

1 INTRODUCTION

2 COVID-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and includes a
3 several characterization, from asymptomatic patients to respiratory failure, cardiac and cardiovascular
4 complications, thromboembolic and inflammatory complications. Pregnancy does not appear to increase
5 susceptibility to this infection, but physiological changes during pregnancy, such as reduced functional residual
6 volumes, diaphragm elevation, and altered cell immunity may be at increased risk for severe disease
7 necessitating maternal intensive care unit admission, mechanical ventilation, and in rare cases, extracorporeal
8 membrane oxygenation^{1, 2}. Deaths have been reported equally in pregnant as in non-pregnant women of
9 reproductive age³. Among pregnant women, especially who develop COVID-19 pneumonia, there is an
10 increased risk of preterm and cesarean delivery due to fever and hypoxemia⁴.

11 The aim of this report is to describe a case of a third trimester pregnant woman with severe acute respiratory
12 syndrome from COVID-19, treated with convalescent plasma and undergoing urgent cesarean section with
13 livebirth without evidence of COVID-19.

14 MATERNAL MANAGEMENT

15 On 24 May 2020 a 34-year-old Asian woman at 28 weeks and 4 days of gestation, presented to Villa Sofia
16 Cervello Hospital, Palermo, with fever, dyspnea and pelvic pain, rapidly deteriorating without benefiting from
17 paracetamol intake. Negative personal history; obstetric history revealed two livebirths with vaginal delivery
18 and two miscarriages. At admission, a fetal ultrasound showed a live fetus with regular biometry, without
19 evaluation of the fetal anatomy in consideration of the gestational age and the clinical condition of the patient;
20 physical examination showed decreased breath sounds to both lungs basis. Furthermore, arterial blood gases
21 (ABG) showed: ph 7,439; PaCO₂ 33, 6 mmhg; PO₂ 38, 9 mmhg; SO₂ 70% in room air. Body temperature was
22 39, 5 °C, blood pressure 125/70 mmhg, pulse rate 124 beats for minutes, and the patient was thachypneic with a
23 persistent severe hypoxia and a P/F (PaO₂- FiO₂ ratio) of 64.4. The laboratory findings included a leukocyte
24 count of 14 x 10³μl, neutrophils of 12, 15 x 10³μl, lymphocytes of 1,22 x 10³μl, C-reactive protein of 14,47
25 mg/dl, lactate dehydrogenase (LDH) of 445 UI/ml, hypokalemia with 2.9 mEq/L, D-dimer of 474 ng/ml (normal
26 value in pregnancy). The other exams were within limits. Molecular nasopharyngeal swab for SARS-Cov-2 was
27 performed with a positive result. The patient was transferred to a negative-pressure isolation room where O₂
28 flow was increased from initial 5 to 15 L/min and non-invasive ventilation (NIV) was attempted without
29 improvements in respiratory failure. So after six hours she was moved to intensive care unit (ICU) and a lung
30 ultrasound showed thickening of the pleura and multiple irregular confluent pleural lines (B-lines) as from

