

# Assessing Disease Outcome in COVID-19 Pregnancies in a Tertiary Referral Center in South India: A Single-center Retrospective Cohort Study

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## ABSTRACT

**Aim:** To study the outcome in COVID-19-positive pregnancies.

**Materials and methods:** Data collected and analyzed retrospectively from COVID-19-positive pregnant women admitted to our hospital between April and September 2020.

**Results:** 78.85% of women below 30 years of age, 60.57% multigravidae, 53.71% above 37 weeks of gestation. 76.85% no comorbidities, 73.42% no history of travel/contact with COVID-19 cases. 84.57% asymptomatic, two had a severe acute respiratory infection (SARI), requiring intensive care. 74.57% diagnosed using reverse transcriptase-polymerase chain reaction (RT-PCR). 91.42% turned negative within 6–10 days. The SARI patients required intensive care unit (ICU) care, one expired. 81.42% discharged between 8 days and 14 days of admission, returned for delivery at term. 83.42% required no medication. 96.28% had normal investigation reports. 83.14% of patients discharged, 16.57% required emergency obstetric intervention. Cesarean section rate 52.28%, the previous cesarean section most common indication (43.16%). Two babies were stillborn. 99.20%, Apgar > 7 at 5 minutes. Two required resuscitations. Nine required neonatal intensive care unit (NICU) admission. Two hundred and seven babies isolated from their mother, four turned positive. Forty-four were roomed in with mothers, 30 turned positive. One hundred and sixty-seven were breastfed, included 34 positive babies. Affected babies were asymptomatic.

**Conclusion:** COVID-19 runs a milder course in pregnancy, possibly due to altered immune status. However, severe cases can deteriorate rapidly. There is evidence of community spread. COVID-19 seemed to increase cesarean rates. Neonatal transmission appeared higher following vaginal deliveries, rooming-in, and breastfeeding.

**Clinical significance:** There is a dearth of adequate data to formulate guidelines about COVID-19-positive pregnancies despite numerous studies. We hope that our findings make a humble addition to ongoing research and provide further impetus to the global fight against this pandemic.

**Keywords:** Abortions, Cesarean section, Coronavirus, Doppler sonography, Fetal distress, Fetal outcome, Hemorrhage, Maternal death, Obstetric outcome, Perinatal outcome.

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## INTRODUCTION

COVID-19 (corona SARS 2 virus) has turned the world topsy-turvy infesting it like the plague, continues to spread with no signs of relenting. It has brought in its wake a novel problem pregnancy with COVID-19. The disease being a mystery presenting in myriad ways, its pregnancy course has baffled experts.

The overall risk of COVID-19 in pregnancy is low. However, pregnant women with COVID-19 appear more likely to develop respiratory complications requiring intensive care and more likely to be placed on a ventilator.

Risk factors for severe COVID-19 during pregnancy include older maternal age, a high body mass index, preexisting diabetes, or hypertension. Some researches suggest that pregnant women with COVID-19 are more likely to have premature birth with babies more likely to be admitted to a neonatal unit.

Various studies are going on around the world to attempt and get a clearer picture of this calamity.

We, as a tertiary referral center cater to a thickly populated large area in Northern Kerala, a South Indian state, having received 350 COVID-19-positive pregnant women to date.

In our study, we have studied the outcome and course of disease in these women.

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**Conflict of interest:** None

## MATERIALS AND METHODS

We examined records of these patients for the course taken by the disease, in 350 women admitted and treated for COVID-19 between April and September 2020.

This is a retrospective study.

We studied the patient characteristics:

- Age.
- Parity.
- Period of gestation at diagnosis.

- Medications other than Fe, Ca.
- Vaccinations taken.
- Obstetric complications.
- Epidemiology
- Symptoms
- Type of test.

Number of days from onset of symptoms to a positive test.  
 Time for seroconversion (first positive test to negative).  
 Number of days from admission to discharge.  
 Treatment drugs.  
 Abnormal investigations.  
 Course of disease.  
 Obstetric outcome and complications.  
 Neonatal outcome

- Was infant stillborn
- Apgar at 5 minutes
- Needed resuscitation, neonatal intensive care unit (NICU) admission
- Isolated from mother
- Feeding
- Neonatal infection and severity

The approval of the institutional ethical committee was taken.  
 The data were entered in a Microsoft excel sheet and analyzed with relevant statistical software.

