

Original Research

Does SARS-CoV-2 in Pregnancy Affect Newborn Outcomes?

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Abstract

Background: The aim of this study was to show the frequency and epidemiological characteristics of pregnant women who tested positive for SARS-CoV-2 during childbirth as well as the course, mode and outcome of their newborn treatment and diet after discharge. The aim is also to show individual symptoms developed by newborn from pregnant women who test positive for SARS-CoV-2. **Method:** The study included all the infants born to the pregnant women who tested positive for SARS-CoV-2 on a PCR test 24 hours prior to delivery or, had already been confirmed positive for the infection and had developed symptoms of the virus or had started treatment for SARS-CoV-2 several days prior to delivery. **Results:** 43/3237 (1.32%) of the pregnant women tested positive for the SARS-CoV-2 virus or had been infected prior to admission and were positive during delivery. A total of 45 newborn infants were transferred to a special room for the care of newborn infants born to SARS-CoV-2-positive mothers at the Department of Neonatology. Specifically, 30/45 (66.7%) of the newborn infants developed symptoms within the first hours of birth which withdrew spontaneously within 24–48 hours after birth. The symptoms referred to are not specific for SARS-CoV-2 infection and are not particularly indicative of infection. **Conclusions:** The conclusion of this short 21-month study is that prenatal and postnatal duration and outcome in infants is not aggravated by pregnant women who tested positive for SARS-CoV-2. Despite the individual symptoms described above and the pathological states the children developed during hospitalization, all the newborn infants were discharged from hospital in full health, and they were all breastfeeding following discharge in conditions which respected all the epidemiological preventive measures.

Keywords: pregnancy; newborn; COVID-19 infection; pandemic

1. Introduction

Corona Virus 2 (SARS-CoV-2) has been rapidly spreading around the world since late December 2019, triggering a global pandemic, and becoming a public health problem across the globe [1,2]. Two years have nearly passed since the first case was identified in our hospital and we are still battling with the virus which is eroding our public health system. Health workers are highly aware of these facts that add to already high levels of stress, particularly amongst health workers directly concerned with neonates and their mothers. Despite significant increases in both incidence and prevalence, little is known about COVID-19 in the perinatal period [3,4]. Neonatologists are especially faced with a hard dilemma: despite constant updates of recommendations, the main issues are still how to survive the pandemic with as little stress as possible, and how not to separate newborn infants from mothers who tested positive for COVID-19, particularly in the first days of life which are emotionally irreplaceable. Present research indicates that there is no difference in the risk of neonatal SARS-CoV-2 infection whether a newborn infant is accommodated with

or separated from its mother who is suspected of being or has tested positive for SARS-CoV-2 [5,6]. Research conducted in 2020 suggests that perinatal SARS-CoV-2 infections could have detrimental effects on the newborn, causing conditions such as dyspnea, fevers, feeding intolerance, premature labor, respiratory distress syndrome, and thrombocytopenia; however, the same study did not confirm vertical transmission of SARS-CoV-2 [7,8]. A Chinese study [9], a study conducted in America [10] and the initial guidelines issued by the American Academy of Pediatrics (AAP) when our first case was reported recommended temporary separation of the newborn from infected mothers as the safest means of preventing infection of the newborn [11]. However, a prospective study from New York that tested and monitored newborn and mothers who tested positive for SARS-CoV-2 concluded that postnatally none of infants tested positive where safety precautions were implemented regarding accommodation and breastfeeding [12]. A study conducted in Italy produced similar results [1]. A recently published global study indicates that newborn infants were separated from their mothers as a safety precau-



tion if the mother tested positive for COVID-19 in half of the countries in the world [13] during the last year, which was also the case in our hospital (University Clinical Hospital Mostar). As incidence and disease progression in pregnant women was the same as in the general population [14], a greater challenge for us at the Clinical Hospital was the organization of antenatal care, pregnancy termination time and manner, and postpartum care, which was predominantly concerned with the separation of the mother from the newborn and breastfeeding, because research findings on these issues were contradictory.

(1) The aim of this research is to show the frequency and epidemiological characteristics of the pregnant women who tested positive for SARS-CoV-2 during childbirth as well as the course, mode and outcome of the treatment and feeding of the newborn upon discharge.

(2) The research also aims to identify the individual symptoms developed by the newborn of the pregnant women who tested positive for SARS-CoV-2 during hospitalization.

