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CASE SERIES

Maternal mortality due to Covid-19: a retrospective case series

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ABSTRACT

Objective: To determine the clinical course of critically ill, SARS-CoV-2 positive pregnant women and to critically analyze the circumstances which led to their mortality. **Methods:** A retrospective review of case records examined to analyze the clinical condition with which critically ill SARS-CoV-2 positive pregnant patients were admitted, the in-patient management protocol followed and subsequent clinical course which led to their deaths. **Results:** There were a total number of 13 maternal deaths which were directly attributed to COVID-19 pneumonia during the study period. Many of these patients had reported with poor oxygen saturation at the time of admission. Oxygen therapy, plasma therapy, antiviral drugs and immunomodulators were administered as part of in -patient management protocol. **Conclusion:** There is an urgent need of dedicated COVID care facilities for pregnant women. Maternal mortality has always been a matter of concern during any pandemic. Specific needs of pregnant women during this pandemic require urgent attention.

Keywords: SARS-CoV-2, COVID-19, maternal mortality.

Coronavirus disease-19 (COVID-19), as the name suggests, is the disease caused by the novel Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2). The disease, which has been declared a pandemic by World Health Organization (WHO), has varying symptomatology ranging from mild upper respiratory illness to severe pneumonia.[1-3] This was initially reported as an outbreak from a wet market in Wuhan, China in December 2019. Within a short span of time, the disease spread all over the world, infecting nearly 2 billion people while causing more than 4 million deaths.[4] Proportionately, India, the second most populous country in the world, also has witnessed more than 30 million cases and 400,000 deaths so far (till 07 July 2021).[4] By early April 2021, a major second wave of infections gripped the country with severe destructive consequences. On 30 April 2021, India became the first country to report over 400,000 new cases and nearly 3,500 deaths in one day.[5]

Maternal mortality is a matter of concern during any pandemic. Initially, during the first wave of the pandemic, it was believed that pregnant women were not at a higher risk of contracting the disease or becoming critically ill, as compared with the general population. However, in two separate studies conducted in Mexico and Brazil, it was observed with concern that there was an increase in maternal mortality ratio by 60% in the year 2020.[6,7] In India, it was observed that there was a significant drop in the number of pregnant women receiving adequate ante-natal check-ups and a proportionate decline in institutional deliveries during the months of national lockdown from April to June 2020 as compared with the same period in 2019.[9] All these factors must have directly or indirectly contributed significantly towards maternal morbidity and mortality during this pandemic.

Materials and methods

This retrospective case series was conducted in a tertiary

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care high-risk obstetrics referral center situated at the National Capital Territory of India. This center is also a 1000 bedded, designated COVID facility. The study was approved by the Institute Ethics Committee and written informed consent for publication of data was taken from the next-of-kin (NoK) of every deceased patient. Case documents of all reported cases of maternal death registered in the hospital database between April and Jun 2021 were retrieved and scrutinized. The data so collected included the patient profile, period of gestation (POG) at the time of presentation, comorbid condition if any, presenting complaints, patient's clinical condition at the time of hospitalization, in-patient management and clinical course. Any obstetric or surgical procedure the patient underwent, during this period, also was recorded.

Results

The patient profile of each case at the time of presentation to the hospital is as depicted in table 1. In-patient management of all patients was executed by a team of doctors comprising obstetrician, intensivist and respiratory physician. The treatment protocol followed as well as the clinical course of the patient is as depicted in table 2 and figure 1. Blood investigation results and chest X-ray findings are as depicted in table 3 and table 4 respectively. A brief clinical summary of each case is as below.

Case 1: This 25year old primigravida at 15weeks period of gestation (POG) presented with dry cough and breathlessness of 2 days duration. She didn't have any known comorbid conditions complicating pregnancy. On evaluation, her oxygen saturation (SpO2) was found to be 70-75% on room air. She was immediately intubated and shifted to the designated COVID – intensive care unit (ICU) for ventilatory support. The response to treatment was poor as evidenced by progressive desaturation. She was declared dead on the same day.