**RESULTS**

78.85% of women were below 30 years of age. 60.57% multigravida. 53.71% of women had presented after 37 weeks of gestation, 13.14% below 28 weeks. 98.57% had singleton pregnancies. There were five cases (1.42%) of twin gestation. 82.47% of women were on iron and calcium tablets at diagnosis, while 17.42% were on drugs like thyroxine, bronchodilators, antihypertensives, etc. 94.57% of women had been booked outside and referred to our hospital at diagnosis. 38.85% were nullipara, 35.42% previous vaginal delivery, 28% had a history of the previous cesarean. 97.15% had previously delivered babies of weight 2.5–3.5 kg.

73.42% of women had no history of travel or exposure to COVID-19 cases, pointing toward community transmission. 98.57% of women had a history of BCG vaccination. 84.57% of women asymptomatic with the diagnosis being made on routine testing done for all pregnant women as part of state protocol. 74.57% of women were diagnosed by reverse transcriptase-polymerase chain reaction (RT-PCR). 15.71% were symptomatic at diagnosis, diagnosed within a week of onset of symptoms (Table 1).

91.42% turned negative within 6–10 days. There was one maternal death. 81.42% of women were discharged within 8–14 days.

**Table 1:** Symptoms

	<i>n</i>	%
Respiratory symptoms	38	10.85
Fever	31	8.85
SARI	2	0.57
Diarrhea	7	2
Fatigue	1	0.28
Asymptomatic	296	84.57
Anosmia	5	1.42

SARI: severe acute respiratory infection

83.42% were treated conservatively receiving only iron, calcium, and ongoing medications while symptomatic patients had been treated using hydroxychloroquine, azithromycin, and oseltamivir.

96.28% had normal investigation reports. 83.14% had disease resolution, discharged, got readmitted at term for delivery. 16.57% required obstetric intervention. Two patients required critical care, one of whom expired despite intensive care (Tables 2 and 3).

183 (52.28%) underwent cesarean section for various indications. Seventy (20%) delivered vaginally. Seventy-three pregnancies were ongoing and on follow-up at the time of data collection for this study. Ten first trimester patients had miscarriages. There was one case of scar ectopic, managed medically. In 13 patients, labor was induced at term (Table 3A).

The most common indication for cesarean was previous cesarean (including elective and emergency cases) (43.16%). There seemed to have been fear of attempting a trial of labor due to uncertainty of outcome in COVID-19-positive pregnancies. 19.67% of cases were due to fetal distress.

Of the 253 women who delivered, 248 (98.02%) women had no obstetric complications. Two (0.79%) had a postpartum hemorrhage, of whom one had to undergo an obstetric hysterectomy. Two women required intensive care unit (ICU) admission, of whom expired due to severe respiratory failure.

Of babies born, 181 (98.90%) of cesarean cases, were <3.5 kg with 3 babies (1.16) >3.5 kg. Of vaginally delivered babies, 63 (90%) were <3.5 kg and 7 babies (10%) were >3.5 kg.

Breast milk or amniotic fluid samples had not been analyzed.

Of the babies born, 144 (56.91%) were female and 109 (43.08%) male.

Two infants (0.79%) were stillborn, one a case of severe intrauterine growth restriction, and another admitted as a case of intrauterine death (macrosomia, found macerated at delivery).

Ten babies (3.98%) had an Apgar score <5 at 1 minute after birth, of which two required active resuscitation. At 5 minutes, the Apgar score was <7 in only two babies (0.79%).

Nine babies required NICU admission, six for observation of which four had a low Apgar at 1 minute after birth. One baby was admitted due to meconium-stained amniotic fluid, one had transient tachypnea of the newborn, and one had sepsis.

In view of inadequate guidelines regarding the isolation of the baby from the mother and breastfeeding, there was a lack of uniformity regarding the same with decisions regarding rooming and breastfeeding based on the wishes of the mother. Forty-four

**Table 2:** Time for seroconversion from positive to negative

<i>Days</i>	<i>n</i>	%
<6	17	4.85
6–10	320	91.42
>10	12	3.42

One case of maternal death

**Table 3A:** Obstetric outcome

<i>Outcome</i>	<i>n</i>	%
Abortion	10	2.85
Induction of labor	13	3.71
Vaginal delivery	70	20
Cesarean section	183	52.28
Ongoing pregnancy	73	20.85



babies (17.52%) were roomed-in with the mother of which 30 babies (68.18%) subsequently were diagnosed to be positive by RT-PCR taken after 24 hours of birth (Table 3B, Figs 1 and 2).

