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Effects of COVID-19 on the body of a pregnant woman with preeclampsia: Birth outcomes (literature review)

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ABSTRACT

In contemporary obstetrics, increasing attention is being paid to identifying problems diagnosed during pregnancy that are believed to increase the risk of complications during pregnancy and labor. The effect of COVID-19 on the body of the pregnant woman as well as its association with preeclampsia and their combined effect on the organisms of the mother and fetus, as well as the specifics of the effect on the course and outcome of labor, have emerged as significant and well-studied problems in obstetric.

The aim of this study was to analyze the effects of COVID-19 on pregnant women with preeclampsia, including possible maternal and/or fetal complications, birth outcomes, delivery methods, and the influence of existing extragenital pathology.

The authors conducted a detailed analytical review of the scientific literature published from 2020 to 2022 on the study topic, gathering information from various sources, such as conference proceedings, technical reports, journal articles, abstracts, and papers available through databases, such as Medline, Google Scholar, and PubMed.

Based on current scientific evidence, pregnant women with COVID-19 have a high incidence of preeclampsia, preterm labor, and operative delivery. The existence of intrauterine vertical transmission has not been reliably proven. The frequency of complications in newborns corresponds with general population indicators.

Keywords: review; COVID-19; preeclampsia; preterm labor; chorioamnionitis; cesarean section; respiratory infections; intoxication; placental detachment; endotheliitis.

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Влияние COVID-19 на организм беременной с преэклампсией. Исходы родов (обзор литературы)

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На современном этапе акушерства все больше внимания уделяется проблемам, диагностируемым во время беременности, которые, предположительно, повышают риск осложнений при беременности и родах. Значимой и изучаемой проблемой в акушерстве стало влияние COVID-19 на организм беременной, а также его связь с преэклампсией и их совокупное воздействие на организмы матери и плода, особенности влияния на течение и исход родов.

Цель работы — проанализировать влияние COVID-19 на организм беременной с преэклампсией: возможные осложнения у матери и/или плода, исходы родов и методы родоразрешения, а также влияние имеющейся экстрагенитальной патологии.

Авторы провели подробный аналитический обзор научной литературы за 2020—2022 годы по исследуемой теме, поиск информации из различных источников: материалов конференций, технических отчётов, журнальных статей, рефератов и статей с использованием баз данных Medline, Google Scholar и PubMed.

Заключение. Согласно современным научным данным, у беременных с COVID-19 наблюдается высокая частота преэклампсии, преждевременных родов и оперативного родоразрешения. Существование внутриутробной вертикальной передачи инфекции достоверно не доказано. Частота осложнений у новорождённых соответствует общепопуляционным показателям.

Ключевые слова: обзор; COVID-19; преэклампсия; преждевременные роды; хориоамнионит; кесарево сечение; респираторные инфекции; интоксикация; отслойка плаценты; эндотелиит.

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In obstetrics, increasing attention has currently been paid to problems that occur during pregnancy, which presumably increase the risk of complications during pregnancy and childbirth. The most significant problem in obstetrics is the impact of COVID-19 on the pregnant woman's body, association between COVID-19 and preeclampsia, and their combined effect on the body of the mother and fetus and course and outcome of childbirth.

Yu.E. Dobrokhotova has reported complications during pregnancy in 26 (76.5%) female patients with COVID-19 [1]. Preeclampsia complicated the course of pregnancy in 13/34 (38.2%) patients, whereas moderate preeclampsia was identified in 9/34 (26.8%) pregnant women and severe preeclampsia in 4/34 (11.8%). Moreover, preeclampsia complications were identified in 3/34 (8.8%) patients, including HELLP syndrome in 2/34 (5.9%) patients, and preterm placental abruption was detected in 1/34 (2.9%) patients. The threat of premature birth was identified in 12/34 (35.3%) cases.