2. Materials and Methods

This research is a retrospective epidemiologic study for the period from 1/3/2020 to 22/12/2021. The study was conducted at the Clinic of Gynecology and Obstetrics and the Department of Neonatology at the Clinic for Children's Diseases of the University Clinical Hospital Mostar. In the period encompassed by the study, 3237 infants were born at the Clinic of Gynecology and Obstetrics. The study includes all the pregnant women who tested positive for the SARS-CoV-2 virus, that is, those who had a positive polymerase chain reaction (PCR) result from a nasopharyngeal or oropharyngeal swab up to 48 hours prior to labor or during labor. In addition, the study included all the positive pregnant women who had developed symptoms of the COVID-19 virus and whose treatment had started 15 days prior to labor. The parameters that were analyzed in the pregnant women were: age, parity, labor type, pathological conditions during pregnancy (gestational diabetes, infections, hypertension), medication in pregnancy, clinical picture of the COVID-19 infection (asymptomatic, mild, moderate or severe), and mode of treatment of the COVID-19 infection. The study also included all the infants born to the pregnant women who tested positive for SARS-CoV-2 on a PCR test. The parameters analyzed in the newborn were: gender, gestational age, birth mass, Apgar score, COVID-19 test, other pathological conditions (jaundice, hypoglycemia, infections), manner and duration of treatment, incubation period, feeding tolerance times, laboratory parameters (leukocytes, C-reactive proteins (CRP), total bilirubin), breastfeeding upon discharge and eventual symptoms connected to the COVID-19 infection. Hypoglycemia is defined as plasma glucose levels <2.5 mmol/L after 72 hours of life in a term or preterm infant. Hyperbilirubinemia is a condition defined as elevated serum or

plasma bilirubin levels above the reference range of the laboratory (>100 $\mu\text{mol/L}$), due to metabolic disorders of bilirubin. Neonatal infection may be confirmed or suspected, accompanied by clinical symptoms and laboratory parameters (C-reactive protein >10 mg/dL). Perinatal infection is any infection accompanied by an increase in inflammation parameters (C-reactive protein) in the first 24 hours of life with or without other signs of infection [15]. Every pregnant woman who tested positive and who gave birth vaginally was accommodated in a special labor room, and the pregnant women who delivered via C-section were accommodated in the operating theatre for C-sections, with all participants in the labor process adhering strictly to all epidemiological protective measures. The newborn infant was immediately transferred to the Neonatal ward at the Clinic for Children's Diseases, where the infant was accommodated in a separate room for newborn infants equipped with all the necessary medical apparatuses and monitors for monitoring the infant. In the period under analysis, data was collected from the case histories of the newborn infants, the transfer and discharge letters for the newborn infants and telephone calls to the parents which noted whether the infants were breastfeeding upon discharge from hospital. The main criteria for the inclusion of a pregnant woman in the study was a positive polymerase chain reaction (PCR) result from a nasopharyngeal or oropharyngeal swab. The most frequently used method for etiological diagnosis of SARS-CoV-2 was the RT-PCR (real-time polymerase chain reaction). Although this method has been defined as the golden standard for diagnosing COVID-19, its sensitivity level is 70%, and specificity level 95%. The tests were conducted by the Microbiology Institute of the UCH Mostar, and the results were available a couple of hours after the pregnant women were admitted for childbirth and after the infant was transferred and separated from the mother. This retrospective study was conducted according to all ethical principles.

Statistical data were analyzed in IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA). Categorical data are expressed as number and percentage. The Chi-squared test was used to determine the significance of differences. The Shapiro-Wilk test was used to check the normality of the distribution of numerical data. The results of the numerical data are expressed as the median of the first and third quartile.

3. Results

In the period from 1/3/2020 to 22/12/2021, 3237 women went into labor at the Clinic of Gynecology and Obstetrics. 43/3237 (1.32%) of the pregnant women tested positive for the SARS-CoV-2 virus or had been infected prior to admission and were positive during childbirth. A total of 45 newborn infants (41 single births and 2 sets of twins) were transferred to a special room for the care of newborn infants born to COVID-19-positive mothers at the Department of Neonatology. Every newborn underwent

Table 1. Distribution of the characteristics of the pregnant women who tested positive for the SARS-CoV-2 virus prior to childbirth or tested positive several days prior to the childbirth and the infection had progressed.

