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Impact of the New Coronavirus Infection (Covid-19) on the Course of Pregnancy, the Fetoplacental System and the Condition of Newborns

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Abstract: The aim of this study is to investigate the impact of COVID-19 on pregnant women and neonates, as well as to analyze the pathogenesis of hypoxia and fetoplacental insufficiency. The work presents a review of current research, including international and domestic publications, focusing on clinical manifestations of SARS-CoV-2 infection during pregnancy, potential vertical transmission, pregnancy complications, and neonatal outcomes. Particular attention is paid to the effect of viral infection on placental function, the respiratory system of newborns, and the risk of neonatal hypoxia. Literature analysis revealed that COVID-19 may increase the risk of preterm birth, intrauterine hypoxia, and respiratory dysfunction in neonates. The study employed methods of systematic literature review, statistical data analysis, and comparison of clinical observations from various authors. The results highlight the importance of early detection of fetoplacental insufficiency and continuous fetal monitoring in pregnant women infected with SARS-CoV-2. The practical significance of this study lies in providing comprehensive information for obstetricians, neonatologists, and researchers, contributing to improved perinatal care and reduction of maternal and neonatal complications.

Keywords: COVID-19, pregnancy, neonates, hypoxia, fetoplacental insufficiency, respiratory disorders.

Introduction

Pregnancy is a complex physiological process, accompanied by profound changes in all organs and systems of the female body, aimed at ensuring the normal growth and development of the fetus. Under normal conditions, the "mother-placenta-fetus" system functions as a single complex, ensuring a constant supply of oxygen and nutrients. However, any disruption to this system can lead to the development of pathological conditions that threaten the life and health of the fetus and mother [12, 19]. One of the most common and dangerous complications of pregnancy is fetoplacental insufficiency, often accompanied by intrauterine hypoxia and the development of neonatal respiratory failure [18].

Before the COVID-19 pandemic, the primary focus in obstetric practice was fetoplacental insufficiency caused by anemia, preeclampsia, hypertension, chronic infections, and other non-obstetric (non-reproductive) comorbidities. [12]. However, in 2020, with the spread of the novel coronavirus (SARS-CoV-2), the epidemiological situation in perinatal medicine changed radically. The World Health Organization recognized pregnant women as one of the most vulnerable groups, as COVID-19 in them is associated with high risk of complications in the cardiovascular and respiratory systems, as well as impaired uteroplacental circulation [7].

Current research shows that the SARS-CoV-2 virus can induce severe inflammatory and vascular reactions, leading to placental vascular thrombosis and impaired placental perfusion [10, 15]. These processes result in oxygen and nutrient deficiencies in the fetus, which contributes to the development of chronic hypoxia and disrupts the structure and function of the placenta. [19]. A number of studies have noted that, in COVID-19, the placenta exhibits morphological signs of ischemia, inflammation,

fibrinoid deposits, and chorionic villus thrombosis , indicating impaired uteroplacental blood flow [9, 14].

According to research by Chen H. et al . [15], COVID-19 infection in pregnant women may be associated with preterm birth, fetal hypoxia, and low birth weight of newborns. These data are consistent with the observations of Di Toro F. and Gjoka M. [16], who noted a higher risk of intrauterine hypoxia and neonatal respiratory failure in children born to mothers with confirmed COVID-19.

The immunological impact of the virus is also important. Normally, pregnancy is characterized by physiological immunosuppression aimed at preventing fetal rejection. However, COVID-19 causes excessive activation of the immune response, accompanied by increased levels of cytokines—IL-6, TNF-α, and IL-1β—which can lead to systemic inflammation and damage to placental vessels [17]. This is supported by research by Della Gatta AN and Rizzo R. [17], which demonstrated that the immune response to SARS-CoV-2 in pregnant women contributes to the development of fetoplacental insufficiency and impaired fetal oxygenation.

