



A STUDY ON CLINICAL SPECTRUM, OUTCOME AND FOLLOW UP OF INFANTS BORN TO COVID-19 POSITIVE MOTHERS IN A TERTIARY CARE HOSPITAL: A PROSPECTIVE COHORT STUDY

Paediatrics

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ABSTRACT

INTRODUCTION: Covid-19 disease caused by SARS-CoV-2 which started as an outbreak of atypical pneumonia has affected all the age groups. Elderly people with co-morbidities are more likely to develop a severe form of disease. The potential harm of the disease in neonates remains unknown. Although neonates acquire infection through horizontal transmission, recent literature suggests an emergence of vertical transmission. So, the following study was undertaken to know the clinical spectrum, outcomes and follow up of neonates born to Covid-19 infected mothers. **AIMS AND OBJECTIVES:** To study the clinical spectrum, outcomes and follow up of newborn babies born to COVID-19 positive mothers. **MATERIALS AND METHODS:** A prospective observational study was done in 100 babies born to Covid-19 positive mothers. All the babies were tested for Covid-19 infection with Rapid Diagnostic Kit Test (RDT) within 24 hours, at the time of discharge or at 72 hours and were followed up to 14 weeks. **RESULTS:** Out of 100 neonates 82% were term babies (≥ 37 week) and 18% were preterm babies (< 37 weeks). Only one (1%) was tested positive for Covid-19. None of them showed symptoms. All babies tested negative at the time of discharge or 72 hours. Follow up was done only in 63 neonates at 7-14 days, 6, 10, 14 weeks of age and none of them developed any symptoms and signs. All had normal development and completed their vaccination as per schedule. **CONCLUSION:** In the study only 1% of the babies were positive for Covid-19 infection without any clinical manifestations which suggests that the chance of vertical transmission in neonates from Covid-19 positive mother is very low if strict Covid-19 protocols followed.

KEYWORDS

COVID-19, SARS-CoV-2, RDT(Rapid Diagnostic Test), Preterm, Infants, Neonates.

INTRODUCTION:

Corona virus disease-19 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which started as an outbreak of atypical pneumonia in December 2019, has since become a global pandemic^[1].

All age groups are susceptible, but people with co-morbidities or the elderly are more likely to develop a severe form of the disease. Although children seem to have less severe clinical symptoms when infected^[2], the potential harm of this novel disease remains largely unknown in neonates, especially in preterm infants. Neonates represent a vulnerable population, in which we have limited knowledge of the natural history, optimal management, and outcomes. An important knowledge gap in neonatal literature exists regarding the mode of transmission of SARS-CoV-2 infection in neonates. Many studies have suggested a horizontal mode, with frequent detection in the first 2 weeks of life^[3-5]. However, substantial evidence is emerging on vertical transmission in neonates^[6-8]. First, such a case report suggested transplacental passage of the virus from an infected mother in the third trimester as a proposed mechanism for detection of SARS-CoV-2 antigen by reverse transcriptase-polymerase chain reaction (RT-PCR) in maternal and neonatal tissues^[8]. Current understanding on vertical transmission is based on detection of SARS-CoV-2 antigen in neonates and in products of conception such as placenta, amniotic fluid and fetal membranes^[9], interleukin-6 in cord blood and neonatal samples^[10,11] and IgG and IgM antibodies in neonates^[10-12].

Laboratory investigations in neonates with COVID-19 were often normal, though leucopenia or leukocytosis, lymphopenia, and raised lactate dehydrogenase (LDH) and creatine kinase (CK) have been reported^[13,14]. A large review on neonatal COVID-19 described lymphopenia (14.4%) and transaminitis (4.1%) and raised inflammatory markers (C-reactive protein) (15.5%)^[17]. In SARS-CoV-2-infected neonates, pneumonia has been documented in few case reports^[15,16]. A recent review detected an interstitial-alveolar pattern in chest X-ray or lung ultrasound and ground-glass opacities in computed tomography scans^[17].

