ORIGINAL ARTICLE

Retrospective Analysis of Clinical Characteristics and Outcomes of Pregnant Women with SARS-CoV-2 Infections Admitted to Intensive Care Units in India (Preg-CoV): A Multicenter Study

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Abstract

Aim: The aim was to examine the outcomes of pregnant women admitted to intensive care unit with coronavirus disease-2019 (COVID-19) infection during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in India. The primary outcome of the study was maternal mortality at day 30. The secondary outcomes were the intensive care unit (ICU) and hospital length of stay, fetal mortality and preterm delivery.

Materials and methods: This was a retrospective multicentric cohort study. Ethical clearance was obtained. All pregnant women of the 15–45-year age admitted to ICUs with SARS-CoV-2 infection during 1st March 2020 to 31st October, 2021 were included.

Results: Data were collected from nine centers and for 211 obstetric patients admitted to the ICU with a confirmed diagnosis of COVID-19. They were divided in to two groups as per their SpO_2 (saturation of peripheral oxygen) level at admission on room air, that is, normal SpO_2 group ($SpO_2 > 90\%$) and low SpO_2 group ($SpO_2 < 90\%$). The mean age was (30.06 ± 4.25) years and the gestational age was 36 ± 8 weeks. The maternal mortality rate was10.53%. The rate of fetal death and preterm delivery was 7.17 and 28.22%, respectively. The average ICU and hospital length of stay (LOS) were 6.35 ± 8.56 and 6.78 ± 6.04 days, respectively. The maternal mortality (6.21 vs 43.48%, $p < 0.001$), preterm delivery (26.55 vs 52.17%, $p = 0.011$) and fetal death (5.08 vs 26.09%, $p = 0.003$) were significantly higher in the low SpO_2 group.

Conclusion: The overall maternal mortality among critically ill pregnant women affected with COVID-19 infection was 10.53%. The rate of preterm birth and fetal death were 28.22 and 7.17%, respectively. These adverse maternal and fetal outcomes were significantly higher in those admitted with low SpO_2 (<90%) at admission compared with those with normal SpO_2.

Keywords: Coronavirus disease-2019, Intensive care unit, Maternal mortality, Obstetric critical care, Pregnant women.

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Highlights

Obstetric critically ill patients pose significant challenge due to physiological changes. It may become more challenging when comorbid conditions are present. Compared with women with normal oxygenation status, those who were admitted to an intensive care unit during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic and had hypoxia at the time of admission experienced considerably increased rates of mortality, premature birth, and fetal death. Obstetric patients in the intensive care unit needed specialized yet personalized care.

Introduction

The pandemic caused by (SARS-CoV-2) known as coronavirus disease-2019 (COVID-19) since December 2019 had grappled the entire globe with millions of people affected by the virus. It affected people across nations irrespective of age and gender.[1] Patients with comorbid conditions like diabetes mellitus, hypertension, malignancy, chronic kidney disease, chronic obstructive pulmonary diseases, and cardiovascular disease were more likely to develop severe COVID-19 infections.

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Though pregnancy is considered a physiological state, it is a risk factor for the severe form of COVID-19 due to various changes in physiology, immunity, and respiratory mechanics during pregnancy. These changes predispose them to decompensate at an accelerated rate in case the COVID-19 illness advances from moderate-to-severe. More so, pregnant women of age >35 years, having obesity, with chronic and/or gestational hypertension, diabetes, and preeclampsia were also at increased risk of developing a severe form of COVID-19.[2,3]

There were challenges in managing pregnant patients with COVID-19-related ARDS (CARDS) due to limitations imposed by anatomical and physiological changes related to pregnancy and limited resources because of sudden surge. The protective lung ventilation strategy usually followed for ARDS patients was difficult to practice in the obstetric population. Furthermore, if there were associated risk factors like preeclampsia or gestational diabetes mellitus or peripartum cardiomyopathy, the outcome tended to be worse. Along with increased maternal morbidity and mortality, there were also higher incidences of premature delivery and adverse perinatal outcomes for patients admitted to intensive care unit (ICU). Pregnant women with COVID-19 were more likely to be admitted to the ICU, but no specific recommendations for COVID-19 ICU management were made.[4,5]

To the best of our knowledge, this is the first multicenter study across various clinical settings examining the clinical characteristics and outcomes of pregnant patients with COVID-19 in the Indian scenarios. Therefore, we planned the retrospective data collection to study the clinical characteristics and outcomes of pregnant women with COVID-19 in India (Preg-CoV).