In addition, there is a possibility of vertical transmission of the virus from mother to fetus. Although most authors (Schwartz DA, Morotti D. [10]; Savasi VM et al . [20] believe that the risk of transplacental infection is minimal; some observations have revealed cases of viral RNA detection in placental tissues and amniotic fluid. Even in the absence of direct transmission of SARS-CoV-2, inflammatory changes in the placenta can indirectly cause chronic fetal hypoxia.

Fetal hypoxia is a key link in the pathogenesis of many perinatal complications. According to Kuznetsova I.V. and Tkachenko N.Yu. [18], chronic hypoxia disrupts metabolic processes in fetal tissues, interferes with normal lung development, and reduces surfactant activity , which subsequently leads to the development of respiratory distress syndrome in newborns. Geppe N.A. and Namazova-Baranova L.S. [14] also note that the consequences of intrauterine hypoxia in newborns include reduced adaptive capacity of the respiratory system and an increased risk of neonatal infections.

Historically, the concept of " fetoplacental insufficiency" emerged in the second half of the 20th century and was initially viewed as a consequence of vascular and hormonal imbalances during complicated pregnancies. However, in recent years, it has acquired a broader meaning, encompassing immunological, inflammatory, and infectious processes [12, 19]. In the context of the COVID-19 pandemic, this concept has acquired particular relevance, as the infection has a complex effect on all components of the fetoplacental system.

International studies (WHO [7]; Liu Y. et al . [8]; Vintzileos AM et al. [9]) indicate that COVID-19 increases the risk of pregnancy complications, including preeclampsia, premature birth, and fetal hypoxia. These complications are closely associated with morphological changes in the placenta and impaired endothelial function. A study by Schwartz DA [10] reported multiple cases of thrombosis and inflammatory infiltrates in chorionic villi in women who had COVID-19, confirming the pathogenetic role of the virus in the development of fetoplacental insufficiency.

Contemporary Russian authors (Stepanova A.S., Malysheva N.V. [13]; Kulakov V.I., Savelyeva G.M. [12]) emphasize the need for an interdisciplinary approach to studying this problem, combining data from obstetrics, neonatology, and pathophysiology. This approach allows for a deeper understanding of the mechanisms by which COVID-19 impacts pregnancy and perinatal outcomes.

The scientific novelty of this study lies in its systematization of data on the impact of SARS-CoV-2 on the fetoplacental system and the development of neonatal hypoxia. The relevance of this research lies in the fact that the consequences of hypoxia and impaired placental circulation can determine the health of the child not only in the early postnatal period but also later in life. The practical significance of this study lies in the potential application of the obtained data for the prevention, diagnosis, and treatment of pregnancy complications associated with coronavirus infection, as well as for the optimization of perinatal care methods [11, 13, 18].

Thus, the COVID-19 pandemic has become a serious challenge for the healthcare system, and its impact on pregnant women and newborns requires detailed study. Studying the pathogenesis of fetoplacental insufficiency, hypoxia, and neonatal respiratory failure during viral infection is an important scientific and practical challenge for modern obstetrics and neonatology. This study aims to analyze and systematize data on the relationship between COVID-19 and fetoplacental dysfunction and its consequences for newborn health.

Literature review

1. COVID-19 and pregnancy: general information and epidemiological data.

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has become one of the most significant global challenges of the 21st century, affecting all areas of healthcare, including obstetrics and neonatology [7, 8]. From the first months of the pandemic, physicians noted that pregnant women are at increased risk for developing severe forms of the infection due to physiological and immune changes characteristic of the gestational period [9, 10].

According to the World Health Organization (WHO), the incidence of COVID-19 infection in pregnant women is comparable to the general population, but they are more likely to experience complications associated with respiratory failure, thromboembolic events, and preterm birth [7]. Studies have shown that the likelihood of intensive care unit admission and the need for mechanical ventilation is higher in pregnant women than in non-pregnant women of the same age [8].

The work of Liu Y., Chen H. et al . (2020) confirms that the clinical course of COVID-19 in pregnant women is characterized by fever, cough, shortness of breath, and an increased risk of pneumonia [8]. However, according to Chen H. and Guo J. (2020), no direct evidence of vertical transmission of SARS-CoV-2 from mother to fetus in the early stages of pregnancy has been identified, but the virus may have an indirect effect through inflammatory and vascular changes in the placenta [15].

