

ORIGINAL PAPER

Obstetrical and Neonatal Outcome of Pregnancies Complicated with SARS-CoV-2 Infection

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Abstract

COVID-19 pandemic had an impact without precedent. Pregnant women are part of the vulnerable population and the extent of SARS-CoV-2 infection consequences on obstetrical and neonatal outcome are still studied. It's been speculated, based on what is known about other pathogenic viruses, SARS-CoV-2 virus can interfere with placental defense mechanisms and increase the miscarriage and preterm birth rate. Often, pregnant women infected with SARS-CoV-2 virus develop mild pneumonia. Severe pneumonia occurs very rarely and is statistically significant related to neonatal death. Our study has been conducted in a multidisciplinary hospital unit and included 184 pregnant women with SARS-COV-2 infection who gave birth in our hospital, diagnosed through polymerase chain reaction. There have been analyzed data regarding the maternal symptomatology, the gestational age, the method of giving birth, complications that have occurred during birth, the newborns weight and neonatal outcome through Apgar score. There have been three cases of severe infection with maternal death and one case with neonatal death. Overall, 20% of patients had mild symptomatology, 2% had severe form and the rest of the patients were asymptomatic. We found a high rate of preterm birth and intrauterine growth restriction and an increase incidence of acute fetal distress followed by caesarean section. SARS-CoV-2 virus affects both the mother and the fetus as a whole and, subsequently, individually. Our results show the adverse obstetrical and neonatal outcome in peripartum period complicated with SARS-CoV-2 infection even in asymptomatic and mild-symptomatic cases.

Keywords: SARS-CoV-2, pregnancy, obstetrical outcome, neonatal outcome.

Rezumat

Pandemia COVID-19 a avut un impact fără precedent. Femeile gravide fac parte din populația vulnerabilă, iar amploarea consecințelor infecției cu SARS-CoV-2 asupra prognosticului sarcinii și asupra evoluției neonatale sunt încă studiate. S-a speculat, pe baza a ceea ce se știe din fiziopatologia virală, că virusul SARS-CoV-2 poate interfera cu mecanismele de apărare placentară și poate crește rata de avort și naștere prematură. Adesea, femeile însărcinate infectate cu SARS-CoV-2 dezvoltă simptomatologie moderată. Pneumonia severă apare foarte rar și are o legătură semnificativ statistică cu decesul neonatal. Studiul nostru a fost realizat într-un spital multidisciplinar și a inclus 184

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de femei gravide cu infecție SARS-CoV-2 diagnosticate prin reacția în lanț a polimerazei. Au fost analizate datele privind simptomatologia maternă, vârsta gestațională, modul de naștere, complicațiile apărute în timpul nașterii, greutatea la naștere și statusul neonatal analizând indicii Apgar. Au fost trei cazuri de infecție severă care au avut ca rezultat decesul matern și un caz de deces neonatal. Per total, 20% dintre paciente au prezentat simptomatologie medie, 2% au avut o formă severă a bolii, iar restul au fost asimptomatice. În cadrul studiului s-a decelat o rată crescută de naștere prematură și restricție de creștere intrauterină, precum și o incidență ridicată a suferinței fetale acute urmate de naștere de urgență prin operație cezariană. Virusul SARS-CoV-2 afectează și mama și fătul atât ca un întreg cât și individual. Rezultatele noastre au arătat ca prognosticul obstetrical și neonatal este influențat de infecția maternă în perioada perinatală chiar și în cazurile asimptomatice și mediu-simptomatice.

Cuvinte cheie: SARS-CoV-2, sarcină, prognostic obstetrical, prognostic neonatal.

INTRODUCTION

COVID-19 pandemic has an impact without precedent. Until March 2022, more than 476 million of confirmed cases and more than six million deaths related to SARS-CoV-2 infection have been registered. In Romania, until the end of April 2022, more than 2.8 million cases have been confirmed with a rate of mortality estimated at 3%¹. However, these significant numbers have not offered clear answers regarding the differences of the infection's mechanisms, the disease path, the associated complications or the outcome.

Pregnant women are part of the vulnerable population and the extent of SARS-CoV-2 infection consequences on obstetrical and neonatal outcome are still studied. It's been speculated, based on what is known about other pathogenic viruses, that SARS-CoV-2 virus can interfere with placental defense mechanisms and increase the miscarriage and preterm birth rate².

