Case Report

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Experience of Veno-venous Extracorporeal Membrane Oxygenation in a Pregnant Woman with Severe Acute Respiratory Distress Syndrome Caused by the SARS-CoV-2 Virus

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SUMMARY Pregnant women occupy a special place in the incidence structure of the new coronavirus infection COVID-19. Taking into account the likelihood of a more severe course of acute respiratory syndrome (ARDS) in this group, it is worth remembering the possibility of timely use of veno-venous extracorporeal membrane oxygenation (IV ECMO) in order to correct life-threatening hypoxia. At the Lapino Clinical Hospital, a cesarean section was successfully performed in a 37-year-old female patient at 20–21 weeks of gestation against the background of IV ECMO with further decannulation and discharge from the hospital.

Keywords: viral pneumonia, acute respiratory distress syndrome, novel coronavirus infection, veno-venous extracorporeal membrane oxygenation, pregnancy

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APTT – activated partial thromboplastin time

ARDS – acute respiratory distress syndrome

BiPAP – bilevel positive airway pressure

CPAP – continuous positive airway pressure

CT CO – computed tomography of the chest organs

FiO_2 – fraction of inspired oxygen

MV – mechanical ventilation

PEEP – positive end-expiratory pressure

P_{insp} – inspiratory pressure
PS – pressure support
SpO_2 – oxygen saturation
VV ECMO – veno-venous extracorporeal membrane oxygenation

AIM OF STUDY

To illustrate the effectiveness of veno-venous extracorporeal membrane oxygenation (VV ECMO) in the complex treatment of severe acute respiratory distress syndrome (ARDS) caused by the *SARS-CoV*-2 virus.

INTRODUCTION

The novel *SARS-CoV*-2 coronavirus infection, which originated in China in December 2019, has spread rapidly around the world. The World Health Organization (WHO) designated this infection as a pandemic on March 11, 2020. According to WHO statistics, the total number of new coronavirus infection cases approached 125 000 000 by March 2021 worldwide [1]. In February 2020, WHO experts in China created a group to study the infection caused by the *SARS-CoV*- 2 virus, where a special role is played by the study of the characteristics of the course and its treatment in pregnant women [2]. As the number of confirmed cases grows, more data is emerging on the mechanisms of transmission and morbidity in the general population, while our knowledge of the effects of *SARS-CoV*- 2 infection on mothers and neonatal outcomes remains limited. Pregnant women are believed to be no more susceptible to *COVID* -19 than the general population.

International data on the severity of *COVID* -19 in pregnant women are contradictory [3, 4]. Comparing with other respiratory viral diseases (*SARS-CoV*-1, *MERS,* influenza *H*1*N*1), it can be assumed that *COVID* -19 may be more severe in pregnant women than in non-pregnant patients of reproductive age: an increase in the number of hospitalizations in intensive care units and the need for mechanical ventilation (MV) [5].

Some physiological changes in the respiratory system that occur during a normal pregnancy can cause a more rapid onset of critical hypoxemia: an increase in oxygen consumption by 20%, a decrease in functional residual lung capacity by 30%, associated with a rise in the diaphragm level up to 4 cm due to the pregnant uterus, as well as an increase in the volume of closure of the lungs [6].

The most formidable complication of coronavirus pneumonia is ARDS, a clinical syndrome characterized by refractory hypoxemia. ARDS develops in approximately 14.8% of hospitalized patients with *COVID* -19 [7], but ARDS is more common in pregnant women than in the general population, with a reported mortality rate of up to 40% [8]. This can be explained by the peculiarity of the functioning of the immune system during pregnancy [6, 9, 10].

A severe course of ARDS requires treatment in the intensive care unit (ICU) and switch to mechanical ventilation.

If adequate oxygenation is not possible on the background of mechanical ventilation and the risk of death is high, VV ECMO can be used. VV ECMO is aimed at maintaining oxygenation and unloading the pulmonary circulation, which increases the necessary time limits for the restoration of lung tissue. The most popular VV ECMO approaches are cannulation with a drainage cannula of the right femoral vein and a return cannula for the right jugular vein. Oxygenated blood flows directly to the right heart to participate in circulation, reducing pulmonary resistance and right ventricular afterload.

The indications for VV ECMO are [11]:

1. PaO_2/FiO_2 <80 mm for more than 6 hours.
2. PaO_2/FiO_2 <30 mm for more than 30 hours.
3. pH <7.25 with $PaCO_2$ > 60 mm Hg more than 6 hours.