Aim and Objectives

The primary outcome of the study was maternal mortality of pregnant women on the day 30 affected with COVID-19 infection admitted to ICU. The secondary outcomes are the ICU LOS, and hospital and fetal outcome which included fetal mortality and preterm delivery.

Materials and Methods

This was a retrospective multicentric study carried out in Indian ICUs after approval from the individual institutions' institutional ethical committees (IEC). The adult COVID-ICU admission registry was searched for patients admitted between March 1, 2020 and October 31, 2021. All pregnant women of the 15–45-year age group admitted to COVID-ICUs in various hospitals with SARS-CoV-2 infection, confirmed by a real time reverse transcriptase polymerase chain reaction (RT-PCR) assay of a nasopharyngeal swab specimen during this period were included in this study. There were no exclusion criteria. Consent was waived off in view of the retrospective design of the study. A clinical research form (CRF) was formulated. The Indian Society of Critical Care Medicine (ISCCM) endorsed the study and the invitation to participate was e-mailed to all ISCCM members.

Data Collection

Pre-designed CRF were used to collect data which include: (a) demographic parameters, such as age, period of gestation, COVID vaccination status, and duration of pregnancy; (b) comorbid conditions, such as obesity, diabetes mellitus (DM), gestational diabetes mellitus (GDM), preeclampsia, eclampsia, hypertension, kidney disease, asthma, cholestasis of pregnancy, noncirrhotic portal fibrosis, transaminitis, hypothyroidism, presence of any blood disorders; (c) clinical parameters at the presentation including duration of symptoms, respiratory status, organ support like oxygen requirement (oxygen flow with nasal cannula or mask, high flow nasal cannula (HFNC)/reservoir mask), the requirement of mechanical ventilation (noninvasive ventilation (NIV) and invasive ventilation), vasopressors and dialysis; (d) laboratory investigations, such as arterial blood gas (paO_2/FiO_2) ratio, renal function test (RFT), liver function test (LFT); (e) treatment-related parameters, such as the kind of steroids given their duration, heparin (subcutaneous or intravenous infusion), remdesivir, tocilizumab, ivermectin, vitamin C, vitamin D, Zinc, immunomodulators, plasma therapy; (f) outcome parameters, such as ICU admission, ICU LOS, hospital length of stay, maternal mortality, pulmonary embolism, cerebral venous sinus thrombosis, mucormycosis; and (g) obstetric parameters, such as placental issues, delivery plan, obstetric hemorrhage, Posterior reversible encephalopathy syndrome (PRES), HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, fetal ultrasound status, fetal complications, termination of pregnancy (induced labor or cesarean section), infections if any, bleeding complications, fetal status at delivery, preterm status at delivery, intrauterine death (IUD), vertical transmission at delivery and maternal death. The patients would be divided into two groups i.e. normal saturation of peripheral oxygen (SpO_2) and low SpO_2 on room air based on oxygenation status at admission for studying the variations if any, in the outcome parameters. Patients with $SpO_2 > 90\%$ on room air on admission were included in normal SpO_2 group, while those with less than or equal to 90% on room air at admission were included in low SpO_2 group.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) according to normal distribution, and categorical variables as numbers (percentages). Between-group (normal SpO_2 and low SpO_2 group) comparisons were performed by Student or Mann–Whitney tests for continuous variables and by Pearson's Chi-square or Mann–Whitney test for categorical variables. Descriptive statistics were carried out on the available data. All tests were two-sided, and a p-value < 0.05 was taken as significant. All analyses were carried out with SPSS version 28.0 (SPSS, Chicago, Illinois, USA).

Results

From the COVID-ICU registries of nine collaborating centers, data pertaining to 211 pregnant women infected with COVID-19 was gathered. Out of these 211 cases, 2 cases were excluded from the final analysis (one case was excluded for age >45 years, and second

