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Original Research Article

COVID-19 in pregnant women: a comparative observational study of pregnancy outcome in three waves of COVID-19 in district hospital, Ballari

Suyajna D. Joshi*, Vijayalakshmi G., Ruksar Banu,
Jayasakthi G., Shrilakshmi R. A.

Department of Obstetrics and Gynecology, District Hospital, Ballari, Karnataka, India

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*Correspondence:

Dr. Suyajna D. Joshi,

E-mail: suyajnajoshi@gmail.com

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ABSTRACT

Background: A three wave pattern of corona virus has been seen in many countries during the 2020 pandemic. Observed data show that the effects of the virus do vary between the three waves. Differences in severity of the disease have been reported, although the comparative characteristics of the three waves still remain largely unknown.

Methods: This was a prospective cross sectional study continuation of our first paper comparing 133 pregnant COVID-19 positive patients in the first wave and 251 patients admitted during second wave and 92 patients in third wave who delivered at district hospital, Bellary.

Results: In the present study 72.8% patients were in the age of 20-30 years, 85.87% patients belong to lower socio-economic status, mild anaemia about 32.6% in third wave, moderate anaemia seen in 10.8% in third wave, and 3.44% had severe anaemia. Non-severe pre-eclampsia was present in 10.8% of the patients, severe pre-eclampsia was seen in 6.52% of the cases and. Mode of delivery was 29.34% FTND, 3.26% FTVD emergency LSCS was 63.06% in third wave, and preterm delivery was seen in 4.34% in third wave. Elevated levels of D-dimer were found 25% in third wave. 0 deaths being reported in third wave.

Conclusions: This study compared the obstetric and clinical outcome in COVID-19 positive patients who are in labor in first, second, and third wave of COVID-19 infection. Although our conclusions are limited, the finding so obtained are important for understanding the clinical parameters, obstetric parameters and perinatal outcome in three waves.

Keywords: Coronavirus, COVID-19, Pandemic, Pneumonia, Pregnant women, SARS-CoV-2

INTRODUCTION

Ever since the end of 2019, the novel coronavirus (SARS-CoV-2), causative agent of the coronavirus disease 19 (COVID-19), has been the major concern of physicians, public health specialists and researchers. Major global public health initiatives are being implemented and rapid investigations of the biology of the virus and pathogenesis of COVID-19 are being conducted in research institutions all around the world severe acute respiratory syndrome Coronavirus 2 (SARS-

CoV-2), is quickly spreading from its origin in Wuhan City of China to the rest of the world.¹ Sequence analysis has revealed that all human coronaviruses have animal origins, including the highly pathogenic ones SARS and MERS causing coronaviruses, as early cases of these infections were traced to individuals being exposed to infected animals. Bats are likely the major natural reservoir of coronaviruses.² SARS-CoV-2 are enveloped positive sense ribonucleic acid (RNA) viruses with spike like projections on its surface (crownlike appearance) hence the name corona virus.³ There have been two events in the past two decades. The first such event was

in 2002-2003, when a new corona virus which originated in bats crossed over to humans via palm civet cats in the Guangdong province of China. Again in 2012, the Middle East respiratory syndrome corona virus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host.⁴ In December 2019, an increased number of patients in Wuhan, started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that traded live animals. On December 31st 2019, China alerted the outbreak to the world health organization (WHO) and on 1 January the human seafood market was closed. On 7th January the virus was identified as a corona virus. All ages were susceptible. Infection spreads mainly through droplets either by inhalation or touching surfaces tainted by them.⁵ The incubation period varies from 2 to 14 days. As per many studies, virus enters the respiratory mucosa, through Angiotensin receptor 2 (ACE2).⁶ The clinical features of coronavirus-2019 (COVID-19) varies, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction, undifferentiated from other respiratory infections. In few patients due to various reasons, by the end of first week the disease can progress to pneumonia, respiratory failure and death, due to rise in inflammatory cytokines.⁷ Diagnosis is by specific molecular tests on respiratory samples. Previous smaller coronavirus outbreaks (i.e., severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)) said to have associated infection in pregnancy with more serious illness and preterm birth.⁸ Pregnant patients of SARS-CoV-2 are predominantly asymptomatic and if symptomatic presents with fever, cough, dyspnea and shortness of breath. In this study we explored threats of SARS-CoV-2 infection amongst pregnant women with in our hospital in all three waves of COVID. Current study was aimed to compare the characteristics and outcomes of patients during three wave periods.

