



## Original Research Article

## Pregnancy &amp; Covid 19 infection: Our experience

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## ABSTRACT

Corona virus disease also known as Covid -19 pandemic has represented major impact to health system and societies world-wide. There is no particular high risk seen among mother and fetus. In addition to these aspects specifically to Covid -19 and gestation that should be known by specialist in order to correctly diagnose disease, classify severity, distinguish obstetric complications with specific signs of Covid -19 and for taking most appropriate management decision.

The pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has exposed vulnerable populations to global health crisis. Mother and fetuses are particularly susceptible to poor outcome. There are very limited data how SARS-CoV-2 behaves in pregnant women & their infants. We pearly reviewed 52 gravida infected with covid-19 pneumonia. Out of which 25 symptomatic patients admitted to our hospital while 27 asymptomatic but Covid positive patients care taken on OPD basis followed by home quarantine for 14 days.

**Aims & Objectives:** 1) To summarize the clinical features of Covid-19 in pregnancy; 2) Any intervention helps for better maternal and perinatal outcome. 3) Safety profile of Remdesivir in third trimester of pregnancy with Covid-19 pneumonia.

**Materials and Methods:** This was a single-centre; meta-analysis performed at Sunshine global hospital Vadodara Gujarat designated hospitals for pregnancy with COVID-19 in the epicentre of the SARS-CoV-2 outbreak and medical consultation/collaboration with Scientific Research Institute, Surendranagar, Gujarat. We included pregnant women with COVID-19 from inpatient & outpatient department.

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## 1. Introduction

The novel coronavirus first time identified in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread around the world.

Possibility of vertical transmission is highly unlikely and has not been demonstrated in Chinese Covid -19 outbreak or in previous epidemics by other similar Corona viruses {SARS-CoV-2 & Middle East Respiratory Syndrome (MERS-CoV)}.<sup>1,2</sup> During 2009 H1N1 influenza pandemic

pregnancy caused higher risk of ARDS, Severe Pneumonia, Mechanical Ventilation and death when compare with reproductive aged non- pregnant women.<sup>3</sup>

Similar results were also reported with SARS and MERS epidemics where pregnant women may develop organ dysfunction and may be it will lead to death. In current Covid-19 outbreak, pregnant women may have had fewer maternal and neonatal adverse effects than were reported for SARS and MERS.<sup>4</sup> There is no evidence of presence of virus in genital fluids, amniotic fluid, urine, or breast milk; according to some limited data.<sup>5</sup>

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There are nearly 3.5 million global cases of SARS-CoV-2, with nearly 250,000 deaths at present. In India total 10208725 cases of SARS-CoV-2. Out of those 9782669 cases are recovered. Treatments during this deadly pandemic are rapidly evolving and certain drugs are remained under trial as potential therapies for COVID-19 patients who are critically ill. Antiviral treatment options proposed and which are safe during pregnancy include several drugs for example, hydroxychloroquine, remdesivir, and lopinavir/ritonavir. Remdesivir is a nucleoside analogue, an inhibitor of RNA-dependent RNA polymerase with in vitro activity against both SARS-CoV-1 and Middle East respiratory syndrome (MERS-CoV).<sup>6–9</sup>

The novel coronavirus disease (COVID-19) is the most challenging health crisis that we are facing today in worldwide. Against this health crisis, it becomes imperative to study the effects of COVID-19 on pregnancy and its outcome. Therefore, the present study was undertaken for evaluating effects of COVID-19 on course of labour and neonatal outcome as well and on maternal morbidity and mortality.

Lower segment caesarean section (LSCS) was done for several obstetric indications like non-progress of labour, foetal distress, etc. Majority of neonates were born with a normal Apgar index (7–10) with average birth weight of (2.5–2.9 kg), according to the characteristics of the newborns.

Pregnancy is an indication for aggravated risk of adverse obstetrical and neonatal outcomes due to several viral or other infections. The systemic effects which propagate the risk of complications from respiratory infections may arise due to the altered physiological and immunological state that is a typical component of pregnancy. The respiratory and cardiovascular components of these changes, along with the development of an immunological adaptation that allows the maternal body for tolerating the antigenically diverse fetus; which inflate the risk towards development of severe respiratory diseases.

