Original Article

Characteristics and outcomes of parturients with COVID-19, admitted to a critical care unit: A single-center retrospective observational study

Ananya Ray[1]*, Tanvir Samra[1]*, Varun Mahajan[1], Karan Singla[1], Naveen Naik B[1], Bharti Joshi[2], Vighnesh Ashok[1], Vanita Suri[2], Mini Singh[3], Arnab Ghosh[3], Goverdhan Dutt Puri[1]

Departments of [1]Anaesthesia and Intensive Care, [2]Obstetrics and Gynaecology and [3]Virology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
** Both contributed equally as first authors*

Abstract

Background: Data on outcomes of coronavirus disease 2019 (COVID-19) in pregnancy are scarce, although they represent a unique physiological state affecting both the mother and child. We present collated data from a tertiary care center in North India, encompassing the outcome, clinical characteristics, and management of these patients. **Materials and Methods:** Parturients ≥ 18 years old, with COVID-19 reverse transcriptase polymerase chain reaction positive for severe acute respiratory syndrome coronavirus 2, requiring intensive care unit (ICU) admission at a tertiary care hospital were included. Data were retrospectively collected from April 2020 to November 2021. **Results:** In all, 26 parturients were admitted to ICU with COVID-19. Five patients were admitted during the first wave, and all were asymptomatic. Twenty-one patients presented during the second wave (March 2021 onward), among which four were asymptomatic and 17 symptomatic (all with severe pneumonia). Three patients presented in the second trimester, all with critical disease, out of which one did not survive. Two patients had twin gestation, and others were singleton pregnancies. Seven patients (27%) were primigravida, and five patients (19.2%) had more than third pregnancy. Twenty critically ill women (77%) delivered during the hospital stay. Six patients died during the second wave, and four deaths (66.7%) were because of COVID-19 acute respiratory distress syndrome (ARDS). **Conclusions:** The number of admissions and mortality related to COVID-19 ARDS was higher in the second wave than in the first. We report the safe use of remdesivir and tocilizumab in our patients.

Keywords: Acute respiratory distress syndrome, COVID-19, obstetric patients, parturient, pregnant

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2019 (SARS-CoV-2), led to much morbidity and mortality and collapse of the health infrastructure in many countries. Although much data have emerged regarding COVID-19 in the normal adult population, the course and outcomes in pregnancy, a unique physiological state, are deficient. Managing pregnant women with severe COVID-19 pneumonia is a challenge for clinicians worldwide as the outcomes of both the mother and child are at stake. There is limited research regarding the management of COVID-19 in pregnant women, and many lacunae exist regarding the

Address for correspondence: Dr. Varun Mahajan, Assistant Professor, Department of Anaesthesia and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: v.varun88@gmail.com

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management and outcomes. With a birth rate of 17.644/1000 people, the need for the same in our country seems to be justified.[1] The incidence of 'home delivery' in India is 22%, and the lack of accessibility to a health care facility for antenatal and postnatal check-up worsened during the pandemic.[2]

At our tertiary care referral hospital, a dedicated COVID-19 care unit and intensive care (ICU) facility has been functional from April 2020. The cumulative admissions of COVID-19 patients have crossed 5602 with 1996 admissions in ICUs by November 2021. The number of patients enrolled in the Obstetric Screening out-patient department (OPD) since the start of the pandemic has crossed 8415. Mild asymptomatic illness because of SARS-CoV-2 has been successfully managed with home isolation, but severe illness requiring critical care admission has been associated with a grave prognosis.

In the existing data, Adhikari *et al.*[3] in their study on 3374 pregnant women on an out-patient basis have showed that SARS-CoV-2 infection is not associated with increased incidence of adverse pregnancy outcomes. On the other hand, in another study, the maternal mortality in COVID-19 pneumonia was reported to range from 0.7% in the first wave to 5.7% in the second wave (February 1 to May 14, 2021) in India.[4]

In light of these limited and contradictory data, in this report, we elaborate the demographic characteristics and outcomes of obstetric patients admitted in the ICU of our tertiary care hospital in North India during the first and second waves of the pandemic.

Materials and Methods

Study setting: An ICU of a tertiary care hospital in North India.

Study population: All critically ill parturients aged ≥18 years, diagnosed with COVID-19 and confirmed with reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2.

Study duration: April 1, 2020 to September 30, 2021.

Study design: Retrospective cohort study.

Sample size and sampling: All consecutive parturients with COVID-19 admitted to ICU during the study period were included.

Data collection: We collected data related to demographic, bio-chemical, and clinical characteristics; disease course; and medications from the daily medical records.

