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Original research article

CLINICAL SPECTRUM OF DISEASE IN NEONATES BORN TO MOTHERS WITH COVID-19 IN A TERTIARY CARE HOSPITAL

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Abstract: *COVID-19 infection during pregnancy presents potential risks to neonates, yet the full clinical spectrum in newborns born to COVID-19-positive mothers remains under investigation. Understanding the clinical outcomes in these neonates is essential for guiding management and care.* ***Objective:*** *To study the spectrum of clinical presentations in neonates born to mothers who tested positive for COVID-19.* ***Methods****: This prospective cross-sectional study was conducted at the Department of Pediatrics, Shifa International Hospital, from April 1, 2020, to April 30, 2021. All neonates born to COVID-19-positive mothers were included in the study and followed daily during their hospital stay. After obtaining parental consent, nasopharyngeal swabs were taken from the neonates for SARS-CoV-2 PCR testing at 24-48 hours of age. After discharge, follow-up calls were made between days 7-14. Data were entered into a predesigned proforma and analyzed using SPSS version 23.* ***Results:*** *A total of 82 neonates were enrolled. Approximately half were born at term, with a mean weight of >2500 grams. Forty-five neonates (53%) underwent SARS-CoV-2 PCR testing within 48 hours of age; all were negative. Sixty-one neonates (74%) were shifted to the mother's care, while 25% required admission to the neonatal intensive care unit (NICU). The most common reasons for NICU admission included respiratory distress (15%), prematurity (6%), and lethargy (5%). Radiological findings included ground-glass appearance in five neonates (6%) and lung consolidation or infiltrates in two (3%). Hematological and biochemical abnormalities included leukocytosis (7%), leucopenia (3.6%), anemia (1.2%), metabolic acidosis (6%), and respiratory acidosis (3.6%). Most neonates (78.6%) received routine care and were fed breast milk. Fourteen neonates (16.7%) required respiratory support, with 13% needing mechanical ventilation. Complications included pneumonia (7%) and respiratory failure (9%). NICU stay varied, with 11 neonates (13%) staying less than 48 hours and 10 (12%) requiring a more extended stay. Four neonates (5%) died due to multiorgan complications.* ***Conclusion:*** *The majority of neonates born to COVID-19-positive mothers remained asymptomatic. However, symptomatic neonates were at risk of serious complications, requiring close monitoring and management, particularly in those with additional risk factors.*

Keywords: COVID-19 infection, fetal-maternal transmission, newborns, well baby.

Introduction

Late in December 2019, a novel -coronavirus called SARS-CoV-2, which causes viral pneumonia, emerged in Wuhan, China (1, 2). The World Health Organization will soon proclaim the 2019 coronavirus pandemic (COVID-19) a worldwide health emergency (3). Studies from previous coronavirus outbreaks suggest adverse perinatal and neonatal outcomes (4). However, the majority of infants and children with COVID-19 are asymptomatic or mildly symptomatic and often remain undiagnosed4. Although most reported cases did not show evidence of maternal-fetal transmission of the SARS-CoV-2 virus (5), it cannot entirely be excluded. There have been instances where neonates with respiratory distress have to be admitted to NICUs. The other conditions warranting admissions were lymphopenia, thrombocytopenia, deranged Liver Function Tests, disseminated intravascular coagulation, and multiorgan failure. Transient hematological disturbances and abnormal radiological findings are also noted in some of the asymptomatic newborns. (5-7). In a systematic review of a total number of 108 pregnancies, only one neonate got a positive qRT-PCR 36 hours after birth despite being isolated from the mother. (8) This study evaluated the clinical presentation and disease spectrum in neonates whose mothers had COVID-19.

Thus, this research aims to study the spectrum of clinical presentation in neonates born to COVID-19-positive mothers.

Methodology

It was a prospective cross-sectional study. All the neonates born to mothers with COVID-19 (from 1st April 2020 to 30th April 2021) were enrolled in the study. Well, babies were transferred with their mothers, and sick newborns were admitted to the Neonatal Intensive Care Unit after initial evaluation by the attending doctor. They were followed daily during a hospital stay. Their clinical symptoms, signs, and hematological, biochemical, and radiological investigations were noted. The complications during the hospital stay and outcome were recorded. A nasopharyngeal swab for SARS-CoV-2 PCR was sent at 24-48 hours of age. After discharge from the hospital, babies were followed between days 7 and 14 by a telephonic call. All the data was entered in a predesigned Performa. SPSS version 23 was used to analyze the data.