Here, we analysed the findings of 52 patients out of which claimed that there were no fetal complications of COVID-19 and it affected pregnant women of them suggested that it does have adverse fetal and neonatal complications. A point that must be stressed upon is that almost all of the mothers that have been included in these studies were in their third trimester, and vertical transmission as well as fetal and neonatal complications, even in previous coronavirus infections, has been prevalent in the first two trimesters and not so much in the third trimester.

## 2. Materials and Methods

### 2.1. Study design and participants

This was a single-centre; metaanalysis performed at Sunshine global hospital Vadodara Gujarat designated hospitals for pregnancy with COVID-19 in the epicentre of the SARS-CoV-2 outbreak<sup>8</sup>. We included pregnant women with COVID-19 from inpatient & outpatient department. COVID-19 was diagnosed by RTPCR. All the COVID-19 patients had positive reverse transcription polymerase chain reaction (RT-PCR) results from respiratory samples.

### 2.2. Patient identification and data collection

All patients consecutively admitted to The Sunshine global hospital Vadodara Gujarat with the diagnosis of COVID-19. Data extracted from the patient records included age, the severity of COVID-19, symptoms, Hemodynamic status, laboratory tests, CT findings, treatments (antivirus regimens, antibiotics, corticosteroids) and length of hospital stay, gestational age on admission, the outcome of pregnancy, and information on neonate were also recorded.

#### 2.2.1. Laboratory and radiological presentations

More leukocytosis ( $> 9.5 \times 10^9/L$ ) (10, 35.7% vs. 2, 3.7%;  $p < 0.001$ ) and elevated CRP levels ( $> 0.6$  mg/dL) (17, 68% vs. 14, 25.9%;  $p = 0.001$ ) were detected in pregnant women. Baseline Hb level (117.5 g/L, IQR 106.75–129, vs. 126 g/L, IQR 121.25–135.5;  $p = 0.018$ ) and albumin level (35.50 g/L, IQR 34.00–38.65 vs. 43.00 g/L, IQR 41.00–43.85;  $p < 0.001$ ) were lower in pregnant patients. Elevated alanine aminotransferase was observed in two (3.7%) non-pregnant women, with no reports in pregnant women ( $p = 0.80$ ). Besides these two pregnant patients, all other pregnant patients showed typical changes on chest CT, with presence of multiple patchy ground-glass shadows.

#### 2.2.2. Patient concerns

We report a clinically confirmed 52 cases of covid-19 with pregnancy. Patients were tested positive for covid-19 before delivery but became negative few days after delivery, out of which 11 patients delivered by LSCS at our hospital,<sup>10</sup> 2 patients delivered vaginally, 3 patients got admitted after LSCS & 9 ANC patients got admitted in 2<sup>nd</sup> trimester & discharged, they delivered at their respective gynaecologist. At 34 weeks of gestation with steroid coverage early LSCS was planned to decrease the materno- fetal vertical transmission. We noted that after delivery recovery of mothers & babies very high. 2 patients who presented very late but reports were very bad they succumbed.

### 2.2.3. Outcome

ANC patients who admitted to our hospital gave birth to a healthy baby after being cured from covid-19 infection. 2 patients came in labour so delivered vaginally. 12 babies were negative on RTPCR, 1 still born delivered in ICU, 1 baby was positive on RTPCR was kept under observation in NICU turned negative after 7 days. 2 patients who presented very late but reports were very bad they succumbed. Average number of hospital stay after LSCS is 5-10 days & after normal delivery 4 days. Pregnant patients with Covid 19 presented with mild to moderate symptoms in early stage recovery chances are high. Chances of vertical transmission cannot be neglected.