From the immunological point of view, the physiopathology of SARS-CoV-2 infection is representing by a decreased number of lymphocytes and monocytes with macrophage infiltration at the level of lung lesions. Also, respiratory failure is a common clinical manifestation in severe cases along with hypercoagulability, thrombosis and the last stage being multiple organ failure. There is a predisposition to severe forms of the disease as mother's body undergoes a series of physiological changes in order to sustain and support the growth of the fetus. There is an increased number of Decidual Natural Killer cells, predominant in the first trimester which have the role to set the trophoblast invasion and arterial remodeling³. Macrophages are implicated in a series of essential function in the early pregnancy, like immunomodulation, blood vessels remodeling and trophoblast invasion and prevention of the rejection phenomena through the production of

prostaglandin E2, interleukin (IL)-10 and indolamine 2,3-dioxygenase⁴.

Cytokines, neurotrophil and chemokines are immune mediators with a crucial role in central nervous system development. If the balance of physiological mechanisms is disrupted this will be translated in impaired neurodevelopment, cognitive and intellectual abilities and a high risk of psychiatric disorders⁵.

Given the above, it is clear the changes that occur in pregnant women make them a vulnerable population for SARS-CoV-2 infection. The cytokine storm interferes with the immunological pregnancy state and can have consequences for the mother and fetus. Data until now show that the most common symptoms in COVID-19 pregnant women are fever and cough. Paraclinical changes in infected pregnant women include lymphopenia, increased levels of C-reactive protein, neutrophil count and alanine aminotransferase (ALT). Often, pregnant women infected with SARS-CoV-2 virus develop mild pneumonia. Severe pneumonia occurs very rarely and it is statistically significant related to neonatal death⁶. Histopathological examination of placenta had shown that SARS-CoV-2 infection is related to an acute placental inflammation, the presence of the infection at the fetal-placental level and a low level of vertical transmission of antibodies⁷.

The microbiota from the materno-placental interface is affected by the viral infection by decreasing the level of beta-interferon secretion which plays a key role in fetal receptivity. So, the SARS-CoV-2 infection by initiating the described inflammatory response, increases the risk of preterm birth.

MATERIAL AND METHOD

Our study has been conducted in a multidisciplinary hospital unit, the University Emergency Hospital of

Bucharest, during COVID-19 pandemic (01.03.2020-31.03.2022) having the hospital's ethical committee approval (22276/21.06.2021). In this retrospective study, we analyzed 184 pregnant women with SARS-CoV-2 infection who gave birth in our hospital. First inclusion criteria were the diagnosis of COVID-19 infection established through polymerase chain reaction (PCR) test at admission. The second inclusion criterion was the birth moment during admission. In our study we reviewed data regarding maternal symptomatology, gestational age, method of birth, complications during childbirth, weight at birth and neonatal outcome representing by Apgar score calculated at 1 minute.

RESULTS

During the studied period, in the Department of Obstetrics and Gynecology of the University Emergency Hospital of Bucharest, 184 women with COVID-19 infection gave birth. Most of them were asymptomatic, but 20% of them had a mild clinical symptomatology. There were three cases of severe infection with SARS-CoV-2 virus which ended with the death of the mother (Figure 1). As we talk about symptomatology, we include fever, cough, anosmia, taste loss or cerebral symptomatology such as cerebral thrombosis or scotomas. The women who were symptomatic were the one who had additional pathologies as diabetes, obesity, heredity thrombophilia or epilepsy.

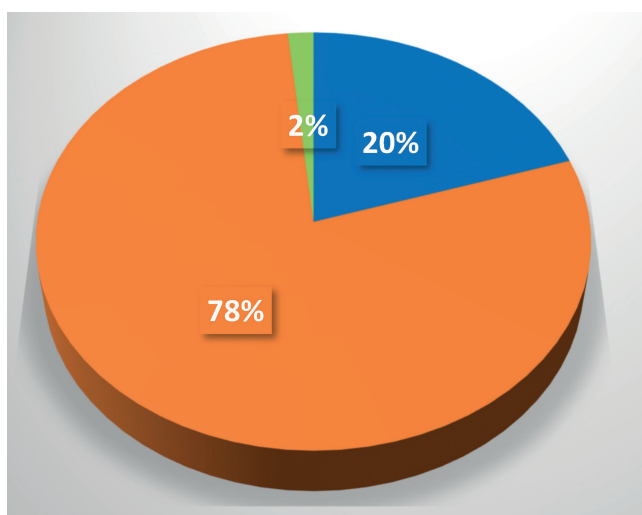


Figure 1. Prevalence of symptomatic vs asymptomatic SARS-CoV-2 infection in pregnant women

The incidence of preterm birth in our study group was 15.7% and the rate of stillbirth was 1.6%, respectively 3 cases (Figure 2). The majority of pregnant women with SARS-CoV-2 infection have delivered at term.

