## Original Article

**Paediatrics Section** 

Clinico-epidemiological Characteristics and Short-term Outcomes of Neonates Born to COVID-19 Positive Mothers at a Tertiary Care Hospital in North Karnataka-A Retrospective Study

MEENAKSHI R SARVI1, CHINMAYI R JOSHI2, PAVAN PUJAR3, K SRIDHAR4,

SHAILESH S PATIL<sup>5</sup>, VIJAYKUMAR B MURTELI<sup>6</sup>, SD JYOTHI<sup>7</sup>

# (CC) BY-NC-ND

## ABSTRACT

**Introduction:** Coronavirus Disease-2019 (COVID-19) infection in pregnant women can have important effects on the perinatal and neonatal outcomes. Multiple modes of transmission of infection from mother to the newborn have been suggested as also the increased risk of complications in COVID-19 infected neonates.

**Aim:** To study the clinico-epidemiological characteristics and short-term outcomes of neonates born to mothers infected with COVID-19 in relation to maternal COVID-19 severity and co-morbidities and to compare the same between COVID-19 infected and non infected neonates.

**Materials and Methods:** This was a retrospective study of 174 neonates born to COVID-19 positive mothers admitted and delivered from 1<sup>st</sup> August 2020 to 31<sup>st</sup> October 2020, at Belagavi Institute of Medical Sciences (BIMS), North Karnataka, India. Data was collected from medical records about the clinical and epidemiological characteristics of the mothers and their neonates, symptoms and severity of COVID-19 and their management and short-term outcomes. Pearson's Chi-square or Fisher's-exact test was used for statistical analysis. The p-value of less than 0.05 was considered statistically significant.

**Results:** Out of 174, 18 (10.35%) neonates tested positive for COVID-19 by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). The rates of prematurity and low birth weight amongst all 174 neonates were 17.24% and 24.14%, respectively. There were no significant differences in demographic features, in the need for resuscitation and incidence of complications like prematurity, low birth weight, birth asphyxia, meconium aspiration syndrome, sepsis between COVID-19 infected and non infected neonates. However, an increased risk of Early Onset Sepsis (EOS) (OR-2.21) in COVID-19 infected neonates. None of the COVID-19 infected neonates required Continuous Positive Airway Pressure (CPAP) or mechanical ventilation and all were discharged subsequently. In this study there were 3 (1.72%) deaths, all among COVID-19 non infected, neonates.

**Conclusion:** The incidence of COVID-19 infection in neonates born to COVID-19 infected mothers in this study was 10.35%. Most of the infections in neonates were of less severity without a significantly increased need for respiratory support and without significant mortality.

# **Keywords:** Continuous positive airway pressure, Coronavirus disease-2019, Sepsis, Severe acute respiratory syndrome-coronavirus-2 infection

# INTRODUCTION

In December 2019, a novel coronavirus emerged in the Wuhan city of China which was named as COVID-19 or Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), which spread worldwide and was declared a global pandemic on 11<sup>th</sup> March 2020 [1]. Globally, as on 8<sup>th</sup> July 2022, there have been 551,226,298 confirmed cases of COVID-19, including 6,345,595 deaths [2].

Multiple modes of transmission have been suggested, including transplacental, through foetoplacental bleed or amniotic fluid, or in postpartum period through breast milk or exposure to aerosolised droplets of viral particles [3-10]. Most recent studies show low risk of intrauterine transmission of SARS-CoV-2, probably because of low levels of SARS-CoV-2 viraemia and the decreased co-expression of angiotensin-converting enzyme 2 and transmembrane serine protease 2 needed for SARS-CoV-2 entry into the cells in placenta

[11-14]. A recent meta-analysis of neonatal SARS-CoV-2 infections attributed 70% and 30% of infections to environmental and vertical transmission, respectively [15]. The study done by Anand P et al., found milder manifestations in COVID-19 infected neonates without any adverse outcomes [16]. Whereas in the study done by Malik S et al., higher risk of adverse outcomes such as neonatal sepsis and death were found in COVID-19 infected neonates [17]. Similar adverse outcomes were also reported by Oncel MY et al., [18].

Emerging studies have shown that SARS-CoV-2 infection during pregnancy is associated with a number of adverse pregnancy outcomes including preeclampsia, preterm birth, and stillbirth, especially among those with severe COVID-19 disease, which in turn can affect neonatal outcomes [11,19-22].

There is a lack of complete knowledge about perinatal COVID-19 and the neonatal outcomes in relation to maternal COVID-19 severity and antenatal co-morbidities, especially from developing countries. This study aims to describe the clinico-epidemiological characteristics of neonates born to mothers with COVID-19 and compare the clinical features and immediate outcomes of COVID-19 infected and COVID-19 non infected neonates. It also aims to study the neonatal outcomes in relation to maternal COVID-19 severity and antenatal co-morbidities.

