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# Evaluation of the clinical efficiency of COVID drug treatment of clinical-paraclinical parameters in a critical case of COVID-19 with severe pulmonary dysfunction after cesarean section

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## Abstract

*On 11 March 2020 World Health Organization declared the Coronavirus disease 2019 (COVID-19) caused by a novel coronavirus (SARS–CoV–2, 2019 – nCoV) a global pandemic. After a year, there are still many unknowns about peripartum women suffering from COVID – 19. In some pregnant women, respiratory failure can rapidly progress to acute respiratory distress syndrome (ARDS) which is requiring extracorporeal membrane oxygenation (ECMO) as a life – saving therapy. This motivated our team to report the case of a 22-year-old pregnant woman suffering from obesity, gestational hypertension with a severe COVID – 19 forms associated with ARDS.*

*We want to highlight the potential benefits of therapeutic management, after an analysis of clinical and paraclinical parameters, especially because the patient was discharge after 40 days with no major complications. The urgent delivery, early initiation of ECMO and the complex pharmacological therapy (including Remdesivir) resulted in favorable maternal– fetal outcomes.*

**Keywords:** COVID-19; ARDS; ECMO; Remdesivir; pregnancy; obesity; gestational hypertension

## INTRODUCTION

COVID-19 disease has become a global pandemic, after the first case of SARS-CoV-2 infection was reported in Wuhan, China, in December 2019. Since then, cases continue generate worldwide multiple questions about clinical evolution and long-term consequences of the infection which remain still uncertain. This lack of scientific clarity becomes particularly worrying in Obstetrics, because pregnant women are at increased risk of viral respiratory infections due to their immune

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compromised status and physiological obstetric changes, including elevation of the diaphragm, high oxygen consumption and edema of the respiratory tract mucosa. Epidemiologically, pregnant women have been particularly susceptible to viral respiratory diseases during outbreaks of SARS and MERS, with increased rates of complications and mortality. Current studies on SARS-CoV-2 infection have shown that pregnant women have similar clinical developments to those of non-pregnant women, often validating only mild symptoms of hyperthermia, cough, shortness of breath, dyspnea, loss of smell and taste, fatigue and physical discomfort [18-28].

Etiologically coronaviruses (CoV) are RNA viruses belonging to order of nidoviruses. Chronologically until December 2019, the family of coronaviruses included a number of six pathogenic species in humans, of which we list in the first instance SARS-CoV and MERS-CoV, and with the advent of SARS-CoV-2, a seventh representative was added to them [8,12,24,13,23].

Genomically, being a new beta coronavirus, specialists show that SARS-CoV-2 shares 79% the identity of the genomic sequence of SARS-CoV and 50% of MERS-CoV. The structural organization of its genome being similar with other beta-coronaviruses, and the six functional open reading frames (ORFs) are arranged in order from 5' to 3': replicase (ORF1a/ORF1b), tip (S), envelope (E), membrane (M) and nucleocapsid (N). In addition, there are seven putative ORFs, which encode accessory proteins interspersed between structural genes [1,4].

Paraclinical, laboratory abnormalities recorded in these cases include lymphopenia, elevated levels of lactate dehydrogenase (LDH), ferritin, aminotransferase, D-dimer and bilateral opacities of ground glass, on chest computed tomography scans [18,13,1,14,5].

The purpose of the study is to present a clinical case report of severe COVID-19 disease which occurred during an early term pregnancy and put in value a biological parameters group, based on the multiverse profile of all parameters, before and after the cesarean section delivery.

## MATERIALS AND METHODS

Pregnant, 22 years old, without obstetric history, is admitted in Obstetrics and Gynecology (OB) IV of Emergency Clinical Hospital Oradea, Romania on the 18.02.2021 with the diagnosis of: IG/IP Non-monetarized pregnancy, with uncertain chronology, ultrasound of 37/38 weeks, live fetus in cephalic presentation, intact membranes, normal pelvis, pregnancy induced hypertension, morbid obesity, acute respiratory failure, suspected SARS-COV-2, negative RH, high-risk pregnancy. With the following objective parameters: blood pressure (BP) = 164/88, AV = 141/min, T = 36, 3o C, Weight = 120 kg, Height = 1.58 cm and saturation in O2 = 96%.

According to the protocol, at admission, biological samples are collected from the nasopharynx in order to perform the RT-PCR test for SARS-CoV-2, which is reactive. Which is why is isolated on the COVID-19 support department of the Hospital according to the same protocol.

