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## Original Research Article

## A study of maternal and perinatal outcomes in first and second waves of COVID-19

Aliya Roohi<sup>1,\*</sup>, V Janaki<sup>1</sup><sup>1</sup>Dept. of Obstetrics & Gynaecology, Gandhi Medical College, KNR UHS, Secunderabad, Telangana, India

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## ABSTRACT

**Background:** The emergence of the corona virus (SARS-COV-2) led to a pandemic. Any pandemic/epidemic is generally associated with poor maternal and child health manifesting as increased maternal and fetal mortality and morbidity.

**Aim:** This study aims to compare the effect of COVID 19 infection on maternal and perinatal outcome in first and second waves of the pandemic.

**Materials and Methods:** A prospective analytical study of 1300 patients was done. Various parameters to measure the maternal and perinatal outcomes were compared among the first and second wave of covid.

All parameters were analyzed using descriptive statistics and compared using the Chi-square test.

**Results:** It was found during the study that fever (48%), cough (30%) and anosmia (40%) were the major symptoms in first wave while majority of women in second wave remained asymptomatic (75%) initially and developed dyspnea later (46%). It was also found that presence of co-morbidities increased the risk of developing severe covid disease. Disease progression was found to be more rapid in the second wave. Maternal respiratory distress accounting as an indication for delivery was higher in second wave (33%) when compared to the first wave (13%). Maternal mortality and preterm delivery rate were higher in the second wave as compared to the first wave.

**Conclusion:** The present study findings can guide and enhance pre-natal counseling and management of pregnant women infected with covid-19.

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## 1. Introduction

In December 2019, pneumonia of unknown cause was first identified in the Wuhan, Hubei province of china, it led to the discovery of the novel corona virus. The virus was named as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) by World Health Organization. The virus went on to spread globally and the World Health Organization declared the outbreak as an emergency of international concern on 30 January 2020, and later declared it as a pandemic on 11 March 2020.<sup>1</sup>

As of September 26, 259,502,031 clinically diagnosed and laboratory confirmed cases have been identified around the world.

Pregnant women are more susceptible to infectious diseases due to the immune suppression.<sup>1</sup>

Pregnancy is an immune condition that is unlike any other. The maternal immune system does not maintain a static immune suppressed state, rather the immunological condition changes along with growth and development of the fetus. In the first trimester, maternal immune system is pro-inflammatory (favorable for implantation of embryo and placentation). In the second trimester, it is anti-inflammatory, (helpful for fetal growth), while in the third trimester, it is pro-inflammatory again, (in preparation for

\* Corresponding author.

E-mail address: [aliyaroohi.dr@gmail.com](mailto:aliyaroohi.dr@gmail.com) (A. Roohi).

parturition).<sup>2</sup>

In a recent study, aghaeepour and colleagues suggested an immunological timing called immune-clock in the peripheral blood. They observed a pregnancy induced increase in signaling across multiple T-cell subsets, including CD25 naive and memory CD4 and CD8 cells.<sup>3</sup>

Systemic maternal viral infections have been shown to have an impact on pregnancy (Racicot et al., 2017).<sup>4</sup> SARS infection during pregnancy has been linked to a high rate of spontaneous abortion, early birth, and intrauterine growth restriction in previous investigations (Wong et al., 2004).<sup>2</sup>

The majority of our second-wave theory is based on the 1918-20 "Spanish Flu," which infected 500 million people worldwide. The presence of waves were explained by increased transmission due to schools.<sup>5</sup>

### 1.1. Pathogenesis of SARS-CoV-2

SARS-CoV-2 is made up of 16 nonstructural proteins and 5-8 accessory proteins, as well as 4 structural proteins including spike (S), envelope (E) glycoprotein, nucleocapsid (N), and membrane (M) proteins.

The surface spike (S) glycoprotein helps the virus integrate into the host cell and is responsible for virus-cell membrane fusion. A receptor-binding domain (RBD) is a critical peptide domain in the pathogenesis of infection.

