1. Introduction

Viral pneumonia occurring during pregnancy is associated with increased morbidity and mortality [1]. Pregnant women are more susceptible to respiratory pathogens because of the pregnancy-related physiological changes [2]. Pregnancy does not seem to aggravate the course of symptoms and clinical characteristics of COVID-19 pneumonia, and the first reports on COVID-19 epidemiology data show an approximately superimposable rate of intensive care unit (ICU) hospitalization [3, 4]. However, optimal management in severe COVID-19 related pneumonia during pregnancy is still debated. After obtaining written informed consent and the ethics committee approval (Comitato Etico Interaziendale, Cuneo, Italy), we report the case of a 28-week pregnant woman with COVID-19 related ARDS.

2. Case report

On 27th of March 2019 a 48-years-old, 27 + 4 weeks gravida 2, para 0 african woman was admitted to our hospital for severe respiratory failure. She was subjected to chest x-ray suggestive for COVID-19 pneumonia (Fig. 1), which was then confirmed by a positive nasal swab. Medical history included hypertension; obesity (BMI 30); sickle-cell trait; stillbirth at 24 weeks. Pregnancy checks showed maternal and fetal wellness. After obtaining written informed consent and the ethics committee approval (Comitato Etico Interaziendale, Cuneo, Italy), we report the case of a 28-week pregnant woman with COVID-19 related ARDS.


TABLE 1. Type of ventilation or oxygen support and arterial blood gas analysis data during intensive care unit stay.

|                          | ICU admission | First day in ICU | 3th day in ICU | 6 hours after prone ventilation | First day after prone ventilation | 5th day after prone ventilation | 14th day after prone ventilation | Day of discharge |
|-------------------------|---------------|------------------|----------------|---------------------------------|----------------------------------|---------------------------------|----------------------------------|-----------------|
| **Type of ventilation or oxygen support** | NIVP with helmet | VCV        | VCV          | VCV prone position        | VCV                             | PSV                             | O₂ nasal cannulas                         | -               |
| **Tidal volume (ml or cmH₂O)** | 8 520 520 520 520 530 20 - - | - 20 20 20 20 - - | 10 10 10 10 12 12 - - | 0.9 0.8 0.8 0.7 0.7 0.7 0.35 0.21 | - - - - - - - - - - - - - - - - - - - - |
| **Respiratory rate** | 20 20 20 20 - - - - | 20 20 20 20 - - - - | 20 20 20 20 - - - - | 0.9 0.8 0.8 0.7 0.7 0.7 0.35 0.21 | - - - - - - - - - - - - - - - - - - - - |
| **Fraction of inspired oxygen** | 0.9 0.8 0.8 0.7 0.7 0.7 0.35 0.21 | - - - - - - - - - - | 0.9 0.8 0.8 0.7 0.7 0.7 0.35 0.21 | - - - - - - - - - - - - - - - - - - - - |
| **Static compliance** | 63.6 86.5 59.9 156 99.9 182 93.2 124 | 31.5 42.2 42.6 41.9 41.4 42.8 32.5 32.8 | 70 108 66.6 222 143 243 207 443 | 91.9 93.5 91.3 99.3 97.7 99.4 93.2 99 | 317 65 65 65 65 65 65 65 | 317 65 65 65 65 65 65 65 |
| **Partial pressure of oxygen in arterial blood sample** | 63.6 86.5 59.9 156 99.9 182 93.2 124 | 31.5 42.2 42.6 41.9 41.4 42.8 32.5 32.8 | 70 108 66.6 222 143 243 207 443 | 91.9 93.5 91.3 99.3 97.7 99.4 93.2 99 | - - - - - - - - - - - - - - - - - - - - |
| **Partial pressure of carbon dioxide in arterial blood sample** | 31.5 42.2 42.6 41.9 41.4 42.8 32.5 32.8 | 70 108 66.6 222 143 243 207 443 | 91.9 93.5 91.3 99.3 97.7 99.4 93.2 99 | - - - - - - - - - - - - - - - - - - - - |
| **Blood oxygen saturation** | 91.9 93.5 91.3 99.3 97.7 99.4 93.2 99 | - - - - - - - - - - | 91.9 93.5 91.3 99.3 97.7 99.4 93.2 99 | - - - - - - - - - - - - - - - - - - - - |

Tv, tidal volume; PS, pressure support; RR, respiratory rate; PEEP, positive end-expiratory pressure; FiO₂, fraction of inspired oxygen; Dp, driving pressure; Cs, static compliance; PaO₂, partial pressure of oxygen in arterial blood sample; PaCO₂, partial pressure of carbon dioxide in arterial blood sample; SpO₂, blood oxygen saturation; NIVP, non-invasive pressure support ventilation; VCV, volume controlled ventilation; PSV, pressure support ventilation.

of severe hypoxia (PaO₂/FiO₂ <100 for > 3 hours), hemodynamic instability (median artery pressure (MAP) <65 mmHg or the need of inotropic/vasoconstrictor drugs) or a life-threatening worsening of maternal conditions.

