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**Case Series** 

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# MATERNAL MORTALITY DURING THE SECOND WAVE OF CORONAVIRUS DISEASE 19 IN INFECTED PREGNANT WOMEN IN A TERTIARY CARE CENTER IN NORTHERN KARNATAKA, INDIA: A SINGLE-CENTER CASE SERIES

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#### Abstract

The coronavirus disease 19(COVID-19) outbreak in its second wave from APRIL 2021 to MAY 2021 was life-threatening to many pregnant women. The nature of the disease in pregnant mothers was devastating. This retrospective study aimed to highlight the clinical presentation, complications, and maternal fatalities that occurred during the second wave of the COVID-19 pandemic by presenting a series of cases. It was observed that the need for intensive care unit admissions and maternal mortality had increased rampantly among pregnant and postpartum women 19 during the second wave when compared to the previous first wave of COVID-19. The data from all patients (n=55) with COVID-19 in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters were compiled for our analysis. Ten among them resulted in mortality. The rest recovered after long hospitalization or had post-COVID sequelae. There was a significant increase in preterm deliveries during 2<sup>nd</sup> wave of COVID-19. Nine out of the 10 reported maternal mortalities were preterm. According to the CT severity score, eighty percent of the mothers were affected with severe disease (>16). An outbreak had brought unpredicted changes to daily well-being. There is growing worry that COVID-19 will impede the provision of maternal and newborn healthcare, particularly in countries with few resources. In this case series, we emphasize the maternal outcome and the perinatal outcome in cases severely affected by COVID-19.

# **INTRODUCTION**

The outbreaks began in 2020, and a pandemic brought on by a new severe acute respiratory syndrome coronavirus has been witnessed globally. Coronavirus disease 19 (COVID-19) is the official name given by the World Health Organisation.

It typically affects pregnant women, mainly disrupting the cardiopulmonary physiology of pregnancy and adaptive immunity leading to increased mortality and morbidity during the intrapartum, and postpartum periods.<sup>[1]</sup>Hemophagocytic

Lymphohistiocytosismight be triggered due to viral

infection, and these patients have fulminant hypercytokinemia and multiorgan failure that eventually cause death.<sup>[2]</sup>

Physiological and anatomical changes during pregnancy decrease maternal tolerance to hypoxia. Vertical transmission in the fetus has a particular interest as the immaturity of innate and adaptive immunity makes them highly susceptible to infection.<sup>[3]</sup> Second wave of the disease increased the incidence of maternal mortality, and perinatal mortality, including Intra Uterine Foetal Demise (IUFD), stillbirth, and prolonged admission to intensive care.

This study helps in formulating treatment protocols for COVID-positive pregnant women, which helps to reduce both maternal and fetal mortality.

#### **Aims and Objectives**

- 1. To evaluate maternal morbidity and mortality among expectant women in the COVID-19 second wave.
- 2. To evaluate the perinatal outcome of newborns of mothers who tested positive for COVID.

# **MATERIALS AND METHODS**

This single-center case series was conducted in pregnant women infected by Coronavirus disease 19 infection during 2nd wave in northern Karnataka, INDIA. The study period was from APRIL 2021 to MAY 2021. The study included an antenatal, and period patient of the postnatal during hospitalization. After clearance from the Ethical Committee of BLDE (Deemed to be University) Shri B M Patil medical college and Research Centre case analysis on maternal death was prepared. The Institutional Ethical Clearance was obtained and the study was registered in the Clinical trial registry of India. Patient identity has been protected by nondisclosure of patient-related data. Consent of patient attenders was taken.

Coronavirus disease 19 infections have been confirmed using rapid antigen test (RAT) using a nasal swab sample, antibody test: using a blood sample, and Real-time polymerase chain reaction (RT-PCR) test by using nasal and throat swab sample was done. High-resolution computed tomography (CT scan) of the chest was done on a pregnant patient by using an abdominal shield to rule out the severity of bilateral lung involvement. Between APRIL 2021 and MAY 2021, there were 55 verified occurrences of severe Coronavirus disease, 10 of which were fatal for mothers. The order of their care or the manifestation of their first symptoms was not taken into consideration when choosing the cases, nor were any publication goals or non-identifying information communicated.