Two hundred and seven babies were isolated with COVID-19-negative attendant, of which four tested positive (1.34%) hinting at the possibility of intrauterine transmission.

One hundred and sixty-seven babies were breastfed (directly/expressed), which included 34 (20.35%) babies found positive.

All infected babies were asymptomatic.

## DISCUSSION

The implications of COVID-19 on pregnancy are largely unknown. Maternal and fetal outcomes in COVID-19 pregnancies warrant detailed research. World Health Organization (WHO) has not found a significant difference in clinical symptoms between non-pregnant and pregnant women of reproductive age.<sup>1,2</sup> Pregnant women did not appear to be at higher risk of developing severe disease.

In our study, only 2 (0.57%) of 350 developed severe disease.

In most studies worldwide, pregnant women presented with mild symptoms like fever, cough, fatigue, and shortness of breath; some may be asymptomatic.<sup>1,3-14</sup> In our study, 84.57% of patients were asymptomatic. Respiratory symptoms like cough, rhinitis, and shortness of breath were seen in 10.85% of our patients. 8.85% presented with fever, remaining presented with diarrhea, fatigue, and anosmia. Two patients presented with a severe acute respiratory infection (SARI).

In a retrospective review by Liu et al.,<sup>15</sup> a comparison of 59 patients, including pregnant and non-pregnant adults, was carried out. They reported no significant difference between various groups regarding the development of clinical features of SARS-CoV-2.

There are changes in the immune system in pregnancy that affect how diseases present in pregnancy.<sup>16</sup> The relative suppression of cell-mediated immunity in pregnancy may be responsible for milder symptoms in COVID-19-positive pregnancies.

Adequate evidence is not available to conclude the definite effect of this virus in pregnancy. Pregnancies with SARS and MERS may help shine a light on the course and outcome of COVID-19 pregnancies.<sup>17,18</sup> Three studies showed no increase in maternal postpartum COVID-19 infection or preterm labor.<sup>1,6,8</sup> Some studies show maternal and fetal problems like preterm labor, preterm rupture of membranes, maternal respiratory distress, and increased incidence of fetal distress.<sup>4</sup> A case report from Iran documented one maternal and resultant intrauterine fetal death, directly linked to COVID-19 infection in pregnancy.<sup>17</sup> In case series from Iran of nine pregnant women with severe COVID-19 disease, seven died, one critically ill and ventilator-dependent, and one recovered after prolonged hospitalization.<sup>19</sup> Baud et al.<sup>20</sup> reported a case of miscarriage during the second trimester of pregnancy in a woman with COVID-19, apparently linked to placental infection with SARS-CoV-2.

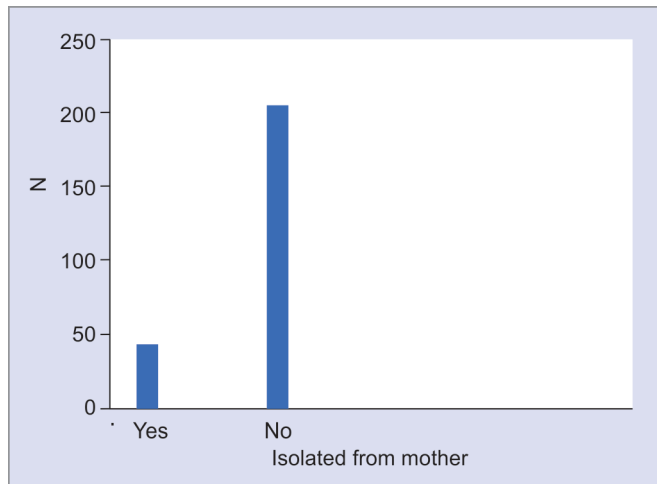
In our patients, we found complications like abortions (2.85%), fetal distress (19.67%), abruption placenta (2.18%), and abnormal umbilical artery fetal Doppler (5.46%). Two patients presented with severe respiratory symptoms requiring intensive care and prolonged ventilatory support. One recovered after delivery, while the other continued to deteriorate even after cesarean section and succumbed to severe respiratory failure. We also found a disproportionate increase in the rate of cesarean sections (52.28%) when compared to an institutional rate of 23% in non-COVID-19 pregnancies. Labor was induced by 3.71% of patients due to COVID-19-related complications.