Following several studies, we have noted that respiratory infections can have a direct embryotoxic effect and cause uteroplacental blood flow disruption in the presence of severe intoxication and hyperthermia. In the present study, 38.2% of pregnant women developed preeclampsia, including severe preeclampsia in 11.8% of patients, whereas the risk of severe preeclampsia in the general population is 1-2%. In 35.4% of the women studied, pregnancy ended in premature birth, which is eight times higher than the general population figure (4.4%; p < 0.001). Furthermore, the rate of surgical delivery in pregnant women with COVID-19 was 2.4 times higher than that in Russia (73.3% versus 30%; p = 0.035).

According to some authors, pregnant women with COVID-19 have a higher incidence of preeclampsia, late pregnancy miscarriages, preterm birth, and surgical delivery than pregnant women without COVID-19. However, the vertical transmission of SARS-CoV-2 from the mother to the fetus has not been confirmed [1].

S. Kurian et al. have investigated 79 pregnant women and revealed 4 cases of early pregnancy termination due to coronavirus infection, where 2 patients had spontaneous miscarriage at weeks 13–18 of pregnancy and 2 patients had their pregnancy terminated for medical reasons because of severe preeclampsia associated with coronavirus infections. Only 1 of 24 cesarean sections was performed because of severe COVID-19. Laboratory tests of swabs from the nasopharynx of newborns for virus RNA were negative in all cases; however, SARS-CoV-2 RNA was detected in the placental tissue of two pregnant women who underwent termination of pregnancy for medical reasons. The overall incidence of preeclampsia, eclampsia, and HELLP syndrome increased to 16.9% [2].

A.L. Arthurs et al. have revealed that pregnant women infected with COVID-19 experience symptoms of preeclampsia, such as edema, hypertension, and proteinuria. This is apparently due to dysfunction of the renin-angiotensin-aldosterone system, which is the target of coronavirus infection.

It has been proven that the course of coronavirus infection in pregnant women is more severe than that in nonpregnant women and is associated with the development of true preeclampsia, spontaneous miscarriages, preterm delivery, pulmonary embolism, and the risk of preterm rupture of membranes. Additionally, SARS-CoV-2 contributes to the development of placental vascular malperfusion, retroplacental hematoma, and chorioamnionitis, which leads to chronic hypoxia, fetal distress, and intrauterine growth retardation. Stillbirths have also been recorded. The opinion regarding vertical transmission of the disease is unclear [3].

A research conducted by M. Jafari indicated the following: the incidence of preterm delivery in women with a new coronavirus infection was 14.3–25.0%, that of preeclampsia was 5.9%, spontaneous miscarriages was 14.5%, premature rupture of membranes was 9.2%, and fetal growth retardation was determined in 2.8–25.0%. The most common postpartum complication in such women in labor is postpartum hemorrhage (54.5%). Cesarean section is performed in more than half (48–100%) of pregnant women with COVID-19 [4].

COVID-19 and preeclampsia have common pathologies, including endothelial cell dysfunction and coagulation disorders. Further, angiotensin-converting enzyme 2 receptors are expressed by endothelial cells, and infection of endothelial cells and immune cell damage to the endothelium have been described in recent scientific studies of the new coronavirus infection. Preeclampsia associated with COVID-19 may result in microvascular dysfunction, thereby causing endotheliitis. Systemic inflammation and microcirculatory dysfunction develop, leading to vasoconstriction and ischemia. Microvasculature alterations contribute to a procoagulopathic state, as evidenced by the high rates of deep vein thrombosis, stroke, and pulmonary embolism that are increasingly observed in COVID-19 patients [5].

