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Original Research Article

Changing trends in fetomaternal outcome in COVID-19 in pregnancy

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ABSTRACT

Background: This study is to provide an overview of the clinical course and outcome of COVID in pregnancy in both first wave and second wave, to study about different parameters affected significantly in both waves.
Methods: This is a retrospective comparative study that was conducted by dividing the patients into group 1 and group 2. Group 1 was treated in 2020 (wave 1) whereas group 2 in 2021 (wave 2). A laboratory confirmed positive cases of COVID-19 infection in pregnant women were included. All the patients were further categorized into mild, moderate and severe subgroups according to the ICMR criteria.
Results: The study of the first (2020) and second (2021) wave of COVID-19. In group 1 and group 2, there were a total of 359 cases and 145 cases respectively. In group 1, there were 54/359 (15.04%) moderate cases and in group 2 there were 17/145 (11.72%) moderate cases. While there were 101/359 (28.13%) and 106/145 (73.10%) severe cases in group 1 and group 2 respectively. Most of severe cases of second group associated with breathlessness, tachypnoea and fall in oxygen saturation level ended with mechanical ventilation by O2 mask (7.54%), NRBM (8.49%), HFNC (14.15%), BIPAP (12.26%), invasive ventilation (22.64%).
Conclusions: The results of study show that hospitalized patients in the second wave were younger, required hospitalization, and had higher mortality rates.

Keywords: COVID-19, Pregnancy, Maternal morbidity, Mortality

INTRODUCTION

SARS-CoV-2 is the strain of coronavirus that causes COVID-19. It was first recognized in Wuhan City, China, at the end of 2019.[1] Other human coronaviruses (HCoV) infections include HCoV 229E, NL63, OC43, and HKU1, which usually cause mild to moderate upper respiratory tract infections, like the common cold, Middle East Respiratory Syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). The world health organization (WHO) on March 11, 2020, has announced the novel coronavirus (COVID-19) outbreak as a global pandemic.[2] Clinical features vary vastly from absence of any symptoms to severe dyspnoea and even death.

However, People are susceptible to CoV-2, the number of mild cases is enormous (accounts for 81% of total no. covid patient).[2] In the second wave, there were more children, pregnant and postpartum women.[3] Pregnancy with co-morbidities like old age, obesity, diabetes mellitus, high blood pressure and coronary artery disease are risk factors for COVID-19 which lead to mortality.[3] Current evidence from a US study suggests that covid positive pregnancies are more likely to develop severe complications, higher need for hospitalization, ICU admission and mechanical ventilation. Among the subset of pregnant females who develop the severe disease, the already complex control of infection may be further complicated by pregnancy.[4] During pregnancy, women have more immunologic and physiologic changes that

could increase risk for more dangerous illness from various infections.[5,6]

Objectives

Objectives of current study were; to provide an overview of the clinical course and outcome of COVID in pregnancy in both first wave and second wave, to study about different parameters affected significantly in both waves.

METHODS

This is a retrospective comparative study carried out in SVP Hospital from April 2020 to May 2021. Our study was conducted by dividing the patients into Group 1 and Group 2. Group 1 comprised of positive patients who were treated at our institute in 2020 (Wave 1) whereas Group 2 consisted of positive patients who were treated in 2021 (Wave 2). A confirmed case of COVID-19 is defined as a positive result by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) or rapid antigen test (RAT) assay of maternal pharyngeal and nasopharyngeal swab specimens. All the patients were further categorized into Mild, Moderate and Severe subgroups according to the ICMR criteria.[5] The study comprises moderate (56/359) and severe cases (99/359) of wave 1 (April 15, 2020, to December 31, 2020) and moderate (21/145) and severe cases (102/145) of wave 2 (April 1, 2021-May 16, 2021). All the mandatory safety precautionary measures- personal protective equipment (PPE) including a jumpsuit, gloves, N-95 mask, splash resistant face shield, goggles were used by all the health care professionals in labour wards and operation theatres. Separate premises were set apart as donning and doffing areas. Complete epidemiologic history, obstetric history, clinical symptoms, signs, specific obstetric condition, laboratory and radiologic investigations, treatment, complications and outcome of data were collected from electronic medical records software ARCUS and curated within customized data collection. All laboratory investigations like complete blood cell count (CBC), liver function test (LFT), renal function test (RFT), C-reactive protein (CRP), serum lactate dehydrogenase (LDH), serum Ferritin, D-Dimer and radiologic assessments like chest X-ray were performed according to the clinical needs of the patients. ICMR Criteria for categorizing the cases into mild, moderate, and severe. As per ICMR criteria[7] Mild case is defined as CRP<20; RR<24; SPO_2> 95%, Moderate case is defined as CRP -20 to 50; RR-24 to 30; SPO_2-90 to 94%; whereas severe case is defined as CRP>50; RR>30; SPO_2<90%. Patients were classified based on the clinical presentation, the severity of illness, fetomaternal outcome, and complications of the disease. Neonatal pharyngeal and nasopharyngeal swab samples were collected immediately after delivery and tested for SARS-CoV-2 using qRT-PCR in wave 1 and the only RAT was done in all new-born babies in the second wave. Sample collection, processing, and laboratory testing complied with WHO guidance. The disease course was monitored and patients were managed by a multidisciplinary team of obstetricians, physicians, pulmonologists, anaesthesiologists and neonatologists as per ICMR guidelines, and investigations were repeated during the hospital stay as per requirement. Data were collected and labelled and analysed with the appropriate statistical test. In this study, fisher exact test was applied and calculated. Statistical tool (software) statistical package for the social sciences (SPSS).