After admission, from the 20.02.2021 the patient complains of dyspnea, dysphagia, bilateral lumbar pain and has a decrease in oxygen saturation, for which the consultation of the on-call ob-gyn is requested, who decides to transfer the pregnant woman to the 2 UCI Obstetrics and Gynecology unit for acute respiratory failure, urinary tract infection and increased platelets for oxygen therapy.

As a result of the acute respiratory pathophysiological alterations occurred on the 2 UCI Obstetrics and Gynecology unit, on the 22.02.2021 for acute respiratory failure with oxygen saturation <84-86%, and fetal tachycardia 166-172/min occurred in an IP with SARS-CoV-2 positive, under spinal anesthesia, an urgent cesarean – section (C-section) was performed. A live female newborn weighing 3200g with Apgar Index 8/9 was extracted. After delivery, placenta is sent in pathology laboratory for specialized evaluation.

After performing the cesarean delivery on the 23.02.2021 (the first day of postpartum) the patient is ventilated non-invasively, continuous positive airway pressure (CPAP) with face mask at FiO2 100% and because the radiographic examination performed reveals multiple opacities of medium intensity, imprecisely contoured, confluent at both lung fields, possibly with a pericardial collection and because the patient requires a computed tomography scan as well as permanent supportive ventilation, it is decided to transfer the patient to the 1st Intensive Care Unit (the 1st ICU) COVID-19 of the Hospital.

At the time of transfer the surgical wound it is being healed, uterus physiologically involved and with lochia corresponding in quantity and appearance to the postpartum day. When arriving at the 1st ICU unit, the general condition is critical, with conscious patient, hardly cooperating, with severe tachypnea, marked inspiratory dyspnea, diminished vesicular murmur on both lung fields, VNI-CPAP FiO2 100%, SpO2 = 80%, hemodynamic stable and diuresis present.

On the 1st ICU COVID-19 unit of the Hospital, the evolution of the patient is unfavorable, with progressive desaturation, so I.O.T. is performed, and the patient is prepared for VV ECMO cannulation. The pharmacological management of the patient mainly was focused on the provision of supportive care, use of recombinant humanized anti-IL-6 receptor monoclonal antibody, recombinant IL-1 receptor antagonist, antiviral therapy, anticoagulation, antibiotic therapy, corticosteroids and other therapeutic agents. Most important therapeutic agents used are noted in Table 1.

The patient benefited from extracorporeal membrane oxygenation (V-V ECMO) therapy, for 14 days, under which the evolution is slowly favorable (as it appears from the paraclinical laboratory and imaging scans given below), after which the mechanical ventilation continues, assisted and subsequently extubating is performed, continuing oxygen therapy, respiratory physiotherapy and progressive resumption of physical activity.

***TABLE 1. Therapeutic agents***

| Class of drugs | Therapeutic substances Concentration pertherapeutic unit |
|---|---|
| Recombinant humanized anti-IL-6 receptor monoclonal antibody | Tocilizumab 20 mg/ml |
| Recombinant IL-1 receptor antagonist | Anakinra 150 mg/ml |
| Antiviral agent | Remdesivir 100 mg/vial |
| Anticoagulation agents | Heparin 5000 IU/ml<br>Enoxaparin 0,8 ml |
| Antibiotics | Ertapenem 1g /vial<br>Meropenem 1 g/ml<br>Vancomycin 1 g/ml<br>Amikacin 500 mg/2ml<br>Gentamicin (80 mg 40 mg/ml-2ml)<br>Moxifloxacin 400 gml/250ml<br>Polymyxin – E 1.000.000 IU powder for solution<br>Ciprofloxacin 100 mg/10 ml<br>Amoxicillin/clavulanic-acid 100 mg/200 mg<br>Metronidazole 5 mg/ml |
| Corticosteroids | Dexamethasone 4 mg/ml<br>Hydrocortisone 100 mg/ml |
| Antihypertensive agents | Enalapril 10 mg/ml<br>Nifedipine 20 mg/ml<br>Methyldopa 250 mg/ml<br>Magnesium Sulfate 2 g/10ml<br>Nebivolol<br>Aspimax cardio 75 mg<br>Atorvastatinum 40 mg |
| Diuretics | Mannitol 200 mg/ml<br>Furosemide 20 mg/ml |
| Mineral Supplements | Aspacardin 39 mg/12mg |
| Oxytocin hormones | Oxytocin 5 Ui/1ml |
| Proton-pump inhibitors (PPI) | Omeprazole 20 mg<br>Pantoprazole 40 mg |
| Analgesics and antipyretics | Paracetamolum 10 mg/ml<br>Metamizolum 1 g/2ml |
| Antiemetic | Domperidonum 2,5 mg/ml |

## RESULTS

**Chest Computed Tomography**

In order to properly evaluate the degree of lung damage and the local evolution, several chest CT were performed. Time series showed different evolution.