METHODS

A prospective study of all hospitalized cases of COVID-19 infected pregnant mothers, admitted in District hospital Ballari, Karnataka between 26 December 2021 and 16 February 2022 was conducted. All pregnant women who were tested positive for COVID-19 were included in the study. Their clinical profile and obstetric profile were documented. Verbal and written consent was taken from all the cases before including them in the study. The clinical and outcome data from December 2021 and February 2022 was compiled and analyzed and compared with the data from the first and second waves from our institute. For the purpose of our study, a laboratory-confirmed case of COVID-19 was defined as a positive result by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) assay of maternal pharyngeal swab specimens. A total of 92 patients were included in this study and their data was compiled and analyzed in detail and compared with first and second

waves results.

Parameters for assessment

Obstetrical behavior and clinical profile of 92 pregnant COVID-19 positive patients were evaluated. Obstetrical behavior of 92 patients during labor, delivery and postpartum period till discharge was highlighted. General physical and detailed systemic examination of all the patients was conducted in a systematic fashion. Complete blood count, coagulation profile, C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, serum ferritin, serum electrolytes, lung function test (LFT), renal function test (RFT) were included, electrocardiography (ECG) done, radiological investigations chest X-ray were done and their reports noted. All the cases in whom labor was induced, the indication for induction and method utilized were noted. Duration of labor and mode of delivery was recorded. Details of all the babies born were documented along with their COVID-19 status. The mother and baby were followed up in hospital till discharge and their morbidity, mortality was noted if any.

Statistical analysis

Data entry and statistical analysis were performed with the help of Statistical package for social sciences (SPSS) version 21.0, while categorical variables are presented as number and percentages.

RESULTS

Clinical/obstetric outcomes of all the COVID positive pregnant women were analyzed and tabulated as given below in the (Tables 1-4). In the present study 72.8% patients were in between the age of 20-30 years, 85.87% patients belonged to lower socio-economic status in third wave as compared to 90% in second wave (Table 1). Mild anemia is seen in 4.5%, 27.4%, 32.6% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Moderate anemia is seen in 11.2%, 16.9%, 10.8% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Severe anemia is seen in 4.5%, 10.35%, 3.44% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Non-severe pre-eclampsia was present in 11.2%, 18.72%, 10.8% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Severe pre-eclampsia was seen in 12%, 9.94%, 6.52% of the patients in 1st wave, 2nd wave and 3rd wave respectively, and 0.7% had gestational hypertension as compared to 1.59% and 0% in second and third wave respectively (Table 2). Elevated levels of D-dimer were found in 9.7%, 34.6%, 25% of the patients in 1st wave, 2nd wave and 3rd wave respectively (Table 3). Mode of delivery was Full term normal delivery (FTND) in 17.4%, 17.9%, 29.43% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Full term vaginal delivery (FTVD) in 9%, 3.77%, 3.26% of the patients in 1st wave, 2nd wave and 3rd wave respectively. Emergency lower segment caesarean section (LSCS) in 67.7%,

74.52%, 63.06% of the patients in 1st wave, 2nd wave and 3rd wave respectively and preterm delivery was seen in 4.5% in first wave and 4.34% in second wave (Table 4).

Table 1: Clinical and obstetric profile of cases.