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Results

A total of 82 neonates were enrolled in the study. About half were born at term with a weight of >2500 grams. (Table 1) Three (3.6%) mothers had respiratory symptoms at delivery. Five (6%) had a history of prolonged rupture of membranes (>18 hours). None of the mothers had a history of diabetes, hypertension, fever, urinary tract infection, chorioamnionitis, or respiratory symptoms in the mother. Forty-five (53%) newborns had SARS-CoV-2 PCR performed within 48 hours of age, and all turned negative.
Sixty-one (72%) were shifted with their mothers. Twenty-one (25%) admissions were made to the Neonatal Intensive Care Unit (NICU), including thirteen (15%) admissions to level III NICU and eight (9%) to level II NICU. Table 2 summarizes common problems and hematological, biochemical, and radiological abnormalities.
The majority, 66 (78.6%), received routine newborn care. Fourteen (16%) required respiratory support, including mechanical ventilation (13%), nasal cannula oxygen (2%), and CPAP (1%). Common complications during hospital stay included pneumonia (7%), respiratory failure (9%), meningitis (4.8%), grade IV IVH, pneumothorax, and renal failure (1% each).
Thirteen (15.5%) received antibiotics, 5 (6%) needed inotropes, and 5 (6%) received blood product transfusion. Six (7.1%) were initially kept NPO and received IV fluids, and the rest of them received breastfeeding 66 (78.6%), Expressed Breast Milk 3 (3.6%), and formula milk 6 (7.1%). During the hospital stay, 6 (7%) developed pneumonia, 8 (9.5%) had respiratory failure, 4 (4.8%) had shock and meningitis, and grade IV IVH, pneumothorax, and renal failure were found in 1 (1%) each.
Eleven (13%) stayed in NICU for < 48 hours, 5 (6%) stayed for 2 to 7 days, and 5 (6%) stayed for > seven days. Four (5%) died of multiorgan complications.
Seventy-eight (95%) went home in stable condition, and 4 (4.8%) of the sick neonate expired.

Table 1: Gestational Age and Birth Weight of babies born to mothers with COVID-19

	Frequency	Percentage
Gestational Age (weeks)		
< 28	5	6
28-31	2	2.4
32-34	6	7.1
35-37	16	19
>37	55	65.5
Birth weight (grams)		
< 1000	4	4.8
1000-1500	3	3.6
1500 – 2500	20	23.8
>2500	52	61.9

Table 2: Clinical problems, laboratory and radiological abnormalities

	Frequency	Percentage
Clinical problems		
Respiratory Distress	12	15
Prematurity	5	6
Lethargy	4	5
Transient Tachypnea of Newborn	2	2
Hypoglycaemia	2	2
Haematological abnormalities		
Leucocytosis	6	7
Leukopenia	3	3
Anemia	1	1
Biochemical abnormalities		
Metabolic Acid ok	5	6
Respiratory Acidosis	3	3
Radiological abnormalities		
Ground Glass Appearance	5	6
Consolidation	2	2
Lung Collapse	2	2

Gestational Age at birth	Observed N	Expected N	Residual
28-31 weeks	1	14.3	-13.3
32-34 weeks	3	14.3	-11.3
35-37 weeks	11	14.3	-3.3
>37 weeks	42	14.3	27.8
Total	57		

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Diagnosis at Admission	Observed N	Expected N	Residual
Sepsis	4	1.8	2.2
Prematurity	1	1.8	-.8
RDS	1	1.8	-.8
TTN	2	1.8	.2
IDM	1	1.8	-.8
Total	9		

Discussion

For over two years now, 489 million individuals worldwide have been infected by COVID-19, and over 6 million have died as a result. (9) even though a lot of research has been done on various aspects of the disease, there are plenty of facts that remain unknown. The spectrum of disease in pregnancy and its relationship with outcome remains unknown. It has been documented in some studies that risk of severe disease is higher in pregnant women. Vertical transmission has been documented, but severe neonatal disease is uncommon. According to specific systematic reviews, the rate of preterm birth among SARS CoV-2 patients is much higher than that of the general pregnant population, (10-12) With regard to pregnancy, multiple cases of loss of fetus and delivering preterm due to fetal distress have been reported in SARS-CoV 2 positive pregnant mothers. (13-15) Mothers with COVID-19 are advised to breastfeed and have skin-to-skin contact but should observe standard contact precautions and use personal protective equipment (16).

The spectrum of disease in neonates born to mothers with COVID-19 has been studied by researchers worldwide. Verdhelli et al reported that out of 793 babies born to COVID-19 positive mothers, 629 neonates (79%) were tested after birth. Of the 629 neonates, just 35 (5.5%) were positive for COVID-19. Of the 35 positive neonates, 14 (40%) were symptomatic. 60 (7.6%) neonates required respiratory support that included mechanical ventilation in 14 (1.8%), non-invasive ventilation in 25 (3%), and nasal oxygen in 21 (2.6%). Like our study, this research concludes that neonatal disease is generally mild, and vertical transmission is the possible transmission route in newborns (17).

