COVID-19 second wave deadlier than first in pregnant women: a comparative observational study and the COVID saga continues

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ABSTRACT

Background: A two wave pattern has been seen in many countries in reported cases of corona virus disease-19 during the 2020 pandemic. Observed data show that the effects of the virus do vary between the two periods. Differences in severity of the disease have been reported, although the comparative characteristics of the two 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 delivered at District Hospital, Bellary, in the first wave and 251 patients admitted during second wave.
Results: In the present study 87.9% patients were in the age of 20-30 years, 90% patients belong to lower socio-economic 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.
Conclusions: This study compared the obstetric and clinical outcome in COVID-19 positive patients who are in labor in first and second 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 both waves with considerable increase in maternal mortality in second wave.

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

INTRODUCTION

An upsurge in cases has occurred following the early spike COVID-19 infections seen in India 2020. In this study we explore threats of SARS-CoV-2 infection amongst pregnant women with in our hospital both in the first wave of infections and more recently. 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]

SARS-CoV-2 are enveloped positive sense ribonucleic acid (RNA) viruses with spike like projections on its surface (crown like appearance) hence the name corona virus.[2]

There have been two events in the past two decades. 1) 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. 2) 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.[3]

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 1st 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.[4] The incubation period varies from 2 to 14 days. As per many studies, virus enters the respiratory mucosa. Through Angiotensin receptor 2 (ACE_2).[5] The clinical features of coronavirus-2019 (COVID-19) varies, ranging from asymptomatic state to acute respiratory distress syndrome and multiorgan 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.[6] 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.[7] Pregnant patients of SARS-CoV-2 are predominantly asymptomatic and if symptomatic presents with fever, cough, dyspnea and shortness of breath.

We aimed to compare the characteristics and outcomes of patients during both time periods.

METHODS

We conducted a prospective study of all hospitalized cases of COVID-19 infected pregnant mothers, admitted in District hospital Ballari, Karnataka between 15 March 2021 and 15 October 2021.

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 April 2021 and June 2021 was compiled and analysed and compared with the data from the first wave 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 transcript as polymerase chain reaction (qRT-PCR) assay of maternal pharyngeal swab specimens. A total of 251 patients were included in this study and their data was compiled and analysed in detail and compared with first wave results.

Parameters for assessment

Obstetrical behavior and clinical profile of 251 pregnant COVID-19 positive patients were evaluated. Obstetrical behavior of 212 patients delivered among 251 women during labor, delivery and post-partum 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 variable are presented as number and percentages.

RESULTS

Clinical/obstetric outcomes of all the COVID positive pregnant women were analysed and tabulated as given below in the Tables 1-4.

In the present study 87.9% patients were in between the age of 20-30 years, 96.3% patients belonged to lower socio-economic status in first wave as compared to 90% in second wave (Table 1).

4.5% patients had mild anemia in first wave as compared to 27.4% in second wave, 11.2% had moderate anemia first wave as compared to 16.7% in second wave, and 4.5% had severe anemia in first wave as compared to 10.35% in second wave. Non-severe pre-eclampsia was present in11.2% of the patients first wave as compared to 18.72% in second wave, severe pre-eclampsia was seen in 12% of the cases in first wave as compared to 9.94% in second wave and 0.7% had gestational hypertension as compared to 1.59% in second wave (Table 2).

Elevated levels of D-dimer were found in 9.7% of the cases in first wave and 34.6% in second wave (Table 3).

Table 1: Clinical and obstetric profile of cases.

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
Age	Below 20	3	2.2	11	4.38
	20-30	117	87.9	219	87.25
	Above 30	13	9.9	21	8.36
Socioeconomic status*	Lower class	128	96.3	226	90.03
	Upper middle class	5	3.7	25	9.96
Gestation	Pretem	27	20.3	65	25.89
	Early term	53	39.8	101	40.23
	Full term	52	39.2	70	27.88
	Late term	1	0.7	15	5.97
Gravida	1	39	29.5	117	46.61
	2	64	48.1	78	31.07
	3	20	15	37	14.74
	4	3	2.2	11	4.38
	5	1	0.7	6	2.39
	6	6	4.5	0	0
	7	0	0	1	0.39
	10	0	0	1	0.39
Parity	0	68	51.1	117	46.61
	1	20	15.1	91	36.25
	2	2	1.5	33	13.14
	3	43	32.3	7	2.78
	4	0	0	3	1.19
Symptoms	Fatigue	53	53	34	13.54
	Cough	26	19.5	102	40.63
	Diarrhea	10	7.5	0	0
	Anosmia	1	0.7	1	0.38
	Sore throat	4	3	10	3.98
	Asymptomatic	39	29.3	77	30.67
	Breathlessness			27	10.75

*modified Kuppuswamy classification.