Characteristics		1 st wave (N=133)	%	2 nd wave (N=251)	%	3 rd wave (N=92)	%
Age (Years)	Below 20	3	2.2	11	4.38	18	19.6
	20-30	117	87.9	219	87.25	67	72.8
	Above 30	13	9.9	21	8.36	7	7.6
Socioeconomic status*	Lower class	128	96.3	226	90.03	79	85.87
	Upper middle class	5	3.7	25	9.96	13	14.13
Gestation	Preterm	27	20.3	65	25.89	8	8.79
	Early term	53	39.8	101	40.23	12	13
	Full term	52	39.2	70	27.88	60	65.21
	Late term	1	0.7	15	5.97	12	13
Gravida	1	39	29.5	117	46.61	36	39.13
	2	64	48.1	78	31.07	31	33.69
	3	20	15	37	14.74	16	17.39
	4	3	2.2	11	4.38	7	7.63
	5	1	0.7	6	2.39	1	1.08
	6	6	4.5	0	0	1	1.08
	7	0	0	1	0.39	0	0
	10	0	0	1	0.39	0	0
Parity	0	68	51.1	117	46.61	45	48.91
	1	20	15.1	91	36.25	30	32.6
	2	2	1.5	33	13.14	13	14.13
	3	43	32.3	7	2.78	4	4.36
	4	0	0	3	1.19	0	0
Symptoms	Fatigue	53	53	34	13.54	46	50
	Cough	26	19.5	102	40.63	18	19.56
	Diarrhea	10	7.5	0	0	2	2.18
	Anosmia	1	0.7	1	0.38	0	0
	Sore throat	4	3	10	3.98	15	16.38
	Asymptomatic	39	29.3	77	30.67	10	10.8
	Breathlessness			27	10.75	0	0

*modified Kuppuswamy classification.

Table 2: Co-morbidities among study subjects.

Characteristics		1 st wave (N=133) Frequency	%	2 nd wave (N=251) Frequency	%	3 rd wave (N=92) Frequency	%
Hypertensive disorders	Gestational hypertension	1	0.7	4	1.59	0	0
	Mild pre-eclampsia	15	11.2	47	18.72	10	10.8
	Severe eclampsia	12	12	25	9.94	2	2.18
	Imminent eclampsia	2	1.5	8	3.18	3	5.17
	Eclampsia			2	0.39	1	1.08
Anemia	Mild	6	4.5	69	27.4	30	32.6
	Moderate	15	11.2	42	16.7	10	10.8
	Severe	6	1.5	26	10.35	2	3.44
	Hypothyroidism	1	0.7	10	3.98	2	3.44
	HELLP syndrome	5	3.7	2	0.79	0	0
	Thrombocytopenia	3	2.2	4	1.59	4	4.34
	HbsAg positive	1	0.7	2	0.79	1	1.08
	HIV positive	0	0	1	0.38	0	0
Others	Bicornuate uterus	1	1.5	0	0	0	0

Continued.

Characteristics	1 st wave (N=133)		2 nd wave (N=251)		3 rd wave (N=92)	
	Frequency	%	Frequency	%	Frequency	%
Gestational diabetesmellitus	1	1.5	1	0.38	1	1.08
Intra-uterine death	4	3	11	4.38	2	3.44
Abruptio-placentae	2	1.5	3	1.19	0	0
Placenta previa	12	1.5	2	0.79	1	1.08
APLA syndrome	1	0.7	0	0	0	0
Retained placenta	1	0.7	0	0	0	0
Overt diabetes	1	0.7	1	0.38	0	0
DCM	-	-	1	0	0	0
Severe MS	-	-	1	0	0	0

Table 3: Distribution of patients based on laboratory findings of COVID-19 and treatment.

Parameters	1 st wave (N=133)		2 nd wave (N=251)		3 rd wave (N=92)		
	Frequency	%	Frequency	%	Frequency	%	
Laboratory parameters	D-dimer (above500)	13	9.7	87	34.6	23	25
	CRP negative	73.70	178	70.91	53	57.61	73.70
	CRP positive	26.30	73	29.09	39	42.39	26.30
Treatment	Radiological findings	15	11.20	51	20.3	6	6.52
	Antibiotic therapy	133	100	251	100	92	100
	Treatment with remdesivir	15	11.20	54	31.87	6	6.52
	ICU admission	1	0.70	19	7.56	0	0
	Corticosteroid therapy	15	11.20	80	31.87	6	6.52

Table 4: Pregnancy outcomes and neonatal outcomes among study subjects.