As the pandemic continues, there is a growing body of evidence on

SARS-CoV-2 infection, but most data originates from the adult population. Current scientific literature in neonates comprises of scattered case reports, case series, and retrospective studies from across the globe^[13-16], with a striking lack of evidence from the Indian subcontinent which has a considerable share of COVID-19 cases. Hence the study was undertaken to know, the clinical characteristics, outcomes and follow-up of SARS-CoV-2-infected neonates from high burden settings are described, which may contribute to the evolving literature in neonates.

Aims and Objectives:

To study the clinical manifestations, outcome and follow up of a neonates born to COVID-19 positive mothers.

Materials and methods:

Type of study: An Observational study.

Study Design: Prospective cohort study design.

Study Area: Study was conducted in ASRAM medical college and hospital, Eluru, West Godavari District.

Study Period: May 2020 to December 2020.

Study Population:

Neonates born to COVID 19 positive mothers from May 2020 to December 2020 were included in analysis. The hospital is a teaching and academic medical college and tertiary referral center for neonatal care. Nearly 380 covid-19 deliveries done in ASRAM hospital from May 2020-December 2020. And we selected 100 Ante-natal mothers by simple random technique during this period with SARS-CoV-2 infection.

Study setting:

The gestational assessment was done by the best estimate of the last menstrual period (LMP), first-trimester ultrasound or by Modified Ballard Score (in case LMP and ultrasound both were unavailable). COVID block with a dedicated labour room and maternity OT was earmarked for delivery of COVID 19 positive women presenting to the

hospital for delivery. The COVID block of the hospital was not equipped with negative pressure, however air conditioning with 12 air exchanges per hour, as per recommendations was followed.

As per the recommendations, all the health care staff followed donning and doffing sequence of complete personal protective equipment (PPE) which included goggles, cap, double layer gloves, N95 mask, shoe covers and overall. Face shields were also used in areas where possible aerosol-generating procedures were done.

Testing policy:

The testing policy was as per national guidelines. Neonates born to mother diagnosed with SARS-CoV-2 infection ante-natally were tested within 24 h of life. Those born to mothers diagnosed with SARS-CoV-2 infection post-natally were tested immediately following maternal diagnosis. Any neonate who developed symptoms was promptly evaluated with a nasopharyngeal swab which was processed using Rapid Diagnostic Kit Test (RDT) for detecting SARS-CoV-2.

Maternal Testing for SARS-CoV-2:

SARSCoV-2 infected mothers were defined as those with a positive SARS-CoV-2 quantitative RT-PCR test in the nasopharyngeal sample during the peripartum period. Neonates born to women with SARS-CoV-2 infection within two weeks prior to or two days after delivery.

Newborn COVID-19 Testing and follow up:

SARS-CoV-2 infected neonates were defined as those with a positive SARS-CoV-2 quantitative RDT test in nasopharyngeal swab within 28 days of birth.

Neonates born to mothers who were diagnosed before delivery were tested within 24 h of birth. Neonates born to mothers detected COVID 19 positive after delivery, during the hospital stay, underwent testing as soon as mother was confirmed positive. Samples (nasopharyngeal/oropharyngeal swabs) were collected under aseptic precautions, after cleaning the neonate. No other sample (blood, anal or rectal swabs) was collected from the neonate. Nasopharyngeal samples were taken under strict aseptic precautions, by the pediatric resident, with a postgraduate qualification. They all underwent training on the technique of appropriate sampling method and collection.

Neonates were tested for SARS-CoV-2 by RDT on a nasopharyngeal swab sample within 24 h, 3rd or 4th day before discharge, and as indicated at subsequent visits. Neonates were assessed at all timepoints for fever, hypothermia, respiratory distress, lethargy, cough, rhinorrhoea, irritability, rash, diarrhoea, and feeding intolerance. These time points were chosen to provide an opportunity for repeat testing and routine neonatal care. The 7–14th day time point was used to allow for routine neonatal follow-up and repeat testing if necessary, along with routine neonate evaluation.