First CT scan was performed in first day post C – section and is showing extensive mixed areas of ground-glass opacities that occupy almost all of the lung parenchyma with the association of variable consolidation foci - ARDS in the context of viral pneumonia (COVID-19) (Figure 1A).

Normally expanded lung, extensive ground- glass opacities associated with condensation areas with air bronchogram that occupy almost all of the lung fields in the context of viral pneumonia (COVID-19). No pleural collections.

After many days in which the CT lung aspect stagnates and shows no signs of imaging improvement, on 09.03.2021 the CT evaluation is highlighting a favorable evolutionary image with significant regression of consolidation areas but persist thickened interlobular and intralobular septa in combination with ground-glass opacities areas distributed diffuse bilaterally (Figure 1B).

Favorable evolutionary aspect compared to the last CT examination from 01.03.2021, with the reduction of pulmonary condensation foci and the resorption of pleural collections.

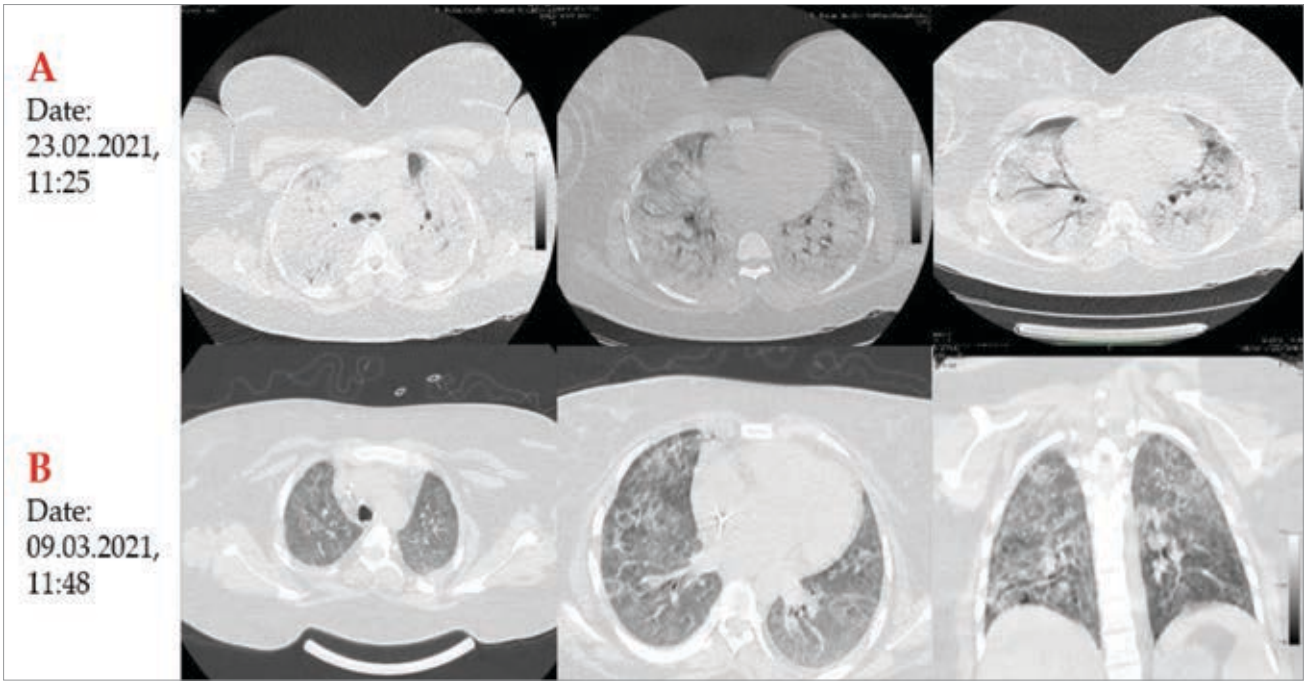


*FIGURE 1. Chest Computed Tomography*

**Histopathological examination of the placenta**

The placenta was fixed in formalin and processed according to a standard protocol used in the Pathology laboratory of our hospital, similar to the international guides [11].

Description of the placenta included the appreciation of the placental weight trimmed of extraplacental membranes and umbilical cord (490 g), the size of the placenta measured in three dimensions (18x15x2cm), the shape (ovoid).

