

Impact of COVID-19 on Pregnancy Outcome in the First Wave, Second Wave, and Third Wave of the Pandemic at a Tertiary Care Centre Mysuru, Karnataka, India: A Prospective Cohort Study

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ABSTRACT

Introduction: The Coronavirus Disease-2019 (COVID-19) pandemic has subjected us all to difficult times in managing patients, particularly pregnant women. Numerous studies have been conducted during each wave, but limited data is available on maternal and neonatal outcomes. Given that people must co-exist with COVID-19, it is crucial to enhance the understanding of antenatal patient management.

Aim: To compare the clinical presentation, co-morbidities, and maternal and neonatal outcomes among pregnant women with COVID-19 during the first, second, and third waves of the pandemic.

Materials and Methods: This prospective cohort study was conducted in the Department of Obstetrics and Gynaecology (OBG) at JSS Hospital, Mysore, Karnataka, India, from January 2020 to February 2022. A total of 33 expectant mothers with COVID-19 presented during the first wave (from January 30, 2020, to the end of February 2021), 50 expectant mothers with COVID-19 during the second wave (from March 2021 to the end of September 2021), and 19 expectant women with COVID-19 during the third wave (from January 2022 to the end of February 2022). Data were collected for each wave, and a comparison of different variables in all three waves was performed. Microsoft Excel was used for data entry, and analysis was conducted using Statistical Package for Social Sciences (SPSS) version 22.0. Chi-square test was employed to compare the different variables as a test of significance.

Results: The mean age of the expecting mothers in the first wave was 27.12±4.35 years, in the second wave was 25.86±3.98

years, and in the third wave it was 24.61±3.98 years, with a p-value=0.103. Symptoms like cough, cold, running nose were highest in the second wave (22 cases, 44.0%), followed by breathlessness in 6 (12.0%) cases, and fever, chills, myalgia, generalised weakness, vomiting in 45 (90.0%) cases. Hypertensive disease of pregnancy was highest in the first wave (8 cases, 24.2%). In the first, second, and third waves, a total of 23 (69.7%), 30 (60.0%), and 12 (63.1%) individuals, respectively, did not have any co-morbidities. The majority of women in the first wave 18 (54.6%) cases and second wave 27 (54.0%) cases were multigravida, while in the third wave, they were primigravida 14 (73.7%) cases. Pre-term deliveries 22 (44.0%) cases and intrauterine deaths 8 (16.0%) cases were highest in the second wave. There was a higher frequency of Preterm Premature Rupture of Membranes (PPROM) and Premature Rupture of Membranes (PROM) in the first wave 6 (18.2%) cases. Neonatal Intensive Care Unit (NICU) admission of babies was found to be highest in the third wave 8 (42.1%) cases, compared to the first two waves. There was no statistically significant association between these parameters and the waves of the pandemic. The mean Haemoglobin (Hb) levels of the study subjects were least in the first wave, compared to those in the rest of the waves (p-value=0.499). Mean Erythrocyte Sedimentation Rate (ESR) levels were significantly lower in the first wave (p-value=0.041), and C-reactive Protein (CRP) was highest in women in the second wave (p-value=0.036).

Conclusion: It is important that always study the features of the disease over a period of time so that the management protocols can be modified.

Keywords: Coronavirus disease-2019, Laboratory investigations, Maternal outcome, Neonatal outcome, Pregnancy

INTRODUCTION

Due to the outbreak of the COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), a global health crisis has been created [1]. Many countries have observed a three-wave pattern, with the first wave starting in January 2020, followed by the second wave in late March 2021 [2], and the third wave in January 2022 [3]. The first case of COVID-19 was reported in India in January 2020 [4]. "In pregnant women, existing co-morbidities such as hypertension, diabetes, high maternal age, and obesity have been recognised as risk factors for severe COVID-19 disease during pregnancy" [5,6]. The present study was conducted to assess the maternal and neonatal outcomes in women with COVID-19 disease

during the first, second, and third waves of the pandemic at a tertiary care centre in Mysuru, India.