The Extracorporeal Life Support Organization (ELSO) calculated that in 2018 the survival rate in case of need for VV ECMO ranged from 58.7 to 73.2% [12]. The experience of using ECMO in *COVID* -19 has demonstrated a mortality rate of up to 40% [13]. A 2020 systematic review of 221 studies (358 patients) requiring ECMO during pregnancy for all indications (the most common indication being ARDS) demonstrated a 75% 30-day maternal survival rate [14]. In Russia, for the first time, the successful use of ECMO in a pregnant woman was registered in 2019 with an infection with the influenza *A* (*H*1*N*1) virus [15]. According to the literature, there are no cases of successful ECMO use in pregnant women with *COVID* -19 in Russia.

Case report

We report a clinical case of the successful VV ECMO in a pregnant patient with severe ARDS caused by *COVID* -19 infection.

Patient S., 37 years old, diagnosed with "Pregnancy, 21-22 weeks, a new coronavirus infection of an extremely severe course, community-acquired bilateral polysegmental pneumonia (lesion volume over 90%)" was delivered to the ICU of the Lapino clinical hospital by an ambulance team from another a medical institution on the 16th day of illness with a positive result of the *SARS-CoV*- 2 polymerase chain reaction (PCR). Of these, she was in the hospital for 12 days. At the previous stages of treatment, antibacterial, anticoagulant and symptomatic therapy was carried out. Upon admission, the patient's condition was assessed as extremely serious. During transportation to the hospital and in the first 12 hours of hospitalization, non-invasive ventilation was performed through a face mask in *CPAP + PS* mode with parameters of positive end-expiratory pressure (PEEP) 9 mbar, $P_{support}$ 10 mbar, oxygen fraction in the inhaled mixture (FiO_2) 90%. The 95% saturation (SpO_2) was achieved, hemodynamics of the patient remained stable, the other organ systems - no dysfunction. On admission, according to ultrasound (ultrasound) and Doppler measurements, the development of the fetus corresponded to the gestational age.

Due to the rapid increase in respiratory failure (tachypnea up to 40 respiratory movements per minute, decrease in saturation to 80%), the patient was put on mechanical ventilation with the following initial ventilation parameters: P_{contr} 28 mbar, with a frequency of 18/min, PEEP 11 mbar, FiO_2 100%, SpO_2 96%. Prolonged sedation with propofol and dexmedetomidine and muscle relaxation were started.

According to the data of computed tomography of the chest organs (CT CO), the volume of the lesion was more than 90% (Fig. 1).

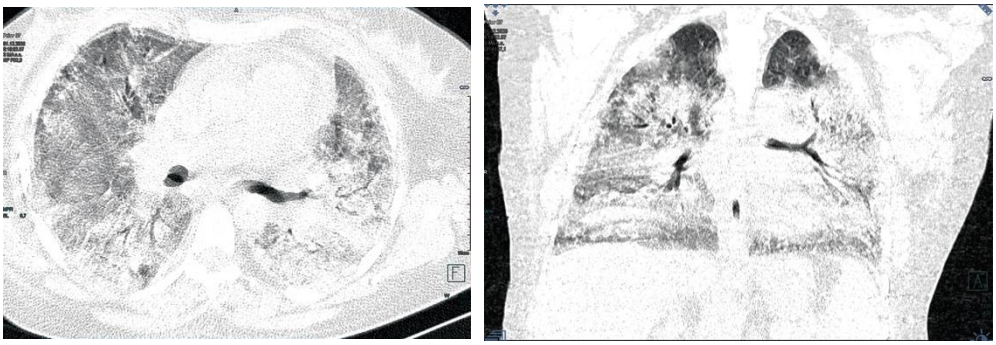

Fig. 1. Computed tomography of the chest upon admission. Subtotal lung damage. The approximate volume of detected changes is more than 75%

She continued antibacterial therapy with broad-spectrum drugs, anticoagulant and anti-inflammatory therapy, symptomatic treatment.

On the 2nd day, hemodynamic instability developed and required the introduction of norepinephrine at a dosage of 0.05 μg/kg/min.

During the first 3 days of treatment in the Lapino Clinic, the patient progressed to hypoxemia with the following parameters of mechanical ventilation: P_{contr} 29 mbar, tidal volume 280 ml, frequency 18 breaths per minute, PEEP 11 mbar, FiO_2 100%. Attention was drawn to a significant decrease in the dynamic compliance of the lungs and tidal volume (Fig. 2). The patient's prone position did not lead to an improvement in oxygenation.