Inclusion and exclusion criteria

Inclusion criteria for current study were; confirmed COVID-19 positive cases by any of the following methods: RAT, RTPCR. Patients with confirmed pregnancy by UPT, USG or β-HCG. Antenatal patients and patients in puerperium (period from delivery to 6 weeks). Exclusion criteria for current study was non-pregnant females.

RESULTS

This is a retrospective, comparative study of the first (2020) and second (2021) wave of COVID-19. In group 1 and group 2, there were a total of 359 cases and 145 cases respectively with the common age group 21-30 years. In group 1, there were 54/359 (15.04%) moderate cases and in group 2 there were 17/145 (11.72%) moderate cases. While there were 101/359 (28.13%) and 106/145 (73.10%) severe cases in group 1 and group 2 respectively.

Moderate cases

Total 54 moderate cases in group 1, 34 (62.96%) were antenatal and 20 (37.03%) were postnatal as depicted in (Table 1). While in group 2 all the 17/17 (100%) cases were antenatal. Associated medical comorbidities like pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM) and hypothyroid were comparable between 2 groups and there was significant difference between the 2 groups (20.38% vs. 52.94%, p=0.014). There was a significant difference between the inflammatory markers of group 1 and group 2. In wave 1, CRP value of moderate cases (20-50) was seen in 54/54 (100%) cases, while in group 2, it was seen in 17/17 (100%) cases. In group 1, raised LDH (>250U/l) in moderate cases was seen in 42/54 (77.77%) cases, while in wave 2 it was 10/17 (58.82%) moderate cases. Likewise, in group 1, raised D-Dimer was seen in 53/54 (98.14%) cases and in group 2 it was 17/17 (100%) cases. In group 1, in moderate cases 2/54 (3.70%) were admitted in HDU and 6/17 (35.29%) in group 2. In moderate cases of group 1, 1/54 (1.85%) required NRBM support and 1/54 (1.85%) required O_2 mask+nasal prongs; and in group 2, 2/17 (11.76%) required NRBM support and 4/17 (23.54%) required O_2 mask+nasal prongs. In NRBM, there was no significant association in both groups. But only in group 2, O_2 mask requirement was more than group 1 (1.85% vs. 23.54%, p=0.0103).

Table 1: Demographic distribution, various lab investigations and outcome of COVID-19 between group 1 and group 2 of moderate cases.

