



## SARS-CoV-2 Infection in Asymptomatic and Symptomatic Pregnant Women: Association with Maternal and Neonatal Morbidity

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### Abstract

**Aim:** To assess the maternal, perinatal, and Neonatal effects of COVID-19 infection in Pregnant women.

**Methods:** A prospective study was performed at Sudha Hospital and Research Institute for 12 months from February 2021 to February 2022. This study was carried out on 78 pregnant women with COVID-19 infection admitted with or without symptoms. Their treatment and outcome of pregnancy were studied.

**Results:** Majority of patients 71.1% presented with symptoms like fever, cough, sore throat and myalgia. There was no significant increase in the incidence of oligohydramnios, preterm labour and Meconium aspiration. Newborn intensive care is significantly needed for babies born during an infective period around 18.4%

**Conclusion:** In the current scenario, pregnant women are more vulnerable to COVID-19 infection. The course, effect and outcome of infection remain still an unsolved problem. Further many studies are necessary to conclude about the after-effects of COVID infection in pregnant women.

**Keywords:** COVID-19, maternal, neonate, oligohydramnios, high-risk pregnancies.

### Introduction

The coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spreading globally<sup>[1]</sup>. SARS-CoV-2 virus can infect a wide range of cells in our body. The virus enters host cells through the receptor for Angiotensin-converting enzyme

(ACE2) which is abundant in type II Alveolar cells of the lung. The virus affects organs expressing ACE2 Receptors like the gastrointestinal tract, cardiovascular system, and nervous system. Hence patients with COVID symptoms present with varied clinical symptoms<sup>[2]</sup>.

According to disease severity COVID-19 is categorised as

1. Mild to moderate:mild symptoms to mild pneumonia (80%)
2. Moderate to severe disease: dyspnea, hypoxia, >50% lung involvement (15%)
3. Very severe disease: respiratory failure, shock, MODS(5%)

The severity of inflammation is directly linked to the severity of cytokine storm<sup>[3]</sup>. This causes adverse effects like acute respiratory distress syndrome, coagulation disorders, and myocarditis. In pregnancy, there is a significant change in immunological response. The immunosuppressive state during pregnancy makes them more vulnerable to infection. The physiological changes in pregnancy cause a reduction in functional residual capacity and expiratory reserve volume of the lungs. Due to the increased risk of respiratory infection in pregnant women, the risk of intrauterine growth restriction, abortion, preterm delivery, increased rate of operative deliveries and maternal hypoxia causing endotracheal intubation is common<sup>[4]</sup>.

The most effective management of COVID-19 includes supportive care, relieving symptoms, oxygen support and medications such as analgesics, antiviral, corticosteroids and ventilation. Remdesvir, a viral RNA inhibitor, is a potential treatment for symptomatic COVID-19 infected mothers<sup>[5]</sup>. In clinical practice, women at risk of imminent preterm delivery receive a short course of dexamethasone or betamethasone to accelerate fetal lung maturity. In severe COVID infections, these patients receive corticosteroids that reduce the inflammatory response. Corticosteroids decrease the adverse effects of pro-inflammatory mediators like TNF alpha, interleukin 1 and interleukin 6. Low dose corticosteroids administered early among symptomatic mothers decrease mortality and morbidity<sup>[6]</sup>. Proinflammatory mediators also increase the risk of venous thromboembolism in COVID infected pregnant mothers. RCOG

recommends the use of low molecular weight heparin prophylaxis in all infected mothers<sup>[7]</sup>.

### Materials and Methods

A prospective study was performed at Sudha Hospital and research institute, Erode over 12 months from February 2021 to February 2022. This study includes 78 pregnant women with COVID positive infection. Inclusion criteria: age 24 to 34 years, confirmation of COVID-19 infection by RTPCR at any week of gestation. Exclusion criteria were age >34 years, Non-pregnant women. A detailed history of maternal age, symptoms, and underlying comorbid conditions are taken. The history and the treatment course in the hospital were documented. The pregnant mothers who had injections of Remdesvir, steroids, and thromboprophylaxis were recorded. They were monitored for complications like oligohydramnios, preterm labour, IUD and meconium aspiration during this period. Mothers delivered were monitored for ICU and NICU care.