Parameters	1 st wave (N=133)		2 nd wave (N=251)		3 rd wave (N=92)		
	Frequency	%	Frequency	%	Frequency	%	
Mode of delivery	Emergency LSCS	90	67.7	158	74.52	58	63.06
	FTND	23	17.4	38	17.9	27	29.34
Second wave (N=212)	FTVD	12	9	8	3.77	3	3.26
	PTVD	6	4.5	8	3.77	4	4.34
	VBAC	1	0.7	1	0.47	0	0
	Breech presentation	4	4.4	2	1.26	7	12.06
Indications 1st wave (N=90)	Fetal distress	13	14.4	59	37.34	11	18.96
	Previous 1 LSCS	41	45.7	45	28.48	18	31.09
	CPD	11	12.20	18	11.39	10	17.24
	Previous 2 LSCS	3	3.3	6	3.79	2	3.44
2nd wave (N=158), 3rd wave (N=92)	Second stage arrest	1	1.1	1	0.63	1	1.08
	Oligohydramnios	6	6.8	38	24.05	4	4.34
	Bad obstetric history	2	2.2	4	2.5	0	0
	Precious pregnancy	3	3.3	4	2.5	2	3.44
	Transverse lie	2	2.2	3	1.89	0	0
	Twin gestation	4	4.4	3	1.89	2	3.44
	Retained placenta	1	0.7	0	0	0	0
Intrapartum complications	Ruptured uterus	2	1.5	0	0	0	0
	Eclampsia			1	0.63	1	1.08
	Postpartum hemorrhage	7	5.2	8	3.77	0	0
Postpartum complications	Secondary PPH	1	0.7	0	0	0	0
	PRES syndrome	1	0.7	0	0	0	0
	Psychosis	1	0.7	2	0.94	0	0
	DIC	2	1.5	1	0.47	0	0
Birth weight	Below 2.5	39	28.5	21	8.37	11	11.96

Continued.

Parameters	1 st wave (N=133)		2 nd wave (N=251)		3 rd wave (N=92)		
	Frequency	%	Frequency	%	Frequency	%	
	Above 2.5	98	71.5	230	91.63	81	88.04
Perinatal outcome	NICU admission	65	47.4	60	23.9	33	35.8
	COVID 19+	7	5.1	8	3.19	0	0
	RDS	8	5.8	15	5.98	0	0
	MAS	12	8.7	6	2.34	1	1.08
	Other causes of RDS	2	1.4	4	1.6	1	1.08
	HIE	9	6.5	6	2.34	0	0
	Sepsis	1	0.7	0	0	2	3.44
	Jaundice	11	8	20	7.97	11	11.96
	Hypoglycemia	1	0.7	1	0.47	0	0
	Dehydration fever	5	3.6	0	0	0	0
	LBW with prematurity	1	3.6	1	0.47	4	4
	IDM	1	0.7	0	0	0	0
MMR	1	0.7	14	5.58	0	0	
PNMR	2	1.5	0	0	0	0	

LSCS: lower segment caesarean section, FTNVD: full term normal vaginal delivery, VBAC: vaginal birth after caesarean section, PPH: post-partum hemorrhage, NICU: neonatal intensive care unit, IDM: infant of diabetic mother, PRES: posterior reversible encephalopathy syndrome, DIC: disseminated intravascular coagulation, CPD: cephalo pelvic disproportion.

DISCUSSION

In the present study 72.8% patients were in the age of 20-30 years, 85.87% patients belong to lower socio-economic status, mild anemia about 32.6% in third wave, moderate anemia seen in 10.8% in third wave, and 3.44% had severe anemia. Non-severe pre-eclampsia was present in 10.8% of the patients, severe pre-eclampsia was seen in 6.52% of the cases and. Mode of delivery was 29.34% FTND, 3.26% FTVD emergency LSCS was 63.06% in third wave, and preterm delivery was seen in 4.34% in third wave. Elevated levels of D-dimer were found 25% in third wave. 0 deaths being reported in third wave.

