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**COVID 19 INFECTION DURING PREGNANCY: STUDY OF
MANAGEMENT, MATERNAL AND PERINATAL OUTCOMES OF
COVID 19 POSITIVE PREGNANT WOMEN IN A TERTIARY CARE
CENTRE**

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INTRODUCTION

The coronavirus disease 2019 pandemic has proven to be a serious impact to healthcare society and communities worldwide. The generation of data about the disease has occurred at a tremendous pace. The mother and fetus seem to be at low risk [1]. However, obstetrics and maternal-fetal medicine practice has undergone profound changes to adapt to the pandemic. In

addition, there are aspects specific to COVID-19 and gestation that needs to be known by specialists in order to properly diagnose the disease, classify the severity, distinguish specific signs of COVID-19 from those of obstetric complications, and take the foremost appropriate management decisions.

The mode of transmission is by respiratory route by direct contact with infected secretions or by respiratory droplets [2]. Vertical transmission has not been demonstrated worldwide and is highly unlikely [3]. Maternal viremia is found to be low and suggests minimal placental seeding [3]. Reported cases of newborn infection worldwide are mostly due to droplet infection. Data on periconceptional and early pregnancy infection is very limited. No evidence of miscarriage or early pregnancy loss is seen [3]. Fetal congenital anomalies have not yet been proven to be occurring because of COVID 19 infection. Only few studies to date have reported, relatively higher rates of adverse birth outcomes in women affected by SARS-CoV-2 at late pregnancy [5]. Rate of preterm birth, Prelabour rupture of membranes is increased but its direct correlation with COVID 19 is not established [3].

AIM: To determine the optimum management in COVID- 19 positive pregnant women and study their maternal and neonatal outcomes

OBJECTIVES:

To detect COVID 19 infection in symptomatic and asymptomatic pregnant women at the earliest.

To study the mode of delivery in COVID 19 positive women in a tertiary care centre.

To study the effectiveness of management protocol for COVID 19 positive women and their neonates followed at a tertiary care centre.

METHODS: The study was conducted at Krishna hospital and medical research centre, Karad among COVID 19 Positive pregnant patients admitted during May 2020 to November 2020 after obtaining a due written, informed consent.

INCLUSION CRITERIA: Pregnant women positive for Covid 19 as detected by real time PCR for SARS CoV 2 infection.

EXCLUSION CRITERIA: Non pregnant Covid positive patients.

MANAGEMENT PROTOCOL:

1) ANTENATAL: Any COVID 19 RTPCR POSITIVE pregnant woman admitted was kept in isolation in ward which was well equipped for isolation and treatment COVID 19 POSITIVE pregnant women.

- Medical history and physical examination including blood pressure, temperature, oxygen saturation (SO₂), and heart and respiratory rate.
- Fetal heart rate auscultation, cardiotocography (CTG), or fetal ultrasound were used depending on gestational age and

maternal symptoms to confirm fetal viability or well-being.

- If there is a clinical indication (respiratory rate > 20 bpm, $SO_2 < 96\%$, presence of dyspnoea, or body temperature $\geq 38^\circ C$):

– Chest X-ray: Measures of fetal protection (abdominal shield) were taken.

Mild infection	Presence of local symptoms in the upper respiratory tract (cough, throat sore, rhinorrhoea, or anosmia) with or without non-specific symptoms such as fever or myalgia and a CURB score of 0 [6].
Moderate infection	Mild pneumonia, considered as pneumonia confirmed by chest X-ray, without presenting severity signs (basal $SO_2 > 90\%$, no need for vasopressors or ventilatory assistance, and CURB score ≤ 1).
Severe infection	<p>Severe Pneumonia. When any of the following criteria are met:</p> <p>1. failure of ≥ 1 organ, basal $SO_2 < 90\%$, respiratory rate ≥ 30 bpm, or need for vasopressors.</p> <p>2. Respiratory Distress. Suggestive clinical findings (dyspnoea, chest retraction, respiratory effort) or radiological evidence of bilateral infiltrates plus oxygenation deficit (SO_2/fraction of inspired oxygen [FiO_2] ratio ≤ 315 [if partial pressure of oxygen (PaO_2) is not available] or PaO_2/FiO_2 ratio ≤ 300).</p> <p>Mild: PaO_2/FiO_2 ratio 200–300; moderate: 100–200; severe: ≤ 100</p> <p>Sepsis. The Sepsis-Related Organ Failure Assessment (SOFA) scale can be used to evaluate sepsis severity⁷ (consider if score > 2). Also quick SOFA with two of the three following criteria: Glasgow ≤ 13, systolic blood pressure ≤ 100 mm Hg, or respiratory rate ≥ 22 bpm.</p> <p>Septic Shock. Arterial hypotension that persists after resuscitation volume and that requires vasopressors to maintain a mean arterial pressure ≥ 65 mm Hg and lactate ≥ 2 mmol/L (18 mg/dL) in the absence of hypovolemia.</p>

