

CLINICAL STUDY

COVID-19 virus and clinical outcome on the newborns at the Neonatal Department of Intensive Medicine in Bratislava, Slovakia

Ingrid BRUCKNEROVA¹, William Christoph BENTO DREYER², Dorothy WASIKE², Jana BRUCKNEROVA³

Neonatal Department of Intensive Medicine Faculty of Medicine, Comenius University in Bratislava and National Institute of Children's Diseases, Bratislava, Slovakia. ingrid.brucknerova@fmed.uniba.sk

ABSTRACT

AIM: The aim of this study was to analyse the group of newborns who were admitted at Neonatal Department of Intensive Medicine in Bratislava Faculty of Medicine Comenius University in Bratislava and National Institute of Children's Diseases in the period from 08.01.2021 until 07.07.2023 who were affected by the COVID-19 virus from mother before birth, from staff or in family or were only in contact with COVID-19 positive person.

RESULTS: Most common symptoms in newborns within our findings included fever, upper respiratory symptoms, and diarrhoea. Detailed analysis of prenatal and postnatal characteristics, clinical findings are presented in tables 1–3.

CONCLUSION: COVID-19 pandemic had a great impact on the pregnant women as well as on prenatal and postnatal development of the child. Our results reveal that the severity of symptoms in COVID-19 infected newborns from our sample was low. It is important to implement adequate neonatal practices for early detection of illnesses, especially in relation to COVID-19 which will subsequently allow early intervention and reduce neonatal mortality. Future challenges for all countries include the implementation of higher hygiene standards, prevention of spreading, more sensitive tests to use in the first day of life (Tab. 3, Ref. 36). Text in PDF www.ellis.sk

KEY WORDS: newborn, COVID-19 virus, complications.

Introduction

On January 30th of 2020, the COVID-19 virus was officially declared a public health emergency (1). This virus originated in the city of Wuhan, China and rapidly spread throughout the globe, leading to a pandemic which affected billions and these repercussions are still felt today. The COVID-19 virus is a single-stranded, enveloped RNA virus (2). It contains four main structural proteins: spike (S), envelope (E), membrane glycoprotein (M) and nucleocapsid proteins (3). Once the virus invades the respiratory cells through ACE2 receptors, the respiratory system is greatly affected with varying symptoms. In chronic and severe cases, this inflammation leads to complications such as diffuse alveolar damage,

acute respiratory distress syndrome and alveolar microvascular occlusion, which can result in chronic respiratory insufficiency and even death (4).

Common symptoms in adults of the respiratory disease include cough, sore throat, loss of smell in more milder manifestations but may progress to tachypnoea and dyspnoea, respiratory and multiorgan failure in more severe cases. The transmission methods are sneezing, coughing and aerosols (5, 6, 7). COVID-19 outbreaks affect elderly people (> 60 years) and those with chronic comorbidities (cardiovascular diseases, impaired immunity, obesity) the most (1). Special categories are pregnant women and its influence on prenatal and postnatal development of the child (8, 9).

Common symptoms among infected newborns include fever, poor feeding, vomiting or diarrhoea and coryzal signs (10, 11). However, the rate of NICU admission isn't substantial. When it comes to the need of respiratory support, supplemental oxygen and non-invasive ventilation are the most common (11). When compared to non-infected mothers, newborns born to COVID-19 positive mothers presented with a lower gestational age, higher antenatal complications, and preterm labour. Additionally, respiratory, and vascular complications (respiratory distress and haemorrhage) were approximately 3 times more common in infected mothers (12).

¹Neonatal Department of Intensive Medicine in Bratislava Faculty of Medicine Comenius University in Bratislava and National Institute of Children's Diseases, Bratislava, Slovakia, ²Faculty of Medicine Comenius University in Bratislava, Slovakia, and ³National Institute of Cardiovascular Diseases, Bratislava, Slovakia

Address for correspondence: Ingrid BRUCKNEROVA, MD, PhD, Prof, Neonatal Department of Intensive Medicine, Comenius University in Bratislava and National Institute of Children's Diseases, Limbova 1, SK-833 40 Bratislava, Slovakia.

Phone: +421.2.59371232

Abbreviations: BW – birth weight, GA – gestational age

Preterm births seem to be more common in pregnancies with symptomatic COVID-19 infections. It's worth noticing that the prevalence of hospital admission due to COVID-19 symptoms is higher in pregnant infected women in their first or second trimester, while infected pregnant women tended to present more often due to obstetric complications.

When it came to COVID-19 disease symptoms, those in the first or second trimester displayed a higher percentage of symptoms of respiratory infection (fever, cough, shortness of breath) than those in the third trimester, which mostly manifested obstetric symptoms. This paper also notes an increased number of preterm births in infected women (13).