#### **Inclusion Criteria**

- 1. All pregnant women were admitted to our hospital and tested positive for COVID-19.
- 2. All COVID-positive women who underwent delivery (either vaginal or cesarean section) at our hospital.
- 3. Every COVID-positive mother who gave birth outside of a hospital (at home or another location) was sent to our facility for COVID management.
- All COVID-positive women had abortions or were admitted to our hospital for the care of ectopic pregnancies.

## **Exclusion Criteria**

All pregnant women who were found COVID negative.

All women who got discharged against medical advice or discharged at request were excluded.

# RESULTS

#### **General Care Management**

Coronavirus disease 19 and related infection in maternal and perinatal outcomes in pregnant women has limited data. Coronavirus disease 19 guidelines provided by the Ministry of Health and Family Welfare, Government of India, and other guidelines of common interest were considered and a standard operating protocol was framed by the Department of Obstetrics and Gynaecology and hospital management of BLDE(DU).

On admission, the patient was segregated based on MEWS score, the need for oxygen, the HFNC machine, and intensive care. Thorough history noted, exposure, and other family members infected. Initial investigations included complete blood count, Coronavirus disease 19 infection test (either by RAT, Antibodies, RT-PCR), HRCT Chest, D-dimer, Lactate dehydrogenase (LDH), C - reactive protein (CRP), Ferritin, other specific investigations (like liver profile, renal profile, coagulation profile) and few investigations repeated (Table No 1). Common management included antibiotics (Piperacillin (4.5g) Tazobactam, Meropenem, third-generation Cephalosporin's, Azithromycin, Doxycycline), antiviral (Remdesivir, Favipiravir), multivitamin, paracetamol, Vitamin С, Ivermectin, Methylprednisolone, Enoxaparin, N Acetylcysteine, etc.

Table 1: Analysis of clinical presentation, treatment and laboratory results among pregnant women during  $2^{nd}$ wave of covid-19 infection.

Cases	1	2	3	4	5	6	7	8	9	10
Maternal age(Years)	25	22	32	29	25	19	21	32	34	22
Obstetric score	G8P2L2	P1L1	G1P0L0	G1	P1L0A1D1	G1P0L0	G2A1	G3A2	G5P2L2A2	G2P1L1
Comorbidities	None	None	Yes	None	Yes	Yes	Yes	Yes	Yes	None
Fever	Yes	Yes	Yes	Yes	Nil	Nil	Yes	Yes	Nil	Nil
Cough	Yes	Nil	Yes	Yes	Nil	Nil	Nil	Yes	Yes	Nil
Dyspnea	Yes									
Medication Antibiotics	Yes									
Antiviral	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Anticoagulants	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Covid 19 test(RAT, ANTIBOD	Positive									
HRCT Severity Score	22/25	11/25	17/25	18/25	15/25	2/25	6/25	18/40	22/25	22/25
CORADS	6	5	5	5	5	3	3	5	5	6
D-DIMER(ng/ml)	524.79	>10000	371	1014	6623	6716	>10000	244	7587.93	>10000
Hemoglobin(g/dl)	11.8	11.9	10.2	10.4	7.8	9.4	10.5	10.4	12	10.7
Platelets	116	37	307	197	17	173	123	296	121	108
WBC	4210	8920	11760	13570	19600	5890	29730	22950	9880	10470
CRP	57	>90	19.5	451		20.5	59.8	46	61.5	68.6
Renal Profile	Normal	Deranged	Normal	Normal	Deranged	Normal	Deranged	Normal	Normal	Normal
Liver Profile	Deranged	Deranged	Normal	Normal	Normal	Normal	Deranged	Normal	Normal	Deranged
S.Feritin	0.5	273.1	81.8			23.3		103	237.79	
LDH	283	583	473	288	896	301	757	215	533	901
INR	0.9	1.5	0.8	1	0.9	0.9	1.59	11	1	0.8

G- Gravida, P- Para, L- Living, A-Abortion, D-Death, RAT- Rapid Antigen Test, RTPCR - Reverse transcription- Polymerase Chain reaction, HRCT-High Resonance Computed Tomography

