Clinical profile and immediate outcomes in neonates born to SARS-CoV-2 positive mothers at a tertiary care centre

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Abstract: Introduction: There is a scarcity of clinical data on the clinical profile of neonates born to COVID positive mothers as well as their immediate outcomes, especially in the Indian context. We aimed to describe the clinical profile and immediate outcomes of neonates born to SARS-CoV-2 positive mothers. Methods: This was a retrospective, chart based observational study conducted in the Neonatal Intensive Care Unit and postnatal wards at a tertiary care centre in Mangalore, Karnataka. All neonates born to women with SARS-CoV-2 infection within two weeks prior to or two days after delivery were included in the study. Data regarding epidemiologic, demographic, clinical features and laboratory tests in neonates born to covid positive mothers were recorded. Data was analysed using descriptive statistics and outcomes expressed as frequency, proportions, percentages and chi square test. Results: From April 2020 to September 2021, 99 babies born to covid positive mothers for were included. 31(32%) neonates were symptomatic and 66(68%) were asymptomatic. Out of the 99 neonates, 84 of the neonates were tested. 81(81.8%) were COVID negative. 3(3.6%) were tested positively by quantitative RT PCR done within 72 hours of life. All the positive neonates were symptomatic and required respiratory support. Infected neonates had no statistically significant difference with noninfected. Conclusions: Covid positivity among neonates born to covid positive mothers was low and majority remained asymptomatic and overall neonates did well. Keywords: Covid Positive Mothers, Neonatal COVID, Clinical Profile, Outcomes.

Introduction

COVID-19 caused by the Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2, has spread worldwide with substantial consequences to public health [1]. As the pandemic evolved, there were significant advances in our knowledge about various aspects of the disease, including epidemiology, clinical features, transmission, detection and management modalities. Pregnant women are a highly vulnerable group of the population who are susceptible to the COVID 19 infection due to the various physiological changes in the immunological and circulatory parameters. As a result, neonates born to these COVID positive mothers are at an increased risk of infection and adverse effects due to the infection [2].

The possibility of mother to fetus transmission of SARS-CoV-2 has implications for the mother, fetus and neonate. In this study, we focus mainly on the neonatal implications. The most common neonatal symptoms are mostly respiratory including respiratory distress, followed by gastrointestinal symptoms like feed intolerance [3]. Unequivocal diagnosis of neonatal infections is made by the detection of the organism in culture or by nucleic acid amplification tests that identify the presence of the pathogen’s RNA or DNA in neonatal blood or body fluid samples [4].

Since the beginning of the pandemic, there were concerns regarding the maternal, fetal and neonatal effects of SARS-CoV-2 infection. The earlier evidence pointed towards pregnancy being considered low risk for the disease. But newer studies reported higher intensive care unit admission rates and mechanical ventilation rates in pregnant women. However, none of these studies specified the fetal or neonatal effects of maternal infection with SARS-CoV-2 [3].
Despite the increasingly recognized impact of the novel corona virus disease, the risk of perinatal transmission and risk of the neonate developing COVID 19 infection during the perinatal period is largely unknown [1]. There is a scarcity of clinical data on the clinical profile of neonates born to COVID positive mothers as well as their immediate outcomes, especially in the Indian context. With this study, we aim to follow up all neonates born to SARS-CoV-2 positive mothers at our hospital and to elicit the demographics, clinical profile and immediate outcomes in these neonates. We wish to throw some light on the outcomes in neonates born to COVID positive mothers and hope to alleviate uncertainties regarding the same, atleast in our setting.

**Material and Methods**

This was a retrospective, chart based observational study conducted in the Neonatal Intensive Care Unit and post natal wards at a tertiary care center in Mangalore, Karnataka. All neonates born to women with SARS-CoV-2 infection within two weeks prior to or two days after delivery were included in the study. Medical records of these neonates, born between April 2020 to September 2021 were reviewed.

SARS-CoV-2 infection in neonates was defined as a positive SARS-CoV-2 quantitative RT PCR test within 28 days of birth [5]. SARS-CoV-2 infected mothers were defined as those with a positive SARS-CoV-2 quantitative RT PCR test during the peripartum period [5].

All mothers were tested by SARS-CoV-2 RT PCR at admission. Testing management were done as per Federation of Obstetric and Gynecological Societies of India and National Neonatology Forum guidelines [6]. SARS-CoV-2 status of the neonate was tested as per guidelines from Ministry of Health and Family Welfare, Government of India and local institutional protocols which was within 72 hours of birth or when the neonate was symptomatic. All neonates were monitored for development of symptoms.

