
Pregnant women with acute respiratory distress syndrome triggered by COVID-19

SHORT REPORT

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Background

Pregnant women with COVID-19 are probably at increased risk of serious illness. The objective of this study was to describe the course of illness in pregnant women admitted to the intensive care unit (ICU) with acute respiratory distress syndrome triggered by COVID-19.

Material and method

Pregnant women with COVID-19 were registered on admission to an ICU at Rikshospitalet, Oslo University Hospital in the period March 2020 to May 2023. We reviewed the patients' medical records retrospectively and describe clinical trajectories, management parameters and laboratory data collected during the period in intensive care. Self-perceived health was surveyed 15 months after discharge from intensive care.

Results

Thirteen pregnant women were admitted in the period from February to December 2021. All met criteria for acute respiratory distress syndrome (ARDS) and were treated with corticosteroids and mechanical ventilation according to current guidelines. None of the patients had been vaccinated against COVID-19. Ten patients were orally intubated after therapeutic failure with non-invasive mechanical ventilation. One patient was treated with extracorporeal membrane oxygenation (ECMO). All patients survived their stay in intensive care, but there were two cases of intrauterine fetal demise. Almost half of the patients reported moderate to significantly reduced self-perceived health and quality of life 15 months after discharge from intensive care.

Interpretation

All pregnant women admitted to an ICU at Rikshospitalet, Oslo University Hospital with ARDS triggered by COVID-19 survived hospitalisation, but several had symptoms that persisted long after their stay in the ICU.

Main findings

Ten out of thirteen pregnant women admitted to Rikshospitalet's intensive care units with acute respiratory failure triggered by COVID-19 were intubated after therapeutic failure with non-invasive mechanical ventilation.

All patients met criteria for acute respiratory distress syndrome (ARDS).

All patients survived hospitalisation, but there were two cases of intrauterine fetal demise.

Almost half of the patients reported moderate to severely reduced self-perceived health and quality of life 15 months after discharge from intensive care.

Acute respiratory failure is a common cause of admission to an ICU in patients with COVID-19. In Norway, mortality among critically ill COVID-19 patients has been moderate [\(1\)](#), but survivors face an increased risk of late complications, known as post-intensive care syndrome. This particularly applies to patients who develop acute respiratory distress syndrome (ARDS) during the course of their illness [\(2\)](#).

In pregnancy, ARDS as a complication of COVID-19 is life-threatening for both the mother and the fetus [\(3\)](#). This report describes the characteristics, treatment and clinical courses of pregnant women referred to Rikshospitalet due to ARDS triggered by COVID-19.

Material and method

Pregnant women with COVID-19 were registered on admission to an ICU at Rikshospitalet, Oslo University Hospital in the period March 2020 to May 2023. Rikshospitalet does not have a dedicated national facility for the comprehensive treatment of critically ill pregnant women, but in collaboration with other hospitals has accepted patients where the risk to the mother and fetus has been deemed particularly high and where evaluation for management with extracorporeal membrane oxygenation (ECMO) is pertinent. We reviewed the patients' medical records retrospectively and describe clinical trajectories, management parameters and laboratory data collected during the period in intensive care.

Fifteen months after discharge, the patients were asked about self-perceived health, quality of life and symptoms of post-traumatic stress. The Euro Quality of Life – Five Dimensions – Five Levels (EQ-5D-5L) and Impact of Event Scale-6 (IES-6) screening tools were employed for this purpose [\(4, 5\)](#). Mean or median values are presented, with measures of dispersion indicated as minimum and maximum values unless otherwise specified. The analysis was conducted using Stata version 17.0 and Microsoft Excel.

The study was approved by the Regional Committee for Medical and Health Research Ethics (REK) South-East (REK number 630377) and the data protection officer at Oslo University Hospital. All patients provided informed consent.

