

Changing trends of Covid -19 in pregnancy - a single centre prospective study

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Abstract:

Objectives: This study aims to assess the effects of covid-19 on maternal and foetal outcomes in both pandemic waves and to compare the differences of adverse effects from first wave to second wave of pandemic. **Methods:** This is a prospective observational study carried out from June 2020 to July 2021 which included 268 proven covid-19 positive pregnant women, out of which 166 patients were in first wave and 102 patients were in second wave. It includes all the patients admitted to the hospital for various obstetric and non-obstetric indications. **Results:** There were total of 4629 deliveries during the study period. The proportion of the symptomatic cases increased from 40% to 55% and the severity of the symptoms both increased in the second wave when compared to first wave. During first wave 90.8% cases had mild symptoms, whereas second wave showed an increase in the moderate to severe illness with 17.2% of moderate, 29.5% of severe and 13.7% of critical Covid illness. The number of patients with sepsis (5 vs 10, p-value 0.026), acute respiratory distress syndrome (1vs 4, p-value 0.071), need for blood/blood products (5 vs 10, p-value 0.026) and the requirement for invasive ventilation (1 vs 6, p-value 0.013) was increased in the second wave. Elevated C-reactive protein (CRP) was the most common (38 cases) abnormal parameter followed by elevated D-dimer levels (14 cases). Radiographic abnormalities of lungs were seen in 25% cases in the second wave while 15% in the first wave which is statistically significant. There was a two-fold increase in the preterm births (7.54 % vs 25%), intrauterine foetal demise (5.6% vs 21 %) and maternal mortality (1.54% vs 6.15%) in the second wave. There were 16 admissions to neonatal intensive care unit (NICU) in the first wave and 25 (52.08 %) admissions to NICU in the second wave. The incidence of vertical transmission was 9% in the second wave and one neonatal death due to multisystem inflammatory syndrome in the second wave. **Conclusion:** Our study shows an increasing trend in the affection and clinical manifestations causing adverse foetal and maternal outcomes in the second wave.

Keywords: Covid-19, pregnancy, second wave, vertical transmission, maternal mortality.

Abnormal uterine bleeding (AUB) is defined as any variation from the normal menstrual cycle, including changes in regularity and frequency of menses, in duration of flow, or in amount of blood loss. It is just a symptom not a disease.¹ More than 70% of all gynecological consultations in the peri and postmenopausal age group is due to AUB.² It occurs in various forms such as menorrhagia, polymenorrhagia, metrorrhagia, and menometrorrhagia.

Coronavirus disease 2019 (covid-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV2). The first case of covid-19 was reported in December 2019 in the province of Wuhan, China following which there has been a steady rise in the number of cases globally. Hence corona virus was declared pandemic on 11th March 2020. Since then there have been more than 180 million cases worldwide with more than 4 million deaths.¹ India is the 2nd worst affected country next only to United States. Since then there has been emerging scientific data regarding etiopathogenesis, clinical spectrum of the disease manifestations, at risk population, high risk factors, investigations and treatment plans. Many countries have faced first wave of pandemic and second wave of pandemic. India faced the first wave from April 1, 2020 - January 31, 2021 and the second wave from February 1, 2021, to June 2021. Changing trends have been noticed during the second wave of covid-19 compared to the first wave of the pandemic in manifestations of covid-19, in infecting different age groups, co-morbidities, clinical presentations and its affection in pregnancy².

In first wave of pandemic there was lack of knowledge of the disease, apprehension regarding the infection in pregnancy, severity, vertical transmission, in-utero infection, intrapartum infection, morbidity and mortality. The data from the early scientific articles didn't show any increased risk, incidence and adverse foetal outcomes in the first wave of pandemic³, but did clear doubts on vertical transmission and transmission of the virus during labour⁴.⁵ Advancing into, second wave of pandemic lead every country into a huge crisis and a massive challenge to the healthcare systems of the country by being more infectious and lethal than the first wave. In the first wave where in elderly and people with comorbidities like diabetes, hypertension, and obesity were affected more. In the second wave the infection rate was higher in young adults and pregnant women. As the pandemic progressed, the available data on the pregnant women with covid-19 has shown that the vertical and intrapartum transmission have been low, but there has been an increase in adverse maternal-foetal outcomes in the second wave⁶. The adverse outcomes in pregnancy noted were preterm birth, oligohydramnios, fresh stillbirth, intrauterine foetal demise and increased incidence of preeclampsia. The proportion of adverse outcome in the pregnancy is directly proportional to the severity of the maternal illness. This study was done to assess the effects of covid-19 on maternal and foetal outcomes in both the waves of the pandemic and to know if there was any statistically significant increase in adverse outcomes in second wave.