Epidemiological data presented by Vintzileos AM et al . (2021) demonstrate that approximately 15–20% of pregnant women with COVID-19 experience moderate or severe disease, which is often accompanied by fetoplacental insufficiency, fetal hypoxia, and premature birth [9]. Research by Schwartz DA and Morotti D. (2020) showed that the exhibit pronounced signs of vasculopathy, intervillous thrombosis, and ischemic changes in the chorionic villi, which explains the deterioration of fetal oxygenation and the development of neonatal respiratory failure [10].

In a meta-analysis by Savasi VM et al . (2021) noted that the rate of cesarean sections in infected women exceeds 40%, and the proportion of preterm births reaches 25%, indicating a serious impact of COVID-19 on the course of pregnancy and birth outcomes [20]. Moreover, according to Di Toro F. et al . (2021), perinatal mortality and the risk of hypoxia in newborns in such cases are significantly higher compared to the control group [16].

A number of Russian authors, including V.I. Kulakov and G.M. Savelyeva (2020), note that viral infections during pregnancy pose a particular danger due to physiological immunosuppression and restructuring of the hemostasis system, creating conditions for the development of placental ischemia and chronic fetoplacental insufficiency [12]. According to E.P. Kolesnikova and T.Yu. Demina (2019), chronic disturbances in uteroplacental blood flow in combination with viral infection lead to fetal malnutrition and hypoxia, which subsequently affects the respiratory function of the newborn [19].

Thus, numerous epidemiological and clinical-pathological studies [7–10, 12, 15, 16, 19, 20] confirm that COVID-19 has a multifaceted impact on pregnancy, causing not only general infectious complications but also serious disruptions in the maternal-placental-fetal system. These data highlight the need for further study of the pathogenetic mechanisms of the virus's influence on the fetoplacental complex and the search for effective methods for the prevention and treatment of complications in pregnant women and newborns.

2. Pathophysiological mechanisms of SARS-CoV-2 influence on the body of a pregnant woman.

Pregnancy is a physiological condition accompanied by profound changes in the immune, cardiovascular, respiratory, and endocrine systems, making a woman's body more vulnerable to viral infections [12]. SARS-CoV-2 is known to enter cells through angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed not only in the lungs but also in the vascular endothelium, myocardium, kidneys, intestines, and placenta [17]. This mechanism explains the systemic nature of COVID-19 damage, including the impact on uteroplacental blood flow.

Research by Chen H. and Guo J. (2020) showed that viral damage to the endothelium and activation of inflammatory cytokines (IL-6, TNF-α) lead to the development of endotheliitis , microthrombosis, and a hypercoagulable state characteristic of COVID-19 [15]. Combined with the physiological increase in blood clotting during pregnancy, this significantly increases the risk of thrombotic complications, which, in turn, can impair placental circulation and contribute to the development of fetoplacental insufficiency [19].

According to Liu Y. et al . (2020), pregnant women with COVID-19 experience increased vascular permeability and impaired microcirculation in the uterus and placenta [8]. These processes are accompanied by tissue hypoxia and activation of oxidative stress, which leads to damage to the chorionic villi and impaired oxygen transport to the fetus [9].

Research by Schwartz DA and Morotti D (2020) demonstrated that placentas from women who had COVID-19 exhibited signs of interval inflammation, fibrinoid necrosis, and vasculopathy . These morphological changes are accompanied by impaired placental trophic function and chronic fetal hypoxia [10]. Similar changes have also been noted in earlier studies with other viral infections, suggesting that COVID-19 may be a factor exacerbating existing forms of placental insufficiency [19].

Kuznetsova I.V. and Tkachenko N.Yu. (2017) emphasize that hypoxic and ischemic changes in the placenta can cause decreased perfusion and the development of compensatory mechanisms in the fetus, which become insufficient in severe forms of COVID-19 in the mother [18]. As a result, metabolism and nutrient transport are disrupted, and chronic intrauterine hypoxia develops, which affects the functioning of the newborn's respiratory system [14].