Moderate cases		Group 1, N (%)		Group 2, N (%)		P value
Total Patients, N (%)		54/359 (15.04)		17/145 (11.72)		0.396
Age (years)	<20	1 (1.85)		1 (5.88)		-
	21-30	36 (66.66)		9 (52.94)		0.389
	31-40	16 (29.62)		6 (35.29)		-
	>40	1 (1.85)		1 (5.88)		-
Antenatal (on admission)	1st trimester	34 (62.96)	0	17 (100)	2 (11.76)	0.106
	2nd trimester		6 (11.11)		6 (35.29)	0.180
	3rd trimester		28 (51.85)		9 (52.95)	0.044
Postnatal (on admission)	LSCS	20 (37.03)	4 (7.40)	-	-	-
	ND		16 (29.62)		-	-
Comorbidities	PIH	6 (11.11)		4 (23.53)		0.014
	GDM	1 (1.85)		1 (5.88)		-
	Hypothyroid	4 (7.40)		4 (23.53)		-
CRP (20-50)		54 (100)		17 (100)		-
LDH >250		42 (77.77)		10 (58.82)		-
Ferritin>282		4 (7.40)		3 (17.64)		-
D-dimer>0.5		53 (98.14)		17 (100)		-
ICU requirement	ICU	0		0		-
	HDU	2 (3.70)		6 (35.29)		-
Oxygen requirement	Invasive	0		0		-
	BIPAP	0		0		-
	HFNC	0		0		-
	NRBM	1 (1.85)		2 (11.76)		0.1404
	O2 mask+NP	1 (1.85)		4 (23.54)		0.0103
RR	24-30/min	2 (3.70)		6 (35.29)		-
	>30/min	-		-		-
SpO2	90-94	2 (3.70)		6 (35.29)		-
	<90	-		-		-
Obstetric outcome	ND	9 (16.66)		0		0.1022
	Preterm ND	1 (1.85)		0		-
	EMLSCS	16 (29.62)		8 (47.06)		0.2419
	ELLSCS	1 (1.85)		0		-
	Hysterotomy	1 (1.85)		0		-
	Abortion	0		0		-
	On going pregnancy	6 (11.11)		9 (52.94)		-
Indication for termination	Obstetrics	18 (33.33)		7 (41.17)		0.3077
	Non-obstetrics	0		1 (5.88)		-
Neonatal outcome	Live birth	30 (96.77) twins-3		8 (100) twins-0		0.5805
	Still born	1 (3.23)		0		-
	Neonatal mortality	2 (6.45)		0		-
	NICU admission	30 (96.77)		0		-
	COVID +ve	0		0		-
Maternal mortality	Antenatal	-	-	-	-	-
	Postnatal		-		-	-

A total of 34/54 (62.96%) pregnant women in moderate cases of group 1, including 3 twins; delivered whom 17/54 (31.48%) required cesarean delivery-emergency 16/54 (29.62%) and 1/54 (1.85%) was elective, 1/54 (1.85%) underwent hysterotomy and 9/54 (16.66%) had full term vaginal delivery and 1/54 (1.85%) had preterm vaginal delivery. While 6/54 (11.11%) were managed conservatively. In group 2 of moderate cases, a total of 17/17 (100%) pregnant women, delivered their babies of whom 8/17 (47.06%) underwent Emergency cesarean section and 9/17 (52.94%) were managed conservatively. All 18/54 (33.33%) cases of group 1 under moderate criteria and 7/17 (41.17%) cases of group 2, which required intervention were terminated due to obstetric indication.

Table 2: Demographic distribution, various lab investigations and outcome of COVID-19 between group 1 and group 2 of severe cases.