Materials and methods

This was a prospective observational study done in the Department of Obstetrics and Gynaecology, Shri Dharmasthala Manjunatheshwara College of Medical Sciences & Hospital, Shri Dharmasthala Manjunatheshwara University, Suttur, Dharwad which is a tertiary care centre and a referral hospital located in North Karnataka. Ethical clearance was taken from the institutional ethical board. Data of all the covid-19 positive pregnant patients from June 2020 to July 2021 was collected. Of which 166 patients were in the first wave April 1, 2020 - January 31, 2021 and 102 patients were in the second wave from February 1, 2021, to July 2021.

Details of the patients like age, parity, gestational age, address, history of contact, comorbidities, intensive care unit (ICU) admissions, pregnancy outcomes like mode of delivery (vaginal/ caesarean), live, term or preterm birth was noted. Neonatal outcome and postpartum recovery were noted. Covid-19 testing of all the pregnant women with symptoms and all the women who came for admission to labour room for various obstetric indications was done according to the ICMR and FOGSI guidelines^{2,7}. Nasopharyngeal swabs were collected and sent in viral transport media (VTM) to microbiology department for testing.

All the pregnant women with RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) and /or Rapid Antigen Test (RAT) positive were enrolled into the study and followed up. Pregnant women were further categorised into asymptomatic and symptomatic and treated accordingly. Similarly, perinatal transmission was tested by nasopharyngeal RT-PCR in a neonate during first 72 hours after birth. This includes intrauterine and intrapartum transmission. Testing is avoided in the first 12 hours to minimize false positives due to superficial colonization. Statistical analysis was done using Fisher's test.

Results

There were 4629 deliveries from June 2020 to July 2021. Our study included all 268 proven covid-19 positive pregnant patients admitted to labour ward or covid-19 ward for various indications during the study period. The gestational age varied from 19 years to 38 years with a mean age was 25 years and mean gestational age was 37

weeks. Of these, 166 patients were in the 1st wave and 102 patients in 2nd wave. Sixty per cent of the patients were asymptomatic in the first wave where as 55% patients were symptomatic in the second wave (figure 1). The severity of illness was classified according to ICMR/MOHFW guidelines^{8,9} (figure 2).