CORADS- Covid 19 Reporting And Data System WBC- White blood cells, CRP - C – Reactive Protein, LDH - Lactate dehydrogenase

#### CASE 1

A 22-year-old multigravida with 19-week gestation came with complaints of fever for 8 days, cough, and breathlessness for 2-3 days. On admission, she was afebrile with 94% saturation on room air with tachycardia (141 bpm) and tachypnoea with a MEWS score of 5. Coronavirus disease 19, IgM and IgG was negative. RT-PCR for Coronavirus disease 19 was tested POSITIVE. CT showed evidence of viral pneumonia in bilateral lungs, CT severity score at admission was 22/25 [Figure 1].



A growth scan was done, and fetal well-being was reassuring. The patient was started on oxygen support due to persistent breathlessness with supportive CORONAVIRUS DISEASE 19 treatment and antibiotics. Increase oxygen demand as the day passed with persistent breathlessness and reached on oxygen 15 liters on the 4th day of admission. The patient started deteriorating further on the 5th day, shifted to intensive care, persistent fall in saturation was recorded, shifted to NIV MODE, and saturation was maintained at 80 % at 100% FiO2. On the 7th day, the patient died due to type 1 respiratory failure due to atypical viral pneumonia.

#### CASE 2

A 22-year-old female on postnatal day one following preterm vaginal delivery was referred because of hypotension with breathlessness.On admission, she presented with tachycardia (140bpm), Tachypnoea (30 CPM), hypotension (70 systolic, 40 diastolic blood pressure), and rapid COVID antigen test negative, RTPCR positive with CT severity score 11/25 and MEWS score 9. The patient started on inotropes (NORADRINALINE 4ml / hour), antibiotics, and supportive treatment was given. The patient blood picture showed thrombocytopenia with normal hemoglobin and total leucocyte count. She was managed in the intensive care unit. Echocardiography showed global hypokinesia, with mild mitral regurgitation with mild tricuspid regurgitation with a left ejection fraction of 40-45% on admission day. Abdominal Ultrasonography showed a normal study with bilateral pleural effusion. CT scan showed evidence of viral pneumonia. The patient was shifted to higher antibiotics, Meropenem, antiviral Remdesvir, and supportive treatment was given. After being diagnosed with coagulopathy and altered inflammatory markers, the patient received fresh frozen plasma and cryoprecipitate. The patient started deteriorating with a fall in saturation and shifted to 15 liters of oxygen support on 2 days of admission, petechial lesion was present over the upper limbs and lower limb. The patient started complaining of breathlessness. The patient shifted to NIV MODE with FiO2 100%, and persistent hypoxia was observed with persistent breathlessness. On 3rd day, cardiac markers deranged. The patient died on the 4th day after unsuccessful cardiopulmonary resuscitative efforts.

#### CASE 3

Patient of age 32 years, multigravida with 32 weeks 3 days of gestation with a known case of hypothyroidism came with complaints of acute onset dyspnoea, complaints of fever, and cough for eight days with a MEWS score of 6. The patient was on treatment for hypothyroidism for 3 years (T. Thyroxin sodium 25 microgram OD). The patient's saturation was 80% on room air, and oxygen support at 15 liters started (89% spo2). The patient presented with persistent hypoxia and shifted to an NIV mask with a Bains circuit on the next day of admission. The patient started with antibiotics and supportive treatment. The blood picture showed normal values. CT scan showed bilateral patches suggesting viral pneumonia, CT severity score was17/25.A growth scan showed fetal well-being to be reassuring. Echocardiography done on the 3rd day showed mild to moderate pulmonary arterial hypertension. Saturation falls were recorded, intubated on SIMV mode with FiO2 100%, with pulse 60bpm with blood pressure not recordable. The patient could not be revived after all resuscitative measures.

#### CASE 4

A 29-year-old previously healthy primigravida at 32 weeks gestation with RTPCR COVID-19 POSITIVE status with a known case of hypothyroidism presented with complaints of fever, dry cough, and dyspnoea. She was admitted with a fever (39°C) and experiencing shortness of breath and was normotensive (120/80 mm Hg) with MEWS core 6. The antepartum testing for the health of the fetus was favorable on the day of arrival, and the chest CT showed characteristics of viral pneumonia. The CT severity score was 18/25 [Figure2].