Results

Thirteen pregnant women with ARDS triggered by COVID-19 were admitted to an ICU at Rikshospitalet in the period February to December 2021. None of the women were vaccinated against SARS-CoV-2 before hospitalisation. Ten women had an immigrant background (6). The duration of illness before admission varied from one to eleven days after symptom onset. All patients met criteria for ARDS, with little comorbidity (Table 1).

Table 1

Patient and management characteristics in 13 pregnant women with ARDS triggered by COVID-19 and admitted to an ICU at Rikshospitalet, Oslo University Hospital in the period March 2020 to May 2023. Values are presented as median (min. – max.) unless otherwise specified.

Patient and management characteristics	Values	Reference values
Age (years)	33 (22–42)	-
Weight at admission (kg)	74 (60–96)	-
Height (cm)	161 (150–170)	-
BMI (kg/m ²)	29 (24–37)	-
Parity	1 (0–3)	-
Gestational age (weeks)	27 (24–35)	-
Comorbidity (n)		-
Musculoskeletal problems	5	-
Mental health issues	4	-
Endocrine disease	4	-
Other	3	-
SAPS II score ¹	38 (21–70)	-
Laboratory findings at admission		
Haemoglobin (g/dL)	9.7 (8.1–11.9)	11.7–15.3
Leukocytes (× 10 ⁹ /L)	8.0 (6.1–18.3)	3.5–10
Neutrophils (× 10 ⁹ /L)	6.9 (5.1–16.5)	1.5–7.3
Platelets (× 10 ⁹ /L)	231 (155–312)	145–390
D-dimer (mg/L)	1.2 (0.5–10)	< 0.50
Fibrinogen (g/L)	4.7 (3.1–6.3)	1.9–4.0
Lactate dehydrogenase (U/L)	353 (241–562)	105–205
Ferritin (µg/L)	126 (42–825)	10–170

Patient and management characteristics	Values	Reference values
C-reactive protein (mg/L)	74 (38–166)	< 4
Procalcitonin (µg/L)	0.2 (0.0–1.0)	< 0.10
Creatinine (µmol/L)	36 (26–71)	45–90
Bilirubin (µmol/L)	8 (4–26)	5–25
Peripheral oxygen saturation (SaO ₂) (%)	96 (88–100)	97–100
Lactate (mmol/L)	1.0 (0.5–1.9)	0.5–2.3
Management data		
Length of hospital stay (no. of days)	16 (10–83)	-
Length of stay in ICU (no. of days)	8 (4–35)	-
Invasive mechanical ventilation (no. of days; n = 10)	8 (1–25)	-
Non-invasive respiratory support (no. of days; n = 13)	1 (0–2)	-
P/F ratio ² (kPa; n = 10) (at admission)	14 (9–36)	> 50
Highest peak pressure (cm H ₂ O; n = 10)	29 (23–32)	-
PEEP (cm H ₂ O; n = 10)	11 (8–15)	-
Tidal volume (mL/kg predicted body weight (PBW); n = 10)	6.1 (2.5–7.4)	-

¹SAPS II = simplified acute physiology score, 2nd edition. Sigmoid scale of 0–150 points, where 38 points (median) corresponds to an expected hospital mortality rate of approximately 20%, 21 points corresponds to a hospital mortality rate of approximately 5%, 70 points corresponds to a hospital mortality rate of approximately 80%.

²P/F ratio = the ratio between the partial pressure of oxygen in arterial blood (PaO₂), expressed in kilopascals, and the fraction of inspired oxygen (FiO₂). PBW, predicted body weight ($45.5 + (0.91 \times [\text{height in centimetres} - 152.4])$).

Ten patients were orally intubated after therapeutic failure with non-invasive mechanical ventilation. All intubated patients were managed with volume- and pressure-limited ventilation (Table 1). Five patients were managed in a modified prone position. Nine patients were given neuromuscular blocking agents and all received corticosteroids.