Severe cases		Group 1, N (%)		Group 2, N (%)		P value
Total Patients, N (%)		101/359 (28.13)		106/145 (73.10)		-
Age (years)	<20	4 (3.96)		1 (0.94)		0.2033
	21-30	70 (69.30)		48 (45.28)		0.0007
	31-40	27 (26.73)		53 (50)		0.0006
	>40	0		4 (3.78)		0.1218
Antenatal (on admission)	1st trimester	55 (54.45)	0	104 (98.11)	5 (4.71)	0.059
	2nd trimester		3 (2.97)		36 (33.96)	0
	3rd trimester		52 (51.48)		63 (59.43)	0.26
Postnatal (on admission)	LSCS	46 (45.54)	35 (34.65)	2 (1.88)	2 (1.88)	0
	ND		11 (10.89)		-	0.0002
Comorbidities	PIH	12 (11.88)		10 (9.43)		0.6544
	GDM	3 (2.97)		7 (6.60)		0.333
	Hypothyroid	9 (8.91)		11 (10.38)		0.8158
CRP	20-50	2 (1.98)		4 (3.77)		-
	>50	99 (98.01)		102 (96.22)		
LDH >250		76 (75.24)		88 (83.01)		-
Ferritin>282		7 (6.93)		35 (33.02)		-
D-dimer>0.5		101 (100)		106 (100)		-
ICU requirement	ICU	11 (10.89)		52 (49.06)		0.0001
	HDU	1 (0.99)		19 (17.92)		0.0001
Oxygen requirement	Invasive	4 (3.96)		24 (22.64)		0.0001
	BIPAP	4 (3.96)		13 (12.26)		0.0001
	HFNC	3 (2.97)		15 (14.15)		0.0055
	NRBM	0		9 (8.49)		0.0033
	O2 mask+NP	1 (0.9)		18 (7.54)		0.0001
RR	24-30/min	4 (3.96)		21 (19.81)		-
	>30/min	8 (7.92)		48 (45.28)		
SpO_2	90-94	3 (2.97)		15 (14.15)		-
	<90	9 (8.91)		64 (60.37)		
Obstetric outcome	ND	9 (16.66)		0		0.4364
	Preterm ND	4 (3.96)		2 (1.88)		0.6217
	EMLSCS	1 (0.9)		3 (2.83)		0.7791
	ELLSCS	42 (41.58)		42 (39.62)		0.053
	Hysterotomy	5 (4.95)		14 (13.20)		1
	Abortion	1 (0.9)		2 (1.88)		-
	On going pregnancy	0		2 (1.88)		-
Indication for termination	Obstetrics	44 (43.56)		28 (26.41)		0.009
	Non-obstetrics	4 (3.96)		30 (28.30)		0
Neonatal outcome	Live birth	53 (98.14) twins-1		63 (92.64) twins-5		0.3299
	Still born	1 (1.85)		5 (7.36)		0.2127
	Neonatal mortality	2 (3.7)		4 (5.88)		0.6034
	NICU admission	53 (98.15)		20 (29.41)		0.0001
	COVID +ve	3 (5.66)		0		1
Maternal mortality	Antenatal	1 (0.9)	-	19 (17.92)	7 (6.60)	0.0001
	Postnatal		1 (0.27)		12 (11.32)	-

While in group 2, 1/17 (5.88%) cases were terminated for non-obstetric indication. There was no maternal mortality recorded in moderate cases in group 1 and group 2.

Severe cases

Total 101 severe cases in group 1, 55 (54.45%) were antenatal and 46 (45.54%) were postnatal as depicted in (Table 2). While in group 2 out of 106 severe cases, antenatal were 104 (98.11%) and postnatal 2 (1.88%). In the age group, 21-30 years (p=0.0007) and 31-40 years (p=0.006) significantly associated in these two groups. In severe cases of group 1, 1/101 (0.99%) and 19/145 (17.92%) cases in group 2 required HDU admission (0.99% vs. 17.9%, p=0.001. None out of 359 required NRBM support in group 1 and O_2 mask and nasal prongs

support was given to 1/101(0.9%). In group 2, 9/106 (8.49%) required NRBM support and O_2 mask + Nasal prongs support was given to 18/106 (7.54%) cases. (p=0.001). 11/101 (10.89%) patients requiring intensive monitoring were admitted to ICU out of which 3 required HFNC, 4 required NIV and 4 patients were intubated and required invasive ventilation in wave 1. Whereas, in wave 2, 52/106 (49.05%) patients 15 required HFNC, 13 required NIV and 24 required intubations, (p=0.001), therefore in group 2 most cases were extremely associated with oxygen requirement to maintain saturation by means of various respiratory modes than group 1 in which oxygen requirement by assisted respiration was less. In all respiratory modes, there is extreme association between these both groups.

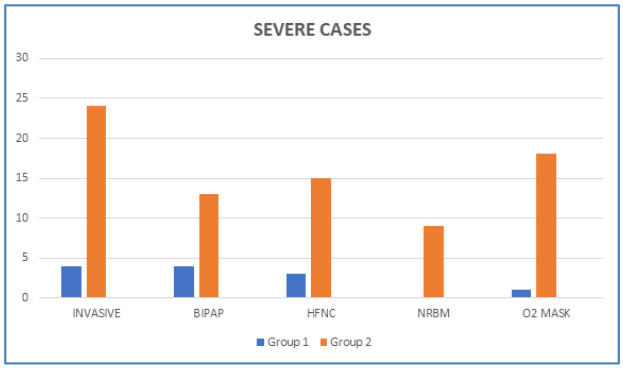

Figure 1: Severe cases.

