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Perinatal outcomes in critically ill pregnant women with coronavirus disease 2019

OBJECTIVE: Early reports suggested that pregnant women were not at an increased risk for severe disease or death from coronavirus disease 2019 (COVID-19). However, few publications have described critical illness in pregnant patients with COVID-19. This study describes the clinical characteristics and outcomes of critically ill mothers and their neonates within our health network since the onset of the COVID-19 pandemic in New Jersey.

STUDY DESIGN: This institutional review board–approved, retrospective case series describes all pregnant women and their neonates requiring critical care for severe COVID-19 within our network’s 2 largest hospitals in March 2020 and April 2020. Maternal demographic information, delivery method and indication, clinical symptomatology, imaging and laboratory findings, and treatment data were collected. Neonatal outcomes were also collected, including real-time polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

RESULTS: There were 1053 deliveries between both hospitals during the study period, with 73 (6.9%) documented symptomatic pregnant patients with COVID-19. Of the 73 patients, 31 (42%) were admitted for management of COVID-19 symptoms. Among the 31 patients, 8 (26%) required intensive care unit (ICU) admission, 6 (19%) required intubation, and 1 (3.2%) was supported with extracorporeal membrane oxygenation (ECMO). Therefore, 8 of 73 (11%) patients who exhibited COVID-19 symptoms developed critical illness.

Table 1 describes the maternal demographics, clinical characteristics, and treatments of the 8 critically ill patients treated during the study period. Mean age and body mass index were 30.5 ± 9.0 years and 34 ± 7.9 kg/m², respectively. Median gravidity and parity were 2.5 (3.5) and 1 (2.75). Mean gestational age at presentation was 30.6 weeks, and mean gestational age at delivery was 31.4 weeks. Of note, 7 (87.5%) of the women were Hispanic, despite the 2 health centers having Hispanic populations of 24.7% and 8%, respectively. Two women had preexisting conditions (chronic hypertension, asthma), and 1 presented with hemolysis, elevated liver enzyme, and low platelet (HELLP) syndrome. Among the 8 critically ill patients, 7 (87.5%) died of disease requiring preterm delivery by cesarean delivery, and 1 is yet to deliver.

Furthermore, among the 8 critically ill patients, 5 had an oxygen saturation less than 94% on admission. Only 1 was febrile on admission, although 5 (62.5%) developed fever during hospitalization. Most had cough (75%) and dyspnea (87.5%). All had elevated transaminases and D-dimer levels. Moreover, C-reactive protein (CRP), lactate dehydrogenase, and interleukin-6 levels were elevated in all women who received these tests.

Treatments are summarized in the Supplemental Figure. All required oxygen supplementation; most received a combination of medical interventions. Of the 8 critically ill patients, 6 (75%) required intubation, and 1 (12.5%) received venovenous ECMO for 12 days. Three women required norepinephrine and prone positioning, which was accomplished after delivery. All women were discharged in stable condition.

Patients 1 through 8 in Table 1 are paired with neonates 1 through 8 in Table 2 (patient 5 is yet to deliver). All neonates were premature and required neonatal ICU admission. Respiratory distress (85.7%) was universal and predominantly severe. Neonatal morbidities were significant. All neonates tested negative by RT-PCR for SARS-CoV-2.

CONCLUSION: Our case series illustrates the potential severity of COVID-19 in pregnant women and provides a model of management that may be useful for obstetrical providers. Most women in our series were Hispanic, which is disproportionately high given the demographics of our institutions. Information on other social determinants of health was not available. This finding warrants further investigation considering emerging racial disparities of COVID-19–related deaths. Most women had rapid onset of disease, developed severe hypoxia, and had significant findings on lung imaging. Fever on initial presentation was uncommon. All had elevation of liver transaminases, CRP, and D-dimer.

There are conflicting data on the risk for preterm delivery associated with COVID-19 in pregnancy. In this study, 7 of 8 women with critical respiratory illness required preterm delivery with the goal of reducing respiratory compromise by decreasing oxygen requirements and enhancing diaphragmatic excursion. Antenatal corticosteroids were not given universally because of the theoretical potential to exacerbate COVID-19 and pulmonary edema. Rapid deterioration was another limiting factor.

All women were discharged home in good health following multimodal and multidisciplinary approaches including intubation, prompt delivery, off-label use of experimental therapies (eg, remdesivir, convalescent plasma), and ECMO. Although there was a significant burden of prematurity, each neonate improved as expected with neonatal intensive care, and there was no evidence of vertical transmission.