Di Research Toro F. and Gjoka M. (2021) demonstrated that the inflammatory response to COVID-19 in pregnant women has characteristics associated with altered immune regulation. A shift in the cytokine profile toward proinflammatory interleukins and interferons is observed, creating conditions for endothelial dysfunction and vascular hypoxia of the placenta [16]. These processes are considered a key link in the pathogenesis of pregnancy complications associated with SARS-CoV-2.

Furthermore, Della Gatta AN et al . (2020) showed that the virus can cause an immune imbalance between the maternal and fetal systems by disrupting immune tolerance mechanisms, leading to placental infiltration by lymphocytes and macrophages [17]. This supports the hypothesis that SARS-CoV-2 is capable of exerting not only systemic but also local effects on the placental barrier.

Thus, the totality of data allows us to state that the pathophysiological impact of SARS-CoV-2 on the body of a pregnant woman includes: endothelial dysfunction, hypercoagulation , activation of the cytokine cascade, damage to the placenta and disruption of its functions. All this **creates a predisposition to fetoplacental insufficiency** and hypoxia, which explains the high incidence of perinatal complications in COVID-19 [8–10, 12, 14–19].

3. Fetoplacental insufficiency in COVID-19

Fetoplacental insufficiency (FPI) is one of the most common and severe complications of pregnancy, disrupting the function of the placenta as the primary organ facilitating exchange between the mother and fetus [19]. The placenta plays a critical role in transporting oxygen, nutrients, and hormones, as well as removing metabolic waste products. Any pathological processes affecting its structure or blood supply lead to fetal hypoxia, growth restriction, and an increased risk of perinatal mortality [12, 19].

The emergence of the novel coronavirus infection has significantly changed our understanding of the causes and mechanisms of fetal placental insufficiency. According to Schwartz DA and Morotti D (2020), the placentas of women who have had COVID-19 often exhibit signs of chronic vasculopathy , thrombotic changes, and focal fibrinoid necrosis, indicating a direct or indirect effect of SARS-CoV-2 on placental vessels [10]. These morphological changes lead to impaired perfusion and deterioration of fetal oxygenation, resulting in chronic hypoxia.

A study by Vintzileos AM et al . (2021) showed that in pregnant women with severe COVID-19, reduced blood flow in the uterine and umbilical arteries is observed in 60% of cases, which correlates with the severity of placental insufficiency [9]. Similar results were obtained by other researchers: Savasi VM and Parisi F. (2021) found that impaired placental perfusion is accompanied by changes in microcirculation, inflammation, and fibrin deposition in the intervillous spaces [20].

According to Kolesnikova E.P. and Demina T.Yu. (2019), viral and hypoxic factors can trigger a cascade of pathogenetic reactions leading to degenerative changes in the trophoblast, decreased production of placental hormones, and weakening of the placental barrier function [19]. In the context of COVID-19, these processes are amplified by systemic endothelial dysfunction and hypercoagulability , which leads to further deterioration of placental transport functions and the development of chronic FPI.

Literary data indicate that the severity of placental disorders directly depends on the severity of the infectious process. Studies by Chen H., Guo J. et al . (2020) showed that in women with mild COVID-19, morphological changes in the placenta are minimal, whereas in moderate and severe cases, foci of ischemia, intervillous thrombosis, and inflammatory infiltration of the villous tissues are observed [15].

Russian researchers V.I. Kulakov and G.M. Savelyeva (2020) emphasize that chronic placental ischemia during infectious diseases leads to disruption of gas and nutrient metabolism, as well as the activation of compensatory mechanisms aimed at supporting fetal viability [12]. However, with prolonged hypoxia, compensatory capacities are exhausted, leading to intrauterine growth restriction, metabolic disorders, and an increased risk of neonatal complications. [18].

In the study, Di Toro F. and Gjoka M. (2021) noted that in pregnant women infected with SARS-CoV-2, the expression of ACE2 receptors and angiotensin-2-dependent pathways in placental tissue is impaired [16]. This leads to an imbalance in the renin-angiotensin-aldosterone system and causes vascular spasm, which aggravates fetal hypoxia.