Data analysis: Statistical analysis was performed with IBM™ SPSS™ version 24 (Armonk, NY: IBM Corp.). The normality of the continuous data was assessed with the Shapiro–Wilk test. Parametric data have been presented as mean ± standard deviation (SD), and non-parametric data have been presented as median [inter-quartile range (IQR)]. Categorical variables have been analyzed with Pearson Chi square or Fisher exact test, whichever applicable. The PaO_2:FiO_2 trend among the symptomatic patients receiving tocilizumab versus those who did not was depicted using the clustered box plot, and survival analysis was performed using the Kalan Meier plot.

Ethical issues: The approval to conduct this retrospective study was obtained from the institute ethics committee (NK/8000/Study/312). The need for obtaining informed consent was waived because of the retrospective nature of the study. The identity of patients has not been revealed in the study.

Guidelines for reporting: This study adheres to the STROBE (Strengthening and Reporting of Observational Studies in Epidemiology) guidelines.

The reference range and cut-offs for laboratory parameters in pregnancy have been adapted from a review article by Abbassi-Ghanavati *et al.*[5] The definition of severity of pneumonia is in accordance to the Ministry of Health and Family Welfare (MOHFW) of India, COVID-19 management protocol.[6]

Results

Disease and demographic characteristics

The data of 442 patients were retrospectively analyzed [Figure 1]. Twenty-six patients were admitted to the ICU during the study period. The overall age (mean [SD]) was 27.5 ± 3.6 years. The incidence of symptomatic patients among those needing ICU admission was 4% (17/442). The common presenting features in symptomatic COVID-19 patients were shortness of breath (14 [82%]), cough (12 [70%]), sore throat (4 [23%]), malaise (3 [18%]), orthopnea (2 [12%]), and palpitations (1 [6%]). The majority (23 [88.5%]) were in the third trimester [Table 1]. The mean ± SD body mass index (BMI) was 27.67 ± 3.55 kg/m^2, with five (19%) patients having BMI >30 kg/m^2. Eight patients had at least one chronic illness. The data regarding the concomitant chronic illnesses have been presented in Table 2.

Of the total ICU admissions (n = 26), five patients presented during the first wave, all asymptomatic for COVID-19 and admitted primarily for other indications, highlighted in Table 2. Twenty-one patients presented during the second wave (March 2021 onward), among which four were asymptomatic and 17 were symptomatic (all with severe pneumonia) [Table 3]. Three patients presented in the second trimester, all with critical disease, out of which one did not survive. Two patients had twin gestation, and others were singleton pregnancies. Seven patients (27%) were primigravida, and five patients (19.2%) had more than the third pregnancy. Twenty critically ill women (77%) delivered during the hospital stay. Out of the total mortality of six patients, all of which were in the second wave, four (66.7%) were attributed to COVID-19 ARDS. The laboratory parameters along with the reference ranges are provided in Table 4.