# MATERIALS AND METHODS

This study was a retrospective study of all neonates born to COVID-19 positive mothers admitted and delivered from 1<sup>st</sup> August 2020 to 31<sup>st</sup> October 2020, at Belagavi Institute of Medical Sciences (BIMS), a tertiary care hospital in North Karnataka, India. The study was planned and executed between November 2021 and July 2022. The collected data was analysed from May 2022. The study was approved by the Institutional Ethics Committee (letter no. BIMS-IEC/177/2021-22). As this was a dedicated COVID-19 hospital during the study period, only COVID-19 positive mothers were admitted.

**Inclusion criteria:** Neonates born to COVID-19 infected mothers admitted in BIMS hospital during the depicted time period of data were included in the study.

**Exclusion criteria:** Outborn neonates born to COVID-19 infected mothers were excluded from the study.

#### Study Procedure

Delivery room practices: Deliveries of COVID-19 positive mothers were conducted by healthcare workers wearing Personal Protective Equipment (PPE) in a separate labour room designated for COVID-19 positive mothers. Mothers performed hand hygiene and wore a mask. All routine practices like delayed cord clamping and immediate skin-to-skin contact in vigorous neonates were encouraged. Those neonates who required resuscitation were resuscitated as per the standard Neonatal Resuscitation Program (NRP) 2015 guidelines in a separate designated area [23]. The babies who required admission were admitted in a separate Neonatal Intensive Care Unit (NICU) designated for babies born to COVID-19 positive mothers (COVID-19 NICU) and managed accordingly.

**Neonatal testing strategies:** The nasopharyngeal swab was sent for all neonates for a real-time RT-PCR assay for SARS-CoV-2 within 24 hours of life as per national policy [24].

Maternal details like age, parity, antenatal risk factors, symptoms like fever, cough, diarrhoea, breathlessness, severity of COVID-19 status, need for ICU care and outcomes were obtained from medical records. Mothers with uncomplicated upper respiratory tract infection and mild symptoms such as fever, cough, sore throat were classified as mild COVID-19 disease, those with pneumonia with no signs of severe disease were classified as moderate disease and those with severe pneumonia were classified as having severe COVID-19 disease. [25]. Demographic features of neonates like age, sex, gestational age, mode of delivery, birth weight and feeding history were noted and their COVID-19 status was documented. The details of the need for resuscitation at birth, need for NICU admission, complications, need for respiratory support in NICU {oxygen/Continuous Positive Air Pressure (CPAP)/mechanical ventilation}, other treatment details as well as outcomes were recorded for all neonates.

# STATISTICAL ANALYSIS

The categorical data were presented as frequencies and percentages. The Odds Ratio (OR) and the corresponding 95% Confidence Interval (95% CI) were calculated using binary logistic regression. To understand differences in outcomes of SARS-CoV-2 infected and non infected neonates, Pearson's Chi-square or Fisher's-exact test was performed. A two-sided p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using International Business Management (IBM) Statistical Package for Social Sciences (SPSS) Statistics Base version 26.0 (SPSS v26.0).

# RESULTS

Out of the 174 COVID-19 infected mothers delivered in this hospital, 172 were asymptomatic for COVID-19, one had mild COVID-19 disease and one had moderate disease for which she was admitted in Intensive Care Unit (ICU). The demographic characteristics, antenatal risk factors and outcomes in COVID-19 infected mothers have been depicted in [Table/Fig-1]. All mothers were managed according to standard COVID-19 protocols and all recovered well.

Serial No.	Maternal variables	Total n (%)			
1.	Age in years (mean age±SD)	24.074±3.890			
2.	Parity				
	≤2	148 (85.05%)			
	>2	26 (14.94%)			
3.	Antenatal risk factors				
	Anaemia	82 (47.13%)			
	Pregnancy induced hypertension	12 (6.89%)			
	Antepartum haemorrhage	2 (1.14%)			
	Gestational diabetes mellitus	2 (1.14%)			
	Premature rupture of membranes	2 (1.14%)			
	Oligohydramnios	4 (2.30%)			
	Prolonged labour	4 (2.30%)			
	Cephalopelvic disproportion	1 (0.57%)			
4.	Outcome				
	Recovered	174			
	Death	0			
<b>[Table/Fig-1]:</b> Demographic characteristics, risk factors and outcome of Coronavirus Disease-2019 (COVID-19) infected mothers.					

Out of 174 neonates, 18 (10.35%) tested positive for COVID-19 by RTPCR. All of them were born to mothers with asymptomatic COVID-19 infection. [Table/Fig-2] shows the demographic characteristics of neonates born to COVID-19 positive mothers. Out of 174 neonates, 97 (55.74%) were male, 30 (17.24%) were born preterm, 42 (24.13%) were Low Birth Weight (LBW) and 79 (45.4%) neonates were delivered by caesarean section. No significant differences were observed in demographic characteristics like gender, gestational age, birth weight, mode of delivery and type of feeding between COVID-19 infected and COVID-19 non infected neonates.

A total of 162 (93.1%) neonates cried immediately after birth, whereas 12 (6.89%) required resuscitation, two being COVID-19 infected and 10 COVID-19 non infected with no statistically significant difference between these two groups (p=0.249). A comparison of complications between COVID-19 infected and COVID-19 non infected neonates is shown in [Table/Fig-3]. No significant differences were found between the two groups in regard to complications.