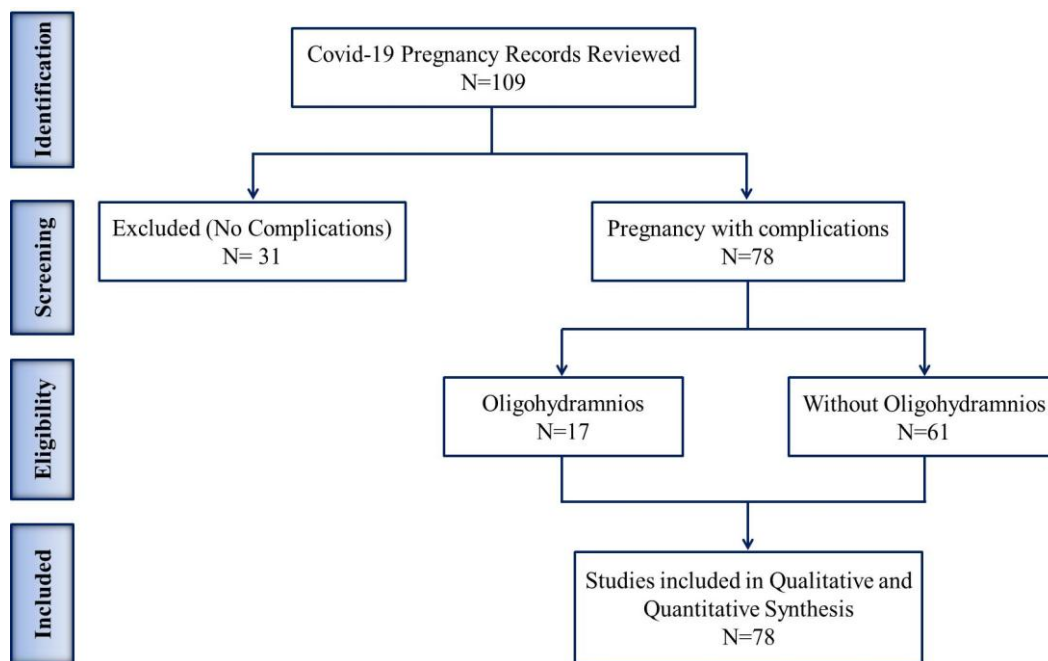
### Results

Table 1 shows the data of symptomatic COVID mothers, their associated illness and the outcome of pregnancy during the study period. Among 78 pregnant women whose Recombinant technology polymerase chain reaction became positive, 22 patients (28.2%) were asymptomatic. Of 78 cases 56 (71.8%) were symptomatic. The most common complaint and symptoms were cough in 38 patients (52.8%) and muscle aches in 31 patients (43.1%). The next common symptom was a fever of low to mild grade occurring on and off without any pattern occurring in about 27 patients (37.5%) and headache in about 29 cases (40.3%). A combination of fever, cough, and muscle aches was reported in the majority of patients.

The next symptom was the loss of smell and taste in about 58.3% of patients being the most prevalent symptom. Other common symptoms prevailing in pregnant women include shortness of breath (30.1%), sore throat (26.4%), nausea

(18.1%), and running nose (6.9%). Around 30 patients have associated obstetric complications like Gestational hypertension in 4 cases (5.1%), gestational diabetes mellitus in 13 cases (16.7%) and thyroid disorders in 13 cases (16.7%) of cases. These 30 patients fall under the symptomatic group exhibiting a range of symptoms from sore throat, and fever to mild

breathlessness. In our study 46 cases were delivered during the study period. Around 16 cases (20.5%) delivered term babies after 37 weeks of gestation. 30 cases delivered preterm around 32 to 36 weeks of gestation. 2 cases went for abortion one less than 12 weeks due to missed abortion and the other case at 18 weeks due to PPRM.



**Figure A:** Flow Chart of Search and Selection Strategy

**Table 1:** Demographic characteristics, symptoms, and underlying medical conditions among Mothers with COVID-19

Characteristics	Values
<b>Age</b>	29.08±5.19
<b>Symptoms Status</b>	
Symptomatic	56 (71.8)
Asymptomatic	22 (28.2)
<b>Symptom reported</b>	
Cough	38 (52.8)
Fever	27 (37.5)
Muscle aches	31 (43.1)
Headache	29 (40.3)
Shortness of breath	22 (30.1)
Sore throat	19 (26.4)
Diarrhoea	9 (12.5)
Nausea or vomiting	13 (18.1)
Abdominal pain	7 (9.7)
Runny nose	5 (6.9)
New loss of taste or smell	42 (58.3)
<b>Underlying medical condition</b>	
PIH	4 (5.1)
GDM	13 (16.7)
Thyroid	13 (16.7)
<b>Delivery</b>	
Term	16 (20.5)
Pre-term	30 (38.5)

Table 2 describes the treatment received during the disease. NICU requirements for newborn and Meconium aspiration were studied. In our study, 20 patients had a course of injection Remdesvir, out of which 12 patients delivered. The maternal and neonatal outcomes had no significant change among the Remdesvir received group and those who had not received. A short course of corticosteroids was given to about 15 patients for

lung maturity. Corticosteroids given for preterm delivery for lung maturity show no adverse effects during recovery. Among 46 delivered COVID affected mothers, 16 neonates required NICU admission (20.5%). Among those 2 neonates had meconium aspiration syndrome. Among symptomatic mothers there was 2 cases of maternal death in spite of effective management due to respiratory complication.