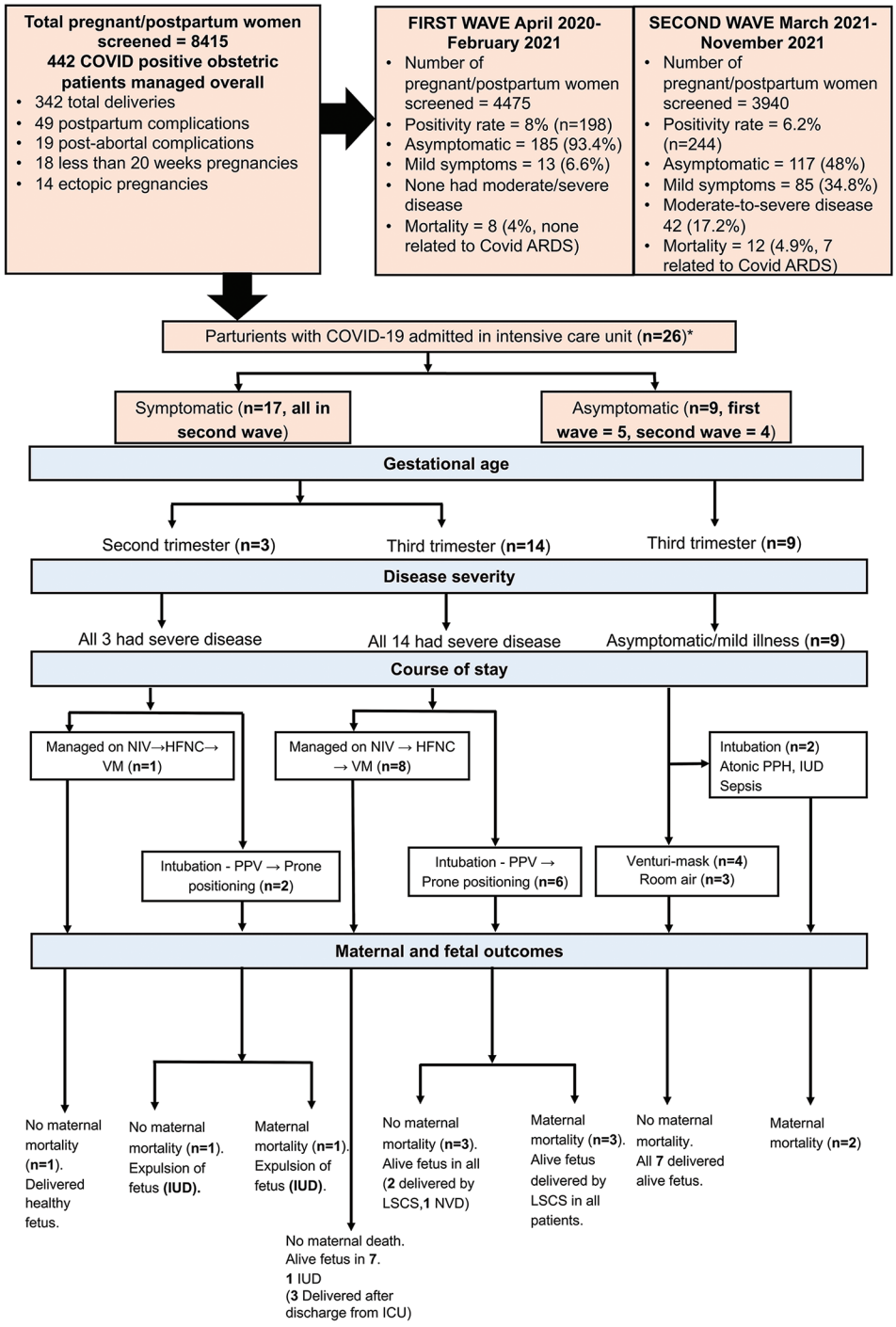

Figure 1: Study flow diagram. COVID-19: coronavirus disease 2019, HFNC: high flow nasal cannula, IUD: intrauterine death, LSCS: lower segment cesarian section, NIV: non-invasive ventilation, NVD: normal vaginal delivery, PaO_2:FiO_2: ratio of partial pressure of arterial oxygen to fraction of inspired oxygen, PPH: postpartum hemorrhage, PPV: positive pressure ventilation. *The numbers depicted are the patients who were admitted to the ICU and whose data was complete

Surgical interventions

Fourteen pregnant patients admitted to ICU underwent lower segment cesarean section (LSCS), of whom 11 (42.3%) underwent emergency surgeries for indications described in Table 1. Five patients admitted to the ICU had vaginal deliveries – three were intra-uterine death (IUD) and two were normal deliveries with a live baby.

Medical management

Steroids, remdesivir, and tocilizumab

All patients (17/26) with pulmonary involvement because of COVID-19 pneumonia and the need for oxygen were administered dexamethasone 6 mg intravenously for 10 days [Table 5]. One patient received dexamethasone for reduction of cerebral edema and one patient received high dose dexamethasone as part of the

trial comparing high-dose dexamethasone (20 mg iv once a day) and tocilizumab in COVID-19 ARDS. Patients with a continued need for high flow or mechanical ventilation were considered for prolonged steroid therapy with oral prednisolone.

A value of C-reactive protein (CRP) ≥ 20 mg/dl is abnormal.[5,7] Patients with CRP ≥ 75 mg/dl or worsening oxygen requirement were considered for tocilizumab administration[8] in the absence of any evidence of bacterial or fungal infection. All patients receiving tocilizumab also received steroids and remdesivir.

