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Experience of COVID-19 infections in neonates in tertiary care centre in north karnataka, India: A prospective cohort study.

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Abstract

Introduction: In neonates, COVID-19 pandemic is emerging as a new challenge to pediatricians. The risk of neonatal transmission from mother during the perinatal and postnatal period is less understood. Hence, we aimed to identify potential risk factors associated with transmission of neonates born to mothers positive for SARS-CoV-2 at time of delivery and to assess the outcome and thereby elucidate the best infection control clinical practices among mother neonate with COVID-19 infection.
Methods: This prospective observational cohort study was conducted during May to October 2020; where all neonates born to mothers positive for SARS-CoV-2 at the time of delivery were enrolled. During the postnatal period, mother and neonate were kept in isolation ward together and initiated breastfeeding after ensuring adequate hand and respiratory hygiene except those requiring NICU admission. At 12-72 hours of life, neonate's samples (nasopharyngeal swabs) for SARS-CoV-2 were collected for real-time PCR. Data regarding maternal and neonatal baseline characteristics and clinical presentation as well as infection control practices in the hospital was documented in structured proforma.
Results: During the study period, 26 (3.6%) mothers tested positive for SARS-CoV-2 of 720 deliveries; Among 28 neonates delivered, 25 neonates were shifted with mother in the isolation ward whereas 3 premature neonate's required NICU admission. Of the 28 neonates, 20 (71%) were born at term, the median gestational age was 37.6 weeks, 17 (61%) were female and 19 (68%) were born by caesarean section. 20 (71%) were breast fed whereas 8 (29%) of 28 neonates were formula fed. All neonates delivered to SARS-CoV-2 positive mothers tested negative for SARS-CoV-2 by rtPCR at 12-72 hours of life.
Conclusion: Mother and primary care providers should be educated and trained about standard respiratory and hand hygiene practices to avoid perinatal and postnatal transmission. Breastfeeding and rooming-in in isolation ward are safe procedures when paired with effective and regular parental education of neonate infection protective strategies.

Keywords: SARS-CoV-2, COVID-19, Neonate, Horizontal transmission.

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Introduction

COVID 19 pandemic has resulted in considerable adverse outcomes in mother and child healths which are yet to be determined [1-3]. Standardized protocols and data regarding the appropriate management of the mother and neonate with SARS-CoV-2 infection need to be established.

In utero transmission of SARS-CoV-2 from mother to fetus is anticipated to be low. Vertical transmission of SARS CoV 2 in neonates is suspected if the mother is positive for SARS-CoV-2 between 14 days prior to birth and 2 days after the birth and the virus is detected in any of the following: 1. Swab of the neonatal respiratory tract in the first 24 hours of life. 2. Amniotic fluid 3. Umbilical cord blood 4. A neonatal blood sample in the first 24 hours of life [4]. Risk of perinatal and postnatal transmission, especially when breastfeeding and rooming in are also less known [5]. Recommendations for management strategies of mother and neonate with COVID 19 vary among different countries and academic bodies like AAP, IAP, FOGSI, NNF due to lack of clinical data [6-12].

This study was done to identify potential risk factors associated with transmission of neonates born to mothers positive for SARS-CoV-2 at time of delivery and to assess the outcome and thereby elucidate the best infection control clinical practices among mother neonate with COVID 19 infection.

Methods

This prospective observational cohort study was conducted between May and October 2020, at Shri B M Patil Medical College Hospital and Research Center, Vijayapura. Inclusion Criteria: All neonates born to mothers who tested positive for

SARS-CoV-2 from a nasopharyngeal swab sample at the time of delivery. All pregnant women presenting in labour were screened for SARS-CoV-2 from a nasopharyngeal swab sample in our labour units from May 2020. Neonates were tested for SARS-CoV-2 by rtPCR on a nasopharyngeal swab sample at 12-72 hours of life and as indicated at subsequent visits. This study was approved by the Institutional Ethical Board.