Characteristic	Number (%) N = 43
Age/year, median (Q1–Q3)	32 (29–36)
Pregnancy	
1	15 (34.8)
2	14 (32.6)
3+	14 (32.6)
Abortion	
No	38 (88.4)
Yes	5 (11.6)
Mode of delivery	
Vaginal	27 (62.8)
Caesarean	16 (37.2)
Course of pregnancy	
Normal course	32 (74.4)
Pathology	11 (25.6)
GBS (Group B streptococcus) positive vaginal swab	1 (2.3)
Hypothyroidism	1 (2.3)
Gestational diabetes	4 (9.3)
Hypertension	3 (7.0)
Urinary tract infection	2 (4.6)
Medications taken in pregnancy	
No	40 (93.0)
Yes (antibiotics)	3 (7.0)
Clinical picture of COVID-19 infection	
Asymptomatic	30 (69.8)
Mild	8 (18.6)
Moderate	4 (9.3)
Severe	1 (2.3)
Hospitalization in COVID-19 department	
No	38 (88.4)
Yes	5 (11.6)
Use of drugs for COVID-19 infection	
No	36 (83.7)
Yes	7 (16.3)
Antibiotics	2 (4.6)
Antibiotics + oxygen	2 (4.6)
Antibiotics + corticosteroids	1 (2.3)
Antibiotics + corticosteroids + anticoagulant therapy	2 (4.6)

primary laboratory tests (leukocytes, bilirubin, CRP) and a PCR test from a nasopharyngeal and oropharyngeal swab on the second day of life which were all negative except for one infant, whose test was repeated and was negative on day seven. Every infant underwent an ultrasound of the brain which indicated no significant pathology. Six newborn infants were placed in incubators. 14/45 newborn infants with neurological symptoms underwent tests for lactate levels in the blood, the results of which were moderate at 3 mmol/L, whereas the reference interval at the Insti-

tute for Laboratory Diagnostics UCH Mostar was 0.5–2.2 mmol/L. None of the newborn developed the typical symptoms of the COVID-19 infection nor did they require any therapy for the coronavirus infection; they did, however, require therapy for other pathological conditions which developed during hospitalization. 44/45 newborn infants were being breastfed ten days following discharge from hospital. This information was obtained via telephone calls to the parents regarding the feeding habits of their infants.

Table 2. The distribution of infants born to pregnant women who tested positive for the SARS-CoV-2 virus before childbirth or tested positive and had developed a COVID-19 infection several days prior to childbirth.

Characteristic	Number (%)
	N = 45
Number of girls/boys	21/24
Birth weight (g), median (Q1–Q3)	3360 (3000–3810)
Gestational age (weeks), median (Q1–Q3)	39 (38–40)
Apgar score	
10/10	44 (97.8)
8/9	1 (2.2)
Other pathological conditions	
No	28 (62.2)
Yes	17 (37.8)
Jaundice	3 (6.6)
Perinatal infection	4 (8.8)
Polycythemia	3 (6.6)
Hypoglycemia	1 (2.2)
Intrauterine growth retardation	1 (2.2)
Cephalhematoma	4 (8.8)
Sepsis and bleeding in the brain	1 (2.2)
Laboratory parameters	
C-reactive protein, median (Q1–Q3)	0.60 (0.18–1.40)
Leukocytes, median (Q1–Q3)	20 (15.6–25.0)
Bilirubin, median (Q1–Q3)	77 (53.5–152.0)
COVID-19 test	
Negative	44 (97.8)
Positive	1 (2.2)
Individual symptoms	
No	15 (33.3)
Yes	30 (66.7)
Length of hospitalization (days)	
–7	40 (88.9)
8+	5 (11.1)
Other therapy	
No	24 (53.3)
Yes	21 (46.7)
Antibiotics	5 (11.1)
Glucose	7 (15.6)
Phototherapy	1 (2.2)
Prophylactic antibiotic therapy + Glucose	3 (6.6)
Prophylactic antibiotic therapy + Phototherapy	2 (4.4)
Glucose + Phototherapy	2 (4.4)
Prophylactic antibiotic therapy + Glucose + Phototherapy	1 (2.2)
Feeding tolerance start (hours)	
In the first hour of life	25 (55.6)
Within 3 to 12 hours after birth	14 (31.1)
12 and more hours after birth	6 (13.3)

During the period under analysis, 30/43 (69.8%) of the pregnant women tested positive and had no symptoms of the COVID-19 infection before going into labor (Table 1). Only 1/43 pregnant woman required mechanical ventilation due to the COVID-19 infection. 2/43 of the pregnant

women needed oxygen support and other therapy before and after childbirth. 11/43 (25.6%) pregnant women had pathological pregnancies, and the most frequent pathological condition of the pregnant women who were part of the sample was gestational diabetes 4/43 (9.3%) (Table 1).