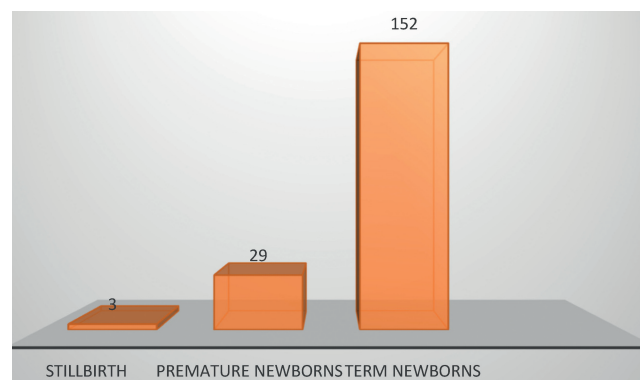


Figure 2. The prevalence of preterm birth and stillbirth among pregnant women with SARS-CoV-2 infection

The preferred method of delivery was through caesarean section with a double incidence than vaginal delivery (Figure 3). The most frequency indications for emergency caesarean section were in order: acute fetal distress, uterine scare and preeclampsia.

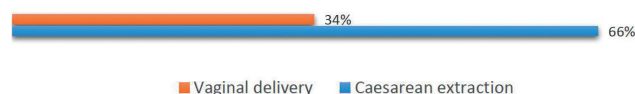


Figure 3. Delivery method in pregnant women with SARS-CoV-2 infection

Regarding the birth weight, more than 22% of the newborns of mothers with peripartum COVID-19 infection had intrauterine growth restriction, having a birth weight below 2.500 grams. In Figure 4 we see the distribution of the newborn from mothers with SARS-CoV-2 virus by their weight.

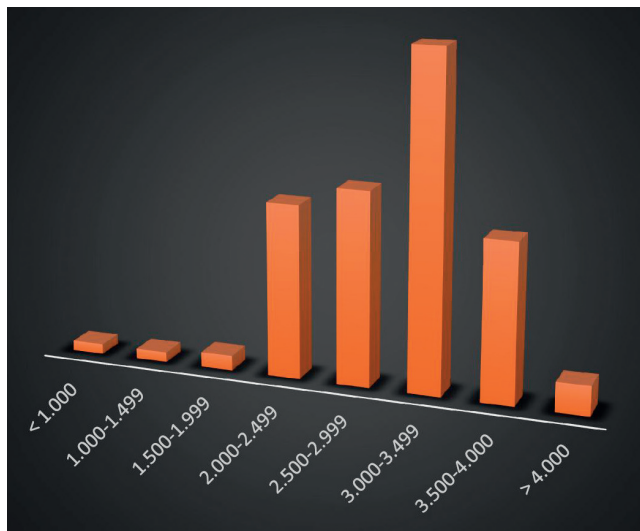


Figure 4. The distribution of the newborns' weight from mothers with COVID-19 infection

Regarding the immediate neonatal status, we analyzed it by the Apgar score calculated at one minute. Only eight cases from our studied group had a difficult postnatal adaptation (Apgar score less than 7), but with subsequent favorable outcome (Figure 5). We have to mention that we had a case of newborn death from COVID-19 infection. The mother was positive for SARS-CoV-2 virus after 11 days post-partum and the newborn the day after. The newborn died 14 days after delivery because of respiratory failure caused by COVID-19 infection.