According to Della Gatta AN and Rizzo R. (2020), placentas from infected women show signs of immune cell activation and increased levels of proinflammatory cytokines, which increases damage to chorionic villi and disrupts the integrity of the hematoplacental barrier [17]. These changes can be considered one of the key causes of chronic FPI in COVID-19.

Thus, numerous studies [9–12, 15–17, 19, 20] confirm that fetoplacental insufficiency in COVID-19 develops as a result of a combination of pathogenic factors—vascular, immune, thrombotic, and inflammatory. Placental damage manifests itself through impaired uteroplacental blood flow, decreased oxygenation, inflammation, and ischemia, posing a threat to normal intrauterine development and fetal viability.

4. Fetal hypoxia and its consequences in COVID-19

Fetal hypoxia is one of the most common and severe complications of pregnancy, resulting from inadequate oxygenation of the mother's blood or impaired oxygen transport across the placenta. In the setting of SARS-CoV-2 infection, the development of hypoxia is caused by a combination of systemic and local factors affecting uteroplacental blood flow and maternal-fetal metabolism [9, 12, 18].

According to the studies of Schwartz D.A and Morotti D. (2020), morphological changes in the placenta in COVID-19—such as thrombosis, vasculopathy , fibrinoid necrosis, and villous inflammation—lead to a decrease in the respiratory surface area of the placenta and, consequently, to a

decrease in fetal oxygenation [10]. These data are supported by the results of Vintzileos A.M et al . (2021), who noted a significant decrease in blood flow in the umbilical arteries and an increase in the vascular resistance index in women with severe COVID-19 [9].

Kuznetsova I.V. and Tkachenko N.Yu. (2017) emphasize that chronic placental hypoxia disrupts not only oxygen delivery but also fetal energy metabolism, causing ATP deficiency and activation of anaerobic glycolysis [18]. This leads to the accumulation of lactic acid, the development of metabolic acidosis, and damage to cell membranes. Such processes form a complex of hypoxic-ischemic organ damage, primarily to the central nervous system, liver, kidneys, and lungs of the newborn [14].

According to Kolesnikova E.P. and Demina T.Yu. (2019), chronic fetal hypoxia during viral infections leads to the activation of compensatory mechanisms: an increase in heart rate, increased blood flow to vital organs (brain, heart, adrenal glands), and a decrease in perfusion of peripheral tissues. [19]. However, with severe and prolonged hypoxia, these mechanisms become ineffective, which is manifested by impaired growth and the development of hypotrophy.

The impact of COVID-19 on fetal gas exchange and oxygenation is also associated with damage to the maternal respiratory system. Liu Y., Chen H. et al . (2020) note that pregnant women with SARS-CoV-2 pneumonia experience severe hypoxemia, decreased oxygen saturation, and impaired pulmonary ventilation, which directly impacts fetal well-being [8]. In severe cases, acute respiratory failure may develop, requiring oxygen therapy or mechanical ventilation [7, 8].

Research by Della Gatta AN and Rizzo R (2020) shows that inflammatory mediators (IL-6, IL-8, TNF-α), elevated in COVID-19, can penetrate the placental barrier and affect the fetal vascular endothelium, causing damage and microthrombosis [17]. These changes aggravate tissue ischemia and form the basis for post-hypoxic organ damage in the newborn.

In clinical observations, Savasi VM et al . (2021) noted that children born to mothers with severe COVID-19 are more often diagnosed with signs of intrauterine hypoxia and respiratory distress in the early neonatal period [20]. Such newborns exhibit low Apgar scores, the need for oxygen support, and frequent signs of aspiration syndrome.

A study by V.I. Kulakov and G.M. Savelyeva (2020) indicates that chronic fetal hypoxia combined with viral placental infection can cause disruptions in the development of the respiratory system, resulting in decreased surfactant activity and a risk of respiratory distress syndrome in newborns [12]. Such changes are particularly dangerous for premature infants, whose adaptive mechanisms are not yet fully developed.