Figure 2:

At the time of admission, she was started on Meropenem, Azithromycin, and supportive care.

After 8 hours, she developed acute respiratory distress syndrome (ARDS), was transferred to the intensive care unit, and was placed on NIV FiO2 100%.; Remdesivir was added. A growth scan was done, which showed severe oligohydramnios with a normal Doppler study on the next day. On the 5th day, fetal well-being was non-reassuring, followed by intrauterine fetal death (IUD) on the same day. Continuous oxygen desaturations directed the beginning of labor, which was followed by the spontaneous vaginal delivery of an IUD baby on the sixth day. She experienced chronic postpartum ARDS, which led to severe hypotension, bradycardia, and death on the eighth day despite CPR attempts.

#### CASE 5

A 25-year-old female on postoperative day immediately following emergency cesarean in view of intrauterine fetal death with abruption, pulmonary edema, HELLP syndrome, and acute renal injury referred to BLDE hospital. She had received blood and blood products before the cesarean section. She was admitted with probable COVID-19 pneumonia, dyspnea (30 breaths per minute respiration), tachycardia (120 beats per minute heart rate), and normotensive blood pressure. Blood tests performed upon admission revealed abnormal blood parameters with a MEWS score of 5. Her chest CT had bilateral patchy ground-glass features with a severity score of 15/25 when she was admitted, and while a nasopharyngeal swab for the Novel Severe Acute Respiratory Syndrome Coronavirus was sent, the results of her RTPCR test were positive, which we learned after she passed away. She began taking Metronidazole (4g), Tazobactam (500mg), and Piperacillin (4g). She had dyspnea and acute hypoxemia (SpO2 82%) over the following several hours, necessitating exogenous O2 supplementation. Within 24 hours, she suffered a cardiopulmonary collapse, acutely decompensated with ARDS, and went into cardiac arrest.

#### CASE 6

A 19 years old previously healthy primigravida at 40 weeks 5 days of gestation with gestational hypertension with moderate anemia with COVID-19 rapid antigen test positive was admitted with a 6hour history of pain abdomen, initiated on Piperacillin (4g) + Tazobactam (500mg), and treatment; fetal wellbeing supportive was reassuring. She was hypertensive on admission (140/90 mm Hg). CT scan revealed patchy bilateral features typical of viral pneumonia, MEWS score 5, CT severity score 2/25, and antepartum fetal monitoring was reassuring. Spontaneous uterine contractions were noted following which she had spontaneous delivery of a live male baby on 2nd day of admission. Following the delivery of a viable neonate, she developed an atonic postpartum hemorrhage which was managed medically, and a blood transfusion was done. The patient experienced

sudden onset of breathlessness, and Favipiravir was added. She had acute hypoxemia (SaO2 89%) requiring O2 supplementation. She started decompensating with a fall in blood pressure and pulse rate and was started on inotrope. She had a cardiopulmonary collapse on the same day and died within 24 hours after failed resuscitative efforts.

#### CASE 7

A 21-year-old woman who was gravida at 35 weeks and 4 days gestation was admitted with severe dyspnea, fever, and a persistent dry cough. She also had a MEWS score of 7, and she arrived at the hospital with decreased fetal activity. An intrauterine fetal demise in the breech presentation was discovered when the patient arrived at the labor room. On arrival, her blood pressure was normal, and a chest CT revealed bilateral patchy groundglass characteristics with a severity score of 6/25 and a positive COVID-19 fast antigen test. The patient was given fresh frozen plasma and had a deranged liver profile and renal profile in addition to a positive typhoid fever test and a coagulopathy Metronidazole, a third-generation diagnosis. cephalosporin, was added. After the IUD fetus was delivered vaginally, she decompensated quickly, and supportive care and stronger antibiotics were administered. The patient developed drowsiness, and random blood sugars had fallen to 53mg/dl, which was corrected. She became hypotensive (70 systolic, 50 diastolic), which led to the need for an inotrope because of her continuous hypoxia, tachypnea, and impending respiratory collapse. Due to ARDS, her condition was progressively getting worse. She experienced a cardiopulmonary collapse and passed away after unsuccessful CPR.