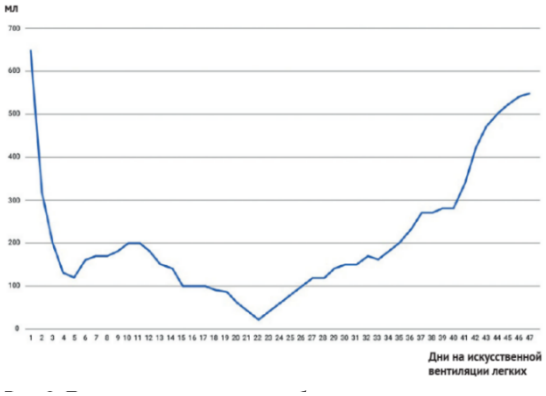

Fig. 2. Dynamics of tidal volume

Despite the ongoing respiratory support and muscle relaxation, the progression of critical hypoxemia continued.

On an urgent basis, a multidisciplinary council was assembled together with specialists from the ECMO Center of the City Clinical Hospital No. 52. It was decided to start the VV ECMO procedure. Cannulas 26 Fr were inserted into the right femoral vein and 19 Fr into the right internal jugular vein. The starting parameters were: blood flow 4.5 l/min, rate 7300 rpm, fresh gas flow 7 l/min, oxygen fraction 100%. SpO_2 90% was reached.

Mechanical ventilation in *BiPAP* mode continued with protective parameters: P_{contr} 20 cm H_2O, tidal volume 180 ml, frequency 16/min, PEEP 10 mbar, FiO_2 70%.

Considering the extremely grave condition of the patient, 6 hours after the start of ECMO, it was decided to terminate the pregnancy by surgery. In the conditions of the intensive care unit, lower midline laparotomy and small caesarean section were performed at the period of 20–21 weeks of gestation. A live premature fetus weighing 420 grams and a length of 24 cm with an Apgar score of 1–3 was removed. Died on the 12th day of life in the ICU of newborns.

After surgery, the patient underwent percutaneous dilated tracheostomy. ECMO continued with the following parameters: flow 4.3 l/min, rate 6500 rpm.

The postoperative period was uneventful. According to the control ultrasound of the pelvic organs, no free fluid was found, the uterine cavity was slit-like. Six hours after the operation, heparin infusion was resumed until the target values of activated partial thromboplastin time (APTT) of 60–70 seconds (Fig. 3). In the morning of the next day, sedation was turned off, normal consciousness was restored.