The umbilical cord was marginally inserted, of 20 cm length, average diameter 1 cm, hyper-coiled 6 coils per 10 cm. The membranes were transparent.

After macroscopic description, at least 4 paraffin blocks were submitted for microscopic examination: 1 block which included a roll of extraplacental membranes and two cross sections of the umbilical cord. Three other blocks were submitted each containing a full-thickness section of normal-appearing placental parenchyma. Grossly we found multiple placental infarctions, thrombosis and retroplacental hemorrhage.

Microscopically, we observed the presence of accelerated villous maturation, chorangiosis, the presence of placental infarctions, acute atherosis, fibrinoid necrosis in the arterial wall, villous agglutination, Tenney-Parker modifications, distal villous hypoplasia. These are suggestive changes for maternal vascular malperfusion (Figure 2A and Figure 2B).

Also, we diagnosed fetal vascular malperfusion secondary to hyper-coiling of the umbilical cord, with obvious stromal karyorrhexis, thrombosis and segmental avascular villi. The inflammatory response was patchy, scattered, reduced.

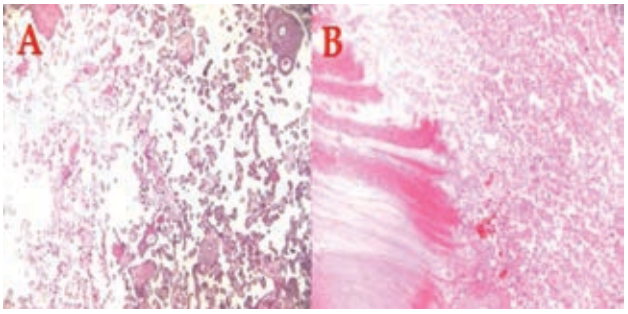


***FIGURE 2. A- Intervillous thrombosis of the placenta (Hematoxylin-eosin, Obx4), B- Early infarction showing crowding and compression of the intervillous spacein the center of the infarct (hematoxylin-eosin, Obx4)***

In Table 2 we will present the chronological evolution of the paraclinical parameters in this case.

As a result of the obvious clinical and paraclinical improvement as can be seen from the table and graphics (fibrinogen, platelets, Prothrombin time (PT),

*TABLE 2. The chronological evolution of the paraclinical*

| Time D/M | Hb g/dl | Hem % | WBC /Ul | PLT /uL | LYM % | Glu mg/dl | ESR mm/h | TQ /sec | APT /sec | Fibr mg/dl | INR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **18.02** | *10.95 | *33.42 | *12.79 | *454.4 | *11.91 | *83 | | 11.1 | 27.2 | 678 | 1.01 |
| **22.02** | *11.97 | *35.94 | *16.76 | 294.9 | *3.668 | *97 | | 10.7 | 34.1 | *460 | |
| **23.02** | 10.93 | *35 | *14.17 | 0 | *6.700 | *123 | *44 | 10.3 | *36.9 | *423 | 0.94 |
| **24.02** | | *30.83 | *12.80 | 103.8 | | *227 | | | 158.3* | 220 | 1.07 |
| **25.02** | *8.764 | 29.75* | 8.78 | 310.9 | 28.33 | *57 | | | 29.8 | 206 | |
| **26.02** | *9.9 | *32.79 | | 317.2 | | | | | *56.6 | *128 | 1.1 |
| **01.03** | *9.556 | *30.98 | 9.235 | 264.6 | | 69 | | | *146 | 129 | *1.42 |
| **03.03** | | | | | | | | | # | *96 | *147 |
| **05.03** | 97.67* | *32.44 | 19.07 | 335 | 6.624 | | | | # | 107 | *134 |
| **06.03** | | | | | | | | | # | *104 | 1.43 |
| **07.03** | 10 | 32.87 | 15.41 | 293.2 | *16.91 | | | | # | *106 | *1.36 |
| **08.03** | *9.439 | | 14.25 | | *14.62 | | | | # | 72 | *2.45 |
| **09.03** | 10.21* | *32.92 | 15.89 | 202.3 | 27.66 | 64 | | | 109.3 | *86 | *8.30 |
| **10.03** | 10.03 | 31.87 | 20.61 | 210.9 | 15.08 | 67 | | | 38.7 | 107 | 1.33 |
| **11.03** | 10.11 | 31.09 | 24.7 | 222.9 | 7.009 | 105 | | | # | | 1.66 |
| **12.03** | 9.5 | 30.8 | 18.1 | 249.7 | 8.611 | 98 | | | 66.7 | 182 | 1.72 |
| **13.03** | 9.838 | 31.61 | 17.96 | 276.7 | 9.415 | | | | 47.9 | | |
| **14.03** | 9.373 | 29.73 | 13.84 | 290.8 | 16.03 | 87 | | | 131 | 230 | 2.33 |
| **16.03** | 9.113 | 30.03 | 12.05 | 296 | 19.83 | 97 | | | 20 | | 2.23 |
| **17.03** | *8.976 | *28.96 | 9.555 | 358.6 | 16.61 | | | | 35 | | 1.5 |
| **19.03** | *8.352 | *28.59 | *11.43 | 370.1 | | | | | | | |
| **22.03** | *9.126 | *30.03 | 10.27* | *499.8 | *18.43 | | 33 | 15.4 | 31.1 | *165 | 141 |
| **25.03** | *8.880 | *29.82 | *10.91 | 501.8 | | *120 | | 13.6 | 28 | 263 | *124 |
| **29.03** | *9.065 | *27.84 | 9.827 | *591 | 25.03 | | | *12.7 | 28.9 | 258 | 1.16 |