#### CASE 8

A 32-year-old previously healthy pregnant woman at 33 weeks gestation with a history of hypothyroidism was referred for inpatient care due to probable COVID-19 pneumonia. Her CT scan had bilateral patchy ground-glass features and a severity score of 18/25. She was also started on Remdesivir, a third-generation cephalosporin, and supportive care. She reported having a fever, dry cough, and myalgia with sporadic dyspnea five days before to admission. She had a MEWS score of 5 and was normotensive upon admission, but within 48 hours she became critically ill and required cesarean delivery. Patient was placed on a bains circuit due to a fall in saturation while receiving maximum exogenous oxygen supply (15 liters/minute); she was started on Piperacillin (4 g) + Tazobactam (500 mg). The patient had ARDS, and despite receiving the most ventilator assistance possible, there was no improvement. She experienced acute ARDS decompensation and died from respiratory failure.

## CASE 9

A 34-year-old gravida patient of 34 weeks gestation presented with imminent eclampsia and was admitted for further management. She had sudden onset of cough following the admission. She was taken up for an emergency cesarean section as fetal well-being was non-reassuring. She had a MEWS score of 8, dyspnea, acute hypoxemia (SpO2 76%), and needed exogenous oxygen supplementation. Laboratory results revealed substantial lymphopenia with RTPCR COVID-19 positive. The CT scan indicated signs of viral pneumonia with a severity score of 22/25 [Figure3].



She was admitted to the ICU, started on Meropenem, and intubated due to acute respiratory distress syndrome (ARDS). Her ARDS did not improve despite the use of all ventilatory assistance (SpO2 - 70-80%). She was supplemented with levofloxacin throughout the ensuing 72 hours. After a futile attempt at CPR, the patient suffered a cardiopulmonary collapse and passed away.

#### CASE 10

A 22-year-old gravida 34weeks 3day gestation was admitted with labor pain with hypoxemia requiring exogenous oxygen support initiated on Piperacillin (4g) + Tazobactam (500mg), with supportive treatment. She had a MEWS score of 5, and because the fetal condition was unsatisfactory upon admission, an emergency cesarean section was performed. She showed bilateral patchy groundglass characteristics on her chest CT at the time of admission, a severity score of 25/25 [Figure 4].



And a positive coronavirus test for novel severe acute respiratory syndrome. She developed acute decompensation in less than 36 hours (SpO2 50%), put on bains circuit, Meropenem, doxycycline, Remdesivir, montelukast, azithromycin, favipiravir, and levofloxacin. Echocardiogram study normal. She suffered end-organ failure and chronic hypoxia while receiving maximum ventilator support. Two days later, despite vain attempts at cardiopulmonary resuscitation, she passed away.

# DISCUSSION

In this case series, the outcome showed severe maternal, and perinatal mortality in COVID-19 POSITIVE pregnant women, especially in the second and third trimesters.<sup>[5]</sup> These trends may be due to physiological changes which make the pregnant patient more vulnerable to coronavirus disease infection in the 2nd wave more than in the 1st wave of the pandemic. Based on initial reports from China, severe acute respiratory syndrome coronavirus 2 does not appear to follow these histological patterns of worsened diseases in pregnancy.<sup>[1]</sup> The most common presentation was fever, cough, and breathlessness. Radiological signs of pneumonia were almost present in all patients.<sup>[4]</sup>[Table 1]

During this infection majority presented with coronavirus disease 19 tested positive, raised inflammatory markers, and few were asymptomatic and discharged without severe morbidity. Data on the maternal and perinatal outcomes of pregnant women infected are limited, and the disease outcome is diverse.<sup>[3]</sup> The perinatal outcome and vertical transmission (mother-to-child) of COVID-19 are presently unclear, and no evidence is currently available.