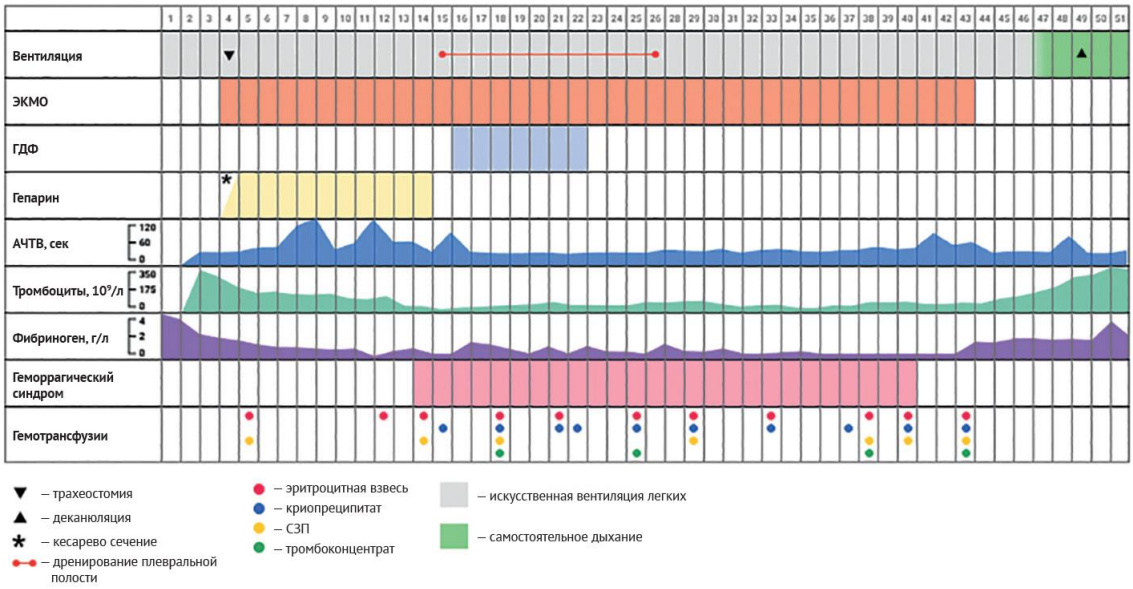

Fig. 3. Dynamics of the patient's condition in the intensive care unit

On the 11th day of ECMO, hypofibrinogenemia and thrombocytopenia (Fig. 3) developed, and caused hemorrhagic and anemic syndromes, which required numerous transfusions of blood components (Table 1). Starting from the 14th day of treatment, further ECMO was performed without heparin administration.

Table 1

The volume of blood transfusion to the patient on the 11th day of ECMO

Component	Transfused in total (l)
Fresh frozen plasma quarantined Fresh frozen plasma anticovid pathogen-reduced	11.84
Pathogen-reduced apheresis platelets	4
Frozen cryoprecipitate	1.35
Erythrocyte suspension leukoreduced	9.3
Total	26.49

On the 17th day of inpatient treatment, despite the ongoing therapy, there was a progression of hemorrhagic syndrome manifested in the development of nosebleeds, bleeding from a tracheostomy, and a postoperative wound. According to ultrasound of the abdominal organs, no free fluid was found, the intervention was limited to revision of the postoperative wound within the subcutaneous fat, hemostatic sutures were applied.

On the 15th day, spontaneous right-sided pneumothorax developed, and the pleural cavity was drained. The lung was expanded, the drainage was removed on the 26th day.

In connection with an increase in the general edema syndrome, in order to control the volemic status, renal replacement therapy was carried out in the mode of hemodiafiltration for 7 days (Fig. 3).

During the entire period of mechanical ventilation, the patient underwent a regular debridement of fibrobronchoscopy for hemorrhagic tracheobronchitis. The improvement of the endoscopic picture occurred on the 46th day. The results of bacteriological research are shown in Table 2.

Table 2

Results of bacteriological and virologic research methods

Microorganisms	Biomaterial	Day of inpatient treatment	Sensitivity
SARS-CoV- 2	scraping	1	
Candida albicans	discharge from the cervical canal		
Klebsiella pneumoniae	broncho-alveolar lavage	11	Co-trimoxazole, Colistin
Acinetobacter baumannii	broncho-alveolar lavage	11	Colistin
Klebsiella pneumoniae	broncho-alveolar lavage	16	Co-trimoxazole, Colistin
Acinetobacter baumannii	broncho-alveolar lavage	16	Colistin
Klebsiella pneumoniae	broncho-alveolar lavage	18	Co-trimoxazole, Colistin
Acinetobacter baumannii	broncho-alveolar lavage	18	Colistin
Enterococcus faecium	blood	25	Linezolid, Vancomycin, Gentamicin, Streptomycin, Tigecycline, Quinupristin/Dalfopristin
Klebsiella pneumoniae	broncho-alveolar lavage	31	Amikacin, Fosfomycin, Gentamicin
Stenotrophomonas maltophilia	blood	40	Co-trimoxazole
Stenotrophomonas maltophilia	blood	43	Co-trimoxazole
Klebsiella pneumoniae	blood	44	Gentamicin, Colistin, Fosfomycin
Stenotrophomonas maltophilia	blood	49	Co-trimoxazole

During hospitalization in the ICU, the patient underwent microbiological monitoring with an assessment of the antibacterial resistance of the detected microorganisms. Correction of antibiotic therapy was carried out according to the research results (Table 2).

During the first 10 days of inpatient treatment, respiratory support was provided in the *BiPAP* mode. By the 22nd day, the maximum deterioration of the elastic properties of the lung tissue was noted: tidal volume decreased to 20–40 ml, compliance - to 10 ml/cm H_2O. When the patient was transferred to the auxiliary ventilation mode, an increase in tidal volume was noted (Fig. 2) and dynamic lung compliance. From the 20th day, against the background of the therapy, there was an improvement in the elastic properties of the lung tissue, restoration of the oxygenating function of the lungs, which made it possible to reduce the volume of ECMO support.