MATERIALS AND METHODS

A prospective cohort study conducted in the Department of Obstetrics and Gynaecology at JSS Hospital, Mysuru, Karnataka, India, from January 2020 to February 2022. It included 33 expectant mothers who presented with COVID-19 during the first wave of the pandemic from January 30th, 2020, to the end of February 2021, 50 expectant mothers with COVID-19 in the second wave from March 2021 to the end of September 2021, and 19 expectant women with COVID-19 in the third wave from January 2022 to the end of February 2022. Institutional Ethical Committee (IEC) clearance

was obtained before the start of the study. A total of 102 pregnant women were enrolled.

Inclusion criteria: Pregnant women who tested positive for COVID-19 by COVID-19 Real Time-Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) in any trimester, irrespective of gestational age, parity, and any associated co-morbidities in all the waves, were included in the study.

Exclusion criteria: Pregnant patients lost to follow-up and those with a negative COVID-19 status, patients in the puerperal period with COVID-19, and non pregnant female patients were excluded.

Study Procedure

The COVID-19 test results were obtained from the microbiology records, and the remaining data were obtained from the study subjects through interviews conducted when they were admitted to the hospital. Maternal outcomes included demographic details, obstetric details, co-morbidities, biochemical investigations, and mode of delivery. Neonatal outcomes included gestational age at delivery (term/preterm), NICU admissions, and COVID-19 results.

STATISTICAL ANALYSIS

Data was entered into MS Excel and analysed using SPSS version 22.0. To compare the different variables, the Chi-square test was

used as a test of significance. A p-value of <0.05 was considered statistically significant.

RESULTS

In the present study, all the subjects in the second wave were symptomatic. Symptoms such as cough, cold, and running nose were highest in the second wave, accounting for 22 (44.0%) cases, followed by fever, chills, myalgia, generalised weakness, and vomiting, which were reported in 45 (90.0%) cases. These symptoms were more prominent in the second wave compared to the first and third waves [Table/Fig-1].

In the second wave, 3 (6%) children tested positive for RT-PCR, while none of the children in the first and third waves were RT-PCR positive [Table/Fig-2].

The majority of women in the first wave 18 (54.6%) and the second wave (27, 54.0%) were multigravida, while in the third wave, the majority were primigravida 14 (73.7%) (p-value=0.089). There was no statistically significant association between preterm delivery, PPRM, PROM, Intrauterine Device (IUD), and the waves of the pandemic [Table/Fig-3].

The majority of deliveries in all three waves were emergency Lower (Uterine) Segment Caesarean Section (LSCS). Preterm vaginal deliveries were highest in the second wave, accounting for 08 (16%)

Parameters	Category	COVID-19 waves			Total n (%)
		1 st (n=33) n (%)	2 nd (n=50) n (%)	3 rd (n=19) n (%)	
Symptoms	Cough, cold, running nose	11 (33.3)	22 (44.0)	06 (31.6)	39 (38.2)
	Breathlessness	03 (9.1)	06 (12.0)	0	09 (8.8)
	Fever, chills, myalgia, generalised weakness, vomiting	13 (39.3)	45 (90.0)	03 (15.8)	61 (59.8)
	None	10 (30.3)	0	12 (63.1)	22 (21.6)
Co-morbidities	Hypertensive disorders of pregnancy	08 (24.2)	09 (18.0)	01 (5.2)	18 (17.6)
	Hyperglycaemia in pregnancy	03 (9.1)	05 (10.0)	02 (10.5)	10 (9.8)
	Seizure disorder	0	0	02 (10.5)	02 (1.9)
	Hypothyroidism	01 (3.0)	06 (12.0)	02 (10.5)	09 (8.8)
	SLE	0	01 (2.0)	0	01 (0.9)
	Psychiatry illness	0	01 (2.0)	0	01 (0.9)
	Cardiac anomalies	01 (3.0)	02 (4.0)	0	03 (2.9)
	Anaemia	01 (3.0)	01 (2.0)	0	02 (1.9)
	Pulmonary oedema	01 (3.0)	01 (2.0)	0	02 (1.9)
	Congestive cardiac failure	01 (3.0)	01 (2.0)	0	02 (1.9)
	None	23 (69.7)	30 (60.0)	12 (63.1)	65 (63.7)

[Table/Fig-1]: Distribution of study subjects based on symptom profile and co-morbidities across three waves of pandemic (N=102).