Time – the study was prepared in 2021 (D / M – meaning day and month). Hb – Hemoglobin. Hem – Hematocrit. WBC – White blood cells, PLT – Platelets, LYM – Lymphocytes, Glu – Glucose, ESR – Erythrocyte sedimentation rates, TQ – Coagulation time, APT – Activated thromboplastin time, Fibr – Fibrin. INR – International Normalized Ratio, PT – Prothrombin time. BUN – Urea nitrogen. CRT – creatinine, UA – Uric acid, AST – Aspartate transaminase, ALT – Alanine aminotransferase, # - not coagulated, * - values that are not in the reference range.

International Normalized Ratio (INR), Activated Partial Thromboplastin time (aPTT), pro-calcitonin, D-dimer, C – reactive protein CRP) including imaging aspects, on the 26.03.2021 the patient is retransferred to the 2 ICU Obstetrics and Gynecology unit. The patient is reevaluated, and the recommended treatment is highlighted in Table 3. Also, a phytocompound-based product with mucolytic and protective properties of the bronchial tree was introduced in the treatment.

On the 2nd UCI Obstetrics and Gynecology unit, on the 40th day after the caesarean delivery, after the

*TABLE 3. Therapeutic substances*

| Class of drugs | Therapeutic substances Concentration per therapeutic unit |
|---|---|
| Antibiotics | Doxycycline 100 mg/caps. |
| Anthistaminic agents | Desloratadine 5 mg/tab. |
| Anticoagulants | Apixaban 5 mg/tab. |
| β-2 adrenergic receptor agonists | Salbutamol 100 Inhaler CFC - Free |
| Corticosteroids | Dexamethasone 4 mg/ml vial |
| Mineral Supplements | Potassium hydrogen aspartate/ Magnesium aspartate 180 mg/ 180 mg |

SARS-CoV-2 infection, patients afebrile, hemodynamically and respiratory balanced, with spontaneous diuresis, present intestinal transit and clearly favorable clinical and paraclinical evolution, as a result on the 30.03.2021 is transferred to OB IV department from where it is discharged on the same day as the recommendations: to continue the treatment recommended by the pulmonologist, listed above; pneumological control in the Ambulatory Service in more than 1 month; obstetrical control after 1 week.

## DISCUSSION

In the case of people with critical forms of COVID-19 disease with ARDS, the available bibliographic sources record superior numerical cases of thromboembolic disorders and hemorrhagic manifestations. COVID-19 can alter pathophysiological the homeostasis coagulation, by a pronounced imbalance in platelet activity and by altering the physiological regulatory mechanisms of coagulation and fibrinolysis. As a pathogenic result, the clinical and paraclinical exteriorization varies from a simple subclinical elevation of laboratory markers and micro thrombi culminating in a series of major thromboembolic events, bleeding and disseminated intravascular coagulation.

As a secondary consequence of an inflammatory trigger episode, the mechanism of activation of the coagulation cascade in COVID-19 disease is represented by the tissue factor pathway, which induces interleukin synthesis and platelet activation, mediated by endotoxin factor and tumor necrosis factor, and as a consequence, the massive infiltration of activated platelets may be responsible for inflammatory infiltration of the endothelial space, as well as thrombocytopenia [11,26,20].

Thus, the diversity of clinical and paraclinical externalizations of coagulopathy confronts the specialist with a difficult question: If and how to ensure quickly an optimal supportive therapeutic approach.