In the case of a previously healthy woman in her late twenties, venovenous ECMO treatment was deemed necessary following unsuccessful management with conventional lung-protective mechanical ventilation with deep sedation, neuromuscular blocking agents, prone positioning and nitrogen monoxide. ECMO could be discontinued after 17 days and the patient was extubated after a total of 25 days of invasive mechanical ventilation. She delivered the child by caesarean section five weeks before the estimated due date.

The median length of stay in ICUs at Rikshospitalet was eight days (Table 1). All patients had single-organ failure. Two patients experienced acute complications: pulmonary embolism, and pneumothorax requiring no treatment. Seven intubated

patients were found to have co-infections, which were treated with antibiotics.

The pregnancy

Upon admission to Rikshospitalet, the patients were in the second or third trimester of pregnancy (Table 1). There was no evidence to suggest that delivery would improve the women's prognosis. In most cases, continuation of pregnancy was considered necessary to avoid severe prematurity and to ensure fetal lung maturation with a two-day course of steroids. All patients were monitored with daily cardiotocography (CTG) and/or ultrasound examination. Emergency plans, including infection control measures, were established to deal with potential cases of perimortem caesarean section.

Three women on mechanical ventilation delivered by caesarean section due to an increasing need for oxygen, repeated episodes of desaturation and haemodynamic instability. Two women had a vaginal delivery following intrauterine fetal demise. In these two cases, placental histopathological examination revealed subacute placentitis and maternal vascular malperfusion.

Self-reported health and quality of life

The median value for self-rated health (EQ-VAS) was 70 (35–100) (Figure 1a). Patients reported minimal issues related to personal care, while pain/discomfort and anxiety/depression were prominent (Figure 1b). Symptoms of post-traumatic stress were most common in women with pre-existing mental health issues (Figure 1c).

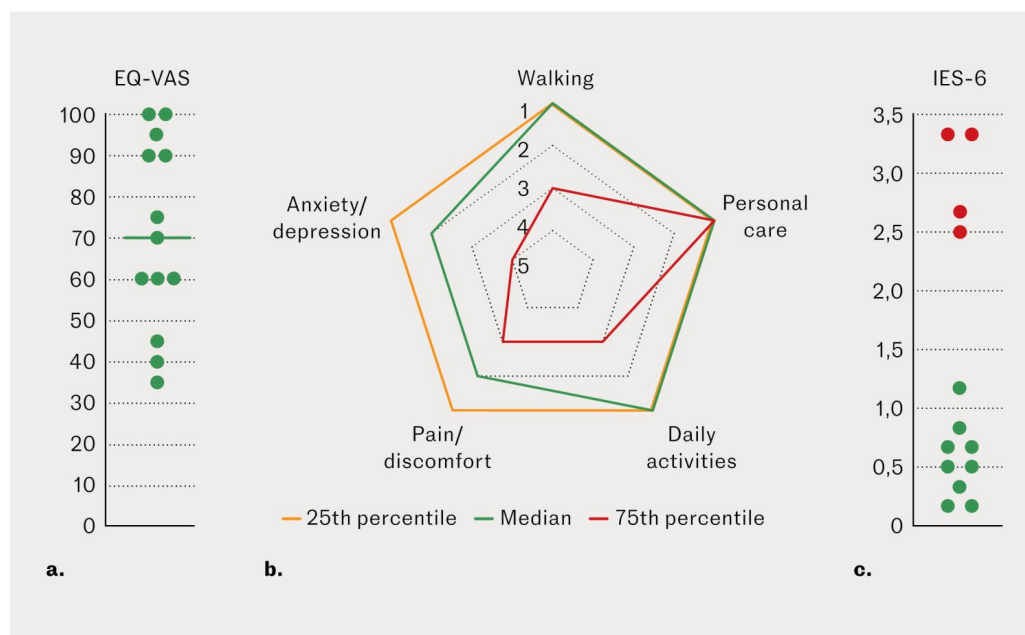


Figure 1 Quality of life and post-traumatic stress measured 15 months after discharge in 13 pregnant women with ARDS triggered by COVID-19 admitted to an ICU at Rikshospitalet, Oslo University Hospital in the period March 2020 to May 2023. a) Self-rated health measured using a visual analogue scale (VAS), where 0 is the poorest and 100 is the best possible health. The median value is 70. b) Self-rated health in five different domains, using EuroQoL-5D-5L (EQ-5D-5L), rated from 1 (no problems) to 5 (very severe problems). c) Symptoms of post-traumatic stress using IES-6 (The Impact of Event Scale-6). A value ≥ 1.75 (red dots) indicates symptoms of post-traumatic stress.