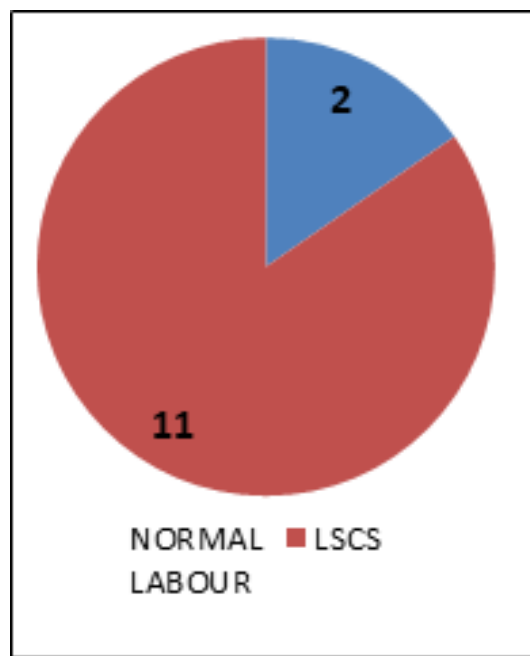


Fig. 1:

### 2.3. Lesson subsections

The Findings of this case report are useful for understanding the possible clinical features of Covid-19 infection in pregnancy, duration of antibody & Passive immunity of the fetus. Pregnant patients with Covid 19 presented with mild to moderate symptoms in early stage recovery chances are high.

#### 2.3.1. Vertical Transmission of COVID-19

There has been a case where the possibility of vertical transmission has been elicited,<sup>1,2</sup> where the neonate had an increased IgM level, which indicated involvement of innate immunity of the neonate. Also, reports suggest that 1 neonate, born to COVID-19 infected mothers, tested positive for SARS-CoV-2, postpartum.

The principal for obstetric management of COVID-19 include rapid detection, isolation, and testing, profound preventive measures, regular monitoring of uterine contractions as well as of fetus, peculiar case-to-case delivery planning based on degree of severity of symptoms, and appropriate post-natal measures is taken for preventing infection. Transmission occurring during birth through contact with infectious vaginal secretions and after birth through respiratory secretions is a concern. Thus, a mother who has confirmed COVID-19 or under investigation should be isolated from her baby until the mother is free from any possible transmission danger.

### 3. Discussion

The recent data have been demonstrated that pregnant women diagnosed with COVID-19 have an increased risk of ICU admission and mechanical ventilation as compared with non-pregnant women.

We have categorized our patients into mild moderate & severe cases depending on 1) RTPCR 2) CT Severity score 3) CALL Score. Total 15 Mild cases, 5 moderate cases & 5 severe cases were admitted. Out of severe cases 2 succumbed 3 patients with use of early Remdesivir early LSCS planned for better outcome. We could successfully save severe cases of covid19 with pregnancy. Decisions regarding emergency delivery are individualized and decisions are taken according to both maternal and fetal status.

Emergency caesarean delivery in ICUs is reserved for such conditions like acute and severe maternal or fetal decompensation; we demonstrate that pregnant women who are critically ill with COVID-19 can be managed in the ICU without the need for emergency delivery. Overall goal oxygen saturation was >95%, in order to ensure adequate fetal oxygenation; our most of the patient required nonbreather, but never mechanical ventilation, to maintain that oxygen saturation except 2 patients required mechanical ventilation.

Pregnancy is a hypercoagulable state in which there is physiologic increase in D-dimer. COVID-19 has been associated with elevations in D-dimer and thrombus formation.<sup>11</sup> Our patient had an elevated D-dimer but no evidence of peripheral thrombi.

Pregnant women who are positive for SARS-CoV-2 are placed on antepartum and postpartum venous thromboembolism prophylaxis according to underlying hypercoagulability in pregnancy and known venous thromboembolic complications associated with COVID-19.

Elevated CRP is also physiologic during pregnancy above non-pregnant values, with difference being detected as early as 4 weeks of gestation.<sup>12</sup> Median CRP values in uncomplicated pregnancy ranging from 3 to 6 mg/L according to population-based studies have been reported. Thus, CRP may not be useful in pregnant patients with

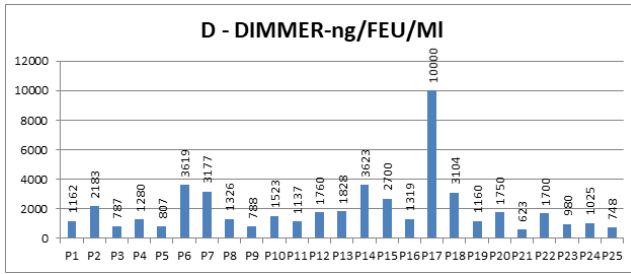


Fig. 2:

COVID-19 to determine the severity of COVID-19 illness.