Table 1: Demographic characteristics of symptomatic and asymptomatic pregnant COVID-19 patients admitted to ICU

	Symptomatic patients (*n*=17)	Asymptomatic patients (*n*=9)
Demographic characteristics		
Age (in years)	29±2.5	24.7±3.8
BMI (kg/m^2)	28.6±3.36	26±3.5
BMI >30 kg/m^2	4	3
Gestational age (in weeks)	33±5	36±2.7
Trimester	Third – 14 Second – 3 (2 IUD)	All third trimester
Gravidity	2 (1,3)	2 (2,3)
Parity	1 (0,1)	1 (0,1)
ICU stay characteristics		
Mortality	4 (23.5%)	2 (22.2%)
ICU stay (in days)[a]	9 (5,13), range 2-52	4 (1,5), range 1-10
Hospital stay (in days)[a]	16 (12,22), range 4-52	10 (7,21), range 5-33
Duration of mechanical ventilation (in days)	6 (4,10), range 1-45 (*n*=8)	Range 6-10, (*n*=2)
APACHE II at presentation	9 (6,10)	9 (5,11)
SOFA score at presentation	3 (2,4)	4 (3,6)

[a]The ICU stay in those who received tocilizumab was 9 (6,10) days and those who did not receive tocilizumab was 9 (4,16) days. The hospital stay was 17 (12,18) and 16 (13,23) days, respectively, in those receiving tocilizumab and not receiving tocilizumab. Data presented as mean±standard deviation, median (IQR), or absolute number (%). APACHE II: Acute physiology and chronic health evaluation score II, COVID-19: Coronavirus disease 2019, IUD: Intra-uterine death, SOFA: Sequential organ function assessment

All patients with alanine aminotransferase (AST)/alanine aminotransferase (ALT) values less than 5 times the upper limit normal (ULN) were considered for injection remdesivir for 5 days. Nine patients were administered this drug. Two of them died.

The Kaplan–Meir survival curve and clustered box plot of the PaO_2:FiO_2 of those receiving tocilizumab and those who did not are provided in Figures 2 and 3, respectively.

Anti-coagulation

Although D-dimers are elevated in normal pregnancy,[5] we administered prophylactic anti-coagulation to all hypoxic patients. Term pregnant patients who were likely to be taken up for surgery at any time received unfractionated heparin (UFH) 5000 IU subcutaneously thrice daily.

Laboratory parameters

The normal ranges for the laboratory parameters and resulting values have been summarized in Table 5.

Imaging studies

Chest radiographs were obtained in all patients, and changes specific to COVID-19 pneumonia were observed in all symptomatic patients (65%, 17/26). Computed tomography for the chest was performed in one patient for suspected fungal pneumonia. This patient was diagnosed with *Aspergillus fumigatus* isolated from the tracheal aspirate. The same patient's non-contrast computed tomography (NCCT) of the head and paranasal sinuses revealed fungal sinusitis as well. In another asymptomatic patient, NCCT head revealed multiple diffuse hemorrhages, possibly because of coagulopathy. Magnetic resonance imaging was performed in two patients because of altered mentation and revealed posterior ischemic reversible encephalopathy (PRES). Ultra-sound imaging to rule out deep vein thrombosis was performed for all patients with severe-to-critical COVID-19 pneumonia, and none revealed any evidence of deep vein thrombosis.

Table 2: Pre-existing and pregnancy-related complications

	Symptomatic (*n*=17)	Mortality (*n*=4)	Asymptomatic (*n*=9)	Mortality (*n*=2)
Pre-existing co-morbidities				
Hypothyroidism	3	1	1	-
Bronchial asthma	1	1	-	-
Seizure disorder	1	-	1	-
Pregnancy-related comorbidities				
Gestational Diabetes mellites	1	-	-	-
Pre-eclampsia	1	-	2	-
Eclampsia	-	-	1	-
LV systolic dysfunction (PP-CMP)	6 (1 severe [RHD])	2	1[a]	-
Posterior reversible encephalopathy syndrome (PRES)	2	-	-	-
PPH	1	-	2	2 (100%)
RPOC	1	-	-	-
Transaminitis + AKI + COVID pneumonia	2	-	1	1 (100%)

[a]This patient had mild LV systolic dysfunction. There were other two patients with rheumatic heart disease (both with severe mitral stenosis, severe tricuspid regurgitation, and moderate-to-severe pulmonary artery hypertension) with normal LV systolic functions. AKI: Acute kidney injury, PP-CMP: peri-partum cardiomyopathy, PPH: peri-partum hemorrhage, RPOC: retained products of conception

Table 3: Severity of lung involvement in symptomatic COVID-19 pneumonia (*n*=17)

Oxygenation				
PaO_2:FiO_2 at admission	Number of patients	Invasive mechanical Ventilation	Tocilizumab	Mortality, *n* (%)
≤100 mmHg	8	2	2	2 (25)[a]
101-200 mmHg	4	2	2[b]	2 (50)[c]
201-300 mmHg	5	-	1	-
Device at admission		**Progression and Outcomes**		
Ventilator	2	1 died		
NIV	8	5 needed IMV and 3 died		
HFNC	6	1 needed IMV. All patients recovered		
VM	1	Recovered		