Table 2: Co-morbidities among study subjects.

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
Hypertensive disorders	Gestational hypertension	1	0.7	4	1.59
	Mild pre-eclampsia	15	11.2	47	18.72
	Severe eclampsia	12	12	25	9.94
	Imminent eclampsia	2	1.5	8	3.18
	Eclampsia			2	0.39
Anemia	Mild	6	4.5	69	27.4
	Moderate	15	11.2	42	16.7
	Severe	6	1.5	26	10.35
Others	Hypothyroidism	1	0.7	10	3.98
	HELLP syndrome	5	3.7	2	0.79
	Thrombocytopenia	3	2.2	4	1.59
	HbsAg positive	1	0.7	2	0.79
	HIV positive	0	0	1	0.38
	Bicornuate uterus	1	1.5	0	0
	Gestational diabetes mellitus	1	1.5	1	0.38
	Intra-uterine death	4	3	11	4.38
	Abruptio-placentae	2	1.5	3	1.19
	Placenta previa	12	1.5	2	0.79

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
	APLA syndrome	1	0.7	0	0
	Retained placentae	1	0.7	0	0
	Overt diabetes	1	0.7	1	0.38
	DCM			1	0
	Severe MS			1	0

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

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
Laboratory parameters	D-dimer (above 500)	13	9.7	87	34.6
	CRP	Negative	73.70	178	70.91
		Positive	26.30	73	29.09
Treatment	Radiological findings	15	11.20	51	20.3
	Antibiotic therapy	133	100	251	100
	Treatment with remdesivir	15	11.20	54	31.87
	ICU admission	1	0.70	19	7.56
	Corticosteroid therapy	15	11.20	80	31.87

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

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
Mode of delivery	Emergency LSCS	90	67.7	158	74.52
	FTND	23	17.4	38	17.9
Second wave (n-212)	FTVD	12	9	8	3.77
	PTVD	6	4.5	8	3.77
	VBAC	1	0.7	1	0.47
Indications	Breech presentation	4	4.4	2	1.26
	Fetal distress	13	14.4	59	37.34
1st wave n-90	Previous 1 LSCS	41	45.7	45	28.48
	CPD	11	12,20	18	11.39
2nd wave n-158	Previous 2 LSCS	3	3.3	6	3.79
	Second stage arrest	1	1.1	1	0.63
	Oligohydramnios	6	6.8	38	24.05
	Bad obstetric history	2	2.2	4	2.5
	Precious pregnancy	3	3.3	4	2.5
	Transverse lie	2	2.2	3	1.89
	Twin gestation	4	4.4	3	1.89
Intrapartum complications	Retained placenta	1	0.7	0	0
	Ruptured uterus	2	1.5	0	0
	Eclampsia			1	0.63
Post-partum complications	Postpartum hemorrhage	7	5.2	8	3.77
	Secondary PPH	1	0.7	0	0
	PRES syndrome	1	0.7	0	0
	Psychosis	1	0.7	2	0.94
	DIC	2	1.5	1	0.47
Birth weight	Below 2.5	39	28.5		
	Above 2.5	98	71.5		
Perinatal outcome	NICU admission	65	47.4		
	COVID 19+	7	5.1		
	RDS	8	5.8		
	MAS	12	8.7		
	Other causes of RDS	2	1.4		
	HIE	9	6.5		
	Sepsis	1	0.7		
	Jaundice	11	8		

Continued.

Characteristics		1st wave (n=133)	%	2nd wave (n-251)	%
	Hypoglycemia	1	0.7		
	Dehydration fever	5	3.6		
	LBW with prematurity	1	3.6		
	IDM	1	0.7		
MMR		1	0.7		
PNMR		2	1.5		

(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)

Mode of delivery was 17.4% Full term normal delivery (FTND) in first wave as compared to 17.9% in second wave, 9% Full term vaginal delivery (FTVD) in first wave as compared to 3.77% in second wave, emergency lower segment caesarean section (LSCS) in 67.7% in first wave as compared to 74.5% in second wave, and preterm delivery was seen in 4.5% in first wave and 3.77% in second wave (Table 4).

