our study is the relatively small size of the group, but the evidenced data are in accordance with those obtained by similar studies. These data are useful for the analysis of the obstetric population, for the knowledge of the risk of infection in this population. We consider that testing all pregnant women at admission to the maternity unit is an important method to reduce the spread of SARS-CoV-2 infection, representing a guide in the approach of delivery in pandemic conditions.

## **Conclusions**

In our study, vertical or perinatal transmission of the infection was not present in any of the neonates. Like in the majority of the cases from other studies, in our case the newborns were negative on RT-PCR testing from the nasopharyngeal swab. The testing allowed excluding the infection and the transfer of the neonates to the non-isolated area. Thus, the hospital stay of the neonates is limited, their discharge to the family being possible when the family members are healthy, unquarantined.

The diagnosis of SARS-CoV-2 infection of the pregnant women was established at admission to the maternity ward. Due this testing, mother's isolation and delivery in safe conditions for the medical staff were possible, using adequate protection equipment to limit their infection and to limit the risk for the newborns.

## **Abbreviations**

SARS-CoV-2 -severe acute respiratory distress syndrome with coronavirus 2

COVID19-coronavirus disease 2019

RT-PCR- real time PCR test

CBC-central blood count

PPE-personal protection equipment

ARDS-acute respiratory distress syndrome

WBC-white blood cells

IgM -immunoglobulin M

IgG -immunoglobulin G

## **Declarations**

**Ethics approval and consent to participate**



Institutional review board and COVID -19 specific research committee approval was obtained for this study .

### **Consent for publication**

Not applicable

### **Availability of data and materials**

All data generated or analysed during this study are included in this published article(and its supplementary information files).

### **Competing interests**

The authors declare that they have no competing interests.

### **Funding**

Nothing to declare.

### **Authors' contributions**

GZ:Conceptualization,methodology,writing –reviewing and editing

MM:data curation, Writing- original draft preparation

MH:software, Validation

TK:Investigation,Visualization

DM :Supervision

All authors have approved the submitted version.

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### **Authors' information**

Not applicable

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