Case 2: 31year old G2P1L0 with In-Vitro Fertilization and Embryo – Transfer (IVF-ET) pregnancy with history of caesarean delivery in the previous pregnancy was admitted with fever for one week, breathlessness and dry cough for two days. She was unable to perceive fetal movements in the previous 24 hours duration. She didn't have any comorbid condition complicating pregnancy. Her SpO2 was recorded as 60-65% on room air. She was immediately intubated and shifted to COVID-ICU for ventilatory support. Intrauterine fetal demise (IUFD) was diagnosed by bedside ultrasonography. Despite all measures, her vital parameters kept on deteriorating and she was declared dead within 13hours post-admission.

Case 3: 30year old primigravida at 25 weeks and 6 days POG admitted with complaint of breathlessness of one day duration. She didn't have any comorbid condition complicating pregnancy. Her SpO2 was recorded as 70-72% on room air. She was immediately intubated and shifted to COVID-ICU for ventilatory support. Since she was near 26week POG with a live fetus in-utero, an urgent consultation with a neonatal intensivist was done anticipating a perimortem caesarean section. However, the NoK of the patient didn't consent for the same. She was declared dead within 15hours post-admission.

Case 4: 33year old G3P1L1A1 with antenatal risk factors such as bronchial asthma, immune thrombocytopaenic purpura and gestational diabetes mellitus, admitted at 33 weeks and 5 days POG with complaints of fever and breathlessness of 3 days duration. She underwent preterm caesarean delivery at 34 weeks and 5 days POG while on oxygen supplementation with NRBM (Non-Rebreather Mask). The baby weighed 2.01Kg and was discharged from the hospital on day 2. The mother was intubated on the third postoperative day as a declining saturation level was observed. Monoclonal antibody (Inj Tocilizumab) was administered. However, her response to treatment was poor and she was declared dead on the fourth postoperative day.

Case 5: 38year old primigravida, IVF-ET pregnancy admitted at 32 weeks POG with complaints of fever, breathlessness and dry cough. Her SpO2 was recorded as 80-82% and was immediately placed on non-invasive ventilation (NIV). An option of immediate caesarean delivery was discussed with the spouse; however, consent for the same was declined. The patient was intubated on day 4 post-admission due to declining oxygen saturation levels. An option of perimortem caesarean section was again discussed with the spouse, but consent was not granted. Despite all resuscitative measures, the patient could not be revived and declared dead on day 4 post-admission.

Case 6: 32year old primigravida admitted at 25 weeks and 3 days POG with the complaint of breathlessness. A very low SpO2 of 55-56% was recorded on admission and she was immediately intubated. There was no improvement in her condition as evidenced by a progressive increase in oxygen requirement and she was declared dead within 18hours post-admission.

Case 7: 30year old multigravida with the antenatal risk factor of gestational diabetes admitted at 32 weeks and 3 days with the complaint of breathlessness. Her SpO2 was recorded as 70% on room air at the time of admission. She was immediately placed on NIV support. She had

Table 1: Patient profile at the time of presentation to the hospital

Cases	Age in yrs	BMI kg/m^2	Gravid / Para	POG (weeks + days)	Comorbidities	Vaccination status	Presenting complaint	SPo_2 on hospitalization (on room air)
Case 1	25	22.6	G1P0	15 + 0	Nil	Not vaccinated	Dry cough, Breathlessness	70-75%
Case 2	31	24.5	G2P1	31 + 2	Nil	Not vaccinated	Dry cough, Breathlessness, Decreased fetal movements	60-65%
Case 3	30	23.8	G1P0	25 + 6	Nil	Not vaccinated	Fever, Breathlessness	70-72%
Case 4	33	26.5	G3P1A1	33 + 5	ITP, Bronchial Asthma, GDM	Not vaccinated	Fever, Breathlessness	93-94%
Case 5	38	27.8	G1P0	32 + 0	Nil	Not vaccinated	Fever, Dry cough, Breathlessness	80-82%
Case 6	32	24.7	G1P0	25 + 3	Nil	Not vaccinated	Breathlessness	55-56%
Case 7	30	26.0	G2P1	32 + 3	GDM	Not vaccinated	Breathlessness	65-70%
Case 8	25	25.8	G2P1	30 + 0	Nil	Not vaccinated	Fever, Dry Cough,Breathlessness	55%
Case 9	30	27.9	G3P1A1	33 + 2	Nil	Not vaccinated	Dry Cough, Breathlessness	80%
Case10	23	28.2	G1P0	26 + 1	Nil	Not vaccinated	Breathlessness	75-76%
Case 11	26	23.4	G1P0	14 + 2	GDM	Not vaccinated	Breathlessness	70-72%
Case 12	23	22.8	G1P0	16 + 0	Nil	Not vaccinated	Breathlessness	75-76%
Case 13	28	28.0	G2P1	32 + 2	Nil	Not vaccinated	Breathlessness	40-45%