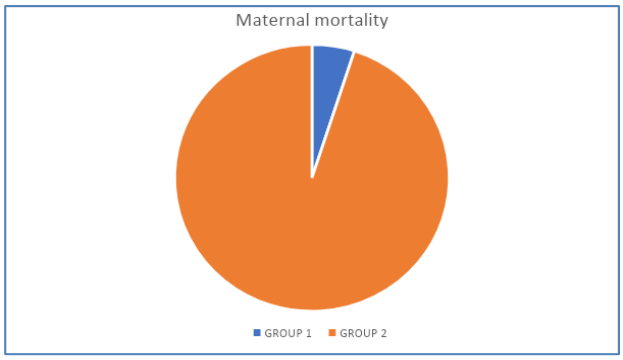

Figure 2: Maternal mortality.

A total of 55/359 (15.32%) pregnant women in severe cases of group 1, including 1 twin; delivered their babies of whom 47/55 (85.45%) underwent cesarean delivery-emergency 42/55 (76.36%) and 5/55 (9.09%) were elective, 1/55 (1.81%) required hysterotomy and 4/55 (7.27%) had full term vaginal delivery and 1/55 (1.81%) had preterm vaginal delivery. While 2/55 (3.63%) were managed conservatively. A total of 104/106 (71.72%) pregnant women in severe cases of group 2, including 5 twins; delivered their babies of whom 56/106 (52.83%) underwent cesarean delivery-emergency 42/106 (39.62%) and 14/106 (13.20%) were elective, 2/106(1.88%) required hysterotomy, 2/106 (1.88%) were aborted and 2/106 (1.88%) had full term vaginal delivery and 3/106 (2.83%) had preterm vaginal delivery. While 39/106 (36.79%) was managed conservatively. Normal delivery is significantly high among group 1 in severe cases (3.96% vs 1.88%, p=0.0002). 44/48 (91.67%) cases of group 1 under severe criteria and 28/58 (48.27%) cases of group 2, were terminated due to Obstetric indication. While in group 1, 4/48 (8.33%) cases and in group 2, 30/58 (51.72%) were terminated for non-obstetric indication. In severe cases of wave 1, there were total 54 deliveries including 1 twins' delivery, amongst which 53/54 (98.15%) were live births and required NICU admission and amongst them 3 (5.66%) tested COVID positive, 1/54 (1.85%) was Still Born and there were 2/54 (3.7%) cases of neonatal mortality. In severe cases of wave 2, there were total 68 deliveries including 5 twins' delivery, amongst which 63/68 (92.64%) were live births and 20/63 (3.17%) required NICU admission, 5/68 (7.36 %) were Still Born and 4/68 (5.88%) cases of neonatal mortality. In severe cases of wave 1, 1/101 (0.99%) postnatal cases of maternal mortality were seen. While in wave 2, 7/106 (6.60%) cases of maternal mortality were antenatal and 12/106 (11.32%) cases were postnatal. Maternal mortality is an extremely significant association in both these groups (0.9% vs. 17.92, p=0.0001).

DISCUSSION

Pregnancy is a state of relative immunosuppression, caused by a change in the maternal immune system to prevent rejection of the semi allogenic foetus.[8] The physiological and mechanical changes associated with pregnancy increase maternal susceptibility to infections and even complicate the intubation and mechanical breathing. This study describes comparison between two groups of COVID-19 pandemic in obstetric cases in our tertiary care centre. Our result showed that the group 2 (73.10%) of disease was associated with a higher incidence of severe cases than group 1 (28.13%). In both groups 21-30 years age group women were more commonly affected. In group 2 younger adults appear to be more prone to infection and many patients of younger age group have succumbed their life, including patients aged between 25 and 50 years.[9] In group 1 majority of cases were mild and moderate with good recovery rate, whereas in group 2 majority of women who were hospitalized presented with severe symptoms and with poor outcome that is explained by total duration of hospital stay and morbidity and mortality comparable to data from Spain, by Vallverdú et al study where the number of hospitalized pregnant women during the wave 2 was ten times higher than in the wave 1, while the total number of patients hospitalized increased by 30% during the same time, indicate that this trend might not be entirely explained by an increase in total number of positive cases.[10] New variants of COVID-19 in the second wave was reported to be more transmissible more deadly and with the potential to escape existing immunity and likely to be changing the disease progression.[11-14] In our study, severe cases in group 2 were 73.10% which was higher than the group 1 (28.13%), similar to ICMR

Symptomatic cases where total cases of wave 2 were significantly higher at 28.7%, compared to the first wave (14.73%).[15]