A retrospective cohort study conducted at Brookdale Hospital Medical Center in New York City from March to May 2020 showed that the babies of COVID-19-positive mothers were three times more prone to have low oxygen saturations than newborns of negative mothers. Additionally, babies of SARS-CoV 2-positive mothers were four times more prone to poor feeding as compared to newborns of COVID-19-negative mothers. Lastly, the babies of SARS-CoV-2-positive mothers were ten times more prone to be symptomatic at the 2-week follow-up. It was also recommended that the nasopharyngeal swab of the newborn should be taken at least 24 hours after birth, and the baby must be observed for any development of any symptom 14 days after birth (18). However, in our study, about two-thirds of babies were transferred with their mothers, had an uneventful hospital stay, and remained well on follow-up assessments.

As in our study, hematological abnormalities have also been noted by Sagheb et al. in a case report of two neonates born to mothers with COVID-19 pneumonia. Both showed low lymphocyte count with high LDH levels and low calcium levels in the blood. They were febrile for many days and were not responding to antibiotics, and other potential causes were ruled out. (19) Similar findings were also observed by researchers in Wuhan, where three out of 33 babies born to moms with COVID-19 tested positive. The most common symptom was breathing difficulty, followed by cyanosis and feed intolerance. All of them had peripheral blood leukocytosis, and the chest x-ray was suggestive of pneumonia. (20)

Shwartz DA analyzed 38 pregnant mothers with COVID-19 and their newborns to assess for maternal-fetal transmission of SARS-COV-2. Neonatal RT-PCR for SARS-COV-2 was found to be negative in 28 of them.

Ten among them developed respiratory distress requiring hospitalization. There was one baby who died of shock and multi-organ failure. (21) In our study, SARS-COV-2 PCR was found negative in all of the 45 newborns who were tested.

A similar study was done by Liu W et al. who assessed the clinical features of 19 neonates born to mothers with COVID-19. These mothers were either clinically diagnosed or confirmed through laboratory to have COVID-19. SARS-CoV-2 was negative in all newborns' throat swabs, feces, and urine. None of the babies developed any clinical or radiological manifestations of the disease. No transmission from mother to child or perinatal complications were noted. (22) Similarly, in a systematic review of 205 infants born to COVID-19 mothers by Bewire GM et al., only 6.3% tested positive. It was concluded that there is a low risk of vertical transmission, and the antibodies against SARS-CoV-2 can be detected in 90% of vertically exposed but otherwise clinically healthy infants. (23)

In contrast to our results, in a retrospective analysis of 524 neonates from India born to mothers who had COVID-19, 6.3% tested positive. These positive-tested neonates were at a higher risk of developing neonatal sepsis and death as compared to non-infected newborns. (24) Similar findings were reported by Mirbeyk et al. in a systemic review of 302 pregnant women with COVID-19. About 5 % tested positive on nasopharyngeal swab testing. Breast milk, placenta, amniotic fluid, and umbilical cord all tested negative except for one amniotic fluid sample. (25)

A multicenter study by the Turkish Neonatal Society in 34 NICUs in Turkey evaluated 125 pregnant women who had yielded a positive RT-PCR test. About 26 % delivered preterm, and 12.8% were low birth weight. Four (3%) of newborns had positive RT-PCR. (26)

Alzamora et al. report one of the earliest reported positive PCR in 16-hour-old babies born to a mother with COVID-19 pneumonia, leading to respiratory failure and requiring mechanical ventilation. (27)

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In our study, 34.5% of babies were delivered preterm (<37 weeks of gestation). Similar findings were reported by Khedmat et al. (28) and Luna et al. (29). Data from the Spanish Society of Neonatology Registry also shows that about 77% of these babies received maternal milk. (29) In our study, more than three-fourths of the babies received mother's milk. In a similar study, mother's milk and skin-to-skin contact safe by Verdheli et al., if performed with masking and appropriate hygienic precautions of the hand and the breast. (17) Zimmermann et al. found that common complications in babies born to COVID-19-positive mothers were respiratory distress syndrome or pneumonia (18%), disseminated intravascular coagulation (3%), and asphyxia (2%). (30) In our study, 7% of babies had pneumonia, 9.5% developed respiratory failure, and 4.8% had shock and meningitis.

Conclusion

The majority of neonates born to mothers who happen to be positive for COVID-19 usually remain asymptomatic. Symptomatic patients can have complications; thus, close observation and monitoring are needed in neonates with additional risk factors.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
It is approved by the department concerned. (IRBEC-SIHISB-232-21)
Consent for publication
Approved
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Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

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