Investigation of COVID-19 Cases That Require Hospital Admission

- Respiratory samples: If not previously performed, a swab of the upper respiratory tract (nasopharyngeal) for PCR testing (COVID-19, seasonal influenza, and syncytial respiratory virus) were performed. In cases of highly suggestive COVID-19 infection with a previous negative PCR, retesting of a lower respiratory tract sample (sputum) was done as per recommendations.

- Chest imaging: If it was not previously performed. Chest tomography can be informative and is not contraindicated in selected cases. In some settings, lung ultrasound was done as an acceptable imaging technique alternative to X-ray.
- Basal electrocardiogram (repeated after 48 hours if medications that may have an effect on the QT interval were administered, such as hydroxychloroquine sulphate, azithromycin, or lopinavir/ritonavir).

Blood sample COVID-19 profile: for haematology, biochemistry, coagulation, and severity markers (ferritin, troponin-I, D-dimer [increased 2–3 times at third trimester]; procalcitonin [if bacterial superinfection is suspected]).

Admission criteria to the intensive care unit:

Major criteria

- Need for invasive mechanical ventilation
- Shock with the need for vasopressors

Minor criteria

- Respiratory rate ≥ 30 bpm
- $\text{PaO}_2/\text{FiO}_2$ ratio < 250
- Multilobar infiltrates
- Confusion/disorientation
- Uraemia (blood urea nitrogen > 20 mg/dL)
- Leukopenia: $< 4,000$ cells/ mm^3
- Thrombocytopenia: $< 100,000$ platelets/ mm^3
- Hypothermia/central temperature $< 36^\circ \text{C}$
- Hypotension in need of aggressive fluid resuscitation

Admission criteria: 1 major criterion or 3 minor criteria. FiO_2 , fraction of inspired oxygen; PaO_2 , partial pressure of oxygen.

RESULTS:

TOTAL NO. OF CASES STUDIED: 180

Of the total of 180 Covid RT PCR positive pregnant women studied 15 were discharged antenatally after observation and supportive treatment of Covid-19 while of the

remaining patients 3 underwent abortion of which 2 were missed abortion and one inevitable abortion. 162 patients delivered during hospitalization (**Table 1**).

Mode of delivery was LSCS for 93 patients (57.40%) while incidence of vaginal delivery was 42.60% among the Covid positive deliveries. Maternal mortality was 1.11% among pregnant women with covid 19 at our institution.

When fatal outcomes were studied among the study subjects 96.95% were Live births, 3 abortions and 2 Intra-uterine fetal death had occurred. There was no incidence of stillbirth although one neonatal death was noted (**Table 2**).

In our study we studied incidence of obstetric complications among Covid positive pregnant women admitted at our institute. Of 180 patients studied 47 patients had an associated obstetric complication. Most common obstetric complication observed was ‘hypertensive disorder in pregnancy’ with 105 overall incidence and constituting 38.29% of all complicated covid positive pregnancies under study. All pregnancy related complications were treated as per obstetric management protocols along with isolation in view of covid positive status (**Table 3**).

Study subjects were categorised into Mild,

moderate and severe infection and were managed accordingly for signs and symptoms of Covid - 19 as per management protocol described above.

82.77% Covid RT PCR positive pregnant women were asymptomatic and were admitted for isolation and observation as per the ICMR guidelines [8].

12.77% pregnant women had mild Covid-19 infection and were given oral Ivermectin and Doxycycline with supplementation of Zinc, calcium and vitamin along with routine antenatal and perinatal management (Table 4).

Pregnant women with Moderate and severe infection were administered full dose of Inj. Remdesivir along with Intravenous antibiotics and steroid treatment.

3 patients who had severe degree of infection were started on Low molecular weight heparin along with Remdesivir, steroids and antibiotic cover (Table 5).

Of the total 159 live births of covid-19 positive patients only 2 neonates (1.25%) were covid 19 positive at birth but did not develop any covid related complication (Table 6).