The development of SARS-CoV-2-induced pneumonia can be divided into two stages: early and late. Direct virus-mediated tissue damage forms the early phase. In late phase, the infected host cells trigger an immune response with the recruitment of multiple mediators causing release of high amounts of cytokines into the circulation, particularly IL-6 and TNF- $\alpha$ , resulting in a local and systemic inflammatory response.<sup>6</sup>

Genetic mutations are the cause for most of the evolutionary changes in organisms. A mutation is a change in the sequence of nucleotides that constitutes an organism's genome.<sup>7</sup>

Analysis of several RNA virus genomes and replication pathways reveals that the natural selection process balances the eradication of existing viruses with the introduction or re-emergence of new viruses.<sup>8</sup>

### 1.2. SARS-CoV-2 Variants of Concern (VOCs)

VOC's include Alpha (B.1.1.7 lineage), Beta (B.1.351 lineage), Gamma (P.1 lineage/GR/501Y), Delta (B.1.617.2 lineage), Epsilon (B.1.427 and B.1.429), Zeta (P.2), Eta and Iota, Theta (P.3), Kappa (B.1.617.1), Lambda (C.37) and Omicron (B.1.1.529).<sup>8,9</sup>

## 2. Materials and Methods

This is a prospective analytical study done in the hospital, being a nodal centre for our entire state also being the only recognized centre by the government for management

of covid -19 in the first wave. The hospital is located at the centre of city and conducts deliveries of approximately 10,000 patients every year.

A total of 1300 patients were included in the study, out of whom 800 were admitted during the first wave of the pandemic between April 2020 and February 2021 and the other 500 patients were admitted during the second wave of the pandemic between March 2021 and August 2021

### 2.1. Inclusion criteria

1. All pregnant women who tested positive for COVID 19 and were admitted at our tertiary care hospital.
2. All Women undergoing vaginal/ cesarean delivery at our hospital.
3. All women undergoing abortion/ admitted for management of ectopic pregnancy in our hospital
4. All women with covid positive statuses who delivered at other hospitals and were referred to our hospital for further management.

### 2.2. Exclusion criteria

1. All women who tested negative for COVID 19.
2. All women who left against medical advice or refused to reveal complete medical history or those with incomplete medical records.

## 3. Aims and Objectives of the Study were

1. To assess the maternal morbidity and mortality due to covid-19 infection in the pregnant women.
2. To assess the perinatal outcome in neonates of covid positive mothers.
3. To compare the severity of covid infection between first and second waves of the pandemic.

Any medical or surgical illness and other relevant history along with demographic data like age, parity, gestational age, area of residence, history of contact, and history of travel were obtained at admission.

Monitoring was continued till delivery and indication for delivery, mode of delivery and condition of the neonate Apgar score and the treatment given to both mother and neonate were duly noted.

Evidence of perinatal transmission of virus was assessed by the SARS-associated corona virus reverse-transcriptase polymerase chain reaction (SARS-CoV RT-PCR)

Patients who required oxygen supplementation or mechanical ventilation were admitted to the maternal intensive care unit and closely monitored by a team of physician, obstetrician, anesthetist, ICU intensivist, and pulmonologists.

Rooming-in was recommended and neonatal swabs were sent within 24 hours.

The Institutional Ethics Committee (IEC) approval was taken for the study.

All the maternal and neonatal parameters were analyzed using descriptive statistics i.e. percentages and proportions were calculated. The Chi-square test was used to compare categorical variables in COVID positive mothers in the first and second wave of COVID-19. P value of less than 0.05 was considered significant.

#### 4. Results

A comparison of symptomatology of covid infection in the mothers admitted in the first wave shows that fever (48%) was the most common symptom followed by anosmia (40%), cough (30%) and sore throat (16%) while majority of the patients admitted in the second wave remained asymptomatic (75%) in the initial phase and later went on to develop shortness of breath (46%).