POG = Period of gestation, ITP = Immune thrombocytopaenic purpura, GDM = Gestational diabetes mellitus

spontaneous preterm premature rupture of membranes (PPROM) on the next day and on examination, compound presentation was diagnosed. She underwent caesarean delivery after endotracheal intubation. The neonate weighed 2.16kg and was handed over to the neonatal intensive care team. The mother's condition further deteriorated in the post-operative period and was declared dead on the fourth post-operative day.

Case 10: 23year old primigravida at 26 weeks and 1 day into spontaneous labour while on NIV support and an emergency caesarean section, in view of fetal distress, was performed after intubating the patient. The neonate weighed 1.96Kg and was intubated immediately at birth; declared dead after one hour. The mother's condition worsened in the post-operative period and was declared dead within 6 hours of delivery.

Table 2: In-patient management of cases

Cases	Duration of hospitalization	Mode and duration of ventilatory support				Antibi-otics	Antiv-irals	Anticoa-gulants	Stero-ids	Plasma therapy	Monoclonal antibody
		FM	NRBM	NIV	ETT						
Case 1	8 hours	-	-	-	8 hours	Yes	No	Yes	Yes	No	No
Case 2	13 hours	-	-	-	13 hours	Yes	No	Yes	Yes	No	No
Case 3	15 hours	-	-	-	15 hours	Yes	No	Yes	Yes	No	No
Case 4	11 days	6 days	4 days	21 hrs	3 hours	Yes	No	Yes	Yes	No	Yes
Case 5	3 ½ days	-	-	3 days	12 hours	Yes	No	Yes	Yes	No	No
Case 6	18 hours	-	-	-	18 hours	Yes	No	Yes	Yes	No	No
Case 7	5 ½ days	-	-	24 hrs	4 ½ days	Yes	No	Yes	Yes	No	No
Case 8	2 days	-	-	24 hrs	24 hours	Yes	No	Yes	Yes	No	No
Case 9	3 ¼ days	-	-	3 days	6 hours	Yes	No	Yes	Yes	No	No
Case 10	9 ¼ days	-	-	9 days	6 hours	Yes	No	Yes	Yes	Yes	No
Case 11	14 days	-	-	13 ¾ days	6 hours	Yes	No	Yes	Yes	No	No
Case 12	8 ½ days	-	24 hrs	7 days	12 hours	Yes	Yes	Yes	Yes	Yes	No
Case 13	8 hours	-	-	-	8 hours	Yes	No	Yes	Yes	No	No

FM = Face mask, NRBM = Non-rebreather mask, NIV = Non-invasive ventilation, ETT = Endo- tracheal tube

Case 8: 25year old multigravida with history of caesarean delivery in the previous pregnancy, admitted at 30 weeks POG with complaints of fever, cough and breathlessness of two days duration. She had a critically low SpO2 level of 55% on room air at the time of hospitalization. She was immediately placed on NIV support and later on was intubated. An option of perimortem caesarean was discussed with the spouse, however, consent was not granted. She succumbed to the illness within 48 hours of hospitalization.