In a study of 15 placentas of women infected with COVID-19, the following findings were noted: COVID-19 positive mothers displayed vascular malperfusion (12/15), villous infarction, peripheral (3/15) and central (1/15), villous agglutination (3/15) and rapid villous maturation (2/15). In 7/15 cases, decidual arteriopathy occurred, as well as atherosclerosis and fibrinoid necrosis of maternal vessels (3/15) and mural hypertrophy of membrane arterioles (5/15) (14).

Additionally, Cimolai mentions reports which reveal that newborns born to infected mothers are at a higher risk for desaturation, poor feeding and more severe episodes of respiratory insufficiency. They also noted that most severe cases were present in newborns with concomitant pathologies and those without any comorbidities were mostly asymptomatic or displayed only mild respiratory symptoms. The study conducted by Kyle and Dumitriu also supports the finding of higher rates of low birth weight and prematurity in newborns born to infected mothers. Most newborns infected with COVID-19 manifest a mild course of infection with lethargy, poor feeding, lower leukocytes yet also not requiring intubation (9, 15, 16).

Due to newborn prematurity or as COVID-19 transmission preventive measures, several postnatal practices such as skin-to-skin contact, delayed bathing and cord clamping may be reduced or avoided in certain hospital settings. An online survey conducted by Rao et al, demonstrated some of the major changes and challenges that impacted neonatal care during the pandemic, these included the redirection of staff responsible for neonates to other COVID-19 related tasks, decrease in available space in the neonatal unit, inattentive mother care, and compromised provision of oxygen to neonates (17). In addition, there was also a decline in newborn follow up, hospital births, and neonatal admissions. This is further supported by an observational study in Nepal by Kc et al, which reported not only a decline in hospital birth during the pandemic but also an increase in institutional stillbirths (18). This, however, may disrupt and impair the normal gut microbiome development of newborns, which can also be severely affected by the growing number of caesarean births in COVID-19 times. These factors, when combined with prematurity, severely affect newborn's natural microbial colonisation, posing risk for future intestinal, respiratory, and metabolic pathologies (19). Regarding imaging, as with adults, the most common findings include diffuse shadows, ground-glass opacity, and multifocal consolidations (20). Additionally, during the COVID-19 pandemic, a great

increase in the rate of Caesarean sections has been reported (13, 21, 22). These procedures have been most common due to the rise of obstetrical complications in COVID-19 infected women (21). Additionally, Zaigham and Andersson note that "foetal distress" comprises a great reason for opting for this emergent procedure (23).

Though Rollins et al mention a report that detected the COVID-19 virus in breastmilk, its reproducing capability was not confirmed. Furthermore, they concluded that breastfeeding measures between mother and neonate should remain with the appropriate safety measures as the benefits of such practice outweigh the risks (24).

Aim

The aim of this study was to analyse the group of newborns who were admitted at Neonatal Department of Intensive Medicine in Bratislava Faculty of Medicine Comenius University in Bratislava and National Institute of Children's Diseases (NDIM FM CU NICHD) in the period from 08.01.2021 until 07.07.2023 who were affected by the COVID-19 virus from mother before birth, from staff or in family or were only in contact with COVID-19 positive person.

Methods

This study was performed through a retrospective analysis of 14 medical records of newborns (4 preterm newborns; 10 term newborns) admitted to the NDIM as well as at a specialised COVID-19 unit in NIDCH in the period from 08. 01. 2021 until 07. 07. 2023.

We took into consideration any gestational problems, date of mother's positivity, delivery report, gestational age (GA) and birth weight (BW), postnatal adaptation, age at admission and reason for admission, clinical complications, and hospitalisation periods.

Results

Characteristics of premature newborns (patients: 1 – 4) and of term newborns (patients: 5 – 14) are presented in Tables 1, 2 and 3 (25).

Two pregnant women of premature newborns (patient 1 and 3) were positively tested before delivery. Patient 1 was COVID-19 positive and had gastrointestinal symptomatology (diarrhoea). Patient 3 was COVID-19 negative and in clinical status complications of prematurity were dominated.

Two pregnant women of premature newborns (patient 2 and 4) were negatively tested before delivery. Patient 2 was also negative. This couple was in contact with COVID-19 positive person. Patient 4 was positively COVID-19 tested and had a mild form of diarrhoea.

Three pregnant mothers of term newborns had unknown COVID-19 status before delivery (mothers of patients 6, 9, 14). One of those (mother of patient 9) was positive on the 3rd day

Tab. 1. Characteristics of premature newborns (1-4).