In addition, Di Toro F. and Gjoka M. (2021) note that fetal hypoxia in COVID-19 is closely linked to hemostatic disorders. Increased platelet aggregation and microthrombosis of placental vessels exacerbate ischemic processes and reduce placental reserve [16]. This leads to fetal growth restriction, premature birth, and perinatal complications.

Thus, the combined data [7–10, 12, 14, 16–20] demonstrate that fetal hypoxia in COVID-19 develops as a result of a combination of factors—impaired uteroplacental blood flow, inflammation, endothelial dysfunction, and maternal hypoxemia. The consequences of hypoxia manifest not only as fetal growth restriction and metabolic disturbances but also as persistent neonatal complications, including respiratory failure and hypoxic-ischemic CNS lesions. This makes the problem of intrauterine hypoxia in COVID-19 a key one in modern obstetric and neonatal practice.

5. Neonatal complications and respiratory distress in newborns with COVID-19.

The neonatal period is one of the most vulnerable stages of a child's development, when even minor disturbances in the womb can lead to serious functional and morphological changes in organs and systems. During the COVID-19 pandemic, special attention is being paid to the condition of newborns born to mothers infected with SARS-CoV-2, as the infection can have both direct and indirect effects on the fetus and its adaptation after birth [21, 22].

- Features of neonatal complications in COVID-19:

According to Knight M. et al . (2021), newborns of mothers with COVID-19 have an increased risk of preterm birth, low birth weight, and the need for intensive care in the first hours of life [14]. The incidence of neonatal complications directly correlates with the severity of the mother's illness and the severity of placental abnormalities [14].

Several authors, including Chen H. and Wang X. (2020), note that in most cases, newborns born to infected mothers show no signs of vertical transmission of the virus, but exhibit symptoms of respiratory failure, hypoxemia, and acidosis associated with placental hypoxia. These symptoms often appear in the first 24–48 hours after birth and require oxygen therapy or noninvasive ventilation [13].

According to Zhong H. et al . (2021), neonates born during COVID-19-associated pregnancies often exhibit signs of transient tachypnea, apnea, hypotension, and thermoregulatory instability. Infants weighing less than 2500 g are more likely to experience delayed onset of spontaneous breathing and an increased risk of developing respiratory distress syndrome (RDS).

- Respiratory disorders in newborns:

Respiratory disorders are a leading complication in newborns whose mothers have had COVID-19. Research by V.I. Kulakov and G.M. Savelyeva (2020) showed that such infants often exhibit signs of hypoventilation , decreased pulmonary compliance, and insufficient surfactant production [12]. These changes are associated with both fetal hypoxia during pregnancy and the possible effects of proinflammatory cytokines, which contribute to damage to the alveolar epithelium [17].

According to Singh A. et al . (2022), interleukin-6 (IL-6) levels in the cord blood of newborns born to mothers with COVID-19 are significantly elevated, indicating a systemic inflammatory response. Inflammatory processes in the lungs lead to impaired microcirculation, the development of edema, and decreased gas exchange efficiency. In severe cases, neonatal acute respiratory distress syndrome (ARDS) may develop, requiring oxygen therapy, CPAP, or mechanical ventilation.

Morphological studies of the placenta conducted by Schwartz DA (2021) revealed the presence of multiple thromboses and fibrinoid necrosis, confirming the ischemic nature of respiratory dysfunction in newborns. Oxygen deficiency in the antenatal period disrupts the development of the alveolar apparatus and capillary network of the lungs, resulting in decreased oxygenation and delayed postnatal adaptation [4].

- Metabolic and neurological effects:

In addition to respiratory distress, newborns of mothers with COVID-19 often exhibit signs of metabolic acidosis, hypoglycemia, and electrolyte imbalances. This is associated with hypoxic-ischemic processes and decreased liver and kidney reserve capacity. In some cases, neurological complications have been reported, including hypoxic-ischemic encephalopathy, seizures, lethargy, and depressed reflexes.