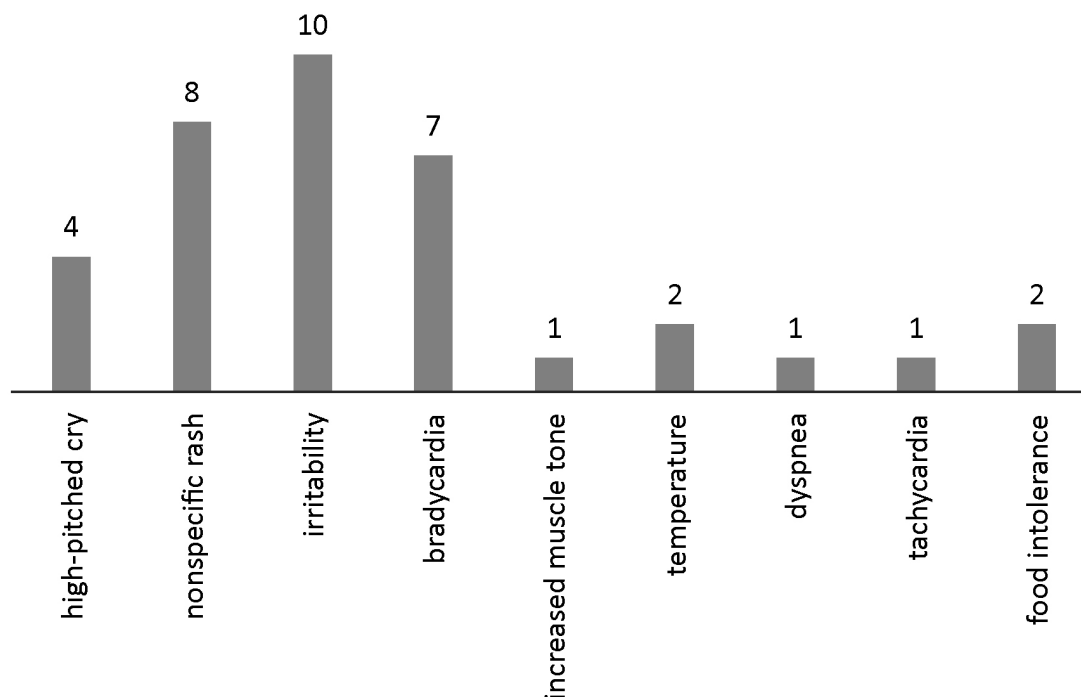


Fig. 1. Distribution of individual symptoms of infants born to pregnant women who tested positive for the SARS-CoV-2 virus before childbirth or tested positive several days before childbirth and had a developed infection.

During the period under analysis, only 2/45 newborn infants required respiratory support due to their young gestational age and other pathological conditions which were not connected to the COVID-19 infection of the mother. 17/45 (37.8%) newborn infants developed other pathological conditions (Table 2). None of the infants required oxygen or any other COVID-19 therapy. 11/45 (24.4%) newborn infants were administered a course of antibiotics for initial signs of infection or an increased concentration of CRP (Table 2). All the newborn infants were tested on day 2 of life, and only one newborn infant tested positive with no symptoms. The newborn infants were still breastfeeding 10 days upon discharge from hospital, and they did not have any symptoms of the infection.

30/45 (66.7%) newborn infants developed symptoms within the first hours of birth which withdrew spontaneously within 24–48 hours after birth. These symptoms were not specific for the COVID-19 infection and were not particularly indicative of infection. Significantly more newborn infants had some unusual symptoms in comparison to asymptomatic infants ($\chi^2 = 4.261$; $p = 0.039$) (Fig. 1). These symptoms could not be connected to other pathological conditions that infants develop during hospitalization. 14/45 (31.1%) newborn infants developed symptoms connected to neurological pathology (shrill crying, irritability, changes in muscle tone) and these symptoms were particularly evident in the first hours after birth (Fig. 1). All of the symptoms mentioned above withdrew spontaneously within 24–48 hours after birth. An undefined rash was de-

veloped by 8/45 infants and withdrew after one day (Fig. 1).