A 74 (42.5%) (six COVID-19 infected and 68 COVID-19 non infected) neonates were admitted to NICU for complications. A comparison between neonatal complications and severity of COVID-19 disease in mothers showed that all of the neonates which were admitted in NICU for complications were born to asymptomatic/mild mothers except one neonate born to mother with moderate disease was admitted in

S. No.	Characteristics	Total neonates (n=174)	COVID-19 infected neonates (n=18)	COVID-19 non infected neonates (n=156)	OR	p-value			
1.	Gender								
	Male	97 (55.74%)	12 (66.6%)	85 (54.48%)	1.07	0.001			
	Female	77 (44.25%)	6 (33.33%)	71 (45.51%)	1.67	0.091			
2.	Birth weight								
	<1000 g	0	0	0					
	1001-1499 g	4 (2.29%)	0	4 (2.56%)	0.99	0.909			
	1500-2499 g	38 (21.84%)	4 (22.22%)	34 (21.79%)	0.99	0.909			
	≥2500 g	132 (75.86%)	14 (77.77%)	118 (75.64%)					
3.	Gestational age								
	<34 weeks	6 (3.4%)	0	6 (3.84%)					
	34-37 weeks	24 (13.79%)	2 (11.11%)	22 (14.1%)	0.72	0.59			
	>37 weeks	144 (82.76%)	16 (88.88%)	128 (82.05%)					
4.	Mode of delivery								
	Normal	95 (54.59%)	10 (55.55%)	85 (54.48%)	1.044	0.001			
	LSCS*	79 (45.4%)	8 (44.44%)	71 (45.51%)	1.044	0.201			
5.	Feeding history					·			
	EBF <sup>†</sup>	44 (25.28%)	6 (33.33%)	38 (24.35%)	4 550	0.050			
	DBF <sup>‡</sup>	130 (74.71%)	12 (66.66%)	118 (75.64%)	1.552	0.658			
6.	Isolation from mothe	r				1			
	Yes	39 (22.41%)	6 (33.33%)	33 (21.15%)	1.00	0.70			
	No	135 (77.58%)	12 (66.66%)	123 (78.84%)	1.86	0.70			

S. No.	Complication	Total neonates (n=174)	COVID-19 infected neonates (n=18)	COVID-19 non infected neonates (n=156)	OR	p-value		
1.	Low Birth Weight (LBW)	42 (24.14%)	4 (22.22%)	38 (24.35%)	1.5	0.091		
2.	Preterm	30 (17.24%)	2 (11.11%)	28 (17.94%)	0.16	0.07		
3.	Birth Asphyxia (BA)	9 (5.17%)	1 (5.55%)	8 (5.12%)	0.68	0.453		
4.	Meconium aspiration syndrome	8 (4.59%)	1 (5.55%)	7 (4.48%)	1.33	0.291		
5.	Early Onset Sepsis (EOS)	4 (2.29%)	1 (5.55%)	3 (1.92%)	2.21	0.061		
6.	Late Onset Sepsis (LOS)	8 (4.59%)	1 (5.55%)	7 (4.48%)	1.22	0.59		
7.	Hyperbilirubinemia	16 (9.19%)	1 (5.55%)	15 (9.61%)	0.066	0.31		
8.	Respiratory distress syndrome	7 (4.02%)	0	7 (4.48%)	-	-		
9.	Anomalies (Tracheo-esophageal fistula)	1 (0.57%)	0	1 (0.6%)	-	-		
10.	*Others	4 (2.29%)	0	4 (2.56%)	-	-		
-	<b>[Table/Fig-3]:</b> Complications of neonates born to COVID-19 positive mother. *Others - 1. Transient tachypnoea of newborn (n=2) 2. shock (n=2)							

view of mother being in ICU [Table/Fig-4]. Out of 18 COVID-19 positive neonates, 6 neonates were admitted to NICU for complications. Neonate 1 and 2 were admitted for LBW, neonate 3 MAS, neonate 4 had Late Onset Sepsis (LOS), neonate 5 was admitted with diagnosis of preterm with LBW with Birth Asphyxia (BA) with Early Onset Sepsis (EOS), neonate 6 was preterm, LBW with hyperbilirubinemia. Among these 18 neonates 2 required resuscitation, 5 required oxygen, however, none of them required CPAP or mechanical ventilation. There were no deaths among COVID-19 infected neonates.

	Maternal COVID-19 severity						
Neonatal manifestations	Asymptomatic/Mild	Moderate					
NICU admission	73	1					
Complications	Complications						
a) LBW	42	0					
b) Preterm	30	0					

c) Birth asphyxia	9	0			
d) Respiratory distress syndrome	7	0			
e) Sepsis	12	0			
f) Anomalies	1	0			
g) MAS	8	0			
h) Hyperbilirubinaemia	16	0			
Outcome					
Recovered	170	1			
Death	0				
<b>[Table/Fig-4]:</b> Neonatal outcomes and complications in relation to maternal COVID-19 disease.					

A comparison between neonatal complications like preterm, LBW, birth asphyxia, sepsis in relation to the maternal co-morbidity no significant difference was observed between newborns of Pregnancy Induced Hypertension (PIH) Vs Non PIH mothers.