In our centre, SARS-CoV-2 testing was done by use of real-time PCR (rtPCR; TRUPCR (3B BlackBio Biotech India Limited, Govindpura, and Bhopal, India) with a turnaround time of 24-36 hours from specimen collection to result reporting. Data collected in predefined structured proforma included maternal and neonatal baseline characteristics, clinical presentation at time of delivery, during hospitalization and rtPCR testing reports. Neonates were examined for fever, respiratory distress in the form of hurried breathing and chest in drawing, lethargy, decreased feed intake and feeding intolerance, cough, irritability, rash, vomiting and loose stools. Mothers were examined during hospital stay for symptoms of fever, cough, and anosmia, shortness of breath, sore throat, rhinorrhoea, myalgia, vomiting and diarrhoea.

In our institute mothers who were positive for SARS-CoV-2 could practice skin- to-skin care and breastfeed in the labour room and postnatal ward using safety measures such as donning a surgical mask (respiratory hygiene) and hand hygiene and breast cleansing. All neonates were kept in a bassinet at 6 feet distance from mother. All mothers were encouraged and educated about the importance of breastfeeding their neonate while in the hospital and after being discharged home. Mothers of neonates admitted to the NICU were allowed to visit the neonate once a day with appropriate respiratory and hand hygiene after being afebrile for at least 72 hours.

Statistical Analysis

Data were represented as proportions for categorical variables and median and simple ranges for continuous variables. Descriptive analysis was done with results on SPSS 23 software.

Results

During the study period, 26 (3.6%) mothers tested positive for SARS-CoV-2 of 720 deliveries; Among 28 neonates delivered, 25 neonates were shifted with mother in the isolation ward whereas 3 premature neonate's required NICU admission. Of the 28 neonates, 20 (71%) were born at term, the median gestational age was 37.6 weeks (range 32-42), 17 (61%) were female and 19 (68%) were born by caesarean section. 20 (71%) were breast fed whereas 8 (29%) of 28 neonates were formula fed. All neonates delivered to SARS-CoV-2 positive mothers tested negative for SARS-CoV-2 by rtPCR at 12-72 hours of life. The most common indication for caesarean sections was Cardio Tocographic abnormalities (80%). Mode of delivery was not affected by SARS-CoV-2 test results.

Among 26 mothers enrolled, 20 (77%) were asymptomatic and 06 (23%) were symptomatic. Of the 6 symptomatic mothers within 7 post natal days, 4 (67%) had cough and 3 (50%) had fever. Of the 28 neonates enrolled, 25 (89%) neonates were kept with the mothers in isolation postnatal ward whereas 3 (11%) required NICU admission due to prematurity and respiratory distress. Of these 25 neonates who were roomed in with mothers, three required 2 days of phototherapy for neonatal hyperbilirubinemia and two shifted to NICU for respiratory distress and feed intolerance. Of the 5 neonates admitted to the NICU, four had a length of stay of 7-10 days where as one neonate had a length of stay of 14 days due to thrombosis and gangrene of right foot.

Among 28 neonates, 20 (71%) were breast fed and the remaining 8 (29%) were formula fed. All neonates delivered to SARS-CoV-2 positive mothers tested negative for SARS-CoV-2 by rtPCR (nasopharyngeal swab) at 12-72 hours of life. 23 (82%) of 28 neonates were discharged home by 4-6 days of life and the remaining five (18%) remained hospitalized in NICU for 7-10 days. Median length of hospital stay for all 28 neonates was 4 days (range 3-10) (Table 1).