The 14-day time point was decided on the basis of what was known about viral shedding and antibody responses at that time and we purported that mothers were unlikely, if asymptomatic, to remain infectious at that time. Thus, if the neonate remained SARS-CoV-2 RDT negative at 14 days, the likelihood of continued risk of transmission from the mother was unlikely. And the neonate was followed up to 14 weeks for the growth monitoring like weight, length, head circumference any symptoms during hospital visits and via the tele consultation which ever is possible for the parents.

Sample size :100.

Study Subjects :

Inclusion criteria:

All the neonates born to the mothers with SARS-CoV-2 positive during 2 weeks prior to the delivery and peri-partum period

Exclusion criteria:

Neonates whose parents are not willing to give consent.

The primary outcomes of the study were:

- 1) To estimate the incidence of perinatal transmission
- 2) To assess the risk factors of transmission such as ante natal complications, mode of delivery, type of feeding and care practices
- 3) To describe the Growth profile of neonates born to SARS-CoV-2 positive mothers.

Data analysis:

We did a descriptive analysis with results presented as proportions for

categorical variables and mean and simple ranges for continuous variables.

RESULTS:

A total number of 380 covid-19 positive deliveries were done in our institute from May 2020 to Dec 2020. Out of which 100 babies were taken into study by simple random sampling technique. Out of 100 neonates 63 babies completed the follow up, at 7-14 days, 6wks, 10wks, 14wks of age.

Out of 100 babies born to COVID-19 positive mothers 58% were males, 42% were females. In which 37 babies were lost to follow up because of various reasons. Most of the mothers were asymptomatic and some of the mothers had mild covid-19 symptoms like cough, rhinorrhoea, headache. No ante-natal mothers had severe symptoms in our study. Most of the ante-natal mothers acquired symptoms during last trimester and 14 days before the delivery. One mother was died on 2nd day of post natal period due to severe disease requiring ventilation.

Other maternal risk factors like Anaemia in 55.5%, Eclampsia in 15.8%, Oligohydromnios in 6.3%, GDM in 4.7%, PROM(>18hrs) in 1.5%, no fetal ultrasonography abnormalities were detected.

Out of 100 neonates 82(82%) were born at term(≥ 37 wks) and 18 were preterm(<37wks) with mean gestational age was 38.1wks(36 - 40+5wks). In which 77(77%) were born through LSCS and 23(23%) through NVD. All the babies born with APGAR SCORE 7@ 1 min and 9@ 5 min.

The neonates were tested with Rapid diagnostic kit test(RDT) due to the limited resources in our hospital settings during that period. The first test was done within 24 hrs of life through the nasopharyngeal swab. Out of 100 neonates one was positive(1%) and neonate does not show any symptoms and signs, baby was observed in post-natal ward along with the family members. The remaining all were negative and does not develop any symptoms and signs. The repeat test was done after 72 hrs of life or before discharge, showing that no neonate tested positive. This showed that there is no vertical transmission from mother to baby in our study.

Out of 100 neonates 78(78 %) babies started on breastfeeding or expressed breast milk(EBM), after counselling regarding transmission risk, hygiene practices, collection of milk, and 12(12%) neonates were started on EBM and formula feed (FF), 10 (10 %) neonates were started on only formula feed (FF). Informed consent taken from the mother and family members.

The mean weight of babies was 2896.7 gms, length 48.4 cms and occipito-frontal circumference (OFC) 33.3 cms noted after birth. Out of 100, 63 neonates were followed at the 7-14 days, 6wks, 10wks and 14 wks period for any symptoms and signs, growth monitoring, vaccination and requirement of further Covid-19 testing. Five (7.9%) out of 63 neonates were consulted through telemedicine at 14th day, 6wks, 10wks, 14wks for any symptoms and vaccination of these neonates done at their respective Anganwadi centers and PHCs.