Neonates born to anaemic mothers were at 1.6 times more risk for low birth weight (p=0.01) as compared to neonates born to non anaemic mothers [Table/Fig-5,6].

Neonatal complications	PIH mothers	Non PIH mother	OR value	p-value
Preterm	2	28	0.08	
LBW	3	39	0.17	
Birth asphyxia	3	6	0.51	0.18
Sepsis	1	11	0.09	
NICU admissions	10	64	0.15	

**[Table/Fig-5]:** Neonatal complications in relation to maternal Pregnancy Induced Hypertension (PIH).

Neonatal complications	Anaemic mothers	Non anaemic mothers	OR value	p-value		
Preterm (n=30)	20	10	0.277			
LBW (n=42)	35	7	1.6	0.01		
NICU admission (n=74)	37	37	0.25			
[Table/Fig-6]: Neonatal complications in relation to maternal anaemia.						

Five COVID-19 infected and 41 COVID-19 non infected neonates needed oxygen therapy, however the difference between these 2 groups was not statistically significant. None of the COVID-19 infected neonates required CPAP or mechanical ventilation, whereas five COVID-19 non infected neonates required CPAP and two required mechanical ventilation. All 75 neonates received antibiotics as per hospital policy. There was no significant difference found between COVID-19 infected and non infected neonates in regard to need for antibiotics, anticonvulsants and duration of hospital stay. There were three neonatal deaths among COVID-19 non infected neonates (3/156 neonates, death rate of 1.9%), but none among COVID-19 infected neonates. A comparison of management strategies between COVID-19 infected and COVID-19 non infected neonates is stated in [Table/Fig-7].

## DISCUSSION

In this study there were 174 COVID-19 infected mothers, among which 173 had asymptomatic/mild disease and one had moderate disease. The reason for higher percentage of mothers being

asymptomatic or with mild symptoms could be due to the strategy of universal testing for COVID-19 in pregnancy and lower thresholds of testing than in the general population. Also, the data collected in the present study was from the first wave, in which the severity of the disease was less with lower positivity rate [26-29]. Similar to the present study, Nayak AH et al., and Singh V et al., reported asymptomatic or mild COVID-19 infection in majority of mothers [30,31]. On the contrary, the studies done by Zambrano LD et al., and Badr DA et al., found increased risks of hospital admission, ICU admission, need for oxygen therapy, and need for mechanical ventilation in infected pregnant women [19,20].

In the present study, common maternal co-morbidities noted were anaemia (47.13%), PIH (6.8%), Gestational Diabetes Mellitus (GDM) (1.14%) and premature rupture of membrane (1.14%). Similarly, Singh V et al., found hypertensive disorders (13.28%), diabetic disorders (10.15%), and anaemia (10.15%) as common co-morbidities [31].

In this study, out of 174, 18 neonates tested positive for SARS-COV-2 with the positivity rate of 10.34%. None of the COVID-19 infected neonates developed severe manifestations of the disease and all were discharged subsequently. This study did not find any significant difference in regard to demographic features, need for resuscitation and respiratory support as well as duration of hospitalisation between the COVID-19 infected and non infected neonates. However there was an increased risk of EOS in COVID-19 infected neonates; although statistically not significant (OR=2.2; p>0.05). The positivity rate in neonates has been found to vary from 3.3 % to 10.7% in various studies. [16-18,32]. Some studies have even shown zero positivity rate [33,34].

In this study, of all neonates born to COVID-19 positive mothers, 30 (17.24%) were preterm, 42 (24.14%) had low birth weight, and 79(45.4%) were delivered by LSCS. In a systematic review by Smith V et al., 63.8% were preterm, 42.8% had LBW, 80% were delivered by LSCS [35]. In the study done by Nanavati R et al., 18.4% were preterm, 36.8% had LBW, and 52% were delivered by LSCS [32]. In the study conducted by Oncel MY et al., 26.4% were preterm, 12.8% had LBW, 71.2% were delivered by LSCS [18], whereas in the study conducted by Malik S et al., 23.6% were LBW and 4.8% were preterm [17]. In the study done by Anand P et al., 40% were preterm, 33.8% had LBW, and 40% were delivered by LSCS

S. No.	Characteristics	Total neonates (n=174)	COVID-19 infected neonates (n=18)	COVID-19 non infected neonates (n=156)	OR	p-value
1	Neonatal resuscitation	12 (6.89 %)	2 (11.11%)	10 (6.41%)	0.24	0.249
2	Need for NICU admission	74 (42.52%)	6 (33.33%)	68 (43.6%)	0.2	0.15
3	Oxygen usage	46 (26.43%)	5 (27.77%)	41 (26.28%)	0.609	0.081
4	CPAP*	5 (2.87%)	0	5 (3.2%)	-	-
5	Ventilator support	2 (1.14%)	0	2 (1.28%)	-	-
6	Antibiotics	75 (43.1%)	9 (50%)	66 (42.3%)	0.55	0.092
7	Anticonvulsants	6 (3.44%)	0	6 (3.84%)	-	-
8	Phototherapy	16 (9.19%)	1 (5.55%)	15 (9.61%)	0.066	0.31
9	Duration of hospital stay					
	0-5 days	56 (32.18%)	4 (22.22%)	52 (33.33%)		
	6-11 days	109 (62.64%)	11 (61.11%)	98 (62.82%)	0.685	0.55
	12-17 days	08 (4.59%)	02 (11.11%)	06 (3.84%)	0.060	0.55
	18-23 days	1 (0.5%)	0	1 (0.6%)		
10	Mean duration of hospital stay (days)		5.07±4.06	6.53±7.12		0.59
11	Deaths	3 (1.72%)	0	3 (1.9%)		-
	Fig-7]: Management of neonates born to C pus positive airway pressure	OVID-19 positive mothe	ers.			