**Table 2:** Maternal Treatment and Follow-up during Pregnancy among Mothers with COVID-19

Variables	Delivered	Ongoing	MTP	Maternal Deaths	p-Value
<b>Remdesivir</b>					
Given	12 (15.4)	5 (6.4)	1 (1.3)	2 (2.5)	0.487
Not Given	34 (43.6)	23 (29.5)	1 (1.3)	0 (0.0)	
<b>Steroid</b>					
Given	11 (14.1)	3 (3.8)	1 (1.3)	2 (2.5)	0.212
Not Given	35 (44.9)	25 (32.1)	1 (1.3)	0 (0.0)	
<b>NICU</b>					
Yes	16 (20.5)	0 (0.0)	0 (0.0)	-	0.004*
No	32 (41.0)	28 (35.9)	2 (2.6)		
<b>Meconium</b>					
Yes	2 (2.6)	0 (0.0)	0 (0.0)	-	-
No	76 (97.4)	0 (0.0)	0 (0.0)		

\*Significant at the 0.01 level (2-tailed).

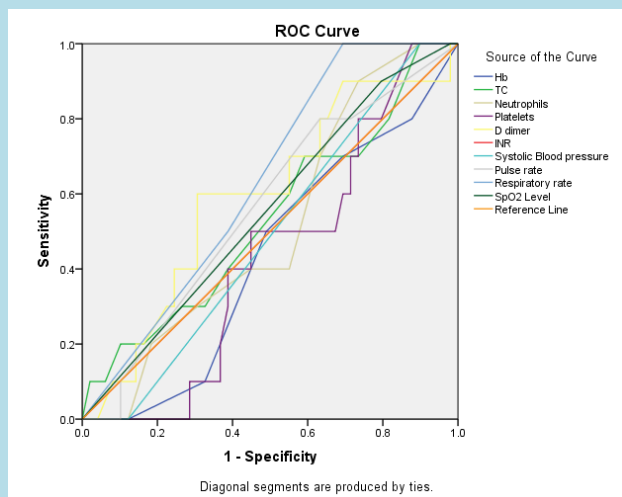
Table 3 describes the clinical and laboratory pictures of COVID infected mothers. Our study shows that 17 patients had significant oligohydramnios compared with others. The laboratory tests showed no significant change except for a slight increase in INR value with a

significant P-value of 0.041. Clinical parameters like systolic and diastolic blood pressure, pulse rate and respiratory rate are normal in our study group. Laboratory parameters like hemogram, leucocyte count, and platelet count were also within normal limits.

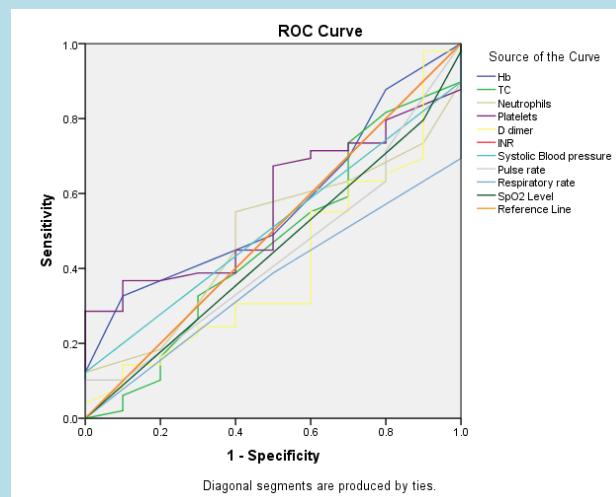
**Table 3:** Clinical and Laboratory Characteristics of COVID-19 Mothers According to their with/without Oligohydramnios in SARS-CoV-2 Infection

Clinical and Laboratory Test	Pregnancy with Oligohydramnios (n=17)	Pregnancy without Oligohydramnios (n=61)	p-Value
Hb	10.57±1.40	10.62±1.59	0.346
TC	9.99±5.10	9.41±4.34	0.574
Neutrophils	7.48±2.45	7.18±2.93	0.512
Platelets	205.31±73.67	244.95±121.27	0.198
D dimer	456.62±358.38	444.91±358.40	0.551
INR	0.94±0.07	0.92±0.05	0.041**
Systolic Blood pressure	101.54±30.51	104.24±24.79	0.563
Pulse rate	87.50±4.10	88.27±4.48	0.828
Respiratory rate	21.50±0.52	20.96±1.06	0.139
SpO2 Level	97.92±0.29	97.57±1.63	0.247

\*\* Significant at the 0.05 level (2-tailed).