A Meta-analysis by Michael grant et al. also shows fever, cough and myalgia to be the major symptoms in their study of 24,410 adults with COVID 19 infection.<sup>10</sup>

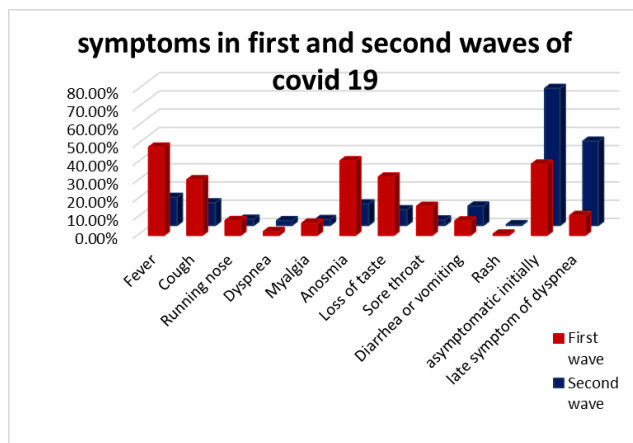


Fig. 1:

In the present study it was observed that there was no significant difference between maternal outcome in different age groups but that observation is limited as age variation among pregnant women in this study was minimal (mean age was 24 with standard deviation of 1 year).

There was no significant difference in maternal outcome with change in gravidity or parity of the pregnant mothers.

In the study, it was found that mothers who were overweight and obese had more severe illness as compared to mothers with normal weight or underweight.

This observation is comparable with the outcome found in a study done by Q cay et al on obesity and COVID 19 severity in a hospital Shenzhen, China. They found that obese individuals were at 3.4 times higher risk of developing severe covid illness.<sup>11</sup>

In our study, the incidence of pre-eclampsia was 13% during the first wave and 10.4% during the second wave. It was also found that presence of pre-eclampsia, eclampsia or other medical complications was associated with poor maternal outcomes both in first and second wave of COVID 19.

It is comparable to the multinational cohort study on maternal and neonatal mortality and morbidity done among pregnant women with covid, done by Jose Villardamong 2130 pregnant women where in presence of pre-eclampsia or other medical complications was found to be associated with increase maternal mortality and morbidity.<sup>12</sup>

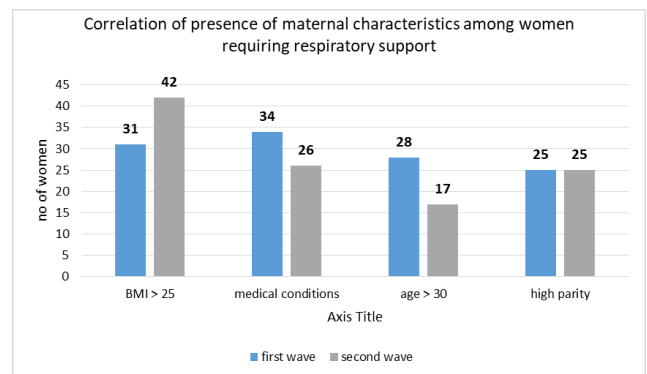


Fig. 2:

It was found that most of the mothers got admitted in the initial two days of developing symptoms during the first wave of covid, while in the second wave majority of the mothers remained asymptomatic initially and did not seek medical attention till the severity of the disease increased to develop shortness of breath. Median duration from onset of symptoms to hospitalization was 1 day in first wave and 10days in second wave.

It was also observed that disease progression from requirement of oxygen supplementation to requirement of invasive ventilation was gradual in first wave and very rapid in the second wave suggesting emergence of more virulent strains of the virus.

It was found that there was significantly raised maternal mortality in second wave of covid compared to the first wave. Previous studies however, have shown no difference between mortality in first and second wave.<sup>13</sup>

In this study high inflammatory markers and high CT severity scoring is found to be associated with higher maternal mortality and morbidity. Treatment with Remedesvir did not show any significant difference in maternal outcome.