Fetal wellbeing was assessed by daily cardiotocogram and periodic obstetric ultrasounds to ensure regular fetal growth, as recommended [2]; in the event of a premature birth, we administered betamethasone (12 mg iv once for two days); no more corticosteroids were administered during ICU stay.

Sedation was achieved with a combination of remifentanil (50-100 ng/kg/min) and midazolam (3-8 mg/h) guided by electroencephalogram parameters in order to use the lowest dose of sedative drugs; cisatracurium was used as a miorelaxant agent (2-3 mcg/kg/min). The patient was kept in a supine position alternating left lateral decubitus. We maintained a tidal volume of 6-8 ml/kg (ideal body weight correct for gestational age), a plateau pressure below 30 cmH₂O and a driving pressure below 15 cmH₂O; PEEP and FiO₂ were set in order to achieve a PaO₂ >70 mmHg and RR set to keep PaCO₂ in normal range (Table 1). Hemodynamic parameters were monitored with a non-invasive advanced hemodynamic monitor. Bed-side ultrasounds were used for daily monitoring of the lungs. According to our institutional COVID-19 treatment protocol, therapeutic dose of enoxaparin was given to prevent thromboembolic complications; serial evaluation of thromboelastography and anti-Xa factor dosage were monitored. Hydroxychloroquine (400 mg bid for the first two days and 200 mg bid for other three days) and Darunavir+Cobicistat (800 + 150 mg once for five days) were also started. Notably, all the given drugs are reported to have a good safety profile in pregnancy [2, 3].

On the third day of ventilation gas exchange worsened; we started a trial of prone ventilation as rescue therapy. The patient was prone positioned with anti-decubitus head ring-rolls protection and foam dressings placed under the shoulders, thighs and legs. In order to avoid abdominal compression the anti-decubitus mattress was deflated at the abdomen level. Arms were aligned with the body keeping the shoulders in a neutral position; the mild anti-Trendelenburg position was chosen to reduce face and head swelling. Prone ventilation lasted 16 hours without hemodynamic derangements. Umbilical artery doppler monitoring ensured fetal well-being before and after prone positioning.

In the following days PaO₂/FiO₂ values remained above 100. Seven days after ICU admission, bronchoalveolar lavage (BAL) cultures tested positive for Klebsiella pneumoniae sensitive to piperacilline/tazobactam which was administered for 10 days, obtaining a negative BAL result at the end of antibiotic course. Body temperature over 38.5°C where solved with paracetamol; no fever was detected after the tenth day of hospitalization.

Fifteen days after ICU admission the patient was able to breathe spontaneously with a decreasing need of oxygen...
supplementation. On the 19th and 20th day of hospitalization she tested negative for COVID-19 on two RNA PCR. Accordingly, she was transferred to the Ob/Gyn ward and at 31 weeks pregnant the patient was discharged at home and scheduled for periodic obstetrics checks.

3. Discussion

ARDS remained the most common cause of ICU maternal and fetal morbidity and mortality. Di Mascio et al. reviewed data of 41 COVID-19 positive pregnant patients, reporting 41.1% preterm birth < 37 weeks, 18.8% premature rupture of membranes, 13.6% preeclampsia, 91.1% cesarean delivery; 2.4% stillbirths, 10% hospitalization in neonatal intensive care and 2.4% neonatal death [5]. Recent case series suggest mothers with severe COVID-19 pneumonia in the third trimester usually need a premature CS upon hospital admission [3], but it is not yet clear whether management of the mother’s respiratory disease is improved by childbirth.

Prone ventilation is often used as a rescue therapy to treat severe ARDS; it allows greater alveolar recruitment of the dorsal lung areas. Benefits are an augmented ventilation-perfusion ratio, a decreased compression by the heart of posterior and medial lung areas, a reduction in hypoxic vasoconstriction and an improvement in cardiac output [6]. In our opinion pregnant patients may have further advantages: diaphragm is moved caudally decreasing the compression of the posterior and caudal pulmonary parenchyma, as described in obese patients [7]; major vessels are less compressed from the uterus if the abdomen is left unsupported.

Despite benefits of pronation in severe ARDS have been widely established [6], data on its use in pregnant patients are anecdotal. Oliveira et al. studied the prone position in awake and spontaneously air breathing patients in 20-
37 week gravida. Prone position was considered safe, comfortable and advantageous to improve oxygen saturation [8], however short duration of pronation was the main limitation. To our knowledge only two case reports describe prone ventilation in pregnant women with severe ARDS. Kenn et al. reported the case of a pregnant woman at 34 weeks of gestation, treated for an ARDS following blunt chest trauma. She obtained benefits from a single prone ventilation cycle [9]. The group of Sukhen describe a 31 weeks of gestation pregnant woman with a refractory ARDS due to H1N1 influenza. Three consecutive cycles of pronation were needed to obtain an improvement in oxygenation [10].

Compared to these cases, our patient is older, some weeks younger in gestational age, and overweight, which makes pronation challenging. During pronation maneuver our ICU staff was extremely careful in positioning and we carried out fetal monitoring before and after positioning. Prone ventilation may be considered to improve respiratory gas exchanges in pregnant women with severe ARDS. Although it was performed only once, prone position allowed us to avoid protracted maternal hypoxia resulting in early premature birth.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

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