[a]One patient receives tocilizumab. [b]Both patients who receive tocilizumab did not require invasive mechanical ventilation and recovered. [c]None of these patients received tocilizumab. Abbreviations: HFNC – high-flow nasal cannula, IMV – invasive mechanical ventilation, PaO_2:FiO_2: ratio of partial pressure of oxygen to fraction of inspired oxygen, VM – Venturi-mask

Table 4: Selected laboratory parameters, Day 1 of ICU admission

Laboratory test	Normal range*		cut-off values[a]	Number (%) of symptomatic patients with deviation from cut-off (*n*=17)	Number (%) of asymptomatic patients with deviation from cut-off (*n*=9)	*P*[b]
	2nd trimester	3rd trimester				
Hemoglobin (mg/dL)	9.7-14.8	9.5-15	<11 gm/dL	10 (59)	8 (89)	0.114
Platelet count (X 10^3/μL)	155-409	146-429	<150 X 10^3/μL	3 (17.6)	7 (77.8)	**0.002**
TLC (X 10^3/μL)	5.6-14.8	5.9-16.9	>16.9 X 10^3/μL	3 (17.6)	2 (22.2)	0.778
D-dimers (ng/ml)	320-1290	130-1700	>1700 ng/mL	6 (35.3)	3 (33.3)	0.920
C-reactive protein (mg/L)	0.4-20.3	0.4-8.1	>20.3 mg/dL	14 (82.35)	7 (77.8)	0.778
AST (U/L)	3-33	4-32	2-5 X ULN	8 (47)	3 (33.3)	0.500
ALT (U/L)	2-33	2-25	2-5 X ULN	6 (35.3)	2 (22.2)	0.492
Total bilirubin (mg/dL)	0.1-0.8	0.1-1.1	>1.1 mg/dL	1 (6)	3 (33.3)	0.065
CK-MB[c] (U/L)	-	1.8-2.4	>25 U/L	10 (59)	6 (66.7)	0.696
Pro-BNP (pg/mL)[c]	-	13.5-29.5	>125 ng/mL[d]	15 (88.2)	7 (77.8)	0.482
Procalcitonin (ng/mL)[c]	-	-	>0.5 ng/mL[d]	4 (23.5)	5 (55.5)	0.102

[a]Cut-off values obtained from Abbassi-Ghanavi *et al.* [b]Pearson Chi-square test. [c]Some cut-off values not obtained from the literature. [d]Cut-off values for the non-pregnant population. $P<0.05$ is significant (highlighted in bold). ALT: alanine aminotransferase, AST: aspartate aminotransferase, CK-MB: creatine kinase-MB, pro-BNP: pro brain-type natriuretic peptide, ULN: upper limit normal, TLC: total leukocyte count. Reference ranges for parameters have been adapted from a review article by Abbassi-Ghanavati *et al.* (doi: 10.1097/aog. 0b013e3181c2bde8)

Table 5: COVID-19-specific medical therapy for symptomatic patients

	Number (%)	Mortality
Dexamethasone[a]	8 (47%)	2 (25%)
Dexamethasone + Remdesivir[b]	4 (23%)	1 (25%)
Dexamethasone + Remdesivir + Tocilizumab[c]	5 (30%)	1 (20%)
Anti-coagulation	UFH – 4	-
	Enoxaparin – 13	-

[a]Injectable dexamethasone 6 mg intravenously was given for 10 days, followed by oral prednisolone till recovery. [b]Injectable remdesivir was administered at a dose of 200 mg on the first day, followed by 100 mg once daily dill day 5. Daily liver function test was performed. The cut-off for stopping remdesivir was AST/ALT elevation above 5×ULN. [c]Injectable tocilizumab 8 mg/kg was given after ruling out the possibility of any secondary infection. [d]Subcutaneous UFH was administered at a dose of 5000 IU thrice daily and Enoxaparin at a dose of 0.6 ml once daily. ALT: alanine aminotransferase, AST: aspartate aminotransferase, UFH: unfractionated heparin

Two-dimensional echocardiography

Two-dimensional echocardiography was performed for all patients admitted to the ICU. Left ventricular dysfunction was found in six patients [Table 2].

Complications in ICU

No patient had any hemorrhagic episode related to anti-coagulation. Two patients had bleeding attributed to post-partum hemorrhage. Other complications are described in Table 6.