Premature newborns								
Number	prenatal history	COVID-19 positivity of mother before delivery	delivery GA (w) BW (g) BL (cm) AS (points)	postnatal history	postnatal COVID-19 positivity	age on admission	days of hospitalisation	clinical signs of COVID-19 infection
1	none	positive before delivery	spontaneous 34+6 days 2360 g 48 cm 7/8	bradycardia, cyanosis, CPAP hyperbilirubinemia (phototherapy)	mother: positive father: positive sibling: positive	28 days COVID-19 positivity subfertility anaemia/leukopenia blood in stool	2 days thinner stools	diarrhoea
2	none	negative	spontaneous 34 w 2000 g 48 cm 2/5/4	resuscitation intubation ventilation	newborn: negative	2 hours	21 days	contact with COVID-19 positive person
3	GDM oligohydramnios asphyxia	positivity 10 days before delivery temperature above 38.5°C	acute c. s. 34 w 1970 g 45 cm 2/5	resuscitation oxygen 100 %, Surfactant ventilatory support/NO pulmonary hypertension Dopamine/Adrenalin	newborn: negative	2.5 hours	15 days	complications of prematurity
4	25 th g. w. -diagnosis of duodenal atresia and CNS haemorrhage	negative	c. s. 36 w 4030 g 48 cm 7/8/8	oxygen 40 % respiratory support	mother: positive newborn: positive	1.5 hour	30 days	diarrhoea

GDM – gestational diabetes mellitus, g. w. – gestational week, c. s. – caesarean section, GA – gestational age, BW – birth weight, BL – birth length, AS – Apgar score, w – week, g – grams, NO – nitric oxide, CNS – central nervous system

Tab. 2. Characteristics of term newborns (5–8).

Term newborns								
Number	prenatal history	COVID-19 positivity of mother before delivery	delivery GA (w) BW (g) BL (cm) AS (points)	postnatal history	postnatal COVID-19 positivity	age on admission	days of hospitalisation	clinical signs of COVID-19 infection
5	Foetus magnus	positive	spontaneous 40+4 days 4520 g 54 cm 10/10	on 2 nd day of life: temperature signs of acute respiratory infection	newborn: positive	4 days temperature leukopenia, thrombocytopenia purulent conjunctivitis	18 days	diarrhoea
6	negative	unknown	spontaneous 41 w 3150 51 cm 10/10/10	no problems	newborn: positive mother, father: positive	11 days lethargy, ↓ appetite temperature capillary refill time prolonged	2 days	upper respiratory symptoms
7	arterial hypertension, GDM foetus – asphyxia	negative not vaccinated	acute c. s. 38 + 5 days 3310 g 50 cm 2/6/8	resuscitation	newborn: positive on 44 th day of age	2.5 hours	diarrhoea 70 days	diarrhoea
8	unknown	positive before delivery with symptomatic course	spontaneous 38 w 3590 g 52 cm 10/10	tachydyspnoea oxygen 30%	newborn negative	5.5 hour	2 days	no clinical problems

GDM – gestational diabetes mellitus, g. w. – gestational week, c. s. – caesarean section, GA – gestational age, BW – birth weight, BL – birth length, AS – Apgar score, w – week, g – grams, NO – nitric oxide

Tab. 3. Characteristics of term newborns (9–14).

Term newborns								
Number	prenatal history	COVID-19 positivity of mother before delivery	delivery GA (w) BW (g) BL (cm) AS (points)	postnatal history	postnatal COVID-19 positivity	age on admission	days of hospitalisation	clinical signs of COVID-19 infection
9	none	contact with positive person before delivery. Positive 3 days after delivery	spontaneous 42 w 4180 52 cm 8/9	temperature upper respiratory symptoms	positive	6 days	1 day	upper respiratory symptoms
10	negative	12 days before delivery	spontaneous 38 w 3980 54 cm 8/9	no problems	newborn: positive	15 days temperature acute rhinitis	1 day	upper respiratory symptoms
11	none	3 days before delivery – dry cough, rhinitis, headache, loss of smell	spontaneous (VE) 41 + 1 day 3800 g 52 cm 6/8/10	resuscitation temperature	newborn: negative	11 days	4 days	no clinical problems
12	none	negative	spontaneous 38 w 2420 g 45 cm 9/10	congenital CMV infection anaemia	newborn: positive mother: positive	47 days	2 days	no clinical problems
13	suspected foetal asphyxia	7 days before delivery: dry cough	caesarean section 38 w 3220 50 8/10	on 2nd day of age: temperature loose stool leukopenia	.newborn: positive	3 days	1 day	subfertility diarrhoea
14	mother: in methadone programme	unknown	spontaneous 38 + 4 days 3310 49 10/10	caput succedaneum hypoglycaemia Neonatal withdrawal syndrome	on 17 th day of age newborn: positive	21 days	42 days	no clinical problems

