# Outcomes of Neonates Born To Mothers Who Were COVID-19 Positive; An Observational Study from Pakistan

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## ABSTRACT

***Objective***: To assess outcomes of neonates born to mothers who were COVID-19 positive.
***Study Design***: Prospective observational study.
***Place and Duration of Study***: Secondary and Tertiary Care Hospitals of the Armed Forces, Pakistan, from Apr to Aug 2020.
Methodology: We studied 106 pregnant women who tested positive for SARS-CoV-2. Stable asymptomatic newborn babies were kept in SARS-CoV-2 specified incubators, at specially designated areas for observation. Nasopharyngeal swabs were taken at first 24 hours and if negative, babies were handed over to clinically stable mothers who were educated regarding use of facemasks and proper hand washing. Neonates who tested positive for SARS-CoV-2 were evaluated for SARS-CoV-2 again at 48 hours and then every 48-72 hours, until found to be negative.
***Results***: Total 106 women were found to be SARS-CoV-2 positive during the study period. All the women delivered singleton babies. Of the 106 babies, 5 (4.71%) were found to be positive for SARS-CoV-2 at 24 hours and only 1 (0.94%) baby was found to be positive at 48 hours and then tested negative at 7th day.
***Conclusion***: Babies born to SARS-CoV-2 mothers were mostly asymptomatic and there was no increased risk of morbidity or mortality to the neonates suffering from the infection.

**Keywords**: COVID-19 positive mothers, Neonates, SARS-CoV-2, Vertical transmission.

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## INTRODUCTION

Corona virus disease is an infectious disease caused by SARS-CoV-2 virus of corona family. First case of COVID-19 was identified in December 2019 in China. WHO declared it as a pandemic on 11th March 2020.[1] In Pakistan the first case of COVID-19 was reported in Karachi on 26th February 2020.By 9th August 2020; there were 284,121 confirmed cases of corona virus disease in Pakistan, resulting in 6082 deaths.[2]

COVID-19 affects all the age groups ranging from neonates to the elderly. Twelve cases of COVID-19 confirmed by SARS CoV-2 PCR have been reported in neonates to date.[3] Common clinical manifestations in COVID positive neonates have been non-specific. These include fever, lethargy, vomiting, poor feeding, respiratory distress, tachypnea, mottling, and cyanosis.[4,5] Laboratory parameters show leukocytosis, lymphopenia, neutropenia, elevated liver enzymes, C-reactive proteins and pro-calcitonin.

It is reported that mode of transmission in majority of the neonates is horizontal via close contact, droplet infection from infected family members and caregivers and hospital acquired infections. Whilst there is no clear evidence of vertical transmission from COVID positive mother to their babies, vertical transmission remains a possibility in neonates with early onset infections.[6] Zheng *et al*, analyzed cell type specific expression pattern of Angiotensin Converting Enzyme -2 (ACE-2) on cells of maternal-fetal interface using single cell RNA-sequencing technology. This revealed very low expression for receptors of ACE-2 on these cells that may be associated with reduced likelihood of vertical transmission.[7]

According to available evidence, neonates have milder manifestation of this disease. There are different presumptions explaining the low risk of neonates of severe infection caused by SARS COV-2. One possibility is the immature functioning of the Angiotensin-Converting Enzyme-2 receptors in neonates, which is a major target of SARS CoV-2. It is postulated that in neonates the ACE-2 receptors are largely immature and high in number leading to low infectivity in neonates. The other possibility is the difference in the number of different types of lymphocytes in neonates and adult

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population. The neonates have a higher CD4 to CD8 ratio due to the presence of thymus in early stages of life.[3] The presence of maternal antibodies in neonates also seems to be protective against SARS COV-2 infection in neonates.

This aim of our study was to determine the clinical and epidemiological profile of neonates born to COVID-positive mothers in Pakistan and see the possible effects of maternal infection on their newborn babies.

## METHODOLOGY

An observational prospective study was carried out at various Secondary and Tertiary Care Hospitals of Armed Forces, Pakistan, from April to August 2020.

**Inclusion Criteria**: All the hospitalized pregnant women who tested positive for SARS-COV-2 were included in the study.

**Exclusion Criteria**: Non-consenting pregnant women were excluded.

Majority of these pregnant women were asymptomatic or had mild symptoms of fever and cough. A study protocol was designed, approved from Institution Review Board (IRB 1045/ Mar 2020) and circulated to all the major secondary and tertiary care hospitals. According to the study protocol, SARS-COV-2 testing was performed on nasopharyngeal swab specimen of all the women, who were admitted to hospital for the delivery of baby. Nasopharyngeal swabs were taken from all the newborns at 24 and 48 hours. Testing was done using real-time PCR (rt-PCR) according to the standard protocol 8. If any sample was positive, repeat samples were performed every 48-72 hours until the result was negative. Baby was kept in SARS COV-2 specified area in NICUs of respective hospitals for observation and then handed over to clinically stable mother. The mothers were educated about handling the baby wearing a facemask, gloves and following droplet precautions. Detailed plan was given to mothers/caregivers for frequent follow-up through 28 days after birth. Mothers were advised about breast feeding techniques and use of facemasks and proper hand washing before and after handling the baby.