Maternal and fetal outcomes

The maternal and fetal outcomes have been described in the flow diagram [Figure 1]. One symptomatic patient gave birth to a child with congenital malformations, and an asymptomatic patient gave birth to a premature child of a birth weight of 1.2 kg.

SARS-CoV-2 Genetic variants

Random testing of samples by next-generation sequencing showed two patients infected with the Delta variant and one patient with a double mutant variant during the second wave.

Discussion

Our retrospective study analyzes and reports demographic and outcome data from a single tertiary care center in North India. We encountered a higher number of ICU admissions and higher mortality in the second wave. Similarly, Mahajan *et al.*[4] in their retrospective analysis of 1530 pregnant and post-partum women with COVID-19 admitted to a hospital in Mumbai, India, have reported a maternal mortality of 10.2/1000 during the first wave and 83.3/1000 live births during the second wave. They also found that the proportion of ICU/HDU admissions increased from 2.4% in the first to 11.6% in the second wave. The case fatality rate increased from 0.7% in the first wave to 5.7% in

Table 6: Complications during ICU stay

	Symptomatic patients (*n*=17)	Mortality among symptomatic patients	Asymptomatic patients (*n*=9)	Mortality among asymptomatic patients
Mechanical ventilation	8 (47%)	4 (50%)	2	2 (100%)
Acute kidney injury[a]	4 (23.5%)	1 (25%)	4 (one patient needed renal replacement therapy)	2 (50%)
Pneumomediastinum and pneumothorax	1 (5.8%)	1 (100%)	-	
Ventilator-associated pneumonia	4 (*Acinetobacter baumannii* [3], *Pseudomonas aeruginosa* [1], *Klebsiella pneumoniae* [1], *Aspergillus fumigatus* [1])[c]	1 (25%)	-	
Blood stream infection	1 (*Enterococcus faecium*, *Klebsiella pneumoniae*)	1 (100%)	-	
Urinary tract infection	1 (*Escherichia coli*)	-	1 (*Escherichia coli*)	-
Hemodynamic instability requiring vasopressors	6 (35%)	3 (50%)	2	2 (100%)

[a]According to the KDIGO guidelines (https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf, page 8. Accessed online on 23 November, 2021). [b]One patient who developed acute kidney injury needed renal replacement therapy. This patient did not survive. [c]One patient had *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Aspergillus fumigatus* isolated from tracheal aspirate during the hospital stay. This patient was discharged after 52 days of hospital stay

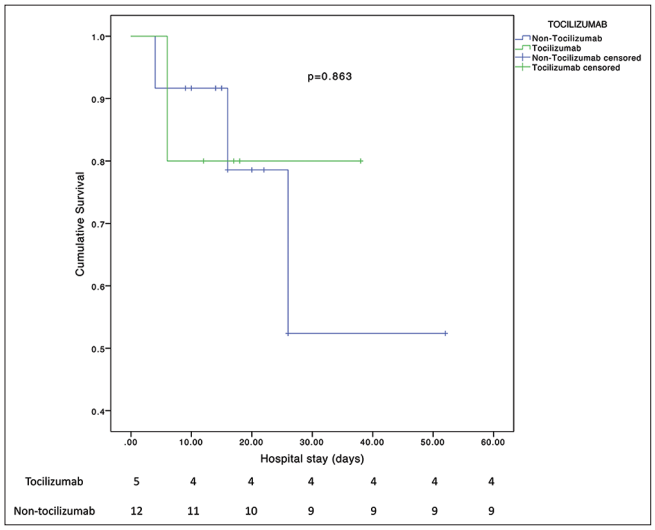

Figure 2: Kaplan Meier analysis of the tocilizumab vs non-tocilizumab cohort. The all-cause in hospital mortality in those receiving tocilizumab was 20% and in those not receiving the drug with only the standard of care with injectable steroids, remdesivir and anticoagulation was 25%. The survival at 3 months post hospital discharge was also same as that at the discharge from the hospital

the second wave.[4] The data on COVID-19 in pregnancy from India are scarce. More studies are needed from other centers for understanding the population characteristics and response to various management strategies.

Disease severity and mortality in COVID-19 in pregnancy

The need for hospitalization related to COVID-19 during pregnancy ranges from 6%[3] to 16%.[9] Maternal mortality in COVID-19 pneumonia ranges from 0.7% in the first to 5.7% in the second wave in India. The severity of the disease and mortality has been reported to increase during the second wave.[4]

Adhikari *et al.*[3] in their study on 3374 pregnant women on an out-patient basis showed that SARS-CoV-2 infection is not associated with increased incidence of adverse pregnancy outcomes. However, we encountered three incidences of IUD in critically ill, symptomatic patients in the second wave. This could have been attributed to the emergence of the more severe and virulent delta strain (B.1.67.2) of SARS-CoV-2 during the second wave. The mortality among the 17 symptomatic patients was 23.5% (4/17), and the mortality among mechanically ventilated patients was 50% (4/8), which is similar to that in the general population.