[16]. In all these studies, there was no significant difference in the demographic parameters between COVID-19 infected and non infected neonates.

In the present study, 12 (6.89%) neonates required resuscitation. In the studies done by Malik S et al., and Anand P et al., 3.6% and 13.8% neonates needed resuscitation, without any significant difference between COVID-19 infected and COVID-19 non infected neonates, similar to our study [16,17]. In this study, 74 neonates (42.5%) required NICU admission for indications like LBW (24.14%), preterm (17.24%), birth asphyxia (5.17%), MAS (4.59%), EOS (2.56%), LOS (4.59%), hyperbilirubinemia (9.15%) and respiratory distress syndrome (4%). In this study, a much higher incidence of EOS was observed amongst COVID-19 infected neonates (5.55%) as compared to COVID-19 non infected neonates (1.92%) (OR 2.21), however the difference was not statistically significant (p=0.06).

In the study done by Malik S et al., 25.2% of babies born to COVID-19 positive mothers required NICU admission. They also found that the COVID-19 infected neonates had significantly higher risk of complications, especially sepsis, poor feeding and respiratory distress, as compared to their non infected counterparts (p-value 0.031, 0.017 and 0.05 respectively) [17]. In the present study, none of the COVID-19 positive neonates needed CPAP or mechanical ventilation, similar to the observations made by Nanavati R et al., [32]. However, in the study by Malik S et al., the need for respiratory support was high among COVID-19 infected neonates; 9.1% required mechanical ventilation while 12.1% required CPAP. Similar findings were reported by Oncel MY et al., [17,18,32].

The present study did not show any significantly increased risk of neonatal complications and adverse outcomes when compared between asymptomatic/mild and moderate COVID-19 infection in the mothers, probably because only one mother out of 174 had

moderate COVID-19 infection, rest all being asymptomatic/mild. Recent studies like those done by Dileep A et al., and Lassi ZS et al., show that more the severity of COVID-19 disease in mothers more likely the risk of maternal complications and adverse neonatal, outcomes like prematurity and LBW [36,37].

In the present study, mean duration of hospital stay was 5.07±4.06 days and 6.53±7.12 days in COVID-19 infected and non infected neonates, respectively. However, this difference was not statistically significant (p=0.59). The probable reason for lesser duration of hospital stay in COVID-19 infected neonates was lesser rate of complications and NICU admissions (33.33%) as compared to COVID-19 non infected neonates (43.58%). Also, most of the mothers (99.4%) had mild/asymptomatic COVID-19 infection without prolonged hospital stay. Similar observations were made by Anand P et al., whereas those made by Oncel MY et al., were in contrast to these findings [16,18].

In this study, there were three deaths, all among COVID-19 non infected neonates (3/156, death rate 1.9%), but none among COVID-19 infected neonates. Similar to this, Anand P et al., reported two deaths among COVID-19 non infected neonates (death rate 3.5%) and none among COVID-19 infected neonates [16]. Similar findings of favourable outcomes in COVID-19 infected neonates with zero mortality have been reported by Oncel MY et al., and Nanavati R et al., [18,32]. In contrast to this, Malik S et al., reported a total of 13 neonatal deaths, death rate being 9% in COVID-19 infected vs 2.04% among COVID-19 non infected neonates. One of the possible reasons for this difference in outcome may be the relatively higher proportion of preterm babies in COVID-19 infected (9%) vs non infected (4.5%) neonates in the study by Malik S et al., [17]. Summary of different articles on impact of COVID-19 infection on maternal and foetal outcomes is depicted in [Table/Fig-8] [16-18,31,32,38].