Data was collected on pre-designed proforma. The proforma along with study protocol was circulated to consultant pediatricians and neonatologists at participating Secondary and Tertiary Care Hospitals. Data regarding gestational age, gender, mode of delivery, appropriateness for gestational age, birth weight, duration of hospital stay, SARS COV-2 status and symptoms were collected regarding the babies born to mothers who were COVID-positive. Maternal data like age, any co morbidities, outcomes of illness and source of acquisition of infection were recorded. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 23. Results were presented as frequency and percentage for categorical variables and mean ± SD for continuous variables.

## RESULTS

All the 106 mothers included in this study were positive for SARS-CoV-2 rt-PCR on nasopharyngeal swab sample. Of 106 newborns born to these mothers, 59 (55.7%) were males and 47(44.3%) were females. Mean gestational age and mean birth body weight were 38.22 ± 1.57 weeks (range: 31–41 weeks) and 3056 ± 508 g (range: 1600–4100g), respectively. Out of 82 (77.35%) babies were born via cesarean section while 24 (22.64%) babies were born via spontaneous vaginal delivery. The commonest indication for LSCS was presence of previous scar.[11] (10.37%) babies were small-for-gestational-age (SGA) and 5 (4.71%) were large-for-gestational-age (LGA). 90 (84.9%) babies were asymptomatic and kept in COVID specified NICU for observation. Of the remaining 16 babies, six had clinical diagnosis of Transient Tachypnea of newborn (TTN), while two were diagnosed to have Respiratory Distress Syndrome (RDS).The remaining eight newborns had birth asphyxia, meconium aspiration syndrome, hypoglycemia, Down syndrome, neonatal sepsis, and minimal respiratory disease. Mean duration of hospital stay was 3.83 ± 2.89 days (range: 1-19 days). None of these babies died. The maternal and neonatal clinic-pathological profile were shown in Table-I.

**Table-I: Clinico-pathological profile of mothers and newborns.**

| Parameters | Mean ± SD |
|---|---|
| Gestational age in weeks (n=106) | 38.20 ± 1.57 weeks |
| Weight of babies (kg) (n=106) | 3.20 ± 2.28 kg |
| Length of babies (n=106) | 48.60 ± 2.84 cm |
| FOC(n=106) | 34.00 ± 1.29 cm |
| Duration of Hospital Stay(n=106) | 3.80 ± 2.9 days |
| TLC of babies (n=51) | 17.08 ± 5.76 x$10^9$/L |
| Haemoglobin of babies (n=51) | 20.92 ± 20.12 g/dl |
| Platelets of babies (n=51 | 236.30 ± 69 x $10^9$/L |
| Age of Mothers (n=106) | 54.33 ± 2.70 years |
| TLC of mothers (n=38) | 12.42 ± 13.78 x$10^9$/L |
| Haemoglobin of mothers (n=38) | 17.55 ± 32.5 g/dl |
| Platelets of mothers (n=38) | 258.24 ± 104 x $10^9$/L |
| LFT of Mothers (=25) | 38.48 ± 22.4 U/L |

Of 106 babies, five were found to be positive for SARS-COV-2 while 101 tested negative for SARS-COV-2 on nasopharyngeal swab specimen as shown in

Table-II. Those babies who tested positive for SARS-COV-2, four were girls and one boy.

**Table-II: COVID Status of Newborns (n=106).**

| RT PCR of Baby | At 24 Hours (n=106) | At 48 Hours (n=72) |
|---|---|---|
| Positive | 5 (4.7%) | 1 (1.4%) |
| Negative | 101(95.3%) | 71(98.6%) |
| Total | 106 | 72(100) |

Out of 102 (96.2%) mothers acquired infection locally while 4 (3.8%) mothers had history of travel abroad. With respect to maternal outcomes, one mother died due to the complications of pregnancy, while 105 mothers were discharged home and recovered completely. Majority of the women were asymptomatic while few had mild symptoms of fever and cough. None of them required any treatment, mechanical ventilation or admission to intensive care unit. The neonatal and maternal characteristics studied in this study were summarized in Table-III.