The hematological clues do not reflect the psycho-somatic improvement begun from the 14$^{th}$ day. Minimum of WBC (leucopenia) was on the 10$^{th}$ day, in the critical status, and the maximum of WBC on the 22$^{th}$ day, in the first week of psycho-somatic amelioration. The minimum level of PLT was on the 21$^{th}$ day followed by a continuous increase, with a maximum on the day of the discharge (in the ameliorating status).

Lymphopenia had at minimal level on the 5 and on the 16$^{th}$ day reflecting the deeply critical status, and on the 22$^{th}$ day in the full improvement status.

The fibrin decreases from the first day and present a minimal plateau from the day 9$^{th}$ (in critical status) until the 19$^{th}$ day (in improved status). The INR had an EKG-like curve with a peak on the 20$^{th}$ day.

The peaks were for the D-dimer on the 7$^{th}$ day (beginning of critical status), for the pro-CALCIT on the 14$^{th}$ day (shifting from critical to ameliorated status) and for FERRI on the 21$^{th}$ day (ending of the first ameliorating week).

We can easily see from the analysis that the hematological, biochemical, coagulation and inflammatory values follows the curve of critical clinical status in the first 14 days, under VV ECMO and after VV ECMO the curve of improved evolution in the next 20-22 days.

The common laboratory changes included lymphopenia, leukocytosis, decreases platelet counts, supraphysiological levels of and D-dimer. The D-dimer levels, along with the clinical condition and severity of pneumonia according to CT scans were used to determine the dosage of Clexane (LMWH).

Laboratory clues were considered in accordance with the severity of the disease. Decreasing in the level of erythrocytes and lymphocytes were main predictors of the severity.

In terms of lab tests and treatment this patient received VV ECMO for 14 days.

The curative approach must be adapted and adjusted by taking into account the estimated and deontological assumed risk of hemorrhage and thrombosis. As the COVID-19 pandemic begins to affect more and more obstetric patients, the choice of the most effective treatment for optimizing the wellbeing of the maternal and fetal binomial is of major importance. Although there are no certified timing guidelines yet on the delivery of pregnant women with severe forms of COVID-19, our case under particularly complex intensive care in the 1$^{st}$ ICU COVID-19 unit began to improve clinical and paraclinical and recover psycho-somatic postpartum.

While previous retrospective studies show appreciable success rates of delivery in pregnant women with COVID-19 disease with mild or moderate respiratory symptoms, our patient had a particularly severe pulmonary pathophysiological status without reserves to tolerate the chronological course of labor. As a result, in patients who are heavily dependent on oxygen supplementation to ensure adequate saturation, we advocate cesarean delivery in order to accelerate labor and avoid fetal distress [11,19].

Anesthetically, in our case, we opted for spinal anesthesia and not for general perioperative anesthesia with intubation, which the patient managed to successfully tolerate. In fact, we believe this is a safer anesthesia technique for both pregnant women with COVID-19, as well as for newborns, having the additional advantage of decreasing the viral exposure of the medical staff [20,10].

The epidemiological possibility of vertical transmission of SARS-CoV-2 infection from a COVID-19-positive mother to the intrauterine fetus remains uncertain, similar to many other studies. We didn't find that the newborn was contaminated, being tested negative immediately after birth and a few days after delivery [28,24,10].

The placenta is an easily accessible organ, constituting a source of information which echoes the intrauterine environment. Known as the "black box" of pregnancy, it provides details regarding the current pregnancy, its evolution and guides the postpartum management [10].

The placenta is considered, however, the least understood organ in the human body. Placental examination can yield important information that may be essential to enhance our understanding of disease pathogenesis and to identify underlying causes of adverse pregnancy outcomes.

In our case, the morphological changes described in the placenta were maternal and fetal vascular mal - perfusion (perfusion abnormalities).

There are no pathognomonic histological findings in human placenta following SARS-CoV-2 maternal infection, as illustrated in a study by Sharps et al. [19] a review on 20 studies, but a higher frequency of maternal vascular mal - perfusion (MVM) of the placental bed was reported in placentas of pregnant women infected with SARS-CoV-2 [27].

It is a recognized pattern of placental injury related to uterine under perfusion, and subsequent hypoxic and ischemic injury. A 93% of the third trimester placenta revealed at least a feature of MVM in a study conducted by Taglauer [22]. Also, fetal vascular mal - perfusion (FVM) was reported in four studies with COVID-19 affected placentas [10]. Fetal vascular thrombosis, abnormal cord insertion, hyper-coiling and maternal hypercoagulable status are among the conditions associated with FVM [7].