Mechanical ventilation/prone ventilation and use of non-invasive ventilation in pregnant patients

Early prone ventilation in mechanically ventilated ARDS has been advocated in the PROSEVA trial, with the majority of the study patients being Influenza A (H1N1) virus infections.[10] The literature regarding the mechanical ventilation and prone positioning in pregnant patients with critical COVID-19 pneumonia is scarce. There are no large-scale studies for making recommendations on initiation of mechanical ventilation, but the present literature supports prone positioning in parturients.[11] In our study, eight patients required invasive mechanical ventilation, of which 50% survived. Prone ventilation was performed in all these patients, and like existing literature, we observed marked improvement in ventilation parameters and paO_2:FiO_2 after prone positioning. Complications after prone positioning were seen in only one patient. This parturient was in the second trimester and had an IUD with spontaneous expulsion after the second day of mechanical ventilation. She succumbed to COVID-19 pneumonia after 26 days.

It is difficult to define a particular cut-off for oxygen requirement and PaO_2:FiO_2 for deciding initiation of invasive mechanical ventilation. To the best of our knowledge and belief, a trial of non-invasive mechanical ventilation is warranted unless absolutely contraindicated to account for reversible causes such as basal atelectasis because of the gravid uterus or a component of excessive extra-vascular lung water because of impaired cardiac

functions. This strategy of a non-invasive ventilation trial has been advocated by other authors in non-pregnant COVID-19 ARDS patients prior to the decision of invasive mechanical ventilation made.[12]

Medical therapy – steroids, remdesivir, tocilizumab, and anti-coagulation

Steroids have been shown to improve survival in the RECOVERY trial when used for patients with peripheral oxygen saturation of <94%.[13] There are no guidelines or definitive recommendations for the steroid regimen in COVID-19 management in pregnancy. Some authors advocate the use of oral prednisolone or injectable hydrocortisone when fetal lung maturity is not a concern.[14] On the other hand, dexamethasone-based regimens are preferred when steroids are indicated for fetal lung maturity, along with the management of COVID-19 pneumonia. Some authors are concerned about the harmful effects of dexamethasone on the fetus such as premature delivery, adverse neurological outcomes, and fetal growth restriction.[14,15] Placental 11ß-hydroxysteroid dehydrogenase metabolises dexamethasone and betamethasone less extensively when compared to prednisolone and hydrocortisone.[16] When fetal maturity is not a concern, hydrocortisone or prednisolone are preferred because of their extensive metabolism by the placental 11ß-hydroxysteroid dehydrogenase. Still, large-scale studies are lacking to support the preference to use oral prednisolone or injectable hydrocortisone.

Limited evidence is available for the safety of remdesivir in COVID-19. In a study by Burwick *et al.*,[17] remdesivir use has been shown to improve recovery rates in pregnant with COVID-19 without an increase in the incidence of serious adverse events. However, there are no recommendations favoring the use of remdesivir in pregnant by the RCOG.

Increasing evidence of benefits of tocilizumab therapy in COVID-19 pneumonia is emerging, with some reporting shortening of hospital stay and reduced likelihood of progression to mechanical ventilation, with no mortality benefits,[18] and others reporting reduction in mortality.[8] However, the mortality in patients receiving tocilizumab therapy was less than that of patients who received standard therapy with or without remdesivir (20% vs 25%); larger randomized controlled trials are needed to make an association with improved survival.

In our study, we encountered no adverse effects with intravenous dexamethasone, remdesivir, or tocilizumab. Administration of tocilizumab may have hastened the recovery as depicted by the faster improvement in the PaO_2:FiO_2 in the tocilizumab group in Figure 3.