Obstetrical providers should be aware of the potential for COVID-19 to progress to critical illness in pregnancy. Without clear guidelines for treatment, providers are left with unproven therapies without sufficient safety data, and
| Patient number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|----------------|---|---|---|---|---|---|---|---|
| **Demographic information** |   |   |   |   |   |   |   |   |
| Age            | 41 | 21 | 36 | 32 | 43 | 26 | 19 | 26 |
| Gravidity/parity | G3P2 | G1P0 | G2P0 | G5P3 | G5P3 | G2P0 | G1P0 | G4P2 |
| BMI (kg/m²)    | 49 | 27 | 26 | 36 | 36 | 33 | 26 | 39 |
| Race/ethnicity | Hispanic | Hispanic | Asian | Hispanic | Hispanic | Hispanic | Hispanic | Hispanic |
| Gestational age at presentation (wk) | 30 5/7 | 33 0/7 | 35 0/7 | 30 0/7 | 26 4/7 | 27 6/7 | 31 1/7 | 30 1/7 |
| Gestational age at delivery (wk)    | 30 5/7 | 33 3/7 | 35 0/7 | 30 1/7 | Undelivered | 28 1/7 | 31 6/7 | 30 2/7 |
| **Medical/obstetrical comorbidities** |   |   |   |   |   |   |   |   |
| Chronic hypertension, hypothyroidism | None | None | Asthma | None | None | None | Preeclampsia | None |
| Delivery method    | Primary CD with tubal ligation | Primary CD | Primary CD | Primary CD | Undelivered | Primary CD | Primary CD | Primary CD |
| Reason for CD      | Respiratory failure | Respiratory failure | Respiratory failure | Respiratory failure | N/A | Respiratory failure | HELLP syndrome | Respiratory failure |
| Clinical data, on admission (maximum) |   |   |   |   |   |   |   |   |
| Oxygen saturation (%) | 78 | 93 | 93 | 97 | 96 | 93 | 98 | 87 |
| Temperature (°F), presentation (Tmax) | 98.9 (100.9) | 97.6 (100) | 100.1 (100.5) | 101.4 (101.4) | 100.3 (100.3) | 99 (101.6) | 97.6 (100.2) | 98.3 (101.5) |
| Cough            | Yes | No | Yes | Yes | Yes | Yes | No | Yes |
| Dyspnea          | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes |
| Chest x-ray/CT findings | Severe diffuse interstitial and airspace disease | Patchy peripheral bilateral lung opacities | Patchy bilateral lower lung infiltrates | Moderate patchy bilateral airspace disease | Low lung volumes, patchy bilateral infiltrates | Left upper lobe and right lower lobe opacities | Negative | Bilateral opacities consistent with pneumonia |
| Ferritin (ng/mL) | 510 (540) | 487 (487) | 1118 (1899) | 57.6 (91) | 64 (114) | 192 (218) | 437 (437) | 183 (183) |
| AST (U/L)        | 73 (84) | 300 (300) | 23 (117) | 30 (107) | 35 (44) | 50 (99) | 20 (1343) | 76 (76) |
| ALT (U/L)        | 27 (49) | 248 (248) | 26 (95) | 14 (74) | 18 (18) | 35 (45) | 6 (246) | 79 (79) |
| D-dimer (µg/mL)  | 2.7 (2.7) | 1.6 (2.9) | 1.3 (1.3) | 1.1 (3.3) | 0.96 (1.1) | 0.93 (1.4) | 26 (46.3) | 0.94 (6.2) |
| WBC (×10³ cells/mL) | 6.3 (14.8) | 3.6 (15.5) | 7.5 (10.5) | 5.9 (16.8) | 11 (18) | 5.4 (12) | 10.6 (20.6) | 3.9 (17.7) |
| Absolute lymphocytes (cells/µL) | 720 | 670 | 2380 | 1620 | 900 | 700 | 2600 | 400 |
| Patient number | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Platelets (×10³ cells/mL) | 229 (413) | 110 (508) | 269 (469) | 169 (376) | 344 (774) | 129 (379) | 280 (322) | 121 (223) |
| C-reactive protein (mg/dL) | 7.8 (14.3) | 6.0 (11.9) | 14.2 (17.7) | 10.6 (13.0) | 17.4 (24.3) | 0.56 (0.56) | 23.6 (23.6) | 16.8 (16.8) |
| LDH (U/L) | 524 (1042) | 379 (465) | 268 (432) | 261 (568) | 226 (386) | 222 (222) | 172 (1785) | 257 (403) |
| IL-6 (pg/mL) | 7 (138) | <5 (39) | 24 (45) | 6 (441) | 17 (17) | N/A | N/A | N/A |
| Standard and critical care treatments |
| Antenatal corticosteroids | No | Yes | No | No | No | Yes | Yes | Yes |
| Supplemental O₂ by nasal cannula | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Hydroxychloroquine | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| Azithromycin | Yes | Yes | Yes | Yes | No | Yes | No | Yes |
| Ascorbic acid | Yes | Yes | No | Yes | No | Yes | No | Yes |
| Methylprednisolone | Yes | Yes | Yes | Yes | No | Yes | No | No |
| Ceftriaxone | Yes | No | Yes | Yes | No | Yes | Yes | Yes |
| Convalescent plasma | No | Yes | No | No | Yes | No | No | No |
| Intubation | Yes | Yes | Yes | Yes | No | Yes | No | Yes |
| Prone positioning | Yes | Yes | No | No | No | Yes | No | No |
| Tocilizumab | Yes | Yes | No | Yes | No | Yes | No | Yes |
| Remdesivir | Yes | Yes | Yes | Yes | No | Yes | No | Yes |
| Heparin/enoxaparin (prophylactic) | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| Vasopressor (norepinephrine) | Yes | Yes | No | Yes | No | No | No | No |
| VV ECMO | Yes | No | No | No | No | No | No | No |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CD, cesarean delivery; COVID-19, coronavirus disease 2019; CT, computed tomography; HELLP, hemolysis, elevated liver enzyme, and low platelet syndrome; IL-6, interleukin-6; LDH, lactate dehydrogenase; N/A, not applicable; VV ECMO, venovenous extracorporeal membrane oxygenation; WBC, white blood cell count.