SLE: Systemic lupus erythematosus

Parameter	Category	COVID-19 waves			Total
		1 st (n=33)	2 nd (n=50)	3 rd (n=19)	
Baby RT-PCR	Negative	33	47 (94.0)	19	99 (97.0)
	Positive	0	03 (6.0)	0	03 (3.0)

[Table/Fig-2]: Distribution of study subjects based on mother and child RT-PCR results.

RT-PCR: Real time-reverse transcriptase-polymerase chain reaction

cases. Foetal distress and previous LSCS were the most common indications for LSCS [Table/Fig-4].

The mean Hb levels of the study subjects were the lowest in the first wave compared to the other waves (p-value=0.499). Mean ESR levels were significantly lower in the first wave (p-value=0.041), and CRP levels were highest in women in the second wave (p-value=0.036) [Table/Fig-5].

Parameters	Category	COVID-19 waves			Total	Chi-square	p-value
		1 st (n=33) n (%)	2 nd (n=50) n (%)	3 rd (n=19) n (%)			
Obstetric score	Primigravida	15 (45.4)	23 (46.0)	14 (73.7)	52 (51.0)	4.81	0.089
	Multigravida	18 (54.6)	27 (54.0)	05 (26.3)	50 (49.0)		
Term/preterm	Preterm	14 (42.4)	22 (44.0)	6 (31.6)	42 (41.2)	0.634	0.771
	Term	19 (57.6)	28 (56.0)	13 (68.4)	60 (58.8)		
PPROM	No	27 (81.8)	42 (84.0)	16 (84.2)	85 (83.3)	0.177	1.000
	Yes	6 (18.2)	8 (16.0)	3 (15.8)	17 (16.7)		
PROM	No	27 (81.8)	44 (88.0)	16 (84.2)	87 (85.3)	2.072	0.878
	Yes	6 (18.2)	6 (12.0)	3 (15.8)	15 (14.7)		

IUD	No	30 (90.9)	42 (84.0)	19 (100)	91 (89.2)	3.293	0.186
	Yes	3 (9.1)	8 (16.0)	0	11 (10.8)		
NICU admission	No	25 (75.7)	32 (64.0)	11 (57.9)	68 (66.7)	2.398	0.316
	Yes	8 (24.3)	18 (36.0)	8 (42.1)	34 (33.3)		
Birth weight		2.64±0.76	2.83±0.78	2.74±0.65			0.507

[Table/Fig-3]: Comparison of obstetric parameters across waves of pandemic. PPRM: Preterm premature rupture of membranes; PROM: Premature rupture of membranes; IUD: Intrauterine device; NICU: Neonatal intensive care unit

Parameters	Category	COVID-19 waves			Total n (%)
		1 st (n=33) n (%)	2 nd (n=50) n (%)	3 rd (n=19) n (%)	
Mode of delivery	Elective LSCS	02 (6.0)	02 (4.0)	02 (10.5)	06 (5.9)
	Emergency LSCS	17 (51.5)	28 (56.0)	12 (63.1)	57 (55.9)
	FTNVD	10 (30.3)	12 (14.0)	04 (21.0)	26 (25.5)
	Preterm vaginal delivery	04 (12.1)	08 (16.0)	01 (5.2)	13 (12.7)
Indications of elective+ emergency LSCS	Oligohydramnios	01 (3.0)	01 (2.0)	0	02 (1.9)
	Breech presentation	03 (9.1)	01 (2.0)	01 (5.2)	05 (4.9)
	Contracted pelvis	01 (3.0)	06 (12.0)	05 (26.3)	12 (11.8)
	Foetal distress	05 (18.2)	09 (18.0)	06 (31.5)	20 (20.6)
	Imminent eclampsia	04 (12.1)	0	0	04 (3.9)
	Previous LSCS in labour	05 (18.2)	13 (26.0)	02 (10.5)	20 (20.6)