It is important to point out that the signs of MVM and FVM are non-specific and can be present in many maternal medical conditions such as hypertensive disorders, lupus anticoagulant and protein C deficiency. So, the results should be interpreted with caution in the context of overall clinical scenarios and may not be attributed to SARS-CoV-2 infection [27, 28].

The case presents maternal and neonatal results postpartum cesarean delivery, our patient validating a significant improvement in postpartum respiratory status under conditions of heroic intensive curative and therapeutic measures, including CPAP, IOT and ECMO on 1 ICU COVID-19 unit, with the newborn showing adequate evolution, without positivity for COVID-19.

We consider that our patient improvement is the result of effective and responsible involvement of the medical team, who applied without omissions, the protocol of delivery and monitoring postpartum the critically ill young mothers on the COVID-19 1 ICU unit calling quickly on CPAP, IOT and especially ECMO.

Published studies report that the vast majority of patients with COVID-19 (>90%) requiring ECMO were assisted using venous VV ECMO for ARDS as in our case report. While the duration of ECMO in COVID-19 may be higher than in non-COVID-19 ECMO patients (14 days in our case), published mortality appears to be similar between the two groups. There is however potential that overall mortality may increase, consequently we strongly encourage participation in data transmission to quantify the optimal use of ECMO in pregnant and postpartum patients in critical forms of COVID-19 [17,2].

Although we still cannot fully explain and highlight the immunological trigger of the patient, medical technology and/or pharmaceutical agents of the

medical which tipped the balance of the clinical and paraclinical evolution of the patient to have a positive evolution, all the more so as there only a few similar cases of survival reported in literature.

Looking forward, we cannot tell whether a possible post-COVID maternal-fetal psycho-somatic syndrome will be validated in the present case, which is being discussed more and more in the medical world. Scientific and clinical evidence on the long-term effects of COVID-19, which affects several systems and organs, suggest that residual effects of SARS-CoV-2 infection, such as fatigue, dyspnea, chest pain, cognitive impairment, arthralgia and decreased quality of wellbeing, cell damage, a robust innate immune response with the production of inflammatory cytokines and a pro-coagulant state induced by SARS-CoV-2 infection may contribute to these sequelae [6,3,8,15,21].

Finally, we acknowledge and promote the urgent need to continue future studies of similar cases, which clarify the timing and the way of delivery, the use of medication, including anticoagulant antivirals and CPAP intensive care techniques, IOT, ECMO, both for the benefit of obstetricians and patients.

## CONCLUSIONS

Urgent parturition is associated with improved materno – fetal outcomes during a severe COVID -19 pneumonias.

We already know that a C – section delivery is a lifesaving surgery for a long period of time, especially in cases with insufficient maternal respiratory reserves associated with coagulation abnormalities, hypertension and obesity. Such pulmonary deficit can occur in a severe COVID -19 form which requires complex therapeutic measures and, in some situations, extracorporeal membrane oxygenation.

In this case scenario the urgent delivery, early initiation of ECMO and the complex pharmacological therapy resulted in favorable maternal and fetal outcome, even if the hematological, biochemical, coagulation and inflammatory values follows the curve of critical clinical status in the first 14 days, under V-V ECMO.

This presentation proves that with up-to-date specialized human and medical resources we are able to solve in a favorable curative-therapeutic way the severe cases of COVID-19 disease that occurred in pregnant and post-partum women. Of course, in such cases an agenda of periodic reevaluations is vital to prevent the occurrence of complex and preventable sequelae.