In the first wave, 87.9% were in age 20 to 30 years. 96.3% patients belong to lower socio-economic status. 4.5% patients had mild anaemia, 11.2% had moderate anaemia and 4.5% had severe anaemia. Non-severe pre-eclampsia was present in 11.2% of the patients, severe pre-eclampsia in 12% and 0.7% had gestational hypertension. Mode of delivery was 17.4% Full term normal delivery (FTND), 9% Full term vaginal delivery (FTVD), emergency lower segment caesarean section (LSCS) in 67.7% cases and preterm delivery was seen in 4.5% of the cases. Elevated levels of D-dimer were found in 9.7% of the cases. One maternal death was reported in the study due to COVID-19 pneumonia.

In the second wave, 87.25% patients were in the age of 20-30 years, 90% patients belong to lower socioeconomic status, mild anemia about 27.4% in second wave, moderate anemia seen in 16.7% in second wave, and 10.35% had severe anemia. Non-severe pre-eclampsia was present in 18.72% of the patients, severe pre-eclampsia was seen in 9.94% of the cases and 01.59% had gestational hypertension. Mode of delivery was 17.9% FTND, 3.77% FTVD emergency LSCS was

74.5% in second wave, and preterm delivery was seen in 3.77% in second wave. Elevated levels of D-dimer were found 34.6% in second wave. 14 deaths being reported in second wave. As per study by KUMAR et al Patients admitted in the third wave were significantly younger than those admitted earlier (46.7±20.5 vs. 54.6±18 yr). The patients admitted in the third wave had a lower requirement of drugs including steroids, interleukin (IL)-6 inhibitors and remdesivir as well as lower oxygen supplementation and mechanical ventilation.

They had improved hospital outcomes with significantly lower in-hospital mortality (11.2 vs. 15.1%). The outcomes were better among the fully vaccinated when compared to the unvaccinated or partially vaccinated. In a study by Seonga et al in comparison with the second wave, the third wave was characterized by delayed strengthening of social distancing policies (3 vs.15 days), longer duration (36 vs. >56 days) and a higher case fatality rate (0.91% vs.1.26%).¹⁴ There were significant differences in transmission chains between the second and third waves (p<0.01). In comparison with the second wave, the proportion of local clusters (24.8% vs. 45.7%) was lower in the third wave, and personal contact transmission (38.5% vs. 25.9%) and unknown routes of transmission (23.5% vs. 20.8%) were higher in the third wave. The most striking difference between the second and third waves was the implementation of public health interventions, and generalized vaccination at various centers at free of cost, unlike the second wave, when social distancing policies were strengthened rapidly, a large number of COVID-19 cases occurred in the third wave within a short time. Due to the short doubling time (3.9 days) and the highly transmissible nature of SARSCoV-2 (omicron variant) and delayed intervention may have led to rapid spread in the community. India started its vaccination campaign from 16th January 2021 onward with two vaccines, a vaccine developed by

Bharat Biotech in association with the Indian council of medical research and National institute of virology named "Covaxin" (BBV152).¹²

The Oxford-AstraZeneca vaccine (AZD 1222), manufactured by the Serum institute of India under the trade name "COVISHIELD". As on September 1 2022, in a remarkable achievement, India's vaccination drive has crossed 219 crore mark of administered doses, with 94.9 crore receiving two doses.¹² Among 92 patients in the 3rd wave 30 patients received one dose of COVID vaccination and 5 received 2 dose of COVID vaccination, rest were not vaccinated.

CONCLUSION

The above study indicates that hospitalized patients in third wave are less morbid requiring less hospital stay, had no mortality. Although majority were asymptomatic in all waves, the severe pneumonic symptoms in second wave stands out as an important difference in all three waves. These characteristics may help to understand the nature of disease in India and its behavior and dangers also and also the effectiveness of proper measures taken by GOI as such vaccination to all for free of cost and stringent screening/quarantine/treatment methods.

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