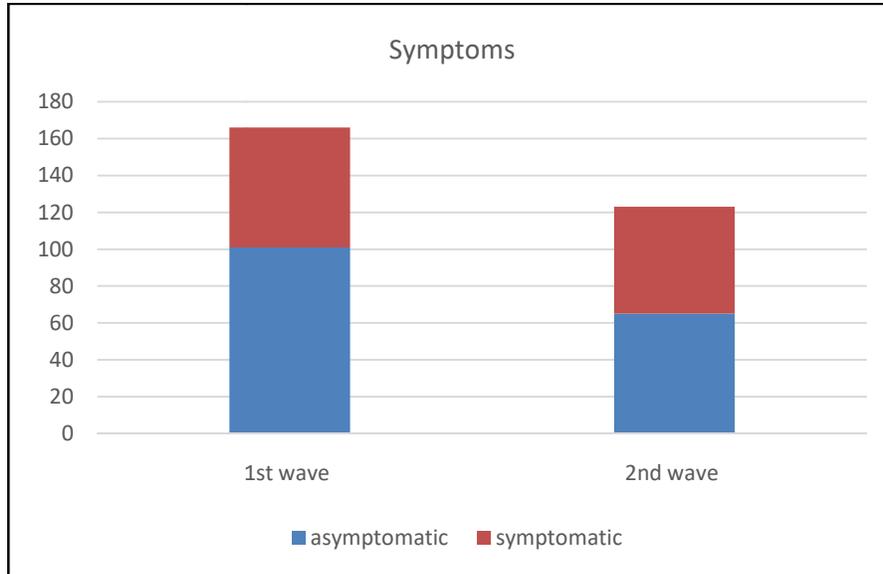


Figure 1: Symptoms in Covid-19

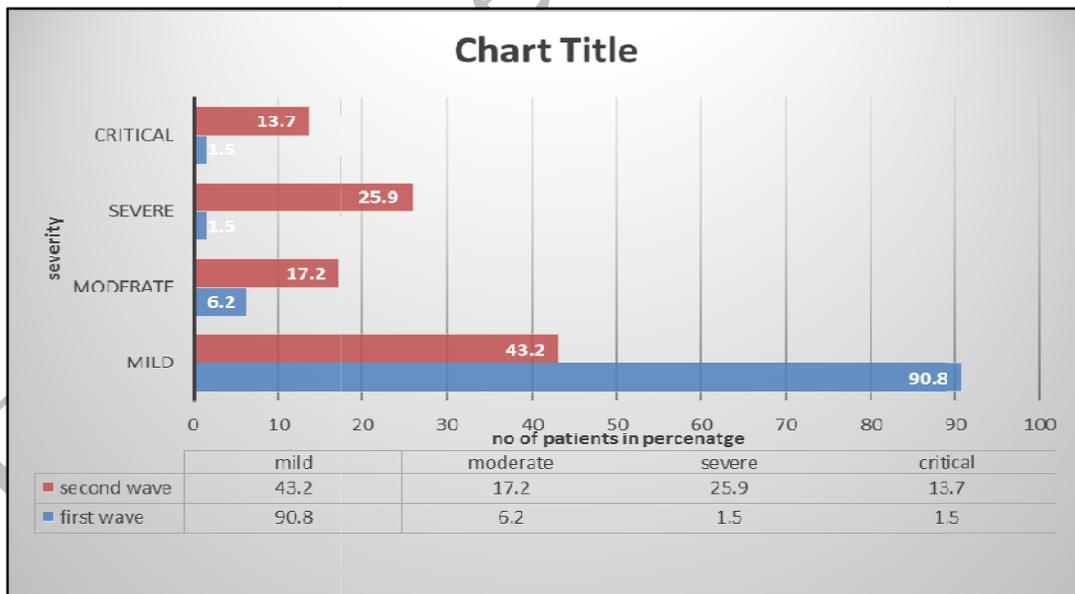


Figure 2: Classification of severity of illness

The proportion of the symptomatic cases and the severity of the symptoms both increased in the second wave when compared to first wave. In symptomatic patient's myalgia, malaise and sore throat were most common presentation, followed by diarrhoea, fever, anosmia and cough (table 1).

Presenting signs and symptoms	Cases in 1 st wave	First wave in percentage	Cases in 2 nd wave	Second wave in percentage
Fever on admission	15	23.07	4	6.89
Cough	10	15.38	9	15.51
Malaise	30	46.15	20	34.48
Dyspnea	2	3.07	4	6.89
Myalgia	35	53.85	20	34.48
Sore throat	30	46.15	18	31.03
Diarrhea	20	30.76	18	31.03
Anosmia	15	23.07	10	17.24

Presentation	1 st wave	Co-morbidity	2 nd wave	Co-morbidity
asymptomatic	101	35	44	20
symptomatic	65	40	58	15

Comorbidities	1 st wave	2 nd wave
Hypertension	28	8
Diabetic	19	11
Hypothyroidism	10	6
Abruption	-	3
Placenta Previa	1	0
Intrauterine growth restriction	9	4
Miscarriage	7	3

There were total of 75 (45%) pregnant women with co-morbidities in the first wave and 35(34.3%) in the second wave (table 2). There was no significant difference in the association of co-morbidities in both symptomatic and asymptomatic group. Hypertension and diabetes were the most common associated co-morbid conditions (table 3).

Complications	1 st wave	2 nd wave	P -value
Sepsis	5	10	0.0269
Cardiac arrest	1	4	0.0711
acute respiratory distress syndrome	1	4	0.0711
Ventilation	1	6	0.0133
Blood product transfusion	5	10	0.0269
Acute kidney injury	1	1	~1
Dialysis	1	1	~1
Shock	1	4	0.0711
Coagulopathy	2	6	0.0569
Deep vein thrombosis	0	1	

The complications in the pregnant covid-19 patients were as mentioned in the table 4. As the proportion of patients with moderate to critical condition was higher in the second wave, the complications were too. The number of patients with sepsis, acute respiratory distress syndrome, and the need for ventilation and the requirement for blood transfusion was increased. There was one covid -19 maternal mortality in first wave and 3 in second wave.