Severe illness appears to be more common in later pregnancy. In this study, 59.43% cases were seen in third trimester which is comparable with UKOSS study, where Symptomatic COVID-19 was principally diagnosed in the third trimester (52%).[16] In group 1 most of the antenatal patients met with good obstetric outcome or continuation of pregnancy without any fetomaternal complication while in group 2 seriousness of disease was high in most of antenatal patients which resulted in early termination of pregnancy to improve maternal outcome. In group 1, comorbidities like gestational hypertension, gestational diabetes mellitus, hypothyroidism have not much affected the course and outcome of patients. Whereas in the second group these comorbidities highly affected the course and outcome of the patients with higher incidence of serious events such as pneumonia, acute respiratory distress syndrome, acute kidney injury, sepsis, ICU admission and mechanical ventilations and death of patients. Inflammatory markers like CRP, LDH, ferritin, D-dimer which suggest the severity of disease were significantly raised in most cases of group 2 compared to group 1 in which inflammatory markers were not so increased. The combination of elevated D-dimer levels was likewise associated with more severe disease and it is seen elevated in all the patients in present study which is comparable to study by turan at el in which it is present in 60% of severely ill and 80% of critically ill positive pregnant women, respectively.[17]

In moderate group 1, HDU admission (3.70%) with NRBM (1.85%) and O_2 mask and nasal prongs (1.85%) support to maintain the oxygen level. While in the second group incidence of ICU and HDU (35.29%) admission were too high. Most of severe cases of second group associated with breathlessness, tachypnoea and fall in oxygen saturation level ended with mechanical ventilation by O_2 nasal prongs and O_2 mask (7.54%), NRBM (8.49%), HFNC (14.15%), BIPAP (12.26%) or invasive ventilation (22.64%). The results were comparable to the study of debolt et al in which the rate of ICU admission 39.5% requiring mechanical ventilation in 26.3% ICU admission with assisted ventilation resulted in long hospital stay, co-infection, organ failure, sepsis and mortality.[18] Cytopathic effects and inflammatory response produced by virus as well as viral evasion of host immune responses are play critical roles in disease severity.[9,10] In group 1 obstetric outcome was good by means of normal vaginal delivery or LSCS or with continuation of pregnancy without any fetomaternal complications while in second group most antenatal women were symptomatic with tachypnoea, respiratory distress and low oxygen level. So, to improve maternal symptomatic conditions early termination of pregnancy was indicated, resulted in high incidence of spontaneous abortion, preterm vaginal delivery, hysterotomy and EMLSCS with poor neonatal outcome. Maternal COVID-19 is associated with an increased rate of cesarean birth (39.62%) where as in UKOSS study, 23.59% of women had cesarean births.[19]

In our study preterm delivery rate was 9.87% comparable to study done by jering et al who reported a 7.2% preterm birth.[20] Pregnant women with symptomatic COVID-19 were more likely to deliver before 37 weeks of gestation, pregnant women with asymptomatic COVID-19 was not, however, at increased risk of preterm baby. For women with symptomatic COVID-19, most of preterm births were iatrogenic. Preterm birth is associated with perinatal mortality and morbidity.[21] The rate of stillbirth (7.36%) and neonatal mortality (5.88%) were higher in group 2 than group 1 comparable with one London hospital reporting an increased incidence of stillbirth during the pandemic.[22] Maternal mortality was significantly high in second group (17.92%) compared to first group (0.9%) there was only one case of maternal mortality which is comparable to, study done at BYL Nair charitable hospital in Mumbai, there were 0.7% maternal mortality in first group and 5.7 % in group 2.[23]

Limitations

A limitation of the present study is the small sample size. This is a study in a medium size hospital, and that covers a relatively small geographical area. And also, we are at the limit of statistical significance for the calculation of mortality differences. So, our findings must be taken with caution. However, these results obtained are relevant since they might be representative of many similar centres which information is yet available on this issue.

CONCLUSION

The results of the present study show that hospitalized patients in the second wave were younger, required hospitalization, and had higher mortality rates. There were differences between those associated with comorbidities and mortality. Study indicate that the characteristics of the infections may change over time. COVID-19 infection was associated with higher rates of cesarean section in pregnant women and their mortality. Based on the results of this study, COVID-19 cannot be considered as an indication for cesarean delivery. So, the timing and mode of delivery should be individualized based on obstetrical indications and maternal condition.

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