**Table-III: Characteristics of newborns and mothers.**

| Characteristics | n (%) |
|---|---|
| **Gender of Newborns** | |
| Male | 59 (55.7) |
| Female | 47(44.3) |
| **Gestational Age** | |
| Appropriate for Gestational Age (AGA) | 90 (84.9) |
| Small-for-Gestational-Age (SGA) | 11 (10.4) |
| Large-for-Gestational-Age (LGA) | 5 (4.7) |
| **Mode of Delivery** | |
| Cesarean Section | 82 (77.3) |
| Spontaneous Vaginal Delivery | 24 (22.4) |
| **Resuscitation** | |
| Yes | 2 (1.9) |
| No | 104 (98.1) |
| **Type of feed** | |
| Breastfeeding | 5 (4.7) |
| Formula Milk | 101 (95.3) |
| **Child's co Morbidities** | |
| Yes | 5 (4.7) |
| No | 101 (95.3) |
| **Symptomatic** | |
| Yes | 15 (14.2) |
| No | 91 (85.8) |
| **Outcome of Mothers** | |
| Discharge | 105 (99.1) |
| Death | 1 (0.9) |
| **Infection Acquired** | |
| Travel | 4 (3.8) |
| Local | 102 (96.2) |
| **C- Reactive Proteins** | |
| Reactive | 5 (8.5) |
| Nonreactive | 54 (91.5) |
| **Co-Morbidities of Mothers** | |
| Yes | 5 (4.7) |
| No | 101 (95.3) |

## DISCUSSION

There are few studies published to date that focus on the impact of SARS-COV-2 infection in mothers and infant but none of them are from Pakistan. Most of the studies so far are based on individual case reports and few case series. Our study was unique as none of the published articles so far, had with such a large sample size from Pakistan.[9-16]

As in other studies, our study also showed that SARS-COV-2 does not cause significant illness in neonates. In our study, 5/106 (4.7%) neonates were found to be positive for SARS-COV-2, which was consistent with studies performed by Wu *et al*.[13] and Salvatore *et al*.[14] In a study conducted by Wu *et al*, there were 5 infected babies born to 29 infected mothers, while in study performed by Salvatore *et al*, there was not a single positive case of SARS-COV-2 in 120 newborns, born to mothers who had tested positive. None of the five babies in our study had any clinical symptoms or radiological features suggestive of clinical infection with SARS-COV-2.

Four out of five babies in our study were delivered via LSCS which was consistent with study performed by Wu *et al*,[13] where all the positive babies were born via LSCS.

In majority of previous studies, the mothers had mild clinical symptom that were consistent with our study. All the five neonates who tested positive for SARS-COV-2, in our study had no clinical feature suggestive of SARS-COV-2 infection. These findings were similar to the report of the Italian Health Ministry who reported 20 newborn babies who tested positive for SARS-COV-2 virus but did not show any symptoms.[17]

An important question at this point is whether intrauterine transmission of SARS-COV-2 virus occurs or not?. Vertical transmission occurs by three routes, via placenta, aspiration of secretions after birth and breast-feeding.

Chen *et al*, analyzed amniotic fluid and cord blood samples obtained from six SARS-COV-2-positive pregnant women and nasopharyngeal swabs from their newborns: all the samples tested negative for SARS-COV-2.[6] A similar study conducted by Lei *et al*, found four pregnant women showing similar results.[14] This study also analyzed vaginal secretions and all were found to be negative for SARS-CoV-2. Chen *et al*, examined neonatal pharyngeal swab samples and placental tissues from three pregnant women who were

positive for SARS-COV-2 but all the samples tested negative for SARS-CoV-2 RNA.[20] Therefore, based on current literature the hypothesis of vertical transmission of SARS-CoV-2, though plausible, remains unproven. Zamaniyan *et al*, reported a critically ill mother who was positive for SARS-COV-2, her amniotic fluid was positive for SARS-CoV-2, the nasal swab of her baby, obtained at 24h of life, was also found to be positive for SARS-CoV-2.[16] This case report, suggested that vertical transmission could be possible in very critically ill mothers perhaps due to large viral load. In another study conducted by Buonsenso *et al*, placental tissue was found to be infected with virus in only one out of total 7 SARS-CoV-2-positive pregnant mothers but their babies were found to be negative.[17] Further studies and longitudinal observation of suspected cases are still needed to resolve this challenge.

Furthermore, Chambers *et al*, has shown, only one of 64 samples of breast Milk was positive for SARS CoV-2 RNA and that too did not reveal any active viral replication. The data is especially reassuring for developing countries where exclusive breast-feeding still remain a challenge.[19]

Transmission of SARS-CoV-2 from infected mothers to their newborn babies is very low. Even in those babies who test positive have a very good prognosis. The gap of knowledge will be filled by seroprevalence studies in mothers and newborns dyads. High quality studies are urgently needed about newborns to better understand the clinical manifestations, clinical course, and prognosis of SARS-CoV-2-positive newborns.

## CONCLUSION

Babies born to SARS-CoV-2 mothers were mostly asymptomatic and there was no increased risk of morbidity or mortality to the neonates suffering from the infection.

**Conflict of Interest:** None.

**Authors' Contribution**

ZA: Conceived the idea, collected and organized the data and helped refining the final draft, AK: Collected and organized the data, wrote main manuscript, TW: Collected data, organized the data, writing of initial manuscript, MA: Writing of initial manuscript and refining the final draft, KNH: Writing of initial manuscript and refining the final draft, RS: Organized the data, writing of initial manuscript and refin-ing the final draft, UES: Collected data, organized the data and wrote the initial manuscript, SF: Collected organized data, QUM: Collected data, organized the data.

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