It is found that higher inflammatory markers were associated with increased incidence of still births and miscarriages, maternal respiratory distress and other maternal complications.

**Table 1:**

Initial symptoms	No of women who developed the symptom in first wave(out if 800)	Percentage of women who developed the symptom in first wave	No of women who developed the symptom in second wave	Percentage of women who developed the symptom in second wave(out of 500)	P value
Fever	387	48.4%	77	15.4%	0.0001
Cough	244	30.5%	62	12.4%	0.0001
Running nose	65	8.1%	17	3.4%	0.08
Dyspnea	17	2.1%	13	2.6%	0.008
fatigue	60	7.0%	14	2.8%	0.06
Myalgia	54	6.7%	16	3.2%	0.06
Anosmia	327	40.9%	59	11.8%	0.08
Loss of taste	256	32%	43	8.6%	0.06
Sore throat	127	15.9%	15	3%	0.06
Diarrhea or vomiting	63	7.9%	53	10.6%	0.08
asymptomatic	313	39.1%	376	75.2%	0.98
Late symptom of dyspnea	87	10.9%	231	46.2%	0.001

**Table 2:**

Baseline maternal characteristics	Median in first wave	Median in second wave	p- value
Median Age	23	25	0.082
Median gravidity	2	2	1
Median parity	1	1	1
Median BMI	25	29	0.0006

**Table 3:** Comparison of medical complications among first and second wave of COVID 19

Underlying conditions	No of women in the first wave having it(among 800)	Percentage of women in the first wave having it	No of women in the second wave having it(among 800)	Percentage of women in the second wave having it	p- value
Pre-eclampsia	104	13%	52	10.4%	0.0006
Eclampsia	22	4.4%	15	3%	0.009
Diabetes	97	12.1%	51	10.2%	0.04
Hypertension	27	3.4%	16	3.2%	0.01
Asthma	53	6.6%	24	4.8%	0.04

**Table 4:** Comparison of disease progression among pregnant women who died in first and second wave of COVID 19

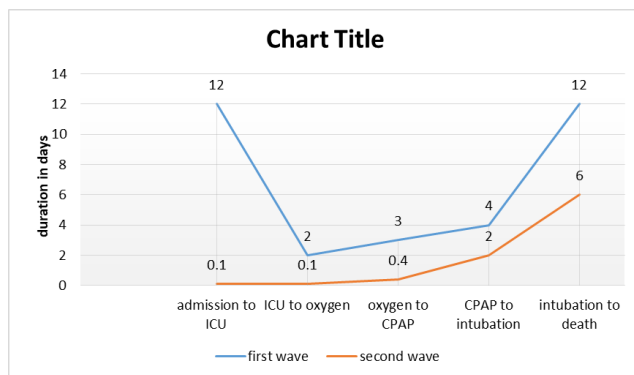
	In first wave(out of 800)	In second wave (out of 500)
Median GA, At diagnosis	36weeks	33weeks
Median GA, At delivery	38.5weeks	34.2weeks
Median Time, from symptoms to admission	1 day	10 days
Median time From admission to ICU(in severe cases)	12 days	1-2 hours
Median time From ICU to oxygen 5L O2	2-3 days	2 hours
Median time from 5L o2 to CPAP	3 days	10 hours
Median time CPAP to intubation	4 days	2 days
Median No of days intubation	12 days	10 days
Median No of days ICU stay	20 days	14 days
Median duration of Hospital stay	32 days	15 days

**Table 5:** Comparison of maternal mortality and severity indicators in first and second wave of COVID 19

	No of women in first wave(out of 800)	Percentage of women in first wave	No of women in second wave (out of 500)	Percentage of women in second wave	P value
Death	56	7%	72	14.4%	0.0013
Recovery after respiratory support	104	48%	83	34%	0.0017
High inflammatory markers	314	40%	302	60%	0.0001
High CT severity score	246	31%	237	47%	0.0019
Maternal complications	104	13%	95	19%	0.0035
Drug regimen Steroid	234	29%	228	46%	0.0001
Remedesvir	74	9%	114	23%	0.0073