Shanes et al.<sup>21</sup> studied placentae of 16 women with severe COVID-19 infection (15 live births and 1 second trimester intrauterine fetal demise). The study found pregnant women with COVID-19, in the third trimester more likely to have placental features suggesting vascular malperfusion/intervillous thrombi. These findings suggest abnormal maternal circulation associated with adverse perinatal outcomes. These may point toward a systemic inflammatory/hypercoagulable state affecting placental physiology. Shanes et al.<sup>21</sup> noted that increased antenatal surveillance for women with COVID-19 may be warranted. In our study, the placental examination was not done.

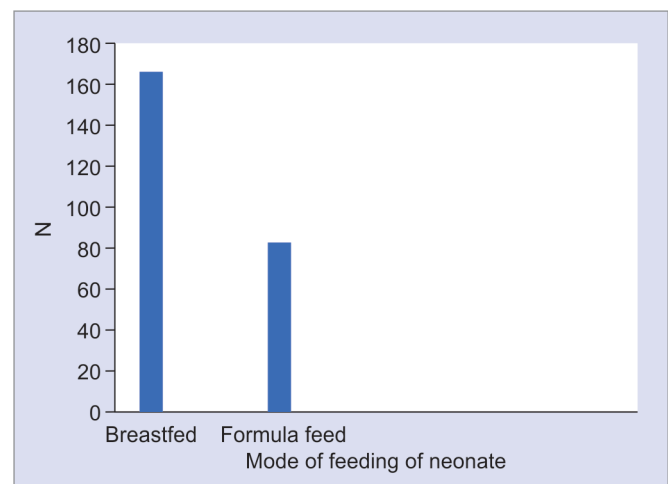
Royal College of Obstetricians and Gynaecologists (RCOG) suggests the possibility of vertical transmission from mother to neonate based on new evidence.<sup>16</sup> Recent studies have reported the possibility of *in utero* COVID-19 transmission by measurement

**Table 3B:** Babies found positive

	n	%
Vaginal delivery	15/70	22.85
Cesarean	19/183	10.92



**Fig. 1:** Neonates isolated from mother



**Fig. 2:** Whether infant breastfed/formula feeds

of fetal IgM blood level.<sup>10,22,23</sup> IgM antibody is not transferred via placenta hence suggesting a fetal immune response to infection.

Earlier case reports from China showed no evidence of vertical transmission. These had tested negative for COVID-19 from amniotic fluid, cord blood, genital swabs, breast milk, and neonatal throat swabs.<sup>1,4,24,25</sup>

One study reported COVID-19 infection in neonates 36 hours after birth.<sup>8</sup> In our study, fetal samples had been taken after 24 hours of birth.

In our study, 34 newborns out of 251 deliveries (13.43%) were found to be positive by RT-PCR. Due to the lack of guidelines regarding the isolation of newborns from mothers, there was no uniformity and had been done according to maternal wish. Forty-four mothers preferred rooming in with babies, while 207 others had preferred to isolate babies with COVID-19-negative relatives. Of the 44, 30 babies turned positive, while only 4 from the other group turned positive. This shows a very high odds ratio of 108.85. However, due to a lack of standardization, we cannot be certain. Similarly of 251 mothers, 167 mothers chose to give direct/expressed milk to babies, the 34 positive babies belonged to this group (20.35%). None of 84 babies given formula feeds developed disease. This could suggest breast milk transmission, however, breast milk samples had not been analyzed.

In a study by Penfield et al.<sup>26</sup> whereof 11 placental/membrane swabs sent after delivery, 3 found positive for SARS-CoV-2, in women with moderate/severe disease at delivery. This study demonstrated the presence of COVID-19 RNA in placental/membrane samples. These findings hint at the possibility of intrapartum viral exposure, suggesting cesarean deliveries as a recommended mode of delivery to decrease the length of exposure and the possibility of vertical transmission.

In our study, of 70 babies delivered vaginally 15 (21.42%) tested positive on day 1, irrespective of rooming-in/isolation, breastfeeding, or formula feeds. Of 183 cesarean deliveries, 19 (10.83%) tested positive. This indicates a cesarean section reducing transmission; however, owing to a lack of uniformity between cesarean and vaginal delivery groups, larger randomized confirmatory studies are required.