4. Discussion

The sudden, unforeseen situation we found ourselves in was difficult for obstetricians and neonatologists who were faced with the need to separate a mother from her newborn infant because of a virus that very little was known about in the beginning [16]. Initial guidelines recommended the separation of the infant from the mother to stop the transmission of the infection [11], which was implemented in the region under analysis during the pandemic. A recently published systematic overview concludes that the COVID-19 infection in infants is rare, and very rare with any of the symptoms of the disease [17]. In our case, maternal transmission of the disease to the infant is not described (except in the case of one infant) even after a period of close contact with the mother and breastfeeding upon discharge. The exception was a COVID-19 positive newborn who was re-admitted to hospital on the fifth day of life because of a one-time fever. The newborn was discharged two days later with a negative PCR test and normal clinical status. This could be explained by a low burden of the virus in the mother [14]. A study conducted at the beginning of the pandemic indicated that 90% of the pregnant women who tested positive gave birth via C-section [18], whereas our study indicates a higher frequency of natural deliveries by the positive pregnant women. There is a lack of convincing evidence that cesarean delivery is protective. The study concludes that vaginal delivery is not contraindi-

cated with COVID-19 [19]. The conclusion that accompanying pathological states in pregnancy (e.g., diabetes, hypertension) increase the risk of more severe incidences of the COVID-19 virus [20] is contradicted by our results. Our study also indicates that the tests for SARS-CoV-2 during the second day of life were negative in infants, although individual infants developed symptoms (shrill crying, irritability and changes in muscle tone) that were not related to the usual symptoms of pathological conditions infants develop during hospitalization. A study conducted in China in 2020 drew a similar conclusion [7]. The longer the pandemic lasts, more and more articles have indicated the reduced risk of transmission of the infection to an infant, allowing hospitals around the world to adapt to the newest information and continue rooming-in policies [5,6,14]. Nevertheless, up until the writing of this article, our health institution has continued to implement its own guidelines and separates infants from their COVID-19-positive mothers, causing greater emotional stress for the parents. Although childbirth is typically considered a happy event, it can become a highly stressful experience and result in acute stress responses. Therefore, it is important to consider the subjective experience of childbirth for the COVID-19 positive pregnant women. Irrespective of the initial separation, 89% of the infants were discharged from hospital with a clean bill of health within a few days (except for four infants who were treated longer) and reunited with their mothers in their home environments. The mothers whose infants were treated in our department were telephoned on the tenth day upon discharge for the purpose of collecting information on whether the infant was breastfeeding and if it was exhibiting any symptoms. Further confirmation can be found in the fact that none of the infants were re-admitted to hospital for treatment after initial discharge (except for the one newborn previously described). Breastmilk offers protection from many viral diseases, and research conducted at the end of 2021 confirms that breastfeeding also protects against the coronavirus [21]. A similar conclusion was reached by a study in Italy published in 2021 whose results indicate that the risk of maternal transmission of SARS-CoV-2 to the infant during interaction was low if the infected mothers did not have severe COVID-19 infections and if they had been educated to adhere to the protective measures (wearing masks and gloves, and hand disinfection) when in contact with, caring for or breastfeeding their infants [7], which is also the recommendation of our study.

5. Conclusions

The conclusion of this short 21-month study is that prenatal and postnatal duration and outcome in infants is not aggravated by pregnant women who tested positive for SARS-CoV-2. Despite the individual symptoms described above and the pathological conditions the children developed during hospitalization, all the newborn infants were discharged from hospital in full health, and they

were all breastfeeding ten days upon discharge in conditions where epidemiological protective measures were maintained. Since the coronavirus outbreak nearly two years ago, many studies have been conducted, and many conclusions have been drawn, yet the hygienic protective measures introduced to prevent the spread of the infection are permanent recommendations, which have been constant over centuries, and formed the basis for the management of SARS-CoV-2 positive mothers and their infants. This is confirmed by our study which indicates that the least expensive measures result in the greater benefits particularly in the interaction of COVID-19 positive mothers and their infants.

Author Contributions

MJR, JB, SG, VB, AM and DŠG designed the research study. MM analyzed the data. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of Clinical Hospital Centre Mostar and valid documentation exists for this matter (number 1034/21).

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Conflict of Interest

The authors declare no conflict of interest.

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