Purposive sampling was done and sample size was calculated as follows:

Sample size calculation:

\[ n = \frac{[DEFF^*Np(1-p)]}{[(d^2/Z_{1-\alpha/2}^2)*Np(1-p) + p^*(1-p)]} \]

where,

- \( N \): population size
- \( p \): hypothesized percentage frequency of outcome factor in the population
- \( d \): confidence limits as percentage

Sample size, \( n = 84 \) at 80% confidence intervals

Data regarding epidemiologic, demographic, clinical features and laboratory tests in neonates born to SARS-CoV-2 positive mothers were recorded. General health status, COVID status of the baby, presence of symptoms, duration of hospital stay and outcomes were also recorded. Data was analysed using descriptive statistics and outcomes expressed as frequency, proportions and percentages. Calculations were done using Microsoft excel software.

**Results**

There were a total of 1766 mothers who delivered at our centre from April 2020 to September 2021 of which 97 mothers tested positive for SARS-CoV-2 fourteen days prior to or two days after delivery (Figure-1).

**Fig-1: Distribution of cases**

A total of 99 neonates, including two sets of twins, born to SARS-CoV-2 positive mothers between April 2020 and September 2021 were included in the study.

Majority of the neonates were born at term. 22 (22.4%) neonates were born preterm of which 2 were born extreme preterm, 1 early preterm and the remaining 19, late preterms. The two extreme preterms did not survive. Caesarian section was the mode of delivery in 42.9% whereas 57.1% were born by normal vaginal
delivery. 52.5% of the neonates were males and 47.5% were females. Most had a favourable extrauterine adaptation with need for resuscitation in only 4 babies, of which two were extreme preterms and did not survive. 31(32%) of the 99 neonates were symptomatic and 66(68%) were asymptomatic.

Out of the 99 neonates born to COVID positive mothers, 15(15.2%) were not tested. 84 of the neonates were tested. 81(81.8%) were COVID negative. 3(3.6%) tested positive for SARS-CoV-2 infection by quantitative RT PCR done within 72 hours of life. None tested positive after 72 hours of life. The three SARS-CoV-2 positive neonates included a set of twins. The twins were born at 35 weeks of gestation whereas the singleton was born at term. All three babies had respiratory distress at birth and required CPAP for 2 days with a total duration of 5 days of hospital stay. None required resuscitation at birth. Blood investigations of all three positive neonates showed respiratory acidosis with all other parameters and chest X ray within normal limits.

Table 1 compares data of SARS-CoV-2 positive and negative neonates born to positive mothers. Neonates infected with COVID 19 had no statistically significant difference with SARS-CoV-2 non infected neonates born to SARS-CoV-2 positive mothers. This could possibly be explained by the small number of SARS-CoV-2 infected cases, making the study inadequately powered to detect a statistically significant difference.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>COVID 19 Negative (n=81) n(%)</th>
<th>COVID 19 Positive (n=3) n(%)</th>
<th>Total (n=84) n(%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43(53.08)</td>
<td>2(66.6)</td>
<td>45(53.5)</td>
<td>0.899</td>
</tr>
<tr>
<td>Female</td>
<td>38(46.9)</td>
<td>1(33.3)</td>
<td>39(44.8)</td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Term</td>
<td>61(75.3)</td>
<td>1(33.3)</td>
<td>62(73.8)</td>
<td>0.339</td>
</tr>
<tr>
<td>Preterm</td>
<td>20(24.6)</td>
<td>2(66.6)</td>
<td>22(26.1)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2.5</td>
<td>24(29.6)</td>
<td>2(66.6)</td>
<td>26(30.9)</td>
<td>0.467</td>
</tr>
<tr>
<td>&gt;=2.5</td>
<td>57(70.3)</td>
<td>1(33.3)</td>
<td>58(71.6)</td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVD</td>
<td>49(60.4)</td>
<td>1(33.3)</td>
<td>50(59.5)</td>
<td>0.732</td>
</tr>
<tr>
<td>LSCS</td>
<td>32(39.5)</td>
<td>2(66.6)</td>
<td>34(40.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>25(30.8)</td>
<td>3(100)</td>
<td>28(33.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>56(69.1)</td>
<td>0(0)</td>
<td>56(66.6)</td>
<td></td>
</tr>
<tr>
<td>Neonatal outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge</td>
<td>79(97.5)</td>
<td>3(100)</td>
<td>82(97.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Death</td>
<td>2(2.5)</td>
<td>0(0)</td>
<td>2(2.4)</td>
<td></td>
</tr>
</tbody>
</table>

Apart from COVID 19 symptoms, of the 81 covid negative neonates, 5 had sepsis, 24 had respiratory distress syndrome and 17 were transient tachypnea of newborn. 52 of the COVID negative babies were healthy. Of the 99 neonates, 22 required oxygen, 2 died during the study and 97 were discharged. The average duration of hospital stay was 2 days.