Discussion

Pregnant women with COVID-19 are believed to be at increased risk of developing a severe clinical course, especially if infected with specific virus variants (Delta) (7). In Norway, however, all pregnant women with COVID-19 admitted to an ICU have survived hospitalisation ($n = 30$, unpublished data from the Norwegian Intensive Care and Pandemic Registry) (8). One of the guiding principles in obstetrics is that seriously ill pregnant women are assessed for critical care on a par with non-pregnant women. However, balancing the decision between prolonging the pregnancy to mitigate extreme prematurity and contemplating the option of delivery or pregnancy termination to enhance maternal care is a complex challenge. Recent international data support our decision to continue our patients' pregnancies (9).

None of the women in our study were vaccinated against SARS-CoV-2 before hospitalisation. At the start of the Norwegian vaccination programme in December 2020, vaccination was not recommended for pregnant women. It was not until January 2022 that the vaccine was extended to all pregnant women irrespective of gestational age (10). The changing guidance on vaccination, lack of targeted information and concerns among pregnant women about potential adverse effects may all have contributed to pregnant women's reluctance to be vaccinated, even after amendments to the vaccine recommendations. Factors such as immigrant background, language barriers and cultural differences may also have impacted attitudes to vaccination in our patient population.

The patients in our study primarily had acute respiratory failure with little extrapulmonary organ dysfunction (Table 1). Most experienced therapeutic failure with non-invasive mechanical ventilation and required endotracheal intubation. Mechanical ventilation is a mainstay in the management of ARDS and gentle ventilation is needed to avoid further lung injury (11). A strong recommendation has been made for the use of corticosteroids (dexamethasone) to treat ARDS triggered by COVID-19 (12). However, dexamethasone crosses the placenta, and WHO recommends switching to equipotent doses of prednisolone or methylprednisolone after a maximum of two days. This also preserves the effect of dexamethasone with respect to fetal lung maturation.

ECMO in pregnant women is associated with a risk of serious complications (13) that must be weighed against the risk of continued conventional ventilation. As we had no prior experience with venovenous ECMO in pregnant women with ARDS, we contacted colleagues at the University of Michigan and the Extracorporeal Life Support Organization (ELSO) to broaden our understanding. Reassuringly, we received confirmation that our standard procedures are applicable to pregnant women as well.

Long-term follow-up of intensive care patients is recommended to identify symptoms of post-intensive care syndrome (2). While ICU admissions are often related to physical issues, our study highlights the significance of mental and cognitive health problems. Fifteen months after discharge from the ICU, patients were not struggling with daily activities to any significant extent. Nevertheless, almost half reported non-specific pain, discomfort, anxiety or depression, and one in three were experiencing post-traumatic stress. Notably, post-traumatic stress was more prevalent in patients with pre-existing mental health issues. The median value for self-perceived health in

our study was comparable with findings in other studies of former intensive care patients, while the proportion with symptoms of post-traumatic stress was slightly higher (14).

Summary

Thirteen pregnant women were admitted to ICUs at Rikshospitalet with ARDS triggered by COVID-19. All patients were discharged alive, but there were two cases of intrauterine fetal demise. Adherence to current guidelines for gentle mechanical ventilation was central to our approach. Just under half of the patients reported a reduced quality of life 15 months after discharge from intensive care, attributed to non-specific pain and discomfort, anxiety and depression, as well as symptoms of post-traumatic stress.

The article has been peer-reviewed.

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