S. No.	Authors	Place	No. of subjects	Objective	Parameters	Conclusions
1	Anand P et al., [16], 2021	New Delhi	65	To describe the clinico- demographic profile and viral load in neonates born to COVID-19 positive mothers.	<ol> <li>Maternal Neonatal E gene cycle threshold (Ct)</li> <li>Maternal neonatal RdRp gene cycle threshold (Ct)</li> <li>Clinical features</li> <li>Demographic features</li> <li>Positivity rate</li> </ol>	Milder manifestation in COVID-19 positive neonates. Maternal viral load was not found to be associated with the positivity status or severity of the illness of neonate.
2	Malik S et al., [17], 2021	Mumbai	524	<ol> <li>To describe the clinical characteristics and management of neonates born to mothers with COVID-19.</li> <li>To compare clinical characteristics and short- term outcomes of the SARS-CoV-2 infected and non infected newborns of the mothers with COVID-19.</li> </ol>	<ol> <li>Demographic features</li> <li>Positivity rate</li> <li>Clinical features, complications, death rate</li> <li>Use of Continuous Positive Airway Pressure (CPAP), Mechanical ventilator, O<sub>2</sub></li> <li><sup>†</sup>usage, resuscitation usage</li> </ol>	Positivity rate of 6%. Higher risk of adverse outcomes such as neonatal sepsis and death in the Severe Acute Respiratory Syndrome- Coronavirus-2 (SARS-CoV-2) infected as compared to the non infected neonates
3	Oncel MY et al., [18], 2021	Multicentre Turkey	125	To evaluate the epidemiological and clinical characteristics of newborns born to women infected with COVID-19.	<ol> <li>Clinical and laboratory characteristics of mothers and neonates.</li> <li>Duration of hospital stay</li> <li>Duration of CPAP/ Mechanical ventilation/Oxygen supplementation.</li> <li>Maternal mortality and neonatal death rate</li> </ol>	COVID-19 in pregnant women has important impacts on perinatal and neonatal outcomes. Maternal mortality, higher rates of preterm birth and caesarean section, suspected risk of vertical transmission, and low rate of breastfeeding
4	Nanavati R et al., [32], 2021	Mumbai	198	To describe clinical characteristics and outcomes of neonatal SARS-CoV-2 infection	<ol> <li>Demographic features</li> <li>Positivity rate</li> <li>Clinical features, complications, death rate,</li> <li>Use of invasive and non invasive ventilation, use of surfactant</li> </ol>	SARS-CoV-2 in neonates has a wide clinical spectrum, though a subset required intensive care

5	Singh V et al., [31], 2021	Jamshedpur	132	To evaluate the clinical presentation of COVID-19 in pregnancy, its course during pregnancy and its effects on maternal and neonatal outcomes.	Details about their age, period of gestation, history of contact, symptoms, associated co- morbidities, mode of delivery and baby details	COVID-19 in pregnancy commonly presents as an asymptomatic or mild disease. It is associated with high rates of preterm births and neonatal admissions to the Intensive Care Unit (ICU).
6	Gurol- Urganci I et al., [38], 2021	England	3527	This study aimed to determine the association between SARS-CoV-2 infection at the time of birth and maternal and perinatal outcomes.	Foetal death at or beyond 24 weeks' gestation (stillbirth), preterm birth, pre-eclampsia, maternal and neonatal length of hospital stay after birth (3 days or more), and 28-day neonatal and 42-day maternal hospital re- admission	SARS-CoV-2 infection at the time of birth is associated with higher rates of foetal death, preterm birth, pre- eclampsia, and emergency caesarean delivery. There were no additional adverse neonatal outcomes, other than those related to preterm delivery.
7	Present study	Belagavi India	174	To study the clinico- epidemiological characteristics and short- term outcomes of neonates born to mothers infected with COVID-19 in relation to maternal COVID-19 severity and co-morbidities and to compare the same between COVID-19 infected and non infected neonates.	<ol> <li>Demographic features of mother and neonates.</li> <li>Positivity rate</li> <li>Clinical features, complications, death rate.</li> <li>Need for resuscitation, use of O2<sup>+</sup>, CPAP, Mechanical ventilator.</li> <li>Correlation of maternal COVID- 19 severity and neonatal outcome.</li> </ol>	Positivity rate was 10.35%. The present study did not show any significant correlation between maternal COVID-19 severity and neonatal outcomes. Neonates born to anaemic mothers were at 1.6 times more risk for low birth weight. Except for increased incidence of EOS in COVID- 19 infected neonates, most of the COVID-19 infections in neonates were of less severity without increased need for respiratory support and without significant mortality.

[Table/Fig-8]: Summary of different studies on impact of COVID-19 on maternal and neonatal outcome [16-18,31,32,38].

## Limitation(s)

The retrospective data collection from a single centre and non availability of COVID-19 non infected mothers and their neonates for comparison were the limitations in the present study.

# CONCLUSION(S)

The incidence of COVID-19 infection in neonates born to COVID-19 infected mothers in this study was 10.35%. The present study did not show any significant correlation between maternal COVID-19 severity and neonatal outcomes. There was no significant difference in neonatal complications between newborns of PIH vs Non PIH mothers however neonates born to anaemic mothers were at 1.6 times more at risk for low birth weight. Except for increased incidence of EOS in COVID-19 infected neonates, most of the COVID-19 infections in neonates were of less severity without increased need for respiratory support and without significant mortality.

Further studies with larger sample size and including neonates born to both COVID-19 infected and non infected mothers, as also followup studies of COVID-19 infected neonates for long-term outcomes are needed. The possible role of maternal COVID-19 severity on the perinatal outcomes needs to be re-evaluated in future studies.

## Acknowledgement

The authors would like to thank the institutional Medical Records Department (MRD) for their help in retrieving the data and statistician Mrs Shantala Kulkarni for her contribution in statistical analysis.