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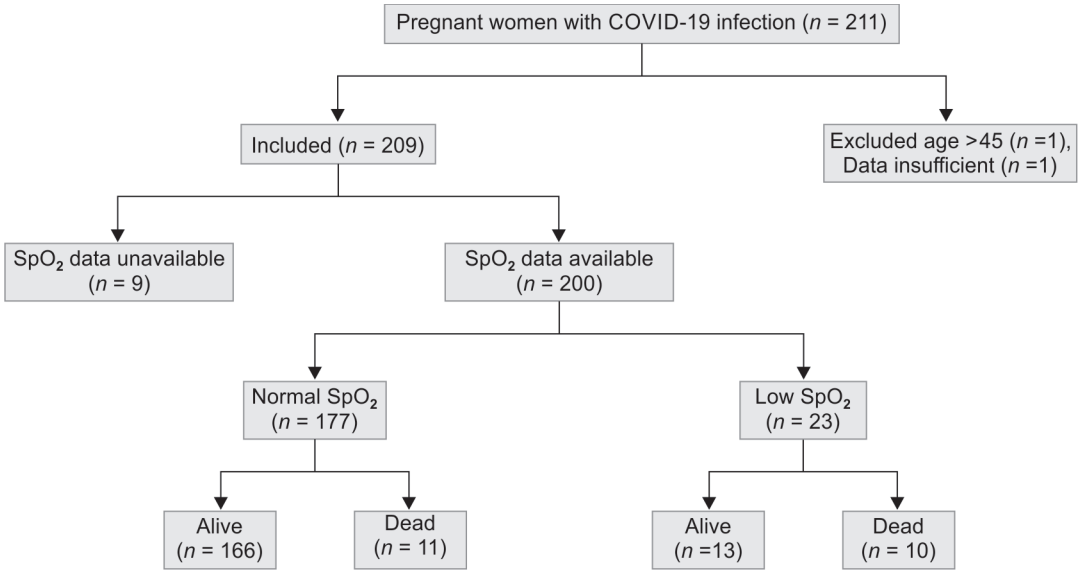


Fig. 1: Overall distribution of patients

Table 1: Baseline characteristics of COVID-19 pregnant patients admitted to intensive care units

Characteristics (n = 209)	*Mean ± SD/Frequency*
Age (Years)	30.06 ± 4.25
Gravida	1.67 ± 0.98
Primigravida	119 (56.94%)
Multigravida	90 (43.06%)
Comorbidities	52 (24.88%)
Pregnancy weeks at admission	36.00 ± 8.00
COVID vaccination 1st dose	16 (7.66%)
COVID vaccination 2nd dose	11 (5.26%)
SpO_2 (%)	94.60 ± 9.17
SOFA score (*n* = 83)	1.90 ± 1.97
Respiratory rate (per min)	23.31 ± 4.99
Systolic blood pressure (mm Hg)	122.01 ± 14.79
Diastolic blood pressure (mm Hg)	76.07 ± 11.54
Heart rate (per min)	97.33 ± 19.37
Steroids	73 (34.92%)
Dexamethasone	40 (19.14%)
Hydrocortisone	7 (3.35%)
Methyl prednisone	26 (12.44%)
Remdesivir	43 (20.57%)
Tocilizumab	9 (4.31%)
Heparin	114 (54.55%)
Ivermectin	8 (3.83%)
Vitamin C	163 (77.99%)
Vitamin D	120 (57.42%)
Zinc	166 (79.43%)
ICU length of stay (days)	6.35 ± 8.56
Prone positioning	11 (5.26%)
ECMO	2 (0.96%)
Hospital length of stay (days)	6.78 ± 6.04
Delivery by cesarian section	143 (68.42%)
Delivery by induction	21 (10.05%)
Maternal mortality	22 (10.53%)
Obstetric hemorrhage	26 (12.44%)
Vertical transmission	2 (0.96%)
PRES	1 (0.48%)
HELLP	6 (2.87%)
Pulmonary embolism	2 (0.96%)
Cerebral venous thrombosis	1 (0.48%)
Mucormycosis	0
Fetal status	
Alive	185 (88.52%)
Dead	15 (7.17%)
Preterm birth	59 (28.22%)

(Contd...)

Table 1: *(Contd...)*

case was excluded due to insufficient data). Figure 1 shows overall distribution of patients. The median age of the patient cohort was 30.06 ± 4.25 years. Around one-fourth of cases had one or more comorbid condition, and hypothyroidism was present in about one-fifth of cases. The mean SpO_2 and mean sequential organ failure assessment (SOFA) score were 94.60 ± 9.17 and 1.90 ± 1.97, respectively. Steroid was prescribed in 35% of cases, remdesivir in 20.57% of cases, 5.26% cases received prone position, and 0.96% cases required extracorporeal membrane oxygenation (ECMO) support. The mean ICU LOS and hospital LOS was 6.35 + 8.56 days and 6.78 ± 6.04 days, respectively. Delivery was conducted by cesarean section in 68.42% cases and only 10.05% cases were delivered by induction of labor. The pregnancy was complicated by obstetric hemorrhage in 12.44% cases, and HELLP syndrome in 2.87% of cases. There was a total of 22 maternal deaths, with mortality rate being 10.53%. In terms of fetal complications, there were 7.17% cases of IUD and 28.22% preterm birth. The details of demographic features, comorbid conditions, clinical parameters, laboratory parameters, therapeutics, as well as complications, and out of this cohort of 209 cases are summarized in Table 1.