Case 9: 30year old multigravida, admitted at 33weeks and 2days POG with dry cough and breathlessness. She went POG, admitted with breathlessness with a SpO2 of 75-76% on room air. Despite continuous supportive measures and convalescent plasma therapy, her condition worsened, and was declared dead on day 10 post-admission. Since the fetus-in-utero had attained 26weeks maturity, an option of perimortem caesarean section was discussed with the spouse, however, consent was not granted.

Case 11: 26year old primigravida with the antenatal risk factor of gestational diabetes admitted at 14 weeks and 2 days POG with the complaint of breathlessness. She had a spontaneous miscarriage while on NIV support and was

subsequently intubated as SpO2 levels deteriorated. She was declared dead on day-14 of hospitalization.

Case 12: 23year old primigravida admitted at 16weeks POG with the complaint of breathlessness. She didn't have

Table 3: Investigation findings

Cases	RT-PCR	Inflammatory Markers					Coagulation Profile			Biochemical markers & Electrolytes					
		CRP	ESR	PCT	IL6	Ferritin	PT-INR	Plt	D-Dimer	Blood Glucose	Liver Enzymes	Creat	Na^+	K^+	$Ca2^+$
Case 1	P	R	R	R	R	N	N	N	N	R	R	R	N	L	L
Case 2	P	N	R	R	R	R	N	N	N	R	R	R	N	L	N
Case 3	P	R	R	R	R	R	N	N	N	R	R	N	N	N	L
Case 4	P	N	R	R	R	R	N	L	R	R	R	R	N	L	L
Case 5	P	R	N	R	R	N	N	N	N	R	R	R	N	L	N
Case 6	P	R	R	R	R	R	N	N	R	R	R	N	N	N	L
Case 7	P	R	N	R	R	R	N	N	R	R	R	R	N	L	L
Case 8	P	N	R	R	R	R	N	N	N	R	R	N	N	L	N
Case 9	P	R	R	R	R	R	N	N	N	R	R	R	N	L	N
Case 10	P	R	R	R	R	N	N	N	R	R	R	N	N	N	L
Case 11	P	R	R	R	R	R	N	N	R	R	R	R	N	L	L
Case 12	P	R	R	R	R	R	N	N	N	R	R	N	N	L	N
Case 13	P	R	R	R	R	R	N	N	R	R	R	R	N	L	N

RT-PCR = Reverse Transcriptase – Polymerase Chain Reaction, CRP = C Reactive Protein, ESR = Erythrocyte Sedimentation Rate, PCT = Procalcitonin, IL6 = Interleukin 6, PT-INR = Prothrombin Time – International Normalized Ratio, Plt = Platelets,Creat = Creatinine,Na^+ = Sodium, K^+ = Potassium, $Ca2^+$ = Calcium,N = Normal, P =Positive, R = Raised, L=Low.

Table 4: Chest X-Ray Findings

Case 1	X-Ray chest was not done as the patient was brought in a moribund condition and expired in 8 hours.	
Case 2	X-Ray chest was not done as the patient was brought in a moribund condition and expired in 13 hours.	
Case 3	X-Ray chest was not done as the patient was brought in a moribund condition and expired in 15 hours.	
Case 4	Day 7 – Bilateral lung infiltrates with peripheral ground glass opacities in lower lobes	Day 9 –Bilateral extensive consolidation
Case 5	Day 1 – Bilateral lung infiltrates	Day 3 – Bilateral extensive consolidation
Case 6	Day 1 – Bilateral extensive consolidation	
Case 7	Day 1 – Bilateral ground glass opacities in lower lobes	Day 4 – Bilateral extensive consolidation
Case 8	Day 1 – Bilateral extensive consolidation	
Case 9	Day 1 – Bilateral consolidation of lower lobes	Day 3 – Bilateral extensive consolidation
Case 10	Day 1 - Bilateral consolidation of lower lobes	Day 7 – Bilateral extensive consolidation
Case 11	Day 1 – Bilateral lung infiltrates with ground glass opacities	Day 8 – Bilateral extensive consolidation
Case 12	Day 1 – Bilateral lung infiltrates with ground glass opacities	Day 7 – Bilateral extensive consolidation
Case 13	X-Ray chest was not done as the patient was brought in a moribund condition and expired in 8 hours.	