Out of 63 babies during 1st visit 48(76%), 2nd visit 52(82.5%), 3rd visit 58(92%), 4th visit 63(100%) were followed up, including the telemedicine consulted neonates. Out of 63 neonates 58(92%) does not require need for the Covid-19 testing, because they were not showing any symptoms and signs.

During the follow up at 7-14 days of age 40(83.33%) out of 48 neonates were put on exclusive breast feeding, 4(8.33%) were on mixed feeding, 4(8.33%) on formula feeding. These babies does not showed any signs and symptoms of Covid-19.

During 6th week 52(82.5%) out of 63 members came for follow up including telemedicine consultancy. We recorded the mean weight, length and OFC in these neonates were 3942.98 gms, 53.66 cms, 36.49 cms respectively. During 10th week mean weight, length, OFC were 4810.98 gms, 58.38 cms, 39.07 cms respectively. During 14th weeks mean weight, length, OFC were 5602 gms, 62.75 cms, 41.47 cms respectively and vaccination done in all the neonates during the respective periods of follow up.

During the follow up period no neonate had symptoms and signs of SARS COVID-19 and no one was admitted for any other symptoms.

All the neonates were healthy and normal growth parameters were observed during follow up.

DISCUSSION:

The present study was conducted in a tertiary care teaching hospital, on the clinical characteristics, outcome and follow up of neonates born to COVID-19 positive mothers. Out of 100 newborns included, only one baby (1%) had SARS-CoV2 virus detected in nasopharyngeal swab by Rapid Diagnostic Kit Test(RDT) in the immediate post-natal period (<24hrs) with asymptomatic clinical course and follow-up. Repeat testing at 72hours of life was negative. No other neonate turned out to be positive for SARS CoV2 during the study period.

Till date, neonates born to mothers with SARS CoV2 infection showed low rates of testing-based vertical transmission and no clinical evidence for neonatal SARS-CoV-2 infection. In our setting we also followed the standard feeding protocols like Direct Breast Feeding (DBF), Expressed breast milk(EBM), both EBM and supplementation with formula (FF) after explaining the COVID precautions, hygiene practices and taken consent from the mother and family members. Repeat testing was done at 72hours of life after rooming-in was done. None of the neonates contracted the infection, which is similar to the findings in a study by Dani Dumitriu, MD, PhD; Ukachi N. Emeruwa, MD, MPH; et al.^[25], in which 82 Well Baby Nursery newborns, showed that lack of evidence for vertical or postnatal transmission was observed while allowing mother-newborn rooming-in, encouraging delayed bathing, and promoting direct breastfeeding with appropriate hygiene.

Rare case reports suggests a possibility of vertical transmission of COVID-19, as reported by Vivanti et al.^[24] The case report described signs of acute and chronic intervillous inflammation consistent with the severe systemic maternal inflammatory status triggered by SARS CoV 2 and demonstration of virus in neonatal samples associated with neurological symptoms thus implying transplacental transmission of SARS CoV 2. Another case report has also raised the concern of positive amniotic fluid for COVID 19 and positive antibody titres in neonates immediately at birth^[25]. Similar case of positive amniotic fluid followed by pneumonia in the neonate is also observed by Zeng et al.^[26]. In this present study, testing of amniotic fluid was not performed. Few earlier reports, however, failed to demonstrate the vertical transmission from mother to neonate by placental and fetal tissue examination^[27-29].

We have included 100 COVID-19-positive mothers and all were tested positive 14 days prior to delivery. Majority of them (93.35%) were asymptomatic, very few (5.65%) had a mild form of the disease like dry cough, rhinorrhoea and headache, only one(1%) presented with severe disease requiring intensive care admission and mechanical ventilation support and died 2days after delivery. Most of the antenatal mothers acquired symptoms during last trimester and 14days before the delivery. Nayak AH, Kapote DS, Fonseca M et al study shows similar findings were seen in a study of 141 patients in Mumbai where most of their patients (97%) were asymptomatic or had mild symptoms^[17]. A living systematic review and meta-analysis in British Medical Journal by Allotey J, Stallings E, Bonet M, et al.also stated that symptoms of fever and myalgia manifest less often in COVID-19 infected pregnant women than in non-pregnant women^[18].