This cohort was divided into two groups based on their SpO_2 level at the time of admission. As baseline admission SpO_2 was not available for 9 cases, the remaining 200 cases were divided into the normal SpO_2 group ($n = 177$), and the low SpO_2/hypoxic group ($n = 23$). There were 11 deaths in the normal SpO_2 group (11 out of 177 cases) compared with 10 deaths in the hypoxic group (10 out of 23 cases), and one mortality among 9 cases for which baseline SpO_2 data were not available. The comparison between the normal SpO_2 and low SpO_2/hypoxic groups has been presented in detail in Table 2. The age and comorbid conditions were comparable in both the groups. As compared with the normal SpO_2 group of patients, the hypoxic group patients had worse clinical as well as biochemical parameters. These patients also had significantly higher SOFA scores, and the steroid prescribing rates were higher in this group.

Similarly, the obstetric and fetal parameters between the two groups of patients are compared and analyzed (Tables 3 and 4). The maternal mortality was significantly higher in the low SpO_2 group than the group with normal SpO_2 at hospital admission (43.48 vs 6.21%, $p < 0.001$) (Fig. 2A, Table 3). The ICU length of stay (LOS) and hospital LOS was comparable among both the groups (Fig. 2B). Non-obstetric maternal complications as pulmonary embolism was reported in two patients (4.35%) in hypoxic group and one case (0.56%) of cerebral venous sinus thrombosis in normal SpO_2 group.

In the normal SpO_2 group, 125 (70.62%) cases had cesarean section for delivery while only 12 (6.78%) cases were induced for labor. However, in the hypoxic group, 14 cases (60.87%) had cesarean section for delivery, whereas only 7 (30.43%) cases were induced for labor and this difference was statistically significant ($p = 0.002$). Fetal USG reported single live intrauterine fetus in 131 (74%) cases in normal SpO_2 group and 7 cases (30.43%) in hypoxic group. There were significantly higher fetal death and preterm delivery in the group of patients with low SpO_2 at hospital admission (Fig. 3, Table 4). There was only one case of vertical transmission of COVID-19 infection in the normal SpO_2 group.

Discussion

To the best of our knowledge, this is the first Indian multicentric study comprising of the largest cohort of pregnant women admitted with COVID-19 infection to the intensive care unit in India. The mean age of the cohort was 30.06 ± 4.25 years, which is similar to the multicentric international study done by Péju E et al.[6] In our cohort of 209 pregnant women infected with COVID-19, 52 (24.88%) cases had comorbid condition. Among other comorbid conditions, DM or GDM, followed by preeclampsia/eclampsia, and hypertension were prevalent. A study of COVID-19-infected pregnant women demonstrated similar trends of comorbid conditions.[2] In this study, 57% women were primigravida, whereas 43% were multigravida. An international multicentric study reported a similar proportion of multigravida and primigravida pregnant women among COVID-19-infected pregnant females admitted to the hospital.[6]

In this cohort, all pregnant ladies who were affected with COVID-19 infection and presented to the hospital were admitted to ICU for monitoring and interventions as required as per decision of the admitting team. This is in contrast to other studies where rate of ICU admission in such population has been low.[2,6] Similarly, the UK national cohort study performed by the UK Obstetric Surveillance System (UKOSS) has reported 5% of hospitalized pregnant women with COVID-19 have required ICU admission.[7] This may be explained by the variation in the clinical severity of the COVID-19 disease in the patient cohort studied as our data were mainly contributed by tertiary care centers, attending to high-risk patients and as per the judgment of the treating team.