**Figure 1:** Clinical and Laboratory Characteristics of COVID-19 Mothers According to their without Oligohydramnios



**Figure 2:** Clinical and Laboratory Characteristics of COVID-19 Mothers According to their with Oligohydramnios

As illustrated in Figure 1 and 2, the ROC curves analysis revealed that Area Under Curve (AUC) = 0.600, p-value 0.273, the results for the retrospective studies were significant. The AUC, calculated as sensitivity and specificity, the study result shows that AUC is less than 0.6 it indicates that the ROC curve will fall on the diagonal and hence suggests that the diagnostic test has no discriminatory ability. It shows that Hb, TC, Neutrophils, Platelets, D dimer, INR, Systolic Blood pressure, Pulse rate, Respiratory rate, and SpO2 level has negative actual state group. So these clinical and laboratory parameters do not affect the COVID-19 mothers doesn't have any correlation with the liquor status of the mother.

**Discussion**

COVID-19 infection poses a great threat to the population. Pregnant women due to an immune suppressive state were more prone to viral infection. There were very few studies carried out on maternal cases for the effect of COVID-19. The results of our study showed symptoms in about 56 (71.8%) pregnant mothers. Common symptoms prevalent are cough, fever and new loss of taste or smell. All other studies also emphasise

fever and sore throat as the common symptoms in pregnant patients.

There is a significant increase in symptoms among pregnant patients infected with COVID. According to Chen et al, pregnant patients showed a significant increase in symptoms like sore throat and fever (75%)<sup>[8]</sup>. The results of our study showed women associated with comorbid conditions have an increased risk of severe symptoms like breathlessness and require antiviral treatment like Remdesvir. According to a clinical update of COVID in pregnancy, high-risk factors like advanced maternal age, pre-existing diabetes, and chronic hypertension were associated with maternal intensive care admissions and endotracheal intubation<sup>[9]</sup>.

Out of 46 deliveries, 30 (38.5%) had delivered before 37 weeks of pregnancy. According to Gao, Yi-Jie et al, the incidence of preterm labour are higher among pregnant women with COVID-19<sup>[10]</sup>. Most preterm deliveries were due to maternal indications like PIH, Diabetes, and Fetal distress. The increased rate of fetal distress increases the rate of newborn intensive care admissions of about 16 cases (20.5%) with a significant P-value.

In our study, 20 patients received injection of Remdesvir in due course of the disease as treatment. Remdesvir has been shown to improve the clinical outcome of pregnant patients. According to Richard M Burwick et al., compassionate use of Remdesvir among pregnant women shows to reduce maternal morbidity and mortality<sup>[11]</sup>. The usual dose of corticosteroids in pregnant women doesn't pose any harm to the patient infected with COVID-19. Similar studies have been conducted to use recovery dose of corticosteroids reduces mortality up to one-third COVID patients in mechanical ventilation.

Our study shows about 17 patients had significant oligohydramnios. Another study by Aliji N showed a significant increase in oligohydramnios due to placental malperfusion.<sup>[12]</sup> But due to limited sources and trials in pregnant women, more data and studies are needed to conclude. There is significant variation in INR value among COVID infected mothers. RCOG recommends that all pregnant COVID-19 infected mothers should receive prophylactic Low molecular weight Heparin. According to the study by Di Renzo GC, the thromboembolic state of pregnancy is further enhanced by inflammation, hypoxia and cytokine storm thus necessitating anticoagulant therapy<sup>[13]</sup>. Our study shows 2 cases of maternal death due to associated co morbid conditions. Another study by villar J, shows COVID-19 in pregnancy was associated with increased risk of morbidity and mortality compared with non-infected mothers.

### Conclusion

This study concludes that COVID-19 infection in pregnant women whether associated with symptoms or not, poses a life-endangering threat to both maternal and fetal outcomes. It includes the respiratory compromise of the mother, intensive care admissions, intrauterine growth restrictions, preterm delivery, oligohydramnios and NICU admissions for the neonate. These complications are comparatively more in COVID infected mothers than non-infected mothers

irrespective of their symptoms making them high-risk pregnancies. Further, to completely understand the after-effects of COVID in pregnancy, we need more studies on pregnant women and more clinical data. Researchers must conduct more studies on COVID and pregnant women in upcoming years.

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