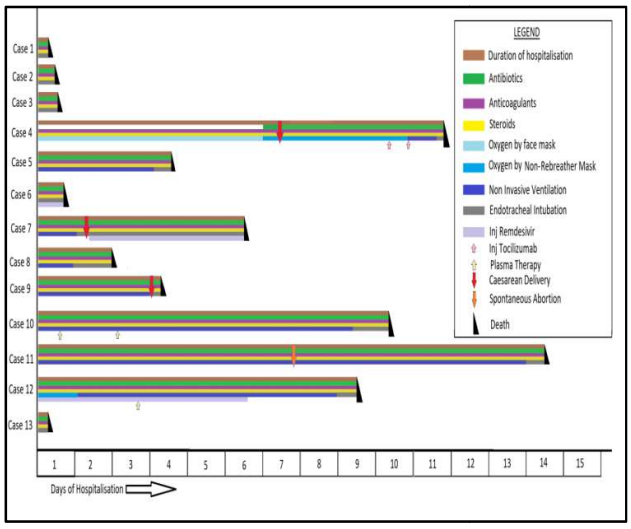

Figure 1: In-patient management and clinical course of patients

any comorbid condition complicating pregnancy. Her SpO2 at the time of admission was recorded as 75-76% on room air. Despite all supportive measures, antiviral therapy and convalescent therapy, she succumbed to the illness on day 11 of hospitalization.

Case 13: 28year old primigravida hospitalized at 32 weeks and 2days POG with breathlessness and critically low SpO2 level of 40-45%. She was immediately intubated and provided ventilatory support. An option of perimortem caesarean section was discussed with the spouse, however, consent was not granted. She was declared dead within 8 hours of hospitalization.

Discussion

Here, we have reported a retrospective case series of 13 cases of maternal mortality due to COVID-19. The study was conducted during the months of April to June 2021. India faced a second wave of COVID-19 pandemic beginning in March 2021 which peaked in the national capital territory during April and May 2021, corresponding with our study period. During the same period of study, our

hospital admission data reveal that there have been 9914 SARS-CoV-2 positive, critically ill patients admitted, out of which 1220 deaths have been reported. This includes 79 SARS-CoV-2 positive, oxygen dependent, pregnant women, out of which 62 delivered during the same period.

In a multinational cohort study of 2130 pregnant women in 18 countries, Villar J et al observed that women with COVID-19 diagnosis were at increased risk of a composite maternal morbidity and mortality index.[9] In the same study, the researchers demonstrated that women with COVID-19 diagnosis were at substantially increased risk of severe pregnancy complications as well as maternal mortality which was 22 times higher than those without COVID-19.

La Verde et al, in a systematic review and meta-analysis of 13 studies involving 154 maternal deaths have analyzed clinical characteristics and comorbid conditions contributing to COVID-19 related maternal deaths.[10] They have found that at least one comorbidity doubled the risk of mortality. They have also concluded that obesity increased the risk of death by two fold while no difference was found in gestational diabetes and bronchial asthma. In our study, none of the patient was obese, three patients were diagnosed to have gestational diabetes and one patient had bronchial asthma.

Clinical management protocol for COVID-19 published and updated by ministry of health and family welfare (MOHFW) was followed in the management of cases in our series.[11] This included oxygen support, immunomodulators, anticoagulants, antivirals and antibiotics. Some of the patients received plasma therapy as well. None of the patients in this case series had received vaccination against SARS-CoV-2 as MOHFW approved vaccination of pregnant women much later.

Conclusion

COVID-19 pandemic has tested the adequacy and preparedness of health care system worldwide. Starting from diagnostic testing to formulating management protocols, our medical world has struggled through. Going forward, there is an urgent need to prioritize safe, accessible, and equitable maternity care in the COVID-19 pandemic and similar situations in the future. Specific needs of pregnant women during this ongoing pandemic should be addressed.

Conflict of interest: None. **Disclaimer:** Nil.

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