Table 1: Outcome in COVID 19 POSITIVE pregnant women

No. Of patients	Underwent vaginal delivery	Underwent LSCS	Underwent abortion	Discharged in the antenatal period	Deaths
180	69	93	3	15	2
Percentage	38.33	51.66	1.66	8.33	1.11

Table 2: Fetal outcome in COVID 19 Positive mothers

No. Of patients	Liveborn	Stillborn	IUFD	Abortions	Neonatal Death
164	159	0	2	3	1

Table 3: Obstetrical complications and their management in COVID 19 POSITIVE pregnancies

Obstetrical risk factor	No. of patients	Management
Missed abortion	2	Post abortive care and observation for 10 days

Obstetrical risk factor	No. of patients	Management
Inevitable abortion	1	Post abortive care and observation for 10 days
Hyperemesis gravidarum	1	Routine Antenatal care and observation for 10 days
Preterm labour	2	Tocolysis, routine Antenatal care and observation for 10 days
Hypertensive disorder of pregnancy	18	Those with no COVID related symptoms : a. NON SEVERE PRE-ECLAMPSIA : Regular BP monitoring, Obsteric USG for fetal maturity,fetal weight,amniotic fluid index, Placental position.Doppler assessment of uterine , Umbilicaland Middle cerebral artery blood flow . Haemogram ,coagulation profile ,Liver and Kidney function tests :if Within normal limits were terminated at 37 weeks. b. SEVERE PRE ECLAMPSIA: terminated between 34 to 37 weeks Specific cases with COVID related have been noted below.
HELLP Syndrome	1	Termination of pregnancy by LSCS for fetal distress with transfusion of blood and blood products . Patient was observed in intensive care unit for 2 weeks.
oligohydramnios	4	Adequate antenatal and intrapartum fetal monitoring .1 patient delivered vaginally after induction of labour. 1 patient was posted for LSCS on maternal request and 2 patients were posted for LSCS for fetal distress.Routine postpartum care and observation for 10 days
IUGR	5	3 vaginal deliveries 2 LSCS for severe IUGR Routine postpartum care and observation for 10 days.
Antepartum hemorrhage	0	-
GDM	2	Both patients were asymptomatic for COVID infection .Oral hypoglycemic agents were started for both patients. Routine postoperative care and observation for 10 days and follow up after 14 days
Meconium stained liquor	6	Patients were posted for LSCS for fetal distress. Routine postoperative care and observation for 10 days
Heart disease in pregnancy	3	1)19 year old primigravida 33 weeks pregnancy with operated case of VSD in her infancy. 2 D echo findings were reassuring . Patient was given routine Antenatal care and discharged after 10 days of observation. 2) 2 cases of peripartum cardiomyopathy
IUFD	2	Induction of labour and vaginal delivery. Routine postnatal care and discharge after observation for 10 days.

Table 4: Management protocols according to severity of COVID 19 infection

Asymptomatic Group A	Management	Mild infection	Management	
			GROUP B (Symptomatic without comorbidities)	GROUP C (symptomatic with comorbidities)
149	Routine Antenatal and postnatal care with observation for 10 days Home isolation for 14 days after discharge.	23	Routine Antenatal and postnatal care . Oral Ivermectin 12 milligrams single dose+ Oral Doxycycline 100 mg BD For 5 days Supportive treatment: oral Zinc , Calcium and Vit C	Antenatal: Oral Ivermectin 12 mg single dose + Oral Doxycycline 100 mg BD For 5 days. Inj. Ceftriaxone 1 g BD Intravenous for 5 days. LMW Heparin 0.4 ml iv OD based on BMI, D-Dimer Postnatal: if Liver and kidney function tests are within normal limits, Inj Remdesivir 200 mg in 40 ml sterile water given in 230 ml 0.9% NS iv on day 1 followed by Inj Remdesivir 100 mg in 20 ml sterile water in 250 ml 0.9% NS iv for 4 days. Alternatively, Oral Favipiravir 1800 mg BD on day 1 followed by Oral Favipiravir 800 mg BD for 6 days.

Moderate infection	Management	Severe infection	Management
5	Inj. Remdesivir for 5 days Inj. Ceftriaxone 1 gm IV BD for 5 days OR Inj. Meropenem 1 Gm IV TID for 5-7 days (If RFT is normal) LMW Heparin 0.4 ml SC or IV OD or BD as per the BMI, INR & D-dimer levels Oral or Inj. Methylprednisolone 40 mg BD and tapered thereafter Supportive treatment	3	Inj Remdesivir for 5 days. Inj Piperacillin +tazobactam 4.5 g 6 hourly 7 days Or Inj Meropenam 1 g iv TID FOR 7 Days(if RFT is normal) Inj LMW Heparin 0.4 ml Iv BD according to BMI , INR D -Dimer Inj Methylprednisolone 40 mgBD and then tapered Plasma transfer Ventilatory support