Laboratory characteristics	1 st wave	2 nd wave	P -value
Leucopenia	5	5	0.51
Lymphocytopenia	4	5	0.31
Thrombocytopenia	10	8	0.62
Elevated C-reactive protein concentration (mg/L)	18	20	0.0495
Elevated D - dimer	4	10	0.011
Radiographic abnormalities on chest imaging	10	15	0.0287

Elevated C-reactive protein (CRP) was the most common abnormal parameter. Both D-dimer along with CRP were notably more in second wave as compared to the first wave which is statistically significant. Lymphopenia and thrombocytopenia were both observed in both the waves of pandemic. Radiographic imaging was the most common modality to check the extent of affection of lungs which was 25% in the second wave with the first wave being 15% and a p value of 0.0287 (table 5). All the patients in both the waves were treated with azithromycin. Ten patients required antiviral in the form of remdesivir and 12 of them received steroids in the second wave. Thirty patients needed anticoagulation of which ten received therapeutic and 20 prophylactic anticoagulation.

Parameters	1 st wave	2 nd wave
Live birth	100	48
Term births	92	35
Preterm birth	8	14
Intrauterine fetal demise	6	12
NICU admission	16	25

There was no statistical difference in the mode of delivery in both waves. 106 patients delivered in the first wave of which 71(67%) patients underwent caesarean section for various obstetric indications. In the second wave 56 patients delivered with 43 (77%) of them undergoing caesarean section. Outcome of the pregnancy did vary in the second wave with incidence of preterm birth, intrauterine foetal demise (IUFD) being higher than the first wave (table 6). The total number of IUFD in the first wave was 51 of which 6 were in covid-19 positive patients. In the second wave the total number of IUFD were 33 of which 12 were in covid -19 positive patients. Of the 12 cases of intrauterine foetal demise 8 were beyond 28 weeks of gestation and 4 lesser than 28 weeks. There were 16 admissions to neonatal intensive care unit (NICU) in the first wave. As the RTPCR testing was not done universally for the new-borns during 2020, risk of vertical transmission not known in the first wave. There were 25 (44.64 %) admissions to NICU in the second wave. During the second wave routine RT-PCR testing was done for all the new-borns, out of which 5 (8.92%) were tested positive for COVID-19 and one (1.78%) neonatal death due to multisystem inflammatory syndrome (MIS).

Fifteen patients in the first wave and 20 patients in the second wave got admitted with symptoms of covid-19. Rest of the patient's got admitted for obstetric indications and were diagnosed as covid-19 in post admission screening. Thirty-six per cent in the first wave and forty-five per cent in the second wave of the covid-19 patients were admitted in the 1st two trimesters for covid-19. Two of these patients had abruption with IUFD at 25weeks.

There were total of 28 covid-19 pregnant women who had severe to critical illness with 5 cases in first wave and the rest 23 in the second wave. Sepsis was seen in 15 patients with 5 in first wave and 10 in the second wave. Ten of them recovered, 4 in the first wave and 6 in second. Eight patients had coagulopathy of which 6 were in the second wave and two in first wave. One patient at 12 weeks came with deep vein thrombosis (DVT) with no pre-existing risk factors for DVT, had medical termination of pregnancy and discharged without adverse outcome.

There were 4 maternal deaths due to covid-19 in which 1 was in the first wave and 3 were in the second. One in the first wave was a primigravida with 7weeks of gestation came with broncho-pneumonia and succumbed within 24 hours of admission to hospital. The rest 3 were in the second wave. All of them had bronchopneumonia of chest imaging, needing ventilation. Two of them succumbed with an average stay of 6 days in the hospital. One among them was postnatal patient who along with bronchopneumonia came with acute kidney injury and arrested with

24hours. There was another patient who came with bronchopneumonia with acute kidney injury and also succumbed within 24 hours, but was tested RT-PCR negative.

Post recovery four patients had oligohydramnios and three patients reported back to hospital with IUFD. One tubal ectopic pregnancy in first wave was managed conservatively. We had one case of scar ectopic with previous three caesareans in second wave, with a hematoma of 5.6X5.7 cms at the scar site which was managed conservatively. Patient was followed with serial beta human chorionic gonadotropin values, which become negative by 6 weeks and the haematoma at the scar site regressed.

Discussion

India is a thickly populated country with 1.3 billion populations, of which 48% constitutes females. At any given time 144/1000 females are pregnant¹⁰. Pregnancy is a high-risk state with altered immune system, vulnerable to infections and adverse outcomes¹¹. The available data suggest increased chance of pregnant women and new mother contracting the infection with higher probability of developing viral pneumonia and adverse outcomes when compared to non-pregnant individuals¹².