S. No	Neonatal Baseline Characteristics	Study Group n=28 (%)
1.	Sex	
	Female	17 (61%)
	Male	11 (39%)
2.	Mode of Delivery	
	Normal Vaginal Delivery	09 (32%)
	Cesarean Section	19 (68%)
3.	Gestational Age	
	Preterm (32-37 weeks)	08 (29%)
	Term (37-42weeks)	20 (71%)
4.	Birth weight (gms)	
	1000-1500	03 (11%)
	1501-2500	11 (39%)
	2500-3500	14 (50%)
5.	Admission of Neonate	
	Isolation Postnatal ward	20 (71%)
	Phototherapy	03 (11%)
	NICU admission	05 (18%)
6.	Feeding History	
	Exclusive Breast Feeding	20 (71%)
	Formula Feeds	8 (29%)
7.	Length of Hospital Stay	
	4-6 days	23 (82%)
	7-14 days	05 (18%)

8.	rtPCR for SARS-COV-2 (12-72 hours of life)	
	Negative	28 (100%)
	Positive	00 (00)

Table 1. Neonates baseline and demographic characteristics.

After 2 weeks of hospitalization, all 28 neonates visited for follow up. 27 (96%) were asymptomatic where as one neonate (4%) was readmitted because of pneumonia, for whom repeat rtPCR upon admission at day 20 of life was positive. Neonate was admitted in isolation NICU ward and started on HHHFNC respiratory support with maintenance intravenous fluids and antibiotics as per unit protocol. Chest X ray was s/o features of pneumonia with elevated CRP and leucocytosis with neutrophil predominance. Prothrombin time and Activated Partial thromoplastin time both were prolonged with elevated inflammatory markers (CRP/Ferritin/Lactate Dehydrogenase) with elevated d-dimer. CRP was further elevated after day 3 of hospitalization; neonate's antibiotics were graded up to second line antibiotics as per unit protocol and a decision was made to add IV IG because of clinical illness with elevated inflammatory markers. 2 D Echo was normal (Table 2).

SARS-CoV-2 Positive Neonate Characteristics	**Observations**
Gestational age	37 weeks
Age at presentation	20 day of life
Gender	Male
Mode of delivery	Caesarian Delivery
Resuscitation at delivery	Cried at birth
APGARS (1 & 5 min)	8, 9
Vital signs on admission	
Temperature (axillary)	100.8°F
Heart rate	180/min
Respiratory rate	76/min
Blood pressure	78/42 mmHg (Mean 50 mmHg)
Oxygen saturation	89% (Preductal)
Presentation	Fever, Respiratory Distress.
Laboratory values	
Complete blood count	
Hemoglobin (g/dL)	11.7
Hematocrit	34.7
White blood cells (µL)	18,670
Neutrophils (%)	69
Lymphocytes (%)	27
Platelets (µL)	4,18,000
C Reactive Protein(mg/dL)	Positive (23.6)
Blood Culture	Negative
Urine analysis	Negative
Urine culture	Negative
Serum Ferritin(ng/ml)	303
D Dimer (ng/ml)DDU	773
Lactate Dehydrogenase	870
PT/INR	22/1.8
Prothrombin Index	92.74%
APTT	38
Chest radiography	Features of Pneumonia
Echocardiogram	Normal
RT PCR for SARS-CoV-2	Detected Positive
Probable mode of transmission	Horizontal
Outcome	Improved

Table 2. SARS-CoV-2 positive neonate characteristics.

On day 7 of hospitalization, neonate was hemodynamically stable on HHHFNC and then weaned to room air. Feeds were initiated on day 3 of hospitalization and were gradually graded up to reach full feeds. The antibiotics were discontinued when the bacterial cultures did not show any growth seven days later. After 10 days of hospitalization, the neonate was discharged with parental education and training on hand hygiene and respiratory hygiene to be followed at home.

Discussion

SARS-CoV-2, a single-stranded RNA virus belongs to the genus Betacoronavirus and is transmitted primarily through respiratory droplets and contact across humans [4]. This is the largest cohort of neonates born to mothers who tested positive for SARS-CoV-2 at time of delivery and who were subsequently followed up clinically up to 2nd week-3rd week of life in North Karnataka, India as per our information. In our study, all neonates tested negative for SARS-CoV-2 virus in the immediate postnatal period (12-72 hours) detected by a rtPCR (nasopharyngeal swab). All neonates were asymptomatic during hospitalization in the isolation postnatal ward. One neonate presented at day 20 of life at follow up clinic with history of hurried breathing, chest in drawing and fever. This finding suggests that, risk of perinatal and postnatal transmission is low if parents and primary care providers are educated with strict infection control practices.