## REFERENCES

- [1] WHO Director-General's opening remarks at the media briefing on COVID-1919 -March 2020. https://www.who.int/docs/default-source/ coronaviruse/transcripts/covid-19-virtual-press-conference---21august.pdf?sfvrsn=ada7ae85\_0.
- Indian Journal of Neonatal Medicine and Research. 2023 Jan, Vol-11(1): PO36-PO42

- [2] WHO Coronavirus Disease (COVID-19) Dashboard n.d. https://COVID-1919.who.int.
- [3] Shende P, Gaikwad P, Gandhewar M, Ukey P, Bhide A, Patel V, et al. Persistence of SARS-CoV-2 in the first trimester placenta leading to transplacental transmission and fetal demise from an asymptomatic mother. Hum Reprod. 2021;36(4):899-906.
- [4] Penfield CA, Brubaker SG, Limaye MA, Lighter J, Ratner AJ, Thomas KM, et al. Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples. Am J Obstet Gynecol MFM. 2020;2(3):100133.
- [5] Facchetti F, Bugatti M, Drera E, Tripodo C, Sartori E, Cancila V, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. EBioMedicine. 2020;59:102951. Doi: 10.1016/j.ebiom.2020.102951. Epub 2020 Aug 17.
- [6] Fenizia C, Biasin M, Cetin I, Vergani P, Mileto D, Spinillo A, et al. Analysis of SARS-CoV2 vertical transmission during pregnancy. Nat Commun. 2020;11:5128. https://www.nature.com/articles/s41467-020-18933-4.
- [7] Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, Abbasi H, Mirjalili SR, Behforouz A, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: A review. Fetal Pediatr Pathol. 2020;39(3):246-50.
- [8] Kulkarni R, Rajput U, Dawre R, Valvi C, Nagpal R, Magdum N, et al. Early-onset symptomatic neonatal COVID-19 infection with high probability of vertical transmission. Infection. 2021;49(2):339-43.
- [9] Groß R, Conzelmann C, Müller JA, Stenger S, Steinhart K, Kirchhoff F, et al. Detection of SARS-CoV-2 in human breastmilk. Lancet. 2020;395(10239):1757-58. Doi: 10.1016/S0140-6736(20)31181-8. Epub 2020 May 21. Erratum in: Lancet. 2020 Sep 12;396(10253):758.
- [10] Chambers C, Krogstad P, Bertrand K, Contreras D, Tobin NH, Bode L, et al. Evaluation for SARS-CoV-2 in breast milk from 18 infected women. JAMA. 2020;324(13):1347-48.
- [11] Jamieson DJ, Rasmussen SA. An update on COVID-19 and pregnancy. Am J Obstet Gynecol. 2022;226(2):177-86. Doi: 10.1016/j. ajog.2021.08.054. Epub 2021 Sep 14.
- [12] Ouyang Y, Bagalkot T, Fitzgerald W, Sadovsky E, Chu T, Martínez-Marchal A, et al. Term human placental trophoblasts express SARS-CoV-2 entry factors ACE2, TMPRSS2, and Furin. mSphere. 2021;6(2):e00250-21.

- [13] Pique-Regi R, Romero R, Tarca AL, Luca F, Xu Y, Alazizi A, et al. Does the human placenta express the canonical cell entry mediators for SARS-CoV-2? Elife. 2020;9:e58716. https://elifesciences.org/articles/58716.
- [14] Edlow AG, Li JZ, Collier AY, Atyeo C, James KE, Boatin AA, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 Pandemic. JAMA Netw Open. 2020;3(12):e2030455.
- [15] Raschetti R, Vivanti AJ, Vauloup-Fellous C, Loi B, Benachi A, De Luca D. Synthesis, and systematic review of reported neonatal SARS-CoV-2 infections. Nat Commun. 2020);11(1):01-10.
- [16] Anand P, Yadav A, Debata P, Bachani S, Gupta N, Gera R. Clinical profile, viral load, management, and outcome of neonates born to COVID-19 19 positive mothers: A tertiary care centre experience from India. Eur J Pediatr. 2021;180(2):547-59.
- [17] Malik S, Surve S, Wade P, Kondekar S, Sawant V, Shaikh M, et al. Clinical characteristics, management, and short-term outcome of neonates born to mothers with COVID-19 in a tertiary care hospital in India. J Trop Pediatr. 2021;67(3):fmab054. Doi: 10.1093/tropej/fmab054.
- [18] Oncel MY, Akın IM, Kanburoglu MK, Tayman C, Coskun S, Narter F, et al; Neo-COVID-19 Study Group. A multicenter study on epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 by Turkish Neonatal Society. Eur J Pediatr. 2021;180(3):733-42.
- [19] Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. CDC COVID-19 response pregnancy and infant linked outcomes team. Update: Characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status-United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(44):1641-47.
- [20] Badr DA, Mattern J, Carlin A, Cordier AG, Maillart E, El Hachem L, et al. Are clinical outcomes worse for pregnant women at ≥20 weeks' gestation infected with coronavirus disease 2019? A multicenter casecontrol study with propensity score matching. Am J Obstet Gynecol. 2020;223(5):764-68.
- [21] Lokken EM, Huebner EM, Taylor GG, Hendrickson S, Vanderhoeven J, Kachikis A, et al. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol. 2021;225(1):77.e1-77.e14.
- [22] Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVID-19 multinational cohort study. JAMA Pediatr. 2021;175(8):817-26.
- [23] Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: Neonatal resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132:S543-60. (18 Suppl 2).
- [24] Chawla D, Chirla D, Dalwai S, Deorari AK, Ganatra A, Gandhi A, et al. Federation of Obstetric and Gynaecological Societies of India (FOGSI), National Neonatology Forum of India (NNF) and Indian Academy of Pediatrics (IAP). Perinatal-Neonatal Management of COVID-19 Infection-Guidelines of the Federation of Obstetric and Gynaecological Societies of India (FOGSI), National Neonatology Forum of India (NNF), and Indian Academy of Pediatrics (IAP). Indian Pediatr. 2020;57(6):536-48.