The course of the new coronavirus infection in pregnant women has not yet been fully studied; however, certain conclusions may be drawn, namely, that pregnancy is a complex process in which the physiological norm may deviate somewhat from the usual process, which should be considered when diagnosing and treating COVID-19. Taking into account the conclusions of the studies, the clinical aspects of the course of the new coronavirus infection in pregnant women do not differ significantly from those in nonpregnant women. In addition, the infectious process can affect the course and outcome of pregnancy, leading to premature birth, spontaneous miscarriages, and preeclampsia, which is pathogenetically related to the development of SARS-CoV-2 infection. Moreover, an increased mortality rate has been noted in pregnant women with a new coronavirus infection [6].

According to I.V. Zhukovets et al., the risk of developing pregnancy complications (preeclampsia, polyhydramnios, oligohydramnios, iron-deficiency anemia, preterm delivery) increased significantly in female patients with pathological changes in the lungs (moderate and severe course of the disease) compared with pregnant women who had mild

COVID-19. The assessment of 112 newborns isolated from mothers with coronavirus infection in the delivery room and early postpartum period showed no vertical transmission of infection from mother to child; 14.5% of newborns were born with varying degrees of prematurity. Growth and development retardation was recorded in every fourth newborn. In the neonatal period, 32% of children who became ill after contact with a sick mother or became infected from other family members had a coronavirus infection of moderate severity, and majority (68%) of such children had a mild course of the disease. It is currently not possible to assess the health status of children aged up to one year or more, and further follow-up and study is required owing to the lack of required data [7].

There is a serious problem of specific categorization of complications in impaired pregnancies due to extragenital diseases and in the case of preeclampsia from complications caused by COVID-19. T.V. Priputnevich et al. have described a clinical case of dichorionic diamniotic pregnancy with severe preeclampsia complicated by COVID-19. A 34-year-old primigravida with arterial hypertension and proteinuria was diagnosed with gestational diabetes mellitus at week 29 of pregnancy. The patient showed signs of pneumonia; thus, PCR testing for COVID-19 was conducted. The test was positive, and the patient was found to have severe preeclampsia complicated by COVID-19. Delivery was performed by cesarean section. The twins had negative nasopharyngeal test results for COVID-19. The problem is that the doctor may underestimate complications that arise during an impaired pregnancy, considering them as manifestations of COVID-19 [8].

Final and reliable conclusions about the characteristics of the course of coronavirus infection in pregnant women and women in labor and postpartum will only be possible when the pandemic ends. Thus, based on the results obtained, we can conclude that the most significant concomitant disease in pregnant women with severe and extremely severe COVID-19 is iron-deficiency anemia; in patients with a poor or fatal outcome, pregnancy is often complicated by gestational diabetes mellitus, preeclampsia, oliqohydramnios, and obesity [9].

In some studies conducted in 2020, no cases of severe preeclampsia were identified in pregnant women examined; moderate preeclampsia associated with SARS-CoV-2 complicated the course of pregnancy in the group of women with a poor outcome almost three times more often (p=0.02). It has been proven that the main link in the pathogenesis of preeclampsia is endothelial dysfunction. Recent studies on the pathogenesis of the new coronavirus infection provide evidence of direct infection of the endothelium and its immune-mediated damage, which can lead to more widespread endothelial dysfunction. In severe cases of SARS-CoV-2 infection, endothelial damage probably contributes to the development of preeclampsia. However, preexisting endothelial dysfunction in patients may be an etiological cause of the development of preeclampsia and may aggravate disease severity. However, identifying the relationship between endothelial damage and the severity of coronavirus infection in pregnant women requires further studies and long-term follow-up [10].

S. Makhmudova has established that the development of severe preeclampsia in pregnant women with COVID-19 was often manifested by increased blood pressure, migraines, visual impairment, proteinuria, and anxiety. During the COVID-19 pandemic, pregnant women with preeclampsia have increasingly complained of headaches, asthenia, malaise, increased blood pressure, palpitations, dyspnea, fear of losing control over themselves, fear of loss of consciousness, and noted feelings of heat or cold, heavy breathing, and dizziness.