Romagano. Perinatal outcomes in critically ill pregnant women with COVID-19. AOGF MFM 2020.
| Neonate | 1 | 2 | 3 | 4 | 5 (undelivered) | 6 | 7 | 8 |
|---------|---|---|---|---|----------------|---|---|---|
| Maternal labor | No | No | No | No | — | No | No | No |
| Length of rupture of membranes | At delivery | At delivery | At delivery | At delivery | — | At delivery | At delivery | At delivery |
| Category II or III fetal heart tracing | No | No | No | No | — | No | No | No |
| Gestational age (wk) | 30 5/7 | 33 3/7 | 35 0/7 | 30 1/7 | — | 28 1/7 | 31 6/7 | 30 2/7 |
| Birthweight (g), size category | 1400, AGA | 2410, AGA | 2680, AGA | 1530, AGA | — | 1250, AGA | 1310, SGA | 1710, AGA |
| Antenatal corticosteroids | No | Yes | No | No | — | Yes | Yes | Yes |
| Sex | Female | Male | Female | Female | — | Male | Female | Male |
| Apgar score (1, 5, 10 min) | 1, 4 | 3, 4, 9 | 7, 9 | 7, 8 | — | 1, 7 | 3, 5, 7 | 4, 9 |
| Resuscitation | O₂, CPAP, PPV, intubation, surfactant | O₂, CPAP, PPV, intubation | O₂, CPAP, PPV | O₂, CPAP | — | CPAP, PPV | O₂, CPAP, PPV, intubation, surfactant, tracheal suctioning |
| Separated immediately after delivery | Yes | Yes | Yes | Yes | — | Yes | Yes | Yes |
| Length of stay (d) | 39 | 15 | 7 | 34+ | — | 35+ | 13+ | 16+ |
| Final disposition | Home | Home | Home | Remains hospitalized | — | Remains hospitalized | Remains hospitalized | Remains hospitalized |
| Respiratory distress present | Yes, RDS | Yes, RDS | Yes, TTN | Yes, RDS | — | Yes, RDS | Yes, RDS | Yes, RDS |
| Respiratory support required | Mechanical ventilation, CPAP, HHFNC | Mechanical ventilation, CPAP, HHFNC | CPAP | Mechanical ventilation, CPAP, HHFNC | — | Mechanical ventilation, CPAP, HHFNC | Mechanical ventilation, CPAP, HHFNC | Mechanical ventilation, CPAP, HHFNC |
| Lowest leukocyte count in first 7 d (×10⁹/µL) | 5.5 | 6.3 | 13.7 | 8.3 | — | 8.6 | 9.1 | 10.3 |
| Lowest neutrophil count in first 7 d (×10⁹/µL) | 1.54 | 2.74 | — | 2.7 | — | 4.6 | 6.4 | 6.0 |