[Table/Fig-4]: Distribution of study subjects based on mode and indications of delivery across three waves of pandemic. LSCS: Lower segment caesarean section; FTNVD: Full term normal vaginal delivery

Parameters	COVID-19 waves Mean±SD			p-value
	1 st	2 nd	3 rd	
Age	27.12±4.35	25.86±3.98	24.61±3.98	0.103
Hb	11.47±1.60	11.55±1.18	11.95±1.14	0.499
PCV	35.04±4.05	35.04±3.26	36.76±2.99	0.133
SPO ₂	96.84±1.79	88.09±2.67	97.94±1.25	0.051
Lymphocytes	17.17±6.75	14.96±5.43	15.41±4.99	0.238
Neutrophils	77.35±7.42	80.59±7.36	78.4±7.05	0.131
Eosinophils	0.73±1.11	0.74±0.79	1.73±2.4	0.029
Monophils	3.53±1.76	3.54±1.26	4.11±1.74	0.402
Basophils	0.412±1.25	1.182±7.04	0.17±0.10	0.683
Platelet	2.28±0.63	2.18±0.71	1.99±0.62	0.330
N:L	6.24±5.42	7.29±3.29	6.38±2.56	0.470
RBS	86.12±23.61	84.04±23.40	92.67±18.54	0.272
Urea	13.36±4.22	14.62±11.21	13.22±4.60	0.720
Creatinine	0.53±0.11	0.54±1.09	0.53±0.10	0.884
Uric acid	4.21±1.60	4.42±1.39	4.72±1.22	0.550
Sodium	136.73±1.79	136.2±2.49	136.67±2.30	0.480
Chloride	100.73±2.49	102.36±2.39	103.94±4.05	0.001
Potassium	4.07±0.48	4.2±0.51	4.13±0.41	0.507
Albumin	3.21±0.28	3.35±0.27	3.36±0.27	0.066
Total proteins	5.87±0.49	6.13±0.45	6.01±0.51	0.062
A:G	1.19±0.20	1.20±0.19	1.23±0.19	0.654
AST	24.64±33.8	31.94±59.8	22.17±11.52	0.666
ALT	14.24±16.57	18.82±32.80	10.67±3.08	0.439
Bilirubin direct	0.25±0.53	0.17±0.12	0.12±0.05	0.357
Bilirubin total	0.46±0.63	0.41±0.24	0.32±0.12	0.474
TSH	2.64±2.25	2.39±1.2	2.53±0.87	0.780
PT	13.18±1.34	13.64±4.08	12.31±1.39	0.358
APTT	30.38±3.63	31.80±8.09	30.68±3.32	0.544
ESR	79.86±19.25	95.57±36.61	99.16±28.13	0.041
INR	0.96±0.24	2.27±5.88	0.92±0.13	0.278
Lactate dehydrogenase	213.33±76.70	283.32±148.12	253.94±92.24	0.970

C-reactive protein	48.84±19.66	55.10±21.35	49.84±30.03	0.036
Ferritin	90.51±74.46	113.97±18.8	75.75±26.63	0.545
D-dimer	0.98±0.93	1.66±1.52	1.61±1.45	0.572

[Table/Fig-5]: Distribution of study subjects based on laboratory investigations across three waves of pandemic. Hb: Haemoglobin; PCV: Packed cell volume; SPO₂: Oxygen saturation; N:L: Neutrophil-to-lymphocyte ratio; RBS: Random blood sugar; A:G: Albumin:globulin ratio; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TSH: Thyroid stimulating hormone; APTT: Activated partial thromboplastin time; ESR: Erythrocyte sedimentation rate; INR: International normalised ratio

DISCUSSION

During the first wave, India registered a low number of COVID-19 positive cases per million people. However, the scenario unexpectedly changed in the second wave, with more than 400,000 confirmed cases per day, resulting in severe consequences [7]. Studies have identified numerous double mutant and triple mutant strains of SARS-CoV-2 in different regions of India [8,9].