In the past, experience with coronaviruses i.e. SARS and MERS in pregnancy have shown evidence of fetomaternal affection. COVID-19 induced systemic endothelial damage may similarly cause hypertensive disorders of pregnancy, coagulopathy and placental dysfunction resulting in adverse maternal and neonatal outcomes like miscarriages, prematurity, oligohydramnios, foetal growth restriction and IUFD.¹³

This study has included pregnant females from 5 weeks to 42 weeks, most of them in third trimester. Compared to 1st wave there was increase in number of symptomatic patients and also increase in severity of illness during the 2nd wave^{2,6}. Though the number of symptomatic patients increased in the second wave but there was no much difference in the symptoms or appearance of new symptoms. Malaise and myalgia was the common symptom followed by fever and cough unlike Gorantla et al¹⁴ where fever and cough was the most common.

There was no much difference in the association of co-morbidities in both the waves and also between symptomatic and asymptomatic patients. Hypertension was the most common comorbidity followed by diabetes mellitus similar to Htun et al¹⁵.

In pregnant patients requiring admission to hospital for covid-19, the proportion of moderate to critical illness was higher in the second wave when compared to the first wave¹⁶. The need for invasive ventilation, ICU admissions and antiviral therapy was higher in the second wave when compared to first wave⁶.

C-reactive protein (CRP) was the most abnormal laboratory parameter in our study followed by elevated d-dimer levels^{17, 18}. Both the laboratory parameters were significantly increased in the second wave. This could be due to the increase in the number of patients with moderate to severe illness. Leucopenia and lymphocytopenia were observed in our study similar to the other studies¹⁸. One of the patients had mildly elevated interleukin -6 who succumbed to complications of Covid-19.

Radiographic abnormalities in the form of focal, multifocal ground glass opacities, with or without consolidation was the most common finding in general population on chest computed tomography (CT)¹⁹. CT scan was the modality used in diagnosing, assessing the severity, planning treatment and assessing the prognosis. To avoid radiation exposure only chest X-ray with abdominal shielding was done in patients with respiratory symptoms. Only selected patients with worsening parameters were subjected to CT scan. There was increase in the radiological abnormalities in the second wave. This could be due to increase in the symptoms and the severity of the patients in the second.

There was no statistically difference noted in the mode of delivery in both the waves in our study. The number of patients undergoing cesarean was higher, probably due to our center is a tertiary referral center¹⁸. There was a significant increase in the number of preterm birth and intrauterine fetal demise in the second wave^{20, 21}. The total number of IUFD in the first wave was 51 of which 6 were in covid-19 positive patients. In the second wave the total number of IUFD were 33 of which 12 were in Covid-19 positive patients².

Vertical transmission was seen in 5(9%) neonates. This incidence was slightly higher in our study when compared to Alexander et al who reported vertical transmission in approximately 3.2% of infected mothers in the third trimester without any significant consequence to the new-borns; this could be probably due to the occurrence in second wave with a variant strain²². We had one neonatal death occurred due to SAR Co-V multi inflammatory syndrome (MIS).

There were many patients admitted for not in labour reasons who were treated for Covid-19 recovered and discharged home. On follow of these patients, they developed oligohydramnios, needing intervention. Four of the patients returned with intrauterine foetal demise on follow up.

Our study was consistent with the other studies where in, it was observed that the proportion of symptomatic pregnant women increased in the second wave²³. The severity of the illness, complications like sepsis, ARDS, acute kidney injury, invasive ventilation, associated morbidity and case fatality increased in the second wave^{6, 14}. The reason for increase in the severity and complications is not determined exactly, which needs further investigation. This could be due to the change in the severity of the affecting strain with mutation or the highly virulent variant strain of concern, which is was considered responsible for the second wave⁶.

Limitation of our study was that, our sample size was smaller. Our centre being a tertiary referral centre, the incidence of complications could be higher. Hence further such studies at population in large to be needed to ascertain the adverse outcomes.

Conclusion

Compared to 1st wave there was increase in number of symptomatic patients and also increase in severity of illness during the 2nd wave this has translated into increase in adverse obstetric outcomes as well. Besides maternal illness, there is evidence of placental and foetal affection as well in the form of increased miscarriages, mid trimester abruptions, foetal growth restriction, oligohydramnios, preterm labour, post Covid-19 oligohydramnios and intrauterine foetal demise.

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