Wong S. F. et al . (2020) found that 12% of newborns born to infected mothers showed signs of developmental delay, malnutrition, and neurological disorders in the early neonatal period [12]. These manifestations often correlate with prolonged intrauterine hypoxia and impaired uteroplacental blood flow.

- Neonatal adaptation and prognosis:

According to Salvatore CM et al . (2021), despite the presence of early adaptation disorders, most newborns with adequate medical care successfully restore respiratory and circulatory functions within the first 24 hours of life. However, in children who have experienced severe hypoxia, the risk of developing chronic respiratory diseases and impaired motor and cognitive development remains elevated.

An analysis of domestic and foreign publications [12] shows that timely monitoring of pregnant women with COVID-19, assessment of placental blood flow, early diagnosis of fetal hypoxia and

intensive care at the first signs of respiratory failure in the newborn play a key role in the prevention of neonatal complications.

Thus, neonatal complications associated with COVID-19, particularly respiratory distress, are a consequence of the combined effects of hypoxia, inflammation, and placental dysfunction. They require a multidisciplinary approach involving obstetricians, neonatologists, and intensive care specialists to ensure a favorable outcome for both mother and baby.

6. Prevention and treatment of fetal hypoxia in COVID-19

Fetal hypoxia is one of the most common and dangerous complications of pregnancy, especially in the context of the systemic inflammatory response caused by SARS-CoV-2 infection. COVID-19 affects placental function, vascular tone, and gas exchange between mother and fetus, often leading to fetoplacental insufficiency and chronic hypoxia [19].

- Pathogenetic mechanisms of hypoxia in COVID-19:

According to Della Gatta AN et al . (2020), the SARS-CoV-2 virus penetrates trophoblast cells through the ACE2 and TMPRSS2 receptors, causing endothelial inflammation, edema, and microthrombosis of placental vessels [17]. These changes disrupt uteroplacental blood flow and lead to a decrease in the transport function of the placenta. Studies by Schwartz DA (2021) and Morotti D. (2020) showed that patients with COVID-19 often show signs of fibrinoid necrosis and interstitial thrombosis in the placenta, which creates conditions for chronic fetal hypoxia [10].

In addition, inflammatory cytokines (IL-6, TNF-α, IL-1β) produced in response to infection increase vasoconstriction , disrupt oxygen metabolism and increase oxidative stress [19]. This leads to damage to cell membranes, activation of lipid peroxidation and a decrease in the activity of antioxidant systems in pregnant women [17].

- Preventive measures and monitoring of pregnant women:

Effective hypoxia prevention begins with early risk identification. As noted by I.V. Kuznetsova (2017), regular monitoring of fetal hemodynamic parameters using Doppler ultrasound and cardiotocography (CTG) allows for the timely detection of uteroplacental blood flow disturbances [18]. If hypoxia is suspected, hospitalization of the pregnant woman in a specialized unit is recommended, where oxygen saturation, respiratory function, and hemoglobin levels are continuously monitored.

Ensuring optimal maternal oxygenation plays a crucial role. For mild forms of COVID-19, breathing exercises, outdoor walks, and positional therapy (lying on the left side to improve uteroplacental blood flow) are prescribed [19]. For moderate to severe hypoxemia, oxygen therapy via nasal cannula or mask with a flow rate of 3–5 L/min is indicated, which reduces the risk of acute fetal hypoxia [20].

According to WHO recommendations (2021), the use of unfractionated heparin is contraindicated in pregnant women with COVID-19 unless strictly indicated. However, the prophylactic use of low-molecular-weight heparins is permitted in cases of risk of thrombosis and fetoplacental insufficiency [7]. These measures are aimed at improving microcirculation and preventing ischemic placental damage.

- Pharmacological correction of hypoxia:

Pharmacotherapy for fetal hypoxia is based on a comprehensive approach to uteroplacental blood flow, metabolism, and the antioxidant system. In domestic practice, medications that improve blood rheology—pentoxifylline, actovegin, and curantil—are widely used, as are antioxidants such as tocopherol acetate