Discussion
In this study, we aimed to describe the clinical profile and immediate outcomes of neonates born to SARS-CoV-2 positive mothers. The proportion of SARS-CoV-2 positive neonates in our study was 3.6 % as compared to 5.1% positive neonates in the NNF registry [7]. The incidence in our study was in line with that of other Indian studies [4, 8] as well as international studies [9-11]. All these neonates tested positive within 72 hours of life. Even though vertical transmission has been described by a few authors, there is still controversy regarding the same and in the absence of serial testing and testing of various body fluids from mother, it is not possible to pinpoint the time of acquisition of infection.
Majority of the neonates (96.4%) born to COVID positive mothers were COVID negative in our study. Of these, 30.8% were symptomatic inspite of testing negative. Similar to our study majority of the neonates were tested negative in Sehra et al’s study [4]. The negativity percentages were similar in other Indian and international studies as well [8, 10-12].

In our study, the median gestational age was 38 weeks and the ratio of male to female was 1.1:1 similar to that described by Kalamdani et al [13]. Normal vaginal delivery rates were higher in these mothers which is in contrast to most studies where caesarian sections were higher [7-8]. However the mode of delivery does not impact the transmission of infection to the baby [6]. The prematurity rate of 22% in our study was significant and was similar to those reported by the NNF registry and the UK registry [7]. This raises concerns about the increase rate of preterm deliveries in SARS-CoV-2 positive mothers. 26% of the babies were born with low birth weight.

All the neonates born to COVID positive mothers were monitored for development of symptoms. 31(32%) of the 99 neonates were symptomatic and 66(68%) were asymptomatic. The most common problems reported among neonates born to COVID positive mothers are respiratory. In our study population also respiratory issues were predominant among the neonates, in both the COVID positive and negative groups. In contrast to our study, all neonates were asymptomatic in Sehra et al's study [4] whereas Nanavati et al observed that two thirds of the COVID positive neonates were asymptomatic while the remaining developed respiratory and gastrointestinal symptoms [8].

As per the NNF COVID 19 registry, SARS-CoV-2 infected neonates were more likely to need resuscitation, be symptomatic, need NICU admission, have abnormal chest Xrays and need respiratory support [7]. Prematurity was noted to be an obvious confounder. In our study, none of the COVID positive babies required resuscitation. All three babies had respiratory distress at birth and required NICU admission and CPAP for 2 days with a total duration of 5 days of hospital stay. Very few studies have described the laboratory abnormalities in these neonates.

Kalamdani et al described elevated LDH levels and mild transamnitis in SARS-CoV-2 positive neonates [8]. In their study, Sehra et al, found that blood investigations as well as Xrays were normal in the COVID negative cohort and leucopenia and elevated CRP, D-Dimer, FDP were observed in COVID positive neonates [4]. Nanavati et al described leucopenia, thrombocytopenia, elevated inflammatory markers and normal chest Xrays in COVID positive neonates [8].

In our study, blood investigations of all three positive neonates showed respiratory acidosis with all other parameters and chest X ray within normal limits. Of the COVID negative neonates, 5 had elevated CRP with other parameters within normal limits. Bernardo et al described radiological abnormalities in 44% of COVID positive neonates, however we did not find any radiological abnormalities in our study. Current evidence does not recommend any blood or radiological investigations in any asymptomatic SARS-CoV-2 positive neonates.

In our study, the neonatal out comes were good. All three SARS-CoV-2 positive neonates were discharged as per local institutional protocols. The average duration of hospital stay of the neonates born to COVID positive mothers was 2 days. All babies were managed as per protocol. Of the 99 neonates, 22 required oxygen (COVID positive and negative), 2 died (extreme preterms) during the study and 97 were discharged healthy.

The limitations of our study were its retrospective nature and small number of subjects. The age of testing of the neonates was non uniform. There was no scope for identification of route of transmission in our study as there testing of biological sources like placenta was not pursued.

**Conclusion**

In conclusion, the study provides data on outcomes in neonates born to COVID positive mothers and their clinical profile and hope to alleviate uncertainties regarding the same in our setting. This would help in making informed decisions in the future.
References


Cite this article as: Adavalath S and Avabratha KS. Clinical profile and immediate outcomes in neonates born to SARS-CoV-2 positive mothers at a tertiary care centre. Al Ameen J Med Sci 2023; 16(2): 162-166.

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