Romagano. Perinatal outcomes in critically ill pregnant women with COVID-19. AJOG MFM 2020. (continued)
TABLE 2
Characteristics, treatments, and outcomes of 7 neonates born to mothers with COVID-19 (continued)

| Neonate | 1 | 2 | 3 | 4 | 5 (undelivered) | 6 | 7 | 8 |
|---------|---|---|---|---|----------------|---|---|---|
| Lowest lymphocyte count in first 7 d ($\times 10^3$/µL) | 3.36 | 2.62 | — | 4.89 | — | 3.6 | 3.8 | 2.4 |
| Lowest hemoglobin in first 7 d (g/dL) | 14.7 | 16.6 | 17.6 | 14.4 | — | 11.5 | 18.5 | 19.4 |
| Highest C-reactive protein in first 7 d (mg/dL) | 0.55 | — | 0.08 | — | — | 0.11 | — | — |
| Other neonatal morbidities | Apnea, hyperbilirubinemia of prematurity, feeding problems, temperature instability, observation and evaluation for sepsis | Hyperbilirubinemia of prematurity, feeding problems, temperature instability | Hyperbilirubinemia of prematurity, extraocular pulmonary sequestration, observation and evaluation for sepsis, feeding problems | Apnea, hyperbilirubinemia of prematurity, temperature instability, IVH | — | Apnea, hyperbilirubinemia of prematurity, anemia of prematurity, NEC, temperature instability | Apnea, hyperbilirubinemia of prematurity, temperature instability, feeding problems | Apnea of prematurity, temperature instability, feeding problems |
| Treatments administered | Antibiotics for 48 h, TPN, surfactant, caffeine, phototherapy | TPN, phototherapy | Intravenous fluids, antibiotics for 48 h, phototherapy | TPN, surfactant, caffeine, phototherapy | — | Antibiotics for 48 h, TPN, surfactant, caffeine, phototherapy | TPN, caffeine, phototherapy | TPN, caffeine, surfactant |
| Head ultrasound results | Normal, day 7 of life | — | — | Unilateral grade 1 IVH on day 8 of life | — | Normal, day 5 of life | Normal, day 5 of life | Normal, day 5 of life |
| SARS-CoV-2 RT-PCR testing done | Yes | Yes | Yes | — | — | Yes | Yes | Yes |
| Specimen type and timing | NP at 24 h and 7 d | NP at 24 h | NP at 24 h and 7 d | NP at 24 h and 7 d | — | NP at 24 h, 72 h, and 10 d | NP at 48 h and 72 h | NP at 48 h and 72 h |
| SARS-CoV-2 test result | Negative | Negative | Negative | Negative | — | Negative | Negative | Negative |
| Type of feeding provided and feeding method | Formula, no maternal breast milk | Formula | Formula, no maternal breast milk | Donor breast milk, no maternal breast milk | — | Donor breast milk | Donor breast milk | Expressed maternal and donor breast milk |
| Discharge | Discharged to father (SARS-CoV-2 negative) | Discharged to father (SARS-CoV-2 negative) | Discharged to father (PUI) | Remains hospitalized | — | Remains hospitalized | Remains hospitalized | Remains hospitalized |

AGA, appropriate for gestational age; COVID-19, coronavirus disease 2019; CPAP, continuous positive airway pressure; HHFNC, humidified high-flow nasal cannula; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NP, nasopharyngeal; PPV, positive pressure ventilation; PUI, person under investigation; RDS, respiratory distress syndrome; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SGA, small for gestational age; TPN, total parenteral nutrition; TTN, transient tachypnea of the newborn.

Romagano. Perinatal outcomes in critically ill pregnant women with COVID-19. AJOG MFM 2020.
although treatment was ultimately successful in all patients, it is impossible to state whether any individual intervention is an improvement over standard supportive care. As research evolves during this crisis, management options will be clarified. Providers should recognize clinical deterioration in pregnant women and intervene swiftly to limit maternal and fetal harm.

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