31 interstitial pneumonia. A high-flow nasal cannula (HFNC) oxygen therapy was attempted (FiO₂ between 80%
32 and 90%; flow 60 lt/min; temperature at 31°C). There was a slight improvement of oxygenation, but tachypnea
33 persisted and the ABG worsened. Therefore, the patient was sedated and endotracheal intubation with invasive
34 mechanical ventilation was started with improvement of clinical and blood gases findings. Venous
35 thromboembolism prophylaxis with enoxaparin sodium (4000 units twice a day) and empiric antibiotic therapy
36 with Clarithromycin (500 mg twice a day) and Ceftriaxone (2 gr daily) to prevent bacterial superinfection were
37 began. Following this was substituted by Vancomycin (2 gr daily) because Staphylococcus Aureus was isolated
38 by bronchoalveolar lavage (BAL) and by hemoculture. Betamethasone (12 mg daily for 2 days) was
39 administered to accelerate fetal lung maturity. During hospitalization serial ultrasound assessments of fetal
40 growth, amniotic fluid volume and Doppler in the umbilical artery were obtained because in patient with severe
41 or life-threatening disease, development of fetal growth restriction is a theoretic concern and has been described
42 with other SARS infections⁵. On 26 May, the patient was placed in prone position ^{6,7}, due to the persistence of
43 respiratory failure, with the use of supports and pads beneath shoulders and hips to prevent aortocaval
44 compression. The patient started a 12-hour daily cycle of pronation, and a progressive improvement of
45 oxygenation was registered, allowing a FiO₂ decrease. The patient underwent a total of four cycles of pronation,
46 lasting 12 hours each. The last cycle was performed on the fourth day of hospitalization, with no consistent
47 changes in respiratory parameters; therefore, no more cycles were performed. On 27 May, after ethic
48 committee's consent, a sack of convalescent plasma (CP) was administered with improvement of clinical and
49 laboratory findings. The following day, a second sack of CP was administered without complications and with
50 the increase of IgG and IgM the following days. A chest radiograph showed bilateral multiple ground-glass
51 opacities, worse on the left lung, confirming interstitial pneumonia. Lung ultrasounds were used for daily
52 monitoring, to reduce the pregnant patient's exposure to ionizing radiations. On 8 June, the antibiotic therapy
53 was modified, with the addition of Meropenem (1 gr three times a day) because of a bronchial aspirate positive
54 for Pseudomonas aeruginosa. The following day the patient's bronchial aspirate came back negative for SARS-
55 CoV-2, but chest radiograph showed an increase of the bilateral opacities, contextually hypoxia and hypercapnia
56 worsened. So on 11 June, at 31 weeks and 1 days of gestation, after a multidisciplinary consultation between
57 obstetrics, pediatrics and anesthetists and after suspension of venous thromboembolism prophylaxis, a cesarean
58 section under general anesthesia (patient was already intubate) was performed without complications. The next
59 day after cesarean section a chest CT scan of the mother confirmed the bilateral ground-glass opacities and
60 broncovascular interstice thickening, as from acute respiratory distress syndrome (ARDS). The patient was

61 underwent to BIPAP ventilation and on 13 June a tracheostomy was done. Then, the clinical conditions and
62 laboratory findings improved gradually. Patient developed CMV infection with also ocular localization, which
63 was treated with Acyclovir. Finally 18 June patient was in spontaneously breathing and lung ultrasound showed
64 an improvement of findings, confirmed at the next chest CT. So on 26 June patient was transferred from ICU to
65 department of pneumology. A maternal chest X-ray on 02 July showed a resolution of infiltrates of both lung
66 fields. Patient was discharged on 6 July, after a total length stay (LOS) of 43 days, in good general conditions,
67 afebrile, without any respiratory symptom/sign.

68 **NEONATAL MANAGEMENT**

69 A preterm female infant weighing 1400gr was delivered with APGAR 3-6-7 at one, five and ten minutes. After two
70 ventilation cycles with FiO₂ increasing from 21 to 30%, the infant was intubated about three minute from birth due
71 to the lack of effective respiratory activity. She was connected to a ventilator in synchronous positive pressure
72 ventilation (SIPPV) with the following parameters: PIP 22 cmH₂O, PEEP 5.5 cmH₂O, FiO₂ 0.30, FR 45 acts/min,
73 SatO₂ 96% and FC 146 bpm. Two hours after birth, after Rx chest and pulmonary ultrasound that showed the
74 prevalence of confluent B lines, signs of Respiratory Distress Syndrome (RDS), surfactant was administered at 200
75 mg/kg. The baby was extubated 24 hours after birth and was placed in nasal continuous positive airway pressure
76 (nCPAP) in ambient air. The patient was subjected to one swab and a BAL for the detection of SARS-Cov2 at birth,
77 at 24 hours and 48 hours of life, with negative results. She received total parenteral nutrition for 24 hours; therefore,
78 minimal enteral feeding was undertaken. The patient was treated with dopamine at 5 mcg/kg/min for pressure
79 support for 72 hours and with broad spectrum antibiotic therapy. A brain ultrasound was obtained and it showed:
80 notes of immaturity, not IVH, moderate dilation of the occipital horns, resistance index of anterior cerebral artery
81 (RI-ACA) 0.8. The echocardiography showed the presence of bidirectional Botallo Arterial Duct; a wide 3.5 mm
82 peri-membranous interventricular defect; a large atrial foramen (3.5 mm); a right ventricular chamber with normal
83 contractility; a slightly dilated pulmonary arterial trunk. Blood tests were normal.
84 Five days from birth, patient was transferred to a pediatric cardiac surgery center in Taormina (Messina) for
85 pulmonary bandaging. This surgical operation was performed at 40 days of life. The child's conditions during
86 hospitalization were satisfactory, with good weight gain. The three serological tests performed at the Pediatric
87 Cardiac Surgery Center showed IgM anti Sars-Cov2 negative and a decreasing of IgG values of probable maternal
88 origin due to transplacental passage.