The COVID-19 vaccination status was poor in this cohort of pregnant patients as only 7.66% (16 cases) were vaccinated with the first dose and 5.26% (11 cases) were vaccinated with the second dose. There was insufficient data available about the immunization status of pregnant females admitted to the hospital with COVID-19 infection. But our study shows that less than 10% of cases were vaccinated with 1st dose of COVID vaccine, whereas only 5% of cases had received 2nd dose of COVID vaccine. This is in coherence with the multicenter international study, in which only about 5% of cases were vaccinated against COVID-19 in spite of strong recommendations for COVID-19 vaccination.[6] The Joint Committee on Vaccination and Immunization (JCVI) endorses the vaccination of pregnant women, as there is no biologically plausible mechanism by which the COVID vaccine will cause harm either in the periconception period, throughout gestation, or during breastfeeding. Hence, all pregnant females should be encouraged to get vaccinated and all their concerns must be addressed by the healthcare professional.[8]

Most of the patients required O_2 support by nasal cannula (39.71%), and lesser number received O_2 face mask (9.57%), reservoir mask (4.78%), and HFNC (5.26%). Noninvasive ventilation support was given to only 15 (7.18%) patients and 14 (6.69%) had received invasive mechanical ventilation. Prone positioning was performed in only 5.26% of cases. There was significantly more requirement for reservoir masks, HFNC, NIV as well as invasive mechanical ventilation in the patients with low SPO_2 levels at hospital admission. Of all (Table 2). Only 2 cases (0.96%) received ECMO. This is in concordance with the UK national cohort study performed using the UKOSS that reported <1% of hospitalized pregnant women with COVID-19 have required ECMO support.[8] In contrast, Péju E et al. reported that about 10% of cases required ECMO support.[6] which may be due to several reasons like severity of disease, liberal policy of initiating ECMO in high-risk group along with greater availability and affordability for ECMO as the study was conducted in patients from France, Belgium, and Switzerland.

In this study, steroids were prescribed in 73 (35%) cases. Steroid prescribing rates in the low SpO_2 group was significantly higher compared with the normal SpO_2 group. This can be attributed to growing evidence in favor of using steroids in hypoxic patients with COVID-19 infections. However, proportion of patients receiving steroids in our cohort was very less as compared with the study by Péju E et al.[6] in which 84% of cases received steroid therapy. The commonest comorbid condition in our cohort was diabetes mellitus or gestational diabetes. The concern of hyperglycemia might have contributed to lesser prescription of drugs like steroids in our cohort. The literature regarding steroid therapy in COVID-19-infected cases shows that the proportion of infected patients who were prescribed steroids varies from 12 to 100%.[9–11] This wide variation in the literature may be due to variability in the institutional policies, inclusion criteria, and clinical severity of cases included in various studies.

Remdesivir was prescribed in about 20% of patients, which is similar to the percentage of cases receiving remdesivir in a multicentric international study. However, the proportion of COVID-19-infected cases treated with remdesivir varied greatly from 0 to 100% in the various studies.[6,9–11] Similarly, in our cohort of 209 cases, tocilizumab was also prescribed in few cases only (4.31%). In contrast to a study compromising of similar cohort of patients, tocilizumab was administered in 13% of the patients.[6] The reason