Preeclampsia can lead to further serious complications, such as intrauterine growth restriction, preterm placental abruption, kidney failure, and eclampsia and even lethal outcomes in the mother and fetus. The highest risk is mainly registered in very early preeclampsia (before week 32 of pregnancy), when the infant mortality rate is 70 times higher than that in term births [11].

Restructuring of the hemostatic system, which is characterized by an increase in the thrombotic activity of the blood against a decrease in the activity of the anticoagulant system, can contribute to the formation of blood clots and is a crucial factor in the development of preeclampsia, placental insufficiency, and intrauterine fetal hypoxia in women who become pregnant after a coronavirus infection [12].

A.I. Shchegoleva et al. have revealed that perinatal complications in newborns arise because of impaired fetoplacental perfusion and against possible thrombotic changes, vasculopathy, and a decrease in the barrier function of the placenta due to inflammatory processes occurring in it in presence of SARS-CoV-2 infection [13–14].

In the cases reported by S. Verma et al., children of mothers with COVID-19 were born with varying degrees of prematurity and required rather long-term intensive care [15].

M.N. Bangash et al. have shown that COVID-19 may cause hepatocyte damage, although other authors have argued that liver damage is directly related to virus-induced cytotoxic T cells and a dysregulated innate immune response or drug toxicity. Further, researchers have noted the dominance of the T-helper type 2 (Th2) system in pregnant women, which reliably provides protection to the fetus and makes the mother vulnerable to viral infections that are more effectively restrained by the Th1 system [16].

Some authors have reported on adverse pregnancy outcomes in women with COVID-19 and determined complications in women and the infants they gave birth to; however, a cause-and-effect relationship with the infection remains unclear. Such complications include very early premature birth at week 22 of gestation, delivery before 36.6 weeks, preterm rupture of membranes, intrauterine growth retardation, low birth weight, intrauterine fetal distress, feeding intolerance, hypoxia and asphyxia, pneumonia and respiratory distress syndrome, and stillbirth [17].

W. Naves do Amaral et al. have reviewed 958 cases of children born to COVID-positive mothers; none of the children had any symptoms of SARS-CoV-2 infection at birth, and all newborns tested negative for SARS-CoV-2 [18].

Additionally, M. Zamaniyan et al. have discovered viral RNA in the amniotic fluid during a cesarean section performed at week 33 of pregnancy. The newborn had a positive reaction to viral RNA, but the disease was completely asymptomatic [19].

M. Mirbeyk et al. have investigated 38 cases that included 301 newborns from mothers with confirmed COVID-19, including 209 full-term and 92 preterm children. Four of the newborns born alive to mothers with COVID-19 were in critical condition [20]. One of them was diagnosed with tachycardia followed by gastric bleeding and refractory shock, which led to death. Another severe case was a premature newborn from a mother who was diagnosed with severe COVID pneumonia [21]. The newborn was extubated and subsequently discharged without any complications.

CONCLUSION

The literature review resulted in the following conclusions:

- 1. Among pregnant women with COVID-19, the incidence of preeclampsia, preterm birth, and surgical delivery is highest.
- Intrauterine vertical transmission of infection has not been confirmed.
- The incidence of complications in newborns corresponds to the general population indicators.
- 4. COVID-19 can lead to fatal outcomes in pregnant women and their fetuses.

The incidence of coronavirus infection among pregnant women has now significantly decreased but has not been eliminated completely, and asymptomatic cases are increasingly being detected. Therefore, considering modern scientific

data, further study on the impact of COVID-19 on the course and outcome of pregnancy, including the search for optimal methods of delivery and possible measures for the prevention and treatment of coronavirus infection in pregnant women, is critical.

ADDITIONAL INFO

Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. The authors declare the compliance of their authorship according to the international ICMJE criteria. L.V. Shchegolikhina — research concept and design, data collection and processing, text writing; A.N. Zainetdinova — research concept and design, editing; L.D. Amirova — data collection and processing, editing.

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