Very few cases indicate the intrauterine vertical transmission of SARS-CoV-2. Data from MBRRACE-UK calls for careful monitoring of affected mothers and neonates.<sup>16</sup> In our study, there were two instances of intrauterine death (0.79%).

RCOG studies have not provided data indicating the risk of teratogenicity/miscarriages in COVID-19.<sup>16</sup> The possibility of vertical transmission needs more research. Fetal outcomes reported, include fetal and respiratory distress *in utero*, prelabor rupture of membranes (PROM), and premature delivery.<sup>1,3-5,7,9,12,17</sup> Whether preterm delivery is iatrogenic or otherwise needs further investigation.<sup>16</sup>

A study by Zhu et al.<sup>4</sup> has reported neonatal COVID-19 symptoms like shortness of breath, fever, vomiting, and abdominal distension. A study by Fan et al.<sup>10</sup> also reported similar symptoms. Numerous studies depict good neonatal outcomes.<sup>1,4,7</sup> Most affected neonates were regularly monitored and managed conservatively and babies recovered well. A study by Yu et al.<sup>8</sup> reported seven pregnant women positive for SARS-CoV-2. Following their cesarean sections, the infants suspected of possible COVID-19 infection were also tested. Only one was found positive at 36 hours after birth, with mild shortness of breath symptoms however recovered well.

In our study, all affected neonates were asymptomatic.

Zhu et al.<sup>4</sup> described 10 neonates of whom 2 had thrombocytopenia and abnormal liver function tests; 1 neonate fully recovered, but 1 died. The neonatal death was attributed to poor immune function, refractory shock due to major viremia, multiple organ failure, and disseminated intravascular coagulation. Fan et al.<sup>10</sup> have reported lymphopenia and mild pneumonia findings in two neonates, with no significant clinical features, born to infected mothers. Wang et al.<sup>11</sup> reported deranged liver function tests and lymphopenia in an asymptomatic neonate born to SARS-CoV-2 infected mother. Neonatal deaths were reported by Karami et al.<sup>17</sup> and Liu et al.<sup>5</sup> where maternal multiple organ dysfunction syndrome was associated with poor neonatal outcomes.

The potential transmission of COVID-19 through breast milk is unknown due to inadequate data. Chen et al.<sup>1</sup> tested breast milk samples from six infected women, and all tested negative. Though this suggests that human milk does not transmit COVID-19, further confirmatory studies are required.

The maternal inflammatory response may have adverse effects on the developing fetus.<sup>27</sup> More studies in this area are recommended.<sup>28-30</sup> Though pregnant women fare better than the elderly population, they have a twice higher rate of preterm prelabor rupture of membranes (PPROM) and three times higher rate of preterm births compared to the general pregnant population. There is inadequate evidence to support vertical transmission. Cautious investigation and monitoring are required in neonates born to COVID-19-infected mothers.

## CONCLUSION

In our study, we found that majority of women had been asymptomatic at presentation diagnosed on routine testing. Most recovered within 8–14 days. The majority required no special treatment. There were complications like abortions, fetal distress, and abnormal Doppler parameters. There was a disproportionate increase in the incidence of cesarean section. The incidence of COVID-19-positive neonates in vaginal deliveries was almost twice that in cesarean deliveries. There was a higher instance of COVID-19 positivity in neonates roomed in with mothers. All positive neonates had been breastfed. However, all positive neonates were asymptomatic.

## CLINICAL SIGNIFICANCE

Our study stresses the importance of testing all pregnant women for COVID-19 irrespective of the presence or absence of symptoms. Community spread being on the rise, contact with affected persons or history of travel has largely lost significance. A larger percentage of patients were diagnosed with RT-PCR than antigen testing, hence that may be a better test. Largely disease had a mild course in pregnancy; however, we must watch out for severe cases since they may deteriorate rapidly.

Our study points toward a need for isolation of babies from affected mothers and withholding breastfeeding till the mother turns negative. The cesarean section seems to reduce the risk of transmission; however, larger, randomized trials may be required for the formulation of guidelines.

There is a need for studying samples of breast milk, amniotic fluid, and placentae to rule out the vertical transmission. This was not done in our patients. The lack of randomization was also an important limitation of our study. However, our study may provide

pointers based on which randomized prospective studies could be done in the future which can strengthen our arsenal in the fight against this deadly pandemic.

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