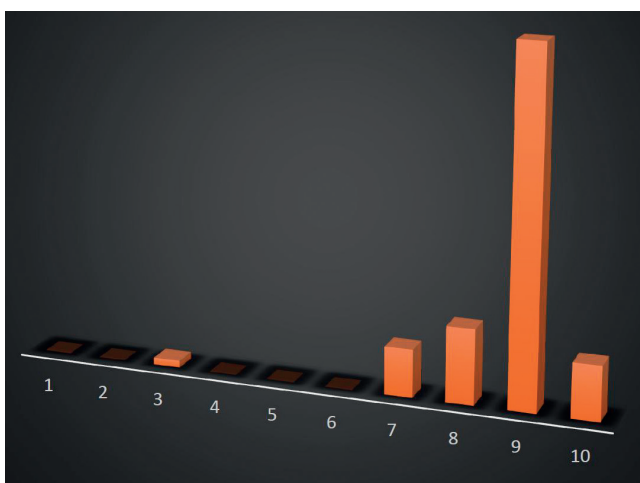


Figure 5. Neonatal status evaluated by Apgar score calculated at 1 minute from mothers with peripartum SARS-CoV-2 infection.

DISCUSSIONS

The latest studies show that due to the physiological, anatomical and immunological pregnancy related changes, pregnant women have an increased risk of developing a severe form of COVID-19 infection⁸. In our study, only 20% of women were symptomatic, with mild symptoms, but for every positive case the monitoring and treatment protocol has been respected. Also, there were three cases of severe infections which needed intensive care and received the latest treatment, but unfortunately, they did not survive. The three severe cases of COVID-19 infection were pregnant women with pregnancy less than 24 weeks of gestation. As we showed, 80% pregnant women with SARS-CoV-2 virus were asymptomatic. So, we can conclude from our study that pregnancy does not accentuate COVID-19 symptomatology.

One possible explanation for the lack of pneumonia cases in our study group could be that during the third trimester, the prenatal medical visits are more frequently, general status and symptomatology were being monitored with more caution. Also, if any suspicion of viral infection comes out, specific paraclinical evaluation takes place.

Secondly, it is worth mentioning that in our study we had a higher incidence of preterm birth compared to general population (about 10%). Data published on this topic agrees on the fact that severe infection associates a higher risk of preterm birth, risk that is insignificant in asymptomatic and mild form of COVID-19 disease⁹. However, the results are controversial as they vary from one study to another. The reason of this variation may be due to a limited number of participants, the known physiopathology of SARS-CoV-2 virus and it is also impossible to exclude other risk factors or pathologies.

In our case, when comparing with data corresponded to pre-pandemic years, respectively 2016-2019, there is clearly an increase incidence of preterm birth. For pandemic period the calculated incidence is 10%, while in the pre-pandemic years the incidence was lower¹⁰.

Another important fact we have noticed is the high incidence of intrauterine growth restriction. The mechanism of fetal growth restriction is multifactorial, resulting from a combination of maternal, placental and fetal factors, but through all these the uteroplacental insufficiency is the dominant cause. Several maternal

non-pathological factors can be reflected in a high risk of fetal growth restriction as height, pregnancy weight, parity and ethnicity¹¹. SARS-CoV-2 infection is an acute event with negative placental effects which lead to severe hypoxemia. The functional receptor for SARS-CoV-2 virus is angiotensin converting enzyme 2 (ACE2) that is mainly expressed in cardiovascular, respiratory and digestive systems. Any changes in maternal homeostasis will affect the fetal growth. Also, there are studies showing that placentas have hemorrhagic modifications or villitis of unknown etiology at histopathological exam, that can be implicated in any maternal and neonatal prognostics^{12,13}.

Since the beginning of the pandemic, the anatomopathological examinations of placentas have confirmed that the inflammatory reaction is extended not only to the placental site but also to the fetus causing fetal distress, preterm birth, miscarriage or other pregnancy complications. Our results show that even in asymptomatic pregnant women with COVID-19 infection there is an increased risk of fetal distress. In our study, 66% of cases needed an emergency caesarean section most of them due to acute fetal distress (Figure 3).

CONCLUSIONS

In conclusion, SARS-COV-2 virus affects both the mother and the fetus as a whole, but also as an individual. Our results show that obstetrical and neonatal outcomes from pregnancies complicated with COVID-19 infection can have appreciable negative effects even in asymptomatic and mild-symptomatic cases. Prompt and safe action from the first moments of suspicion or confirmation of infection is essential for improving the prognosis. A multidisciplinary team formed at least by an obstetrician, a neonatal doctor, an infectious disease doctor, is needed whenever we talk about a COVID-19 infection during pregnancy. As we show in our study, even an asymptomatic form may lead to obstetrical and neonatal complications.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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