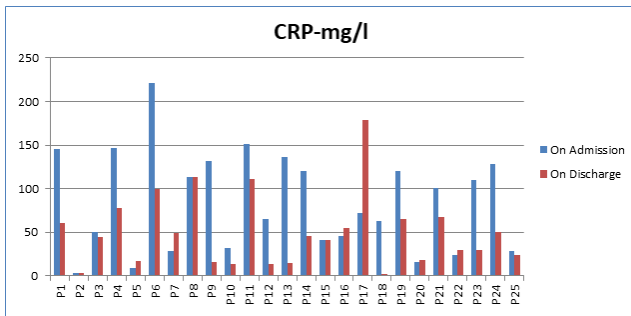


Fig. 3:

Remdesivir is a prodrug which intracellularly metabolized into an adenosine triphosphate analogue which inhibits viral RNA polymerase with in vitro inhibitory activity against SARS-CoV and MERS-CoV.<sup>8,9</sup> After the emergence of SARS-CoV-2, in vitro testing demonstrated that Remdesivir has activity against this virus; however, the data of its use in pregnancy are limited. Manufacturer safety data indicate that in animals there is no reproductive developmental toxicity at clinically relevant doses; but in female animals before conception the embryonic toxicity was only noted when systemically toxic doses were administered to them (Remdesivir Investigator's Brochure, Gilead Sciences). Initial analysis of patients who are treated with compassionate use of Remdesivir demonstrated the possible mortality benefit and low rate of adverse effects. The National Institutes of Health Adaptive COVID-19 Treatment Trial-1 (ACTT-1) study demonstrated that Remdesivir was superior to placebo because it decrease time for recovery in hospitalized adults and may have mortality benefit in patients. However, neither of these studies included pregnant women in their studies. On basis of updated compassionate use protocol of remdesivir, our patient will be included in a forthcoming analysis of patients receiving Remdesivir. An Ebola treatment study included Remdesivir as 1 of 4 arms before covid-19. Total 6 of the 175 patients enrolled in that arm who had a positive pregnancy test at the time of their enrolment. There is no any specific adverse outcomes were recorded in pregnant women in this arm of the study; however, the

study report does not provide specific information regarding the outcomes in these patients. In this study, our patient tolerated the medication very well.

Transaminitis is one of the noted side effects of Remdesivir. This drug may further complicate the interpretation of elevated liver enzymes in a population where they could manifest as pre-eclampsia, any viral effect, or any physiologic elevation. Our patient did develop an increase in transaminases while on Remdesivir treatment; but this increase due to COVID-19 or due to Remdesivir is not clear. Our patient had no proteinuria or hypertension symptoms to suggest pre-eclampsia as a cause of transaminitis.

According to, WHO recommendations, mothers with suspected or confirmed COVID-19 should be encouraged to initiate or continue to breast feed. Counselling of mothers should be done about benefits of breastfeeding substantially outweigh potential risks for transmission.<sup>13</sup> Breast feeding will not spread COVID 19 babies. Infected mother transmit the virus via respiratory droplet.

#### 4. Conclusion

COVID-19 has proven to be a deadlier infection. Pregnancy is a stressful physiological condition and is an indication for immuno-suppression and that's why pregnant women are more susceptible for complications related to COVID-19, as compared to a non-pregnant women. COVID-19's effects are seen on mother and neonate or may be on both. Chances of vertical transmission of COVID-19 are possible across the materno-fetal interface according to fetal complications, by utilization of ACE2 receptors. This is essential in achieving a better prognosis for the mother and preventing infection in the neonate. A number of studies have discussed COVID-19 in pregnant women, our study shows highlight of several important aspects of care of our patients in COVID-19.

#### 5. Source of Funding

None.

#### 6. Conflict of Interest

The authors declare that there is no conflict of interest.

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