The first CT scan after the start of ECMO was performed on the 29th day of inpatient treatment (Fig. 4). Attention was drawn to the appearance of numerous interpleural air accumulations; against the background of a subtotal viral lesion of the lungs, the appearance of air cavities in the right lung was noted; the approximate volume of lung damage is more than 90%.

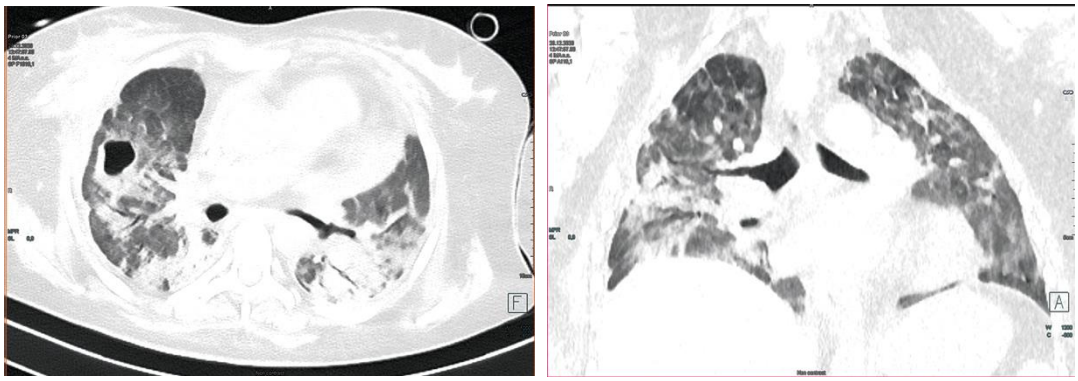

Fig. 4. Computed tomography of the chest organs on the 29th day of inpatient treatment

Subsequent studies showed an improvement in the CT pattern without a significant decrease in the volume of air cavities (Fig. 5), moderate positive dynamics in the form of resolution of reticular changes in the right lung with improved pneumatization of its apex, the total volume of changes was more than 75%, in addition, pneumathocele of the right lung.

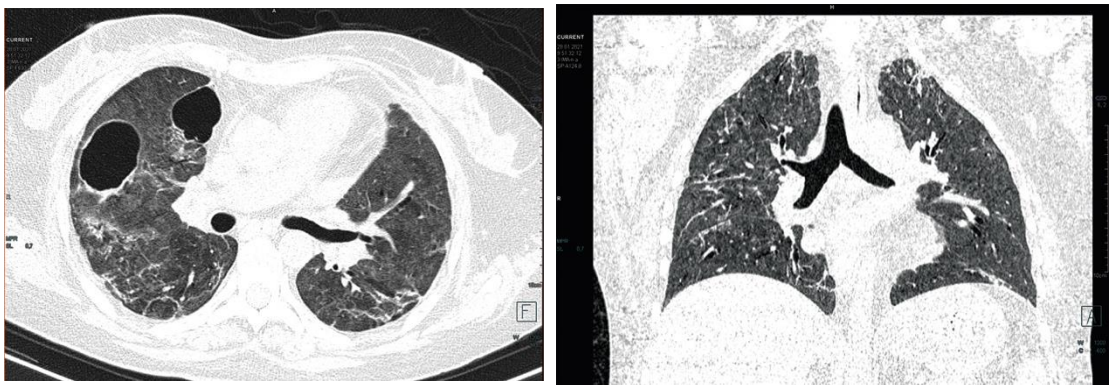

Fig. 5. Computed tomography of the chest organs on the 59th day of inpatient treatment

On the 42nd day of inpatient treatment (58th day of illness) ECMO was discontinued, mechanical ventilation was continued in *CPAP* mode. After 5 days, the patient was successfully weaned from mechanical ventilation. On the 51st day, the patient was transferred to the therapy department of the Lapino CH for further treatment and observation. After a complex of medical and rehabilitation measures, on the 73rd day of inpatient treatment, she was discharged home in a satisfactory condition without oxygen support, recommendations were given for a further period for treatment on an outpatient basis.

After discharge from the hospital, comprehensive rehabilitation treatment was continued. When performing a confirmatory CT scan of the chest organs 30 days after discharge from the hospital, there was a persistent positive dynamics, laboratory tests were within the standard values.

CONCLUSION

Timely initiation of veno-venous extracorporeal membrane oxygenation, according to Russian and international experience and this clinical observation, can improve the outcome of severe acute respiratory distress syndrome against the background of pneumonia caused by the *SARS-CoV*-2 virus.

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