Out of 100 babies born to COVID-19 positive mothers 82.53% were term(>=37 weeks) and 17.47% were preterms (<=37 weeks). And 11.11% were Small for Gestational age(SGA) and 88.89% were Appropriate for Gestational age(AGA) with 25.07 being Low birth Weight which was similar to the study conducted by Ruchi Nanavati, Dwayne Mascarenhas et al.^[30]. Following antenatal complications were reported in the present study like, Anemia (62.8%), Eclampsia(25.5%), Oligohydromnios (10.1%), GDM(4.4%), PROM(>18hrs)[3.15%]. Anemia and Eclampsia were the common comorbidities among antenatal mothers in contrast to findings reported by Nayak et al.^[17] and Gajbhijee et al.^[19] where, hypertensive and diabetic disorders as the most commonly associated co-morbidities. In a prospective cohort study by Antoun et al., 10.5% of patients had severe pre-eclampsia compared to 1-2% risk in the general population, out of which one patient developed hemolysis, elevated liver enzymes and low plateletcount (HELLP) syndrome and disseminated intravascular coagulation^[20]. One possible explanation can be that placental angiotensin-converting enzyme 2 (ACE2) is highly expressed at the maternal-fetal interface and its dysregulation by

SARS-CoV-2 might be involved in the high rates of preeclampsia associated with severe and critical COVID-19-infected pregnant women^[21]. Maternal mortality was higher in the second wave of COVID 19 than the first wave. Although the current study reports only 1% maternal mortality, the data is from first wave of COVID 19.

In our study outcome and follow up of neonates up to 14 weeks done. Out of 100 neonates, we could follow up only 63 of them regarding their health status. Post discharge follow-up during 7-14 days, 6, 10 and 14 weeks does not show any signs and symptoms. Growth parameters were normal with no hospital admission and completed the primary series of routine vaccination.

However, our study has the following limitations. This study is limited by the sample size and a follow-up period of 14 weeks. A larger cohort and longer follow-up with repeat testing with RTPCR based antigen tests and serology might be needed to confirm that perinatal transmission which is unlikely to occur if correct protective strategies are used. The diagnosis of COVID-19 and virus carriage was based on NP swabs. Though the absolute sensitivity of detecting SARS-CoV2 with NP swabs is unknown, the modality is only around 70% sensitive for diagnosing respiratory viral infections^[22]. The study is observational and short term follow up, clearly not powered to detect long term adverse clinical outcomes in the neonate. We were unable to screen for presence of the virus in blood, urine, or stool due to absence of approved testing for these samples during the study period. We used Rapid Diagnostic Kit Test (RDT) due to the resource limited setting and availability of RT-PCR during the first wave of COVID 19.

There is a chance that asymptomatic and mildly symptomatic infants infected with the virus may have been missed in the absence of testing during follow-up, although we would suggest that this is of limited clinical significance. The risk of mother-to-infant transmission of SARS-CoV2, vertically or horizontally, in the perinatal period is very low. Breast feeding and rooming in can be practiced safely with adequate infection control precautions. The risk of adverse outcome to infants born to mothers who have SARS-CoV2 infection at birth is minimal, aside from the risk of premature delivery due to iatrogenic/maternal reasons. However, there are no published long-term outcome data on these infants and further follow-up studies will be needed to fully ascertain any downstream adverse outcomes in this group of infants.

CONCLUSION:

Our data suggest that perinatal transmission is unlikely to occur if correct hygiene precautions are undertaken and that rooming in and breastfeeding are safe procedures when paired with effective parental education of infant protective strategies.

Ethical committee approval number:

IEC/ASR/APPROVAL/030/2021

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