This data is limited due to the unanticipated nature of the coronavirus disease pandemic. A study done by Mishra et al also showed that the second wave was more intense and fatal as compared to the first wave of the COVID-19 pandemic in India with overall higher mortality with cesarean section was noted.<sup>[6]</sup>

There was an increased number of intrauterine fetal demises observed during 2<sup>nd</sup>wave, with preterm deliveries making more vulnerable to perinatal outcomes.<sup>[7-10]</sup> Unknown effects of Antiviral (like Remdesivir, Favipiravir), and harmful x-ray radiation due to HRCT during the 2nd and 3rd trimester on neonates, is concerning. The presentation and onset of the disease are varied resulting in the drastic decompensated state of the mother and fetus leading to maternal death and bad perinatal outcome (IUFD, stillborn, preterm deliveries) [Table 2]. HRCT, Inflammatory markers helped to segregate patient into severity levels, and prompt management could be given. As the majority of pregnant presented in late stages with one or other co-morbidities leading to a bad outcome. In

our study comorbidities like 2 patients with hypothyroidism, 1 with gestational hypertension with anemia, 1 with severe preeclampsia, 1 with HELLP syndrome, 1 with acute fatty liver disease. Few delivered alive babies were admitted to intensive care to look for any viral infection-related

outcome, and feeding was top-up feed and was isolated from the mother to decrease the spread of disease. Few babies showed evidence of viral pneumonia and required an exogenous oxygen supply. Babies showed immense improvement and early discharge within 10-14 days [Table 2].

Outcome	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
IUFD	N/A	NO	N/A	Yes	Yes	No	Yes	NO	No	NO
Gestational	19	34 6/7	32 3/7	33	29 1/7	40 5/7	35 4/7	33 2/7	34	34 5/7
Age (week)										
Neonatal demise	-	NO	N/A	N/A	N/A	No	N/A	YES	No	No
Mode of delivery	-	С	N/A	V	С	V	V	С	С	С
Birthweight (Kg)	-	2.6	N/A	1.7	1.1	3.1	2	2	1.7	2.5
Neonatal pneumonia	-	Yes	N/A	N/A	N/A	Yes	N/A	YES	No	Yes
Need for o2, ventilator	-	Yes	N/A	N/A	N/A	Yes	N/A	YES	Yes	Yes
Hospitalization	-	10	N/A	N/A	N/A	8	N/A	5	15	10
(days)										
CORONAVIRUS	-	Negative	N/A	N/A	N/A	Negative	N/A	Negative	Positive	Negative
DISEASE 19test										
IgG antibodies	-	Not	N/A	N/A	N/A	Negative	N/A	Not	Not	Positive
		done						done	done	

There was no laboratory-confirmed coronavirus disease 19 infections except for one baby; two babies showed clinical, radiological changes of disease. There was the need for ventilator support for two babies, 3 IUFDs, four live birth (3 caesareans, one vaginal delivery), and one perinatal mortality [Figure5].

Roohi et al had done similar research which found that the second wave of infection had greater rates of maternal respiratory distress, maternal ICU hospitalizations, preterm births, NICU admissions, and maternal and neonatal fatalities than the first wave.<sup>[10]</sup>

Coronavirus disease is raising the maternal mortality rate, questioning effective strategies for reducing the same. The obstetrician is in dilemma in managing these cases, which include high mortality during this 2nd wave of Coronavirus disease, which mainly affects the cardiopulmonary system.



Herein, caution is needed in the treatment and management of pregnant ladies (mainly in the second and third trimester period) to reduce the attributable risk, maternal and perinatal mortality.

# **CONCLUSION**

Coronavirus disease-19 pandemic worsened global maternal and perinatal outcomes, with increased maternal death, intrauterine fetal demise, 1sttrimester pregnancy loss, and stillbirth. There is a need to prioritize pregnant women and a safe, accessible, and equitable maternity care response to this pandemic or other outbreaks and future health crises. In order to manage COVID-19 infection during pregnancy, each institution that provides maternity care must use a Multidisciplinary physician/intensivist, approach (obstetrician, physiotherapist).<sup>[12]</sup> anesthesiologist, and To pregnant conclude, women diagnosed with coronavirus disease 19 infection had fatal outcomes and increased perinatal mortality and it becomes very difficult for an obstetrician to make decisions on the management of COVID-positive pregnant women until solid evidence on the possibility of maternal death emerges. The vulnerability mainly depends on lung involvement and immunological changes in response to disease, which was variable from person to person.

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