DISCUSSION

After 2 waves of COVID 19 infection we have demonstrated an increase in the number of obstetric patients with positive SARS-CoV-2 tests. Symptomatic infections were more common in second wave, with more pregnant women presenting with breathlessness and with de-saturation requiring more ICU admissions.

Presently we have extended our study during second wave, even though incidence in both waves was more among 20-30 age groups, compared to first wave more patients presented with deranged CRP and D-dimer levels, in turn more patients required corticosteroids and remdesivir treatment in second wave.

Fatality rate was found to be more in second wave attributing to 14 maternal deaths due to severe COVID pneumonia, compared to 1 maternal death in first wave.

In the present study 87.9% patients were in between the age of 20-30 years, 96.3% patients belong to lower socio-economic status in first wave as compared to 90% in second wave, 4.5% patients had mild anemia in first wave as compared to 27.4% in second wave, 11.2% had moderate anemia first wave as compared to 16.7% in second wave, and 4.5% had severe anemia in first wave as compared to 10.35% in second wave.[8] Non-severe pre-eclampsia was present in 11.2% of the patients first wave as compared to 18.72% in second wave, severe pre-eclampsia was seen in 12% of the cases in first wave as compared to 9.94% in second wave and 0.7% had gestational hypertension in first wave as compared to 1.59% in second wave.[9] Mode of delivery was 17.4% full term normal delivery (FTND) in first wave as compared to 17.9% in second wave, 9% full term vaginal delivery (FTVD) in first wave as compared to 3.77% in second wave, emergency lower segment caesarean section (LSCS) in 67.7% in first wave as compared to 74.5% in second wave, and preterm delivery was seen in 4.5% in first wave and 3.77% in second wave.[9] Elevated levels of D-dimer were found in 9.7% of the cases in first wave and 34.6% in second wave.[9] One maternal death was reported in the study due to COVID-19 pneumonia in first wave as compared to 14 deaths being reported from our center in second wave.[10]

In study by Iftimie et al two hundred and four patients were hospitalized during the first period, and 264 during the second period.[11] Patients in the second wave were younger and the duration of hospitalization and case fatality rate were lower than those in the first wave. In the second wave, there were more children, and pregnant and post-partum women. The most frequent signs and symptoms in both waves were fever, dyspnea, pneumonia, and cough, and the most relevant comorbidities were cardiovascular diseases, type 2 diabetes mellitus, and chronic neurological diseases. Patients from the second wave more frequently presented renal and gastrointestinal symptoms, were more often treated with non-invasive mechanical ventilation and corticoids, and less often with invasive mechanical ventilation, conventional oxygen therapy and anticoagulants.[12-15] Several differences in mortality risk factors were also observed.

Ciapponi et al in there systematic reviews (SRs) summarizing the best evidence regarding the effect of COVID-19 on maternal and child health following Cochrane methods and PRISMA statement for reporting, concluded that the most frequent COVID-19 clinical findings during pregnancy were fever (28-100%), mild respiratory symptoms (20-79%), raised C-reactive protein (28-96%), lymphopenia (34-80%), and pneumonia signs in diagnostic imaging (7-99%).[12] The most frequent maternal outcomes were C-section (23-96%) and preterm delivery (14-64%). Most of their babies were asymptomatic (16-93%) or presented fever (0-50%), low birth weight (5-43%) or preterm delivery (2-69%). The odds ratio (OR) of receiving invasive ventilation for COVID-19 versus non-COVID-19 pregnant women was 1.88 (95% confidence interval and the OR that their babies were admitted to

neonatal intensive care unit was 3.13. The risk of congenital transmission or via breast milk was estimated to be low, but close contacts may carry risks.

However there are few limitations of this study, as this study is conducted with small number of population the results cannot be generalized to all.

CONCLUSION

The above study indicates that hospitalized patients in second wave required more hospital stay, had higher mortality rates, even though treatment were more effective and intensive. Although majority were asymptomatic in both waves, the severe pneumonic symptoms in second wave stands out as an important difference in both waves. These characteristics may help to understand the nature of disease in India and its behavior and dangers also.

ACKNOWLEDGMENTS

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