GDM – gestational diabetes mellitus, g. w. – gestational week, c. s. – caesarean section, GA – gestational age, BW – birth weight, BL – birth length, AS – Apgar score, w – week, g – grams, NO – nitric oxide, CMV – cytomegalovirus, VE – vacuum extractor

after delivery, as well as her child was also positive for COVID-19 infection with upper respiratory symptoms. Patient 6 (upper respiratory symptoms) and patient 14 (no clinical problems) were positively tested after delivery.

Two pregnant women of term newborns had negative tests for COVID-19 before delivery (mothers of patients 7, 12). Patient 7 was infected at hospital and had diarrhoea. Patient 12 with congenital CMV infection, on 47th day of age together with his mother were positively tested for COVID-19. In his clinical status diarrhoea was dominant. They were infected at home.

Two term newborns (patient 5 and 13) of two COVID-19 positive mothers were COVID-19 positive and had diarrhoea; patient 10 of COVID-19 positive mother who was positive, had signs of upper respiratory symptoms.

Patients 8 and 11 of COVID-19 positive mother before delivery tested negative for COVID-19 and did not have clinical problems (diagnosis: the children of COVID-19 positive mother).

Discussion

When comparing the first and second wave of COVID-19 in India, 2 studies concluded that adverse mother and neonatal outcome seemed more severe during the second wave of the pandemic, with higher rates of symptomatic mothers, maternal mortality, missed miscarriages, intrauterine growth restriction, oligohydramnios, caesarean section rates, and need for stronger and more invasive therapies (26). Additionally, Nazer et al. also mentioned an increase in the number of pregnant women infected with COVID-19 who required extracorporeal membrane oxygenation (27).

Among pregnant women, symptoms mentioned are dry cough (mother of patient 13), fever (mother of patient 3) and rhinitis, loss of smell, headache (mother of patient 11). These symptoms are in accordance with symptoms among pregnant patients in the study by Delahoy et al (2020).

Regarding therapy and management, a Serbian report describes different changes between the four different waves of the COVID-19 pandemic. The first wave possessed the highest frequency of antiviral therapy administration, while the third wave displayed the highest rate of LMWH use, as well as CT usage for evaluation. The fourth wave experienced the longest hospitalizations, the highest requirement for non-invasive oxygen therapy as well as the longest use and use of corticosteroids. Additionally, this report also recognizes an increase in frequency of stillbirths and low placental maturity. These findings could be attributed to the increased severity of COVID-19 infection with the emergence of variants of concern as well as the inability of countries to adequately respond to the increase of healthcare demand of pregnant women with COVID-19 due to limited staff or resources (28).

Our results reveal that the severity of symptoms in COVID-19 infected newborns from our sample was low. 7 mothers (patient: 1, 3, 5, 8, 10, 11, 13) were infected before delivery at the end of the 3rd trimester. 42.8% of these patients (1, 5, 13) developed mild gastrointestinal symptoms (diarrhoea) and 14.3% (patient 10) had signs of upper respiratory tract infection without the need of respiratory support. 28.5% (patient 8 and 11) did not contract COVID-19 infection nor developed clinical complications. Additionally, case 5 demonstrated lower levels of thrombocytes. The complications in these cases are in agreement with the study conducted by Zhu et al, where he noted thrombocytopenia, respiratory distress, fever, and gastrointestinal complications present in neonates born to COVID-19 positive mothers (29). We suppose faecal oral and/or aerosol route of transmission due to the lack of adequate hygiene preventive practices (30). Case 3 manifested with prematurity complications (prenatal asphyxia) and imaging results showed respiratory distress syndrome on both lungs of the 3rd and 4th degree, which strengthens the hypothesis of the involvement of the COVID-19 infection in the more pronounced clinical presentation. However, we cannot confirm its relation to prenatal COVID-19 infection as the possible activator since the foetus also presented with oligohydramnios and mother with gestational diabetes mellitus on diet (31, 32). 3rd trimester COVID-19 positivity and caesarean section could pose as a risk for foetal hypoxia in cases 3 and 13, as it was evidenced by previously mentioned studies, a COVID-19 infection during pregnancy severely affects the placenta's vascularity, posing a great risk for foetal development and thriving capability.