- [25] Clinical management protocol: COVID-19. https://www.mohfw.gov.in/ pdf/ClinicalManagementProtocolforCOVID-1919.pdf.
- [26] Strid P, Zapata LB, Tong VT, Zambrano LD, Woodworth KR, Riser AP, et al. COVID-19 severity among women of reproductive age with symptomatic laboratory-confirmed sars-cov-2 by pregnancy status-United States, Jan 1, 2020;2021. Clinical Infectious Disease. 2022;75(supple2):S317-S325.
- [27] Jain VK, Iyengar KP, Vaishya R. differences between first wave and second wave of covid-19 in India, diabetes & metabolic syndrome: Clin Res & Rev. 2021;15(3):1047-48.
- [28] Zirpe KG, Dixit S, Kulkarni AP, Pandit RA, Ranganathan P, Prasad S, et al. The Second- vs First-wave COVID-19: More of the same or a lot worse? A comparison of mortality between the two waves in patients admitted to intensive care units in nine hospitals in Western Maharashtra. Indian J Crit Care Med. 2021;25(12):1343-48.
- [29] Malik S, Jain D, Bokade CM, Savaskar S, Deshmukh LS, Wade P, et al. Outcomes in neonates born to mothers with COVID-19 during the second wave in India. Eur J Pediatr. 2022;181(9):3537-43.
- [30] Nayak AH, Kapote DS, Fonseca M, Chavan N, Mayekar R, Sarmalkar M, et al. Impact of the coronavirus infection in pregnancy: A preliminary study of 141 patients. J Obstet Gynaecol India. 2020:70:256-61.
- [31] Singh V, Choudhary A, Datta MR, Ray A. Maternal and neonatal outcomes of COVID-19 in pregnancy: A single-centre observational study. Cureus. 2021;13(2):e13184.
- [32] Nanavati R, Mascarenhas D, Goyal M, Haribalakrishna A, Nataraj G. A single-center observational study on clinical features and outcomes of 21 SARS-CoV-2-infected neonates from India. Eur J Pediatr. 2021;180(6):1895-906.
- [33] Salvatore CM, Han JY, Acker KP, Tiwari P, Jin J, Brandler M, et al. Neonatal management and outcomes during the COVID-19 pandemic: An observation cohort study. Lancet Child Adolesc Health. 2020:4(10):721-27.
- [34] Liu W, Wang J, Li W, Zhou Z, Liu S, Rong Z. Clinical characteristics of 19 neonates born to mothers with COVID-19. Front Med. 2020;14(2):193-98.
- [35] Smith V, Seo D, Warty R, Payne O, Salih M, Chin KL, et al. Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. PLoS ONE. 2020;15(6):e0234187.
- [36] Dileep A, ZainAlAbdin S, AbuRuz S. Investigating the association between severity of COVID-19 infection during pregnancy and neonatal outcomes. Sci Rep. 2022;12:3024. https://www.nature.com/articles/ s41598-022-07093-8.
- [37] Lassi ZS, Ana A, Das JK, Salam RA, Padhani ZA, Irfan O, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: Clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. J Glob Health. 2021;11:05018.
- [38] Gurol-Urganci I, Jardine JE, Carroll F, Draycott T, Dunn G, Fremeaux A, et al. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: National cohort study. Am J Obstet Gynecol. 2021;225(5):522.e1-22.

## PARTICULARS OF CONTRIBUTORS:

- Assistant Professor, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India.
- 2. Assistant Professor, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India. 3
- Senior Resident, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India. 4 Junior Resident, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India.
- 5.
- Professor, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India. Associate Professor, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India. 6.
- Associate Professor, Department of Paediatrics, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India. 7.

## NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Meenakshi R Sarvi, B5, JNMC Quarters, JNMC Campus, Nehru Nagar, Belagavi-590010, Karnataka, India.

E-mail: mnrai16@gmail.com

## AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA · For any images presented appropriate consent has been obtained from the subjects. NA

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jul 14, 2022
- Manual Googling: Dec 02, 2022 iThenticate Software: Dec 28, 2022 (17%)

Date of Submission: Jul 12, 2022 Date of Peer Review: Sep 06, 2022 Date of Acceptance: Dec 29, 2022 Date of Publishing: Mar 31, 2023

ETYMOLOGY: Author Origin