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## REFERENCES

1. Arsene AL, Dumitrescu IB, Drăgoi CM et al. A new era for the therapeutic management of the ongoing COVID-19 pandemic. *Farmacia*. 2020;68(2):185-196.
2. Badulak J, Antonini MV, Stead CM et al. Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization. *ASAIOJ.* 2021;67:485–95.
3. Carfì A, Bernabei R, Landi F. Gemelli Against COVID-19 Post-Acute Care Study Group Persistent Symptoms in Patients After Acute COVID-19. *JAMA*. 2020;324:603–5.
4. Chan JF-W, Kok K-H, Zhu Z et al. Genomic Characterization of the 2019 Novel Human-Pathogenic Coronavirus Isolated from a Patient with Atypical Pneumonia after Visiting Wuhan. *Emerg Microbes Infect.* 2020;9:221–36.
5. Chen D, Yang H, Cao Y et al. Expert Consensus for Managing Pregnant Women and Neonates Born to Mothers with Suspected or Confirmed Novel Coronavirus (COVID-19) Infection. *Int J Gynaecol Obstet.* 2020;149:130–6.
6. Gupta A, Madhavan MV, Sehgal K et al. Extrapulmonary Manifestations of COVID-19. *Nat Med.* 2020;26:1017–32.
7. Heider A, Fetal Vascular Malperfusion. *Arch Pathol Lab Med.* 2017;141:1484–9.
8. Huang C, Wang Y, Li X et al. Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China. *Lancet*. 2020;395:497–506.
9. Huang C, Huang L, Wang Y et al. 6-Month Consequences of COVID-19 in Patients Discharged from Hospital: A Cohort Study. *Lancet*. 2021;397:220–32.
10. Jaiman S. Gross Examination of the Placenta and Its Importance in Evaluating an Unexplained Intrauterine Fetal Demise. *Journal of Fetal Medicine.* 2015;2.
11. Khong TY, Mooney EE, Ariel I et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. *Archives of Pathology & Laboratory Medicine.* 2016;140:698–713.

12. Lee DH, Lee J, Kim E et al. Emergency Cesarean Section Performed in a Patient with Confirmed Severe Acute Respiratory Syndrome Coronavirus-2 -a Case Report. *Korean J Anesthesiol.* 2020;73:347–51.
13. Liu D, Li L, Wu X et al., Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. *AJR Am J Roentgenol,* 2020;215:127–32.
14. Liu Y, Chen H, Tang K, Guo Y. Withdrawn: Clinical Manifestations and Outcome of SARS-CoV-2 Infection during Pregnancy. *J Infect.* 2020;S0163-4453(20)30109–2.
15. McElvaney OJ, McEvoy NL, McElvaney OF et al. Characterization of the Inflammatory Response to Severe COVID-19 Illness. *Am J Respir Crit Care Med.* 2020;202:812–21.
16. Moore KM, Suthar MS. Comprehensive Analysis of COVID-19 during Pregnancy. *BiochemBiophys Res Commun.* 2021;538:180–6.
17. Panigada M, Bottino N, Tagliabue P et al. Hypercoagulability of COVID-19 Patients in Intensive Care Unit: A Report of Thromboelastography Findings and Other Parameters of Hemostasis. *J ThrombHaemost.* 2020;18:1738–42.
18. Rasmussen SA, Smulian JC, Lednicky JA et al. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What Obstetricians Need to Know. *Am J ObstetGynecol.* 2020;222:415–26.
19. Sharps MC, Hayes DJL, Lee S et al. A Structured Review of Placental Morphology and Histopathological Lesions Associated with SARS-CoV-2 Infection. *Placenta*. 2020;101:13–29.
20. Spiezia L, Boscolo A, Poletto F et al. COVID-19-Related Severe Hypercoagulability in Patients Admitted to Intensive Care Unit for Acute Respiratory Failure. *ThrombHaemost.* 2020;120:998–1000.
21. Sungnak W, Huang N, Bécavin C, Berg M. HCA Lung Biological Network SARS-CoV-2 Entry Genes Are Most Highly Expressed in Nasal Goblet and Ciliated Cells within Human Airways. *ArXiv.* 2020.
22. Taglauer E, Benarroch Y, Rop K et al. Consistent Localization of SARS-CoV-2 Spike Glycoprotein and ACE2 over TMPRSS2 Predominance in Placental Villi of 15 COVID-19 Positive Maternal-Fetal Dyads. *Placenta*. 2020;100:69–74.
23. Tang N, Li D, WangX, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.* 2020;18(4):844–7.
24. Zhu H, Wang L, Fang C et al. Clinical Analysis of 10 Neonates Born to Mothers with 2019-NCoV Pneumonia. *TranslPediatr.* 2020;9:51–60.
25. Varlas VN, Bors RG, Nasui BA et al. Key points in fertility preservation treatment strategies during COVID-19 pandemic. An update on pharmacological therapies. *Farmacia*. 2021;69(2):189-99.
26. Wang X, Zhou Z, Zhang J et al. A Case of 2019 Novel Coronavirus in a Pregnant Woman With Preterm Delivery. *Clin Infect Dis.* 2020;71:844–6.
27. Who Global Status Report on Noncommunicable Diseases 2014 Available online: http://www.who.int/nmh/publications/ncd-status-report-2014/en/ (accessed on 31 May 2021).
28. Wong YP, Khong TY, Tan GC. The Effects of COVID-19 on Placenta and Pregnancy: What Do We Know So Far? *Diagnostics* (Basel). 2021;11(1):94.