**Table 6:**

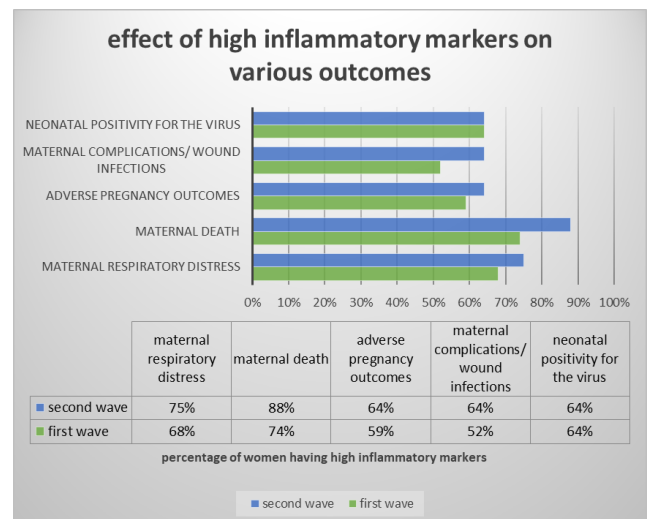
Obstetric outcomes	No in first wave (out of 800)	Percentage in first wave	No in second wave (out of 500)	Percentage in second wave	P- value
Stillbirths	32	4%	24	6%	0.03
Miscarriages	28	3.5%	53	10.6%	0.001
Deliveries	686		413		
Median days between SARS-CoV-2 diagnosis and delivery (IQR)	7 days		11 days		



**Fig. 3:**

In the present study it was found that incidence of abortions, still births, placental abruptions and preterm deliveries was higher in pregnant women infected with covid as compared to non-covid pregnant women. It was also found that the incidence of these conditions was significantly higher in the second wave of covid as compared to first wave.

In the present study the caesarean deliver rate is 46% in the first wave and 57% in the second wave. It was much lower in our study compared with other studies reaching as



**Fig. 4:**

high as 93%.<sup>14</sup>

Cesarean delivery rate was higher in second wave compared to the first wave.

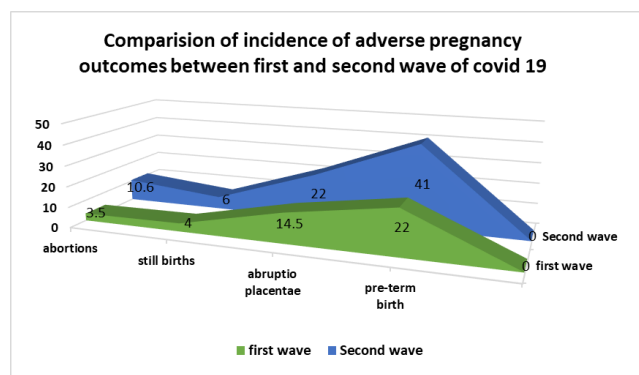
Apart from obstetric indications, maternal deterioration, failure to maintain adequate oxygenation or trouble with mechanical ventilation due to the gravid uterus, and fetal

**Table 7:**

Mode of delivery	No in first wave(out of 800)	Percentage in first wave	No in second wave(out of 500)	Percentage in second wave
Vaginal	370	54%(among all deliveries)	178	43%(among all deliveries)
Cesarean delivery	315	46%(among all deliveries)	235	57%(among all deliveries)