Five newborns (2, 4, 7, 9, 14) were in contact with a positive person while in the hospital. The newborn in case 2 was intubated after birth, even though the mother and newborn tested negative for COVID-19. This could be attributed to the newborn's lung immaturity and low gestational age. Cases 4, 7, 9 and 14 ended up contracting the viral infection. Cases 7 and 4 developed mild gastrointestinal symptoms (diarrhoea). Additionally, along with case 13, cases 4 and 7 were delivered via caesarean section, a procedure which, as postulated by Laubereau et al, oftentimes along with prematurity impacts the normal colonisation of the child's gut microbiome (33). This could have been exacerbated by the COVID-19 infection, leading to gastrointestinal symptoms.

However, case 4 was diagnosed with congenital malformation of the gastrointestinal tract, which does not allow us to attribute these symptoms solely to the COVID-19 infection. Case 14 presented with no COVID-19 clinical complications, while case 9 developed upper respiratory symptoms.

Two cases (6 and 12) contracted COVID-19 prior to hospitalisation. In case 6, all family members developed symptomatic COVID-19 infection and the newborn presented with upper respiratory symptoms but remained stable. In case 12, the infant was admitted for a blood transfusion of erythrocytes due to anaemia, during triage COVID-19 infection was detected hence being transferred to the specialised COVID-19 unit. The infant and mother were asymptomatic for COVID-19 infection. The infant did not manifest any clinical COVID-19 infection complications.

The findings in preterm newborns further demonstrated no correlation between positive prenatal history and adverse clinical course as all preterm newborns' cases with (n=2) and without positive prenatal history (n=2) developed clinical complications. This however was different in term neonates, as in cases where no pathological findings during pregnancy were reported, COVID-19 infected newborns displayed a stable clinical course. Conversely, when congenital defects, infections, gestational diabetes mellitus, arterial hypertension, and drug-dependency were proven during the pregnancy in cases 5, 12, 7, and 14 respectively, the newborns infected with COVID-19 displayed a more eventful clinical course, usually manifesting itself throughout several systems of organs indicating a correlation between pathological findings during pregnancy and development of clinical complications. This confirms the findings of previously mentioned studies, which affirm that just as in adults, newborns with co-morbidities are at a higher risk for complications.

The complications in these cases portray a similar course in comparison to the review conducted by Bulbul et al, with findings mentioning foetal distress, respiratory failure, and gastrointestinal complications present in COVID-19 neonates (34). This further indicates that these complications, as shown, aren't limited to the respiratory system and as such require a multidisciplinary approach and care to minimise disease severity and mortality as well as isolate the newborns from the first day of life and stop the spread of infection.

Due to its high transmissibility and rapid spread, the COVID-19 pandemic had a great impact on the healthcare systems of all countries. This is highly attributed to lack of readily available health resources and prompt response. With pandemic restrictions as a means to curb the spread of the virus, there has been a decline in the application of essential neonatal care practices (skin to skin contact, newborn follow up), subsequently contributing to adverse neonatal health and neonatal mortality. This could pose a challenge for optimal and specific neonatal care.

Various surveys and observational studies noted that despite preventive measures controlling the spread of the virus, they set limitations on important practices such as skin to skin contact, newborn follow up, and institution delivery which may further impact the neonate's quality of life.

Conclusion

Although most newborns, when infected, seem to display an asymptomatic to mild course of COVID-19 infection, this clinical course suddenly suffers a drastic change when preterm births, comorbidities and maternal infection during pregnancy come into play. As such, it is imperative to adequately assess the history course of events which occurred before the infection as it may allow for a better responsive measure from neonatal care staff. Moreover, although COVID-19 virus transmissibility or its protection through breastmilk was not proven, guidelines and several studies confirm that the benefits of breastfeeding highly outweigh the risks (35).

COVID-19, like any other infection, can exacerbate previous complications in newborns and given that little is known regarding the impact in neonatal health, long term follow-up to evaluate future repercussions and cooperation between pneumologists, gastroenterologists, paediatricians, and immunologists in specialised centres is imperative to ensure adequate quality of life.

Furthermore, it is important to implement adequate neonatal practices for early detection of illnesses especially in relation to COVID-19 which will subsequently allow early intervention and reduce neonatal mortality.

Despite its impact on a global scale, low- and middle-income countries faced more adverse changes within healthcare systems, in comparison to developed countries more so within neonatal care (36). This further indicates the necessity of not only promoting education amongst parents and healthcare staff and implementing measures which allow a safe practice of essential neonatal care practices, but also shows the need of global cooperation to reduce neonatal mortality.

Future challenges for all countries include the implementation of higher hygiene standards, prevention of spreading, more sensitive tests to use in the first day of life. Although the Covid-19 pandemic brought about challenges, it provided new opportunities to optimise and improve neonatal healthcare.

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