Zeng et al., Zamaniyan et al., Kirtsman et al. [13-15] studies, have reported positively tested neonates for SARS-CoV-2 within 48 hours of life. However, in none of these case reports, serial rtPCR testing past the first week of life was done [5]. 11 case reports of neonatal COVID-19 detected by SARS-CoV-2 PCR [13,16-18] have been documented till date. Six of case cohorts reported presented within three days of life whereas the remaining presented between day five and twenty eight days of life. In our study, neonate presented at 20th day of life and was tested positive for SARS-CoV-2 upon readmission. In majority

of neonate's cohort, fever is the main presenting symptom of COVID-19 (66%) with favorable prognosis as described [19-22]. In our case study, we suspected COVID-19 in this neonate in light of pandemic where the presenting complaint was respiratory distress along with fever.

In neonates of COVID 19, most common laboratory abnormalities seen include lymphocytopenia, thrombocytopenia, leukopenia, and elevated inflammatory markers [23]. Laboratory abnormalities of neonatal COVID-19 in our study were suggestive of leucocytosis followed by leucopenia with elevated CRP, Serum Ferritin, D Dimer and Lactate Dehydrogenase.

Dumpa et al. [24] postulated that neonatal infection due to COVID 19 infection can be early-onset neonatal infection (first three days of life) or late-onset neonatal infection (4-28 days of life). Our study suits into late onset category probably due to horizontal transmission. There is no evidence to suggest that this infection can be transmitted through breast milk. The majority of the cases reported are due to horizontal transmission as reported previously by Chen H et al. except few cohort studies [1].

To reduce perinatal transmission risk, American Academy of Pediatrics, recommends isolation of the neonates immediately after delivery, formula or expressed breast milk feeding with no contact with the mother for 14 days or at least 7 days from onset of symptoms [9]. WHO advocates for the promotion of breastfeeding and the initial mother–neonate relationship immediately after childbirth [11]. The established advantages of early mother–neonate bonding and breastfeeding should be prioritized during the perinatal period if the risks are deemed low.

In our center, all neonates were allowed to room in with mothers and breast feed except those admitted in NICU. (Neonate was kept 6 feet apart from their mother with attendee unless feeding). All mothers were trained and educated about the importance of following appropriate infection control precautions such as frequent hand hygiene, use of surgical masks at all times, and breast cleansing.

In our center, most neonates were discharged within 4-6 days of life to home, where in mother was the primary care provider and she continued breastfeeding. In our experience, we have shown that rooming in with the mother and breastfeeding are safe if mother and primary care providers are trained with adequate parental education of safe infection control practices similar to case series published in the literature till date.

However, comparable to our center data, there is a case report of neonate who became symptomatic with respiratory symptoms after hospital discharge from Coronado Munoz and colleagues and eventually tested positive for SARS-CoV-2. In our study, contact tracing of SARS-CoV-2 positive neonate showed that one of family members had clinical COVID-19 signs [22]. This observation further establishes the need for careful precautions to prevent horizontal spread of infection.

Conclusion

Currently, data suggesting the possibility of vertical transmission is unclear except in few case cohorts. The most common mode of neonatal transmission of COVID-19 seems to be horizontal while vertical transmission is likely in early-onset neonatal COVID 19 infections. Literature on serological testing from bigger cohorts will give more evidence into the transmission patterns including antenatal and vertical transmissions. Fever is one of the main presenting symptoms of neonatal COVID-19, followed by respiratory distress. Our data suggest that perinatal and post natal transmission is unlikely to occur if mother and primary care providers practice standard respiratory and hand hygiene practices and that rooming in and breastfeeding are safe procedures when combined with effective and regular parental education of neonate infection prevention strategies.

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