89 **DISCUSSION**

90 Majority of pregnant women experience only mild or moderate cold/flu-like symptoms, cough, fever, headache,
91 and smell and taste disturbance whereas shortness of breath, myalgia, sore throat and diarrhea are the less
92 common symptoms⁸. Several studies revealed that pneumonia during pregnancy is associated with increased
93 morbidity, mortality and obstetric complications with perinatal adverse outcomes compared to non-pregnant
94 state especially due to changes in immune responses^{9, 10}. The physiologic changes of pulmonary function during
95 pregnancy are important to consider severity of disease and to guide ventilator FiO₂ parameters. Indeed, during
96 pregnancy, maternal peripheral oxygen saturation (SpO₂) should be maintained greater than 95% and maternal
97 PaO₂ greater than 70 mmHg is desirable to maintain a favorable oxygen diffusion gradient from the maternal to
98 the fetal side of the placenta¹¹.

99 In the presence of ARDS of any etiology, prone positioning has proven beneficial effects on oxygenation and
100 mortality¹². Our data confirmed that pregnant women may be safely prone and this position may improve
101 clinical and blood gasses findings to relieve both diaphragmatic compression from abdominal contents and
102 aortocaval compression from the gravid uterus¹³.

103 The use of convalescent plasma for the treatment of acute viral illnesses is an established therapy that has
104 previously shown benefit in the treatment of SARS, MERS, and Ebola virus patients¹⁴. Our patient's clinical
105 conditions partially improved. Therefore, we think that it may be an efficient therapy but probably complete
106 benefit is reached when given early in the course of severe or life-threatening disease¹⁵ and changes in immune
107 response in pregnant women may influence complete response. Anyway, our case confirms the success and
108 safety of convalescent plasma treatment in pregnant patients, as already described by a limited number of other
109 papers^{16, 17}.

110 We showed like severe maternal respiratory disease improved by delivery. Indeed increased oxygen
111 consumption and reduced functional residual capacity, which are normal in pregnancy, may facilitate maternal
112 deterioration in patients with pneumonia¹⁸. So delivery should be considered as a component of the management
113 of refractory hypoxemic respiratory failure or worsening critical illness in pregnant women. However, maternal
114 care and delivery decisions are best individualized after multidisciplinary discussion with anesthetist, obstetrics,
115 pediatrics to balance risk and benefit for maternal and fetal status.

116 We also confirmed that lung ultrasound examination is an accurate imaging method to detect pulmonary and
117 pleural conditions useful especially to monitor those patients who require serial exams and pregnancy women
118 because it is a radiation free exam^{19, 20}.

119 Some studies report newborn infections and placental infections, so precautions during delivery were necessary
120 to prevent the rare but possible vertical transmission^{21,22}.

121 In the future perspective, other studies on larger numbers of pregnant women with COVID-19 need to be
122 conducted to better understand the correct maternal and fetus care and the efficacy of several therapies, such as
123 convalescent plasma.

124 **DISCLOSURE OF INTEREST**

125 All authors have no conflicts of interest to declare, include relevant financial, personal, political, intellectual or
126 religious interests.

127 **CONTRIBUTION TO AUTHORSHIP**

128 C.G. and T.M.: study concept, data interpretation; M.M.: planning, carrying out and writing of the work; T.D.:
129 writing of the work for neonatal management; C.S.: data collection, writing of the work; L.B.V., G.E.: data
130 interpretation for obstetric management; R.B., D.M.: data interpretation for maternal management; T.F.: study
131 design, data collection, data interpretation.

132 **DETAILS OF PATIENT'S CONSENT**

133 Written informed consent was obtained from the patient for publication of this case report. A copy of the written
134 consent is available for review by the Editor-in-Chief of this journal on request.

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