Anti-coagulation should be a part of standard management in all symptomatic COVID-19 patients. Like COVID-19, pregnancy is a prothrombotic state,[19] although the increased

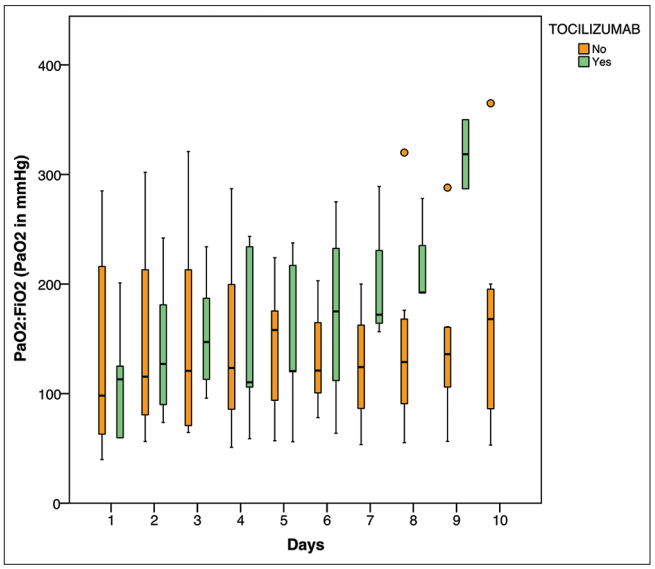

Figure 3: Clustered boxplot showing the trends of PaO_2:FiO_2 in parturients administered tocilizumab vs those who were not. The median (IQR) hospital-stay in those who received tocilizumab, and in those who did not receive the drug was 17 (12,18) and 16 (13,23) days, respectively, and the mortality was 20 and 25% respectively. One patient (20%) needed invasive mechanical ventilation in tocilizumab vs 7 (58%) in non-tocilizumab cohort. PaO_2:FiO_2: ratio of partial pressure of arterial oxygen to fraction of inspired oxygen

risk of thrombosis was not observed in a previously conducted study.[20] The anti-coagulation used should be guided by the timing of delivery and the probable mode of delivery. If delivery or surgery is expected, unfractionated heparin is preferable because of its shorter duration of action and potential for reversal. On the other hand, if delivery is not anticipated, the use of enoxaparin is preferred.[21] This decision is purely clinical and is guided by the dynamics of the mother as well as the fetus. The dosage (prophylactic vs therapeutic) and duration should be based on the institutional protocol. We followed the same practice and observed no thrombotic or hemorrhagic complications in our cohort.

Obstetric management – benefit of early delivery for improving maternal ventilation

Whether early termination of pregnancy has any benefits on maternal ventilation cannot be ascertained from this small sample size study. Theoretically, the lung function should improve by decreasing the effect of the gravid uterus on the lungs and improve the lung function by decreasing atelectasis and V/Q mismatch. We did not observe any overt improvement in the PaO_2:FiO_2 ratio or ventilation parameters after termination of pregnancy.

Routine imaging

We performed chest radiography as and when required for all the parturients. The gravid uterus was shielded with a lead apron. Bedsides, 2D-echocardiography was performed for all patients to rule out any cardiogenic component of the respiratory distress.

Extra-pulmonary involvement in COVID-19

COVID-19 has emerged as a multi-system inflammatory disease with the potential to cause multi-organ dysfunction, including respiratory, cardio-vascular, renal, hematologic, gastro-intestinal, hepatobiliary, endocrine, neurologic, and ophthalmic systems.[22-25] The proposed mechanisms of multi-organ involvement in COVID-19 may include direct toxicity by the virus, endothelial cell damage and thromboinflammation, dysregulation of the immune response, and dysregulation of the renin angiotensin aldosterone system.[25] The association of the organ dysfunction with COVID-19 cannot be made with certainty because of a small sample size.

Vaccination for pregnant women

The last symptomatic parturient at our institute was admitted to ICU in June, 2021. Admissions have declined thereafter, probably because of the vaccination of pregnant women.

Limitations

The comparison of mortality with age-matched pregnant women without associated COVID-19 was not possible in our study. Therefore, a true comparison could not be made between the two subsets of populations. Moreover, the sample size of the study is too small to firmly advocate a particular medical or supportive therapy.

Conclusions

We report an increased number, severity, and mortality of the COVID-19 pneumonia cases among parturients during the second wave of the pandemic, possibly owing to the emergence of the Delta strain. Overall, the proportion of patients requiring admission to ICU was small but associated with a high mortality. We report the safe use of remdesivir and tocilizumab in select parturients. Although we did not report any maternal or fetal adverse events related to tocilizumab use, its safe use in this subset needs to be studied in larger clinical trials. Further conclusions regarding risk factors and therapeutic management require a larger sample size.

The condition of parturients with COVID-19 can deteriorate rapidly from mild to severe disease. Early identification of hypoxic parturients and referral to a tertiary care center are desirable for better maternal and fetal outcomes.

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Conflicts of interest

There are no conflicts of interest.

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