All the participants in the second wave were symptomatic in the present study. In a study by Singh V et al., during the second wave, 10 women had moderate disease and four had severe disease, compared to two women with severe disease during the first wave [10]. There were four cases of maternal mortality due to COVID-19 pneumonia, all of which occurred during the second wave, and none of the individuals were vaccinated for COVID-19 infection [10]. Mahajan NN et al., described advanced rates of severe COVID-19, admissions to the ICU or high dependency unit, case fatality rate, and maternal mortality ratio during the second wave of the pandemic [11]. In a study by Chaudhary D et al., the requirement for mechanical ventilation was higher during the second wave compared to the first wave among COVID-19 positive pregnant women. Additionally, the maternal death rate was significantly higher during the second wave compared to the first wave [12]. Kadiwar S et al., also suggested that pregnant and peripartum women experienced more severe illness in the second wave of the COVID-19 pandemic compared to the first wave [13]. In the study by Singh V et al., the most frequently associated co-morbidities were hypertensive disorders, diabetic disorders, and anaemia. There was no significant difference in the frequency of these co-morbidities between the two waves [10]. Mahajan NN et al., reported similar findings [11].

The majority of women in the first wave 18 (54.6%) and the second wave 27 (54.0%) were multigravida, while in the third wave, the majority were primigravida 14 (73.7%). Preterm deliveries were highest in the second wave, accounting for 22 (44.0%) cases, and there were eight cases of intrauterine deaths or stillbirths (16.0%). The frequency of PPRM and PROM was higher in the first wave, with 6 (18.2%) cases. NICU admissions of babies were highest in the third wave, with 8 (42.1%) cases, compared to the first two waves. In the study by Singh V et al., during the first wave, with a mean gestational age at delivery of 34.65 weeks, 35 (27.78%) women had preterm delivery, while during the second wave, with a mean gestational age at delivery of 33.80 weeks, 21 (24.71%) women had preterm delivery [10]. Chaudhary D et al., also observed similar findings in their study, with high rates of preterm deliveries among COVID-19-affected pregnant women [12]. Many reviewers have described the high incidence of preterm births among pregnant women with COVID-19, but the exact cause remains unclear in these studies [5,14,15]. "The rate of NICU admissions was also high, being 21.31% and 33.33%, respectively, during the two

waves [14,15]. Allotey J et al., have also concluded that pregnant women infected with COVID-19 are more likely to give preterm birth and have a higher incidence of neonatal admissions to the ICU" [5]. However, the rate of intrauterine and neonatal deaths remained low during both waves, and no neonatal deaths secondary to COVID-19 infection were seen in the present study.

The majority of deliveries in all three waves were emergency LSCS. Preterm vaginal deliveries were highest in the second wave, with 8 cases (16%). Foetal distress and previous LSCS were the most common indications for LSCS. This is in accordance with the study by Singh V et al., which found that the caesarean section rate was significantly higher during the second wave compared to the first. Several studies have reported a high rate of caesarean sections during the pandemic [16-18]. The reasons for this could be several factors, such as more women opting for caesarean section in isolated areas and maternal concerns about respiratory function.

Limitation(s)

More pregnant women need to be included in future studies. The present study was conducted at a single center, and a multicenter study should be conducted to obtain a broader perspective. Additionally, vaccination was not included as a factor in the present study.

CONCLUSION(S)

Comparison of all three waves has made us realise that COVID-19 can present with different symptoms. Preterm vaginal deliveries and intrauterine deaths were highest in the second wave. Neonatal COVID-19 infection was only observed in the second wave, but the incidence remained low. However, by comparing all three waves, the authors were able to assess the changes in clinical presentation, co-morbidities, and maternal and neonatal outcomes in women with COVID-19 disease.

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