**Table 8:**

Neonatal characteristics	No in first wave	Percentage in first wave	No in second wave	Percentage in second wave	p- value
Gestational age at birth, weeks, median (IQR)	37 weeks		34 weeks		
>37weeks	371	54%	107	26%	0.0001
<37 weeks	315	46%	306	74%	0.0004
Time from diagnosis to delivery	2 days		14 days		
Birth weight z-score, median (IQR)	2.36Kgs		2.03Kgs		
Birth-weight<10th percentile	151	22%	170	41%	0.0038
Apgar score <7 at 10 min	55	8%	120	29%	0.0001
Umbilical arterial pH, median (IQR)	7.38		7.26		
Neonatal intubation	34	4.9%	84	20%	0.0013
NICU hospitalization	48	7.3%	92	24%	0.002
Neonatal death	14	2.1%	16	4%	0.0135
Neonate SARS-CoV-2-positive	34	5.3%	12	3.1%	0.0142

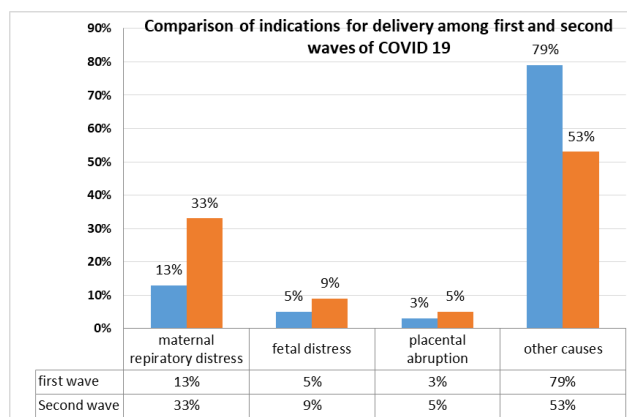


**Fig. 5:**

compromise were all reasons for an early delivery, more so, during the second wave.

Incidence of placental abruption and fetal distress as indication was also increased significantly between first and second wave.

Comparison of neonatal outcome between the first and second wave in the present study shows that there is increased incidence of preterm births among neonates born to covid positive mothers as compared to mothers not infected by covid. This can be explained by the presence of increased inflammatory process in mothers infected by covid.



**Fig. 6:**

Early induction of delivery or early caesarean sections done to rescue the mothers from respiratory distress was also another important reason for increased incidence of preterm births in second wave of covid.

There was also increased incidence of low birth weight, low Apgarscore, NICU admissions and neonatal deaths among neonates born to mothers infected by COVID-19 in the second wave as compared to the first wave.

The results are comparable to similar results found in a systematic reviews by Shin Qin Wei et al. and Danielle Di Mascio et al.<sup>15,16</sup>

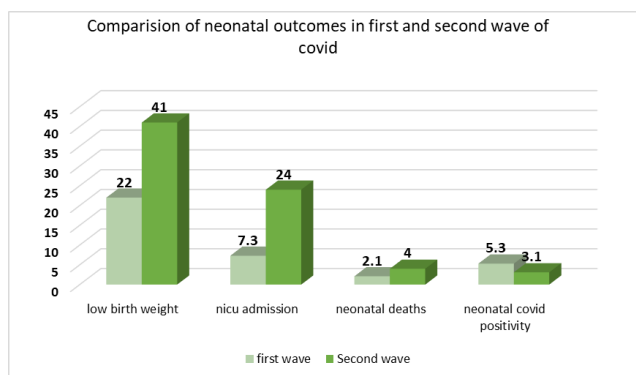


Fig. 7:

## 5. Conclusion

Among mothers hospitalised with COVID-19 infection at Gandhi hospital, higher rates of maternal respiratory distress, maternal ICU admissions, requirement of invasive ventilation, miscarriages, still births, preterm births, NICU admissions, maternal and neonatal deaths were reported during the second wave of infection as compared to the first wave. Above study findings can guide and enhance pre-natal counseling and management of pregnant women infected with COVID-19.

## 6. Source of Funding

None.

## 7. Conflict of Interest


The authors declare no conflict of interest.

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## Author biography

Aliya Roohi, Post Graduate  <https://orcid.org/0000-0002-5302-962X>

V Janaki, Professor

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