Table no. 5: neonatal resuscitation and initial management

	APGAR <7	APGAR >=7	Neonatal resuscitation
APGAR Score at 1 min	19	140	Those neonates with an APGAR score of less than 7 were watched for development of respiratory distress , secondary apnea in a well equipped newborn care corner.COVID RTPCR for nasopharyngeal swab was done .COVID negative neonates were kept in an isolated ward for observation . They were given top feeds and breast feeding was avoided till maternal viral load decreased.
APGAR Score at 5 min	9	150	Those neonates who had respiratory distress , secondary apnea were kept in neonatal ICU in isolation and observed for 10 days .Nasopharyngeal swab tested negative for COVID in these babies. They were given top feeds till maternalviral load decreased.

Table no. 6: Neonatal management

No. of COVID 19 positive neonates	Management	No. of COVID 19 negative neonates	Management
2	The neonates who tested COVID positive at birth were kept with their mothers. They were observed for development of any symptoms and any hematological and biochemical(CBC, INR; Liver function tests,ESR , CRP, IL-6, Sr ferritin , D-Dimer) and radiological pulmonary changes. Breastfeeding was discouraged in these neonates. A repeat Covid swab was done which came to be negative. Immunisation as per National Immunisation schedule.	157	Neonates were kept in isolation for observation for 10 days. Routine postnatal care was given. Top feeding was advocated till maternal viral load decreased. Immunisation as per National immunisation schedule .

DISCUSSION:

This study conducted attempts to establish the optimum management protocol for COVID 19 Positive pregnancies in the present pandemic situation that has grappled the world .

In our study, of the total number of deliveries conducted, 58 % were done by caesarean section and 42% were

vaginal deliveries. None of the terminations were done for COVID 19 related complications. The increased caesarean rate is consistent with findings of other studies done ⁹ although the most common indication for caesarean delivery among these study groups was Covid-19 pneumonia [10]. No significant effect of COVID 19 infection on the course of

labour was observed. The vaginal deliveries and caesarean sections were conducted in well equipped and well isolated labour rooms and operation theatres as per ICMR guidelines [8].

82% of the COVID 19 positive pregnant females did not develop any symptoms or complications and a routine post partum care was adequate for them. This finding of common occurrence of asymptomatic covid-19 infection among pregnant women is consistent with the study done by Metkari *et al* [11] wherein 85% of Covid-19 positive pregnant women were found to be asymptomatic. In our study it was seen that 12 % of the females developed mild infection and the supportive treatment given to them sufficed their covid infection.

Development of complications due to moderate infection was seen in 2.7 % cases. The most common obstetric complication associated was hypertension in pregnancy which was consistent with the results of meta-analysis done by Shu Qin Wei *et al* [12] associating increased incidence of pre-eclampsia among women with Covid -19 infection. Although deterioration was not observed in this study group, the data is very less to generalize the results.

96.9% Neonates of mothers with COVID 19 Positive status were COVID 19 negative at birth and did not develop any complications during the period of observation. From this study, vertical transmission seems to be unlikely. Similar observations were noted from studies by Lopez *et al* [1] and also in the meta-analysis done by Kotlyar *et al* [13]. The usual neonatal resuscitation protocol followed usually in the hospital yielded good results in neonates of COVID positive mothers. The management protocol followed for COVID positive neonates is however very less to conclude significant results in terms of effectiveness. 1 neonatal death that occurred was COVID 19 negative in a low birth weight, preterm neonate under NICU Care and cause of death was sepsis outside of covid 19 infection, the finding is consistent with meta-analysis by Ciapponi *et al* [14] which reported neonatal mortality prevalence was 0.34%.

CONCLUSION:

The stratification followed in pregnant women majorly helped in triage and implementation of the management protocols accordingly.

Most pregnant women with SARS CoV-19 positivity are symptomatic and the high rate

of asymptomatic presentation in pregnant women with COVID-19 may be explained by the screening strategy for COVID-19 and the low thresholds for testing during pregnancy. Pregnant women with COVID-19 are also at an increased risk of receiving cesarean sections. The risk of congenital transmission or transmission via breast milk is estimated to be low to very low, but there is a higher risk of transmission due to close contact by droplet or airborne transmission. It can be concluded that Covid -19 infection in pregnancy does not alter obstetric management although it may cause increased incidence of iatrogenic preterm birth. Overall Maternal and neonatal outcome in pregnancy with Covid-19 is good and comparable to normal population.

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