Table 2: Comparison between normal SpO_2 and low SpO_2 group

Characteristics	*Normal SpO_2 group*		*Low SpO_2 group*		*p-value*
Age (years), Mean ± SD	*n* = 177	30.17 ± 3.90	*n* = 23	29.26 ± 5.88	0.326
Gravida	*n* = 177	1.64 ± 0.98	*n* = 23	1.70 ± 0.93	0.811
Vaccine (Dose 1), *n* (%)	*n* = 177	11 (6.21)	*n* = 23	4 (17.39)	0.056
Vaccine (Dose 2), *n* (%)	*n* = 177	9 (5.08)	*n* = 23	1 (4.35)	0.879
Gestation (weeks)	*n* = 176	32.84 ± 7.96	*n* = 18	32.39 ± 5.80	0.817
Comorbidities					
Obesity (*n*, %)	177	2 (1.13%)	23	0 (0%)	0.246
Pre-eclampsia/eclampsia	177	13 (7.34%)	23	1 (4.35%)	
DM/GDM	177	13 (7.34%)	23	3 (13.04%)	
Hypertension	177	8 (4.52%)	23	1 (4.35%)	
Kidney impairment	177	1 (0.56%)	23	0 (0%)	
Asthma	177	1 (0.56%)	23	0 (0%)	
NCPF	177	1 (0.56%)	23	0 (0%)	
Cholestasis of pregnancy	177	1 (0.56%)	23	0 (0%)	
Transaminitis	177	2 (1.13%)	23	0 (0%)	
Blood disorder (*n*,%)	177	13 (7.34%)	23	1 (4.35%)	0.908
Hypothyroidism	177	35 (19.77%)	23	5 (21.74%)	0.663
Clinical parameters					
SOFA score	*n* = 69	1.41 ± 1.28	*n* = 12	4.73 ± 2.87	**<0.001**
SpO_2 (%)	*n* = 177	97.26 ± 1.96	*n* = 23	74.09 ± 15.26	**<0.001**
RR (per min)	*n* = 177	22.55 ± 3.84	*n* = 21	30.62 ± 6.67	**<0.001**
SBP (mm Hg)	*n* = 177	123.27 ± 13.54	*n* = 22	112.41 ± 20.53	**0.001**
DBP (mm Hg)	*n* = 177	76.69 ± 10.59	*n* = 22	71.27 ± 17.09	**0.038**
HR (per min)	*n* = 177	95.64 ± 16.65	*n* = 22	117.41 ± 16.02	**<0.001**
Blood investigations					
Hb (gm%)	*n* = 174	11.03 ± 1.44	*n* = 22	10.84 ± 2.10	0.072
TLC (*10^3/uL)	*n* = 174	10.85 ± 5.8	*n* = 22	10.13 ± 4.27	**0.003**
Platelet count (per mm^3)	*n* = 174	211332 ± 68160	*n* = 22	198409 ± 75669	0.781
CRP (mg/L)	*n* = 142	134.90 ± 701. 87	*n* = 15	86.33 ± 67.61	0.079
D dimer (ng/mL)	*n* = 138	814.80 ± 635. 34	*n* = 17	512.42 ± 1130.55	**<0.001**
IL 6 (pg/mL)	*n* = 34	48.02 ± 66.81	*n* = 11	60.11 ± 57.72	0.134
Ferritin (mg/L)	*n* = 103	212.82 ± 417.61	*n* = 12	188.93 ± 119.98	0.263
LDH (U/L)	*n* = 85	283.43 ± 397.41	*n* = 10	1161.0 ± 2340.7	**0.004**
ABG parameters					
pH	*n* = 138	7.37 ± 0.07	*n* = 14	7.33 ± 0.12	0.093
PaO_2 (mm Hg)	*n* = 138	84.78 ± 23.95	*n* = 14	69.86 ± 16.04	**0.036**
PCO_2 (mm Hg)	*n* = 137	35.57 ± 10.70	*n* = 14	41.31 ± 15.96	0.137
Lactate (mmol/L)	*n* = 147	3.47 ± 6.77	*n* = 13	2.85 ± 1.95	0.749
Renal functions					
Urea (mg/dL)	*n* = 137	19.49 ± 11. 32	*n* = 15	32.90 ± 54. 74	**0.017**
Creatinine (mg/dL)	*n* = 165	0.62 ± 0.29	*n* = 16	0.85 ± 0.66	**0.012**
Sodium (mmoL/L)	*n* = 158	137.75 ± 3.48	*n* = 15	139.53 ± 5.38	0.074
Potassium (mmol/L)	*n* = 159	4.07 ± 0.52	*n* = 15	3.92 ± 0.71	0.311
Liver function tests					
Total bilirubin (mg/dL)	*n* = 137	0.74 ± 0.90	*n* = 16	1.51 ± 2.46	0.012
AST (U/L)	*n* = 158	114.88 ± 543. 54	*n* = 16	114.93 ± 160. 12	1.00
ALT (U/L)	*n* = 152	88.37 ± 284.0	*n* = 16	103.56 ± 131. 1	0.833
ALP (U/L)	*n* = 133	158.55 ± 92.92	*n* = 16	240.50 ± 110.26	0.001
Albumin (gm/dL)	*n* = 130	2.75 ± 0.46	*n* = 14	2.89 ± 0.49	0.276

(Contd...)

Table 2: *(Contd...)*

Characteristics	*Normal SpO_2 group*		*Low SpO_2 group*		*p-value*
Oxygen-related requirement					
HFNC	*n* = 171	5 (2.82%)	*n* = 13	4 (17.39%)	**0.003**
Reservoir mask	*n* = 169	6 (3.39%)	*n* = 13	3 (13.04%)	**0.001**
O_2 cannula	*n* = 170	21 (11.86%)	*n* = 13	2 (8.70%)	0.735
Face mask	*n* = 169	17 (9.60%)	*n* = 13	2 (8.70%)	**0.008**
NIV	*n* = 124	7 (3.95%)	*n* = 16	8 (34.78%)	**0.001**
Invasive MV	*n* = 175	6 (3.39%)	*n* = 16	8 (34.78%)	**0.001**
Proning	*n* = 174	4 (2.26%)	*n* = 18	6 (26.09%)	**<0.001**
ECMO	*n* = 174	0 (0%)	*n* = 18	2 (8.7%)	**0.008**
Medications					
Dexamethasone	*n* = 177	29 (16.38%)	*n* = 23	10 (43.48%)	**0.024**
Methylprednisolone	*n* = 177	20 (11.30%)	*n* = 23	5 (21.74%)	
Hydrocortisone	*n* = 177	2 (1.13%)	*n* = 23	5 (21.74%)	
Remdesivir	*n* = 177	35 (19.77%)	*n* = 23	7 (30.43%)	0.151
Tocilizumab	*n* = 177	7 (3.96%)	*n* = 23	1 (4.35%)	0.573
Heparin S/C	*n* = 177	98 (55.37%)	*n* = 23	13 (56.52%)	0.484
Heparin IV	*n* = 177	1 (0.56%)	*n* = 23	1 (4.35%)	0.084
Ivermectin	*n* = 177	6 (3.39%)	*n* = 23	1 (4.35%)	0.514
Vitamin C	*n* = 177	152 (85.88%)	*n* = 23	7 (30.43%)	**<0.001**
Vitamin D	*n* = 177	111 (62.71%)	*n* = 23	5 (21.74%)	**<0.001**

The values in bold imply statistical significance. (*n* = number of subjects for whom data were available)

Table 3: Maternal outcome parameters

Maternal outcomes	*Normal SpO_2*	*Low SpO_2*	*p-value*
Maternal death	11 (6.21%) (*n* = 177)	10 (43.48%) (*n* = 23)	**<0.001**
ICU length of stay (days)	6.55 ± 8.8 (*n* = 176)	5.64 ± 8.20 (*n* = 23)	0.751
Hospital length of stay (days)	6.81 ± 5.88 (*n* = 176)	7.09 ± 7.89	0.840

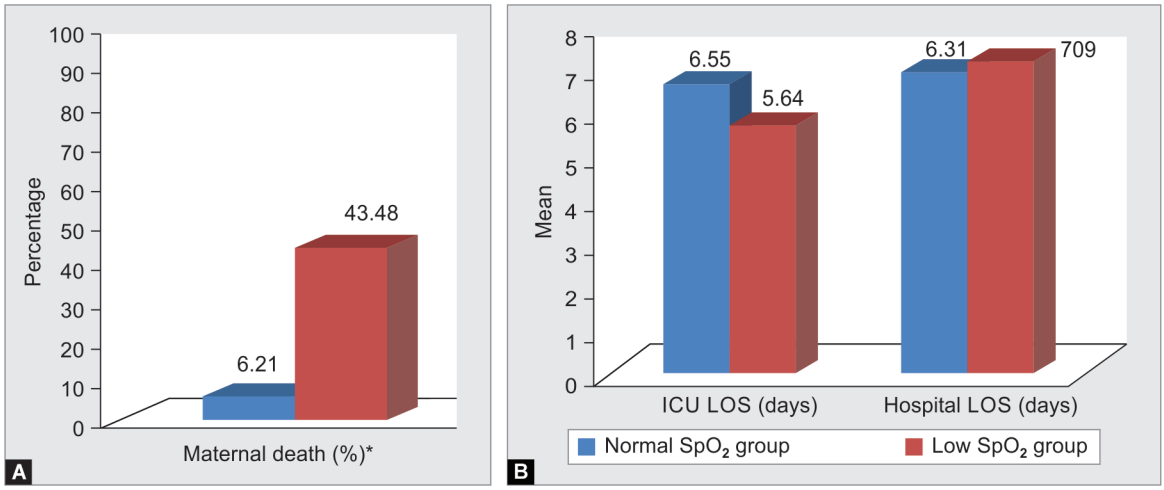
The values in bold imply statistical significance. (*n* = number of subjects for whom data were available)

for this significant variability may be due to insufficient evidence in favor of using this drug and lack of strong recommendations from statutory bodies regarding its use in COVID-19 infections.

More than half of the patients (54.55%) received heparin, mostly in the subcutaneous form, and intravenous heparin was used rarely (0.96% cases). Many patients received vitamin C (78% cases), vitamin D (57.42% cases), and zinc (79.43% cases). The use of vitamin C and Vitamin D was more in case of the patient with normal SpO_2 at the time of hospital admission. Few cases also received ivermectin (3.83% cases).

The mean gestational age of hospitalization in our cohort of COVID-19-infected pregnant women was 36.00 ± 8.00 weeks. The common method of termination of pregnancy was by cesarean section in about 68.42% of cases, whereas only 10.05% of cases were delivered by induction of labor. In an international study, around 90% of cases were delivered by cesarean section. This difference is due to the fact that in their study, more severe COVID-19 cases were delivered, and only 37% of cases were delivered during their ICU stay.[6] However, In our study, there were 28.22% cases of preterm delivery. Various studies show that the rate of preterm birth varies from 27 to 48%. Hence, our results are consistent with the existing literature.[6,12,13] Intrauterine death was reported in 7.17% cases in our cohort and both the preterm delivery and IUD were significantly higher in the hypoxic group in this study. It is highly possible that neonatal complications were most probably related to the severity of the maternal COVID-19 disease and hypoxia leading to an increased risk of prematurity than a direct fetal impact of SARS-CoV-2 infection.[2,4–6,9,12,14]

There was obstetric hemorrhage in 12.44% cases though none was life-threatening. Also HELLP syndrome was reported in 2.87% cases, PRES in 0.48% cases, and vertical transmission of infection to the fetus in 0.96% cases in the cohort of patients. Maternal mortality was 10.53% and was significantly high in the low SpO_2 group compared with the normal SpO_2 group. This higher incidence of maternal complications was due to a more severe COVID-19 disease in these patients. Furthermore, maternal complications appeared to be owing to ICU-related complications as well as obstetric issues, since we found cases of pulmonary embolism (2 cases) and cerebral venous thrombosis (one case) in the population studied.[4,5,11,15,16] The strength of the study remains the high number of obstetric patients in the cohort as compared with previous studies.[6]



Figs 2A and B: Maternal outcomes. (A) Shows the more maternal mortality rate in normal SpO_2 group (6.21%) and hypoxic group (43.48%); (B) The ICU length of stay (LOS) and hospital LOS were comparable among both the groups (depicted in mean of days). *shows that differences were statistically significant ($p < 0.001$)

Table 4: Fetal outcome parameters

Fetal outcomes	*Normal SpO_2 (n = 177)*	*Low SpO_2 (n = 23)*	*p-value*
Preterm birth	47 (26.55%)	12 (52.17%)	**0.011**
IUD	9 (5.08%)	6 (26.09%)	**0.003**

The values in bold imply statistical significance. (*n* = number of subjects for whom data were available)

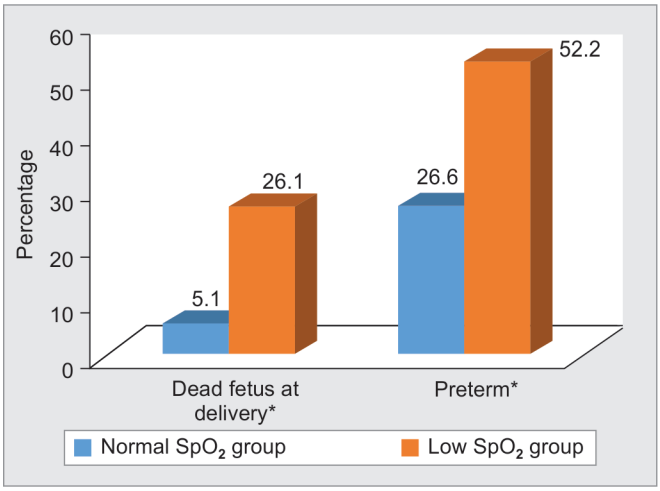


Fig. 3: Fetal outcome parameters. Shows incidence of IUD and preterm in normal SpO_2 group and hypoxic group and the differences among the groups were statistically significant ($p = 0.003$ and $p = 0.011$, respectively)

Limitations

This was a retrospective study and conducted during the COVID-19 pandemic. All data could not be retrieved, and some of the data are missing. Though a large number of centers were expected to enroll, many centers could not participate due to constraints like difficulty in tracking of records of SARS-CoV-2 patients during the pandemic. Selection bias cannot be entirely eliminated as we had data from nine centers only.

Conclusion

The pregnant patients with COVID-19 infection with hypoxia on admission had worse clinical as well as laboratory parameters as compared with the patient group with normal oxygen level at hospital admission. Maternal mortality was significantly higher in the hypoxic group. The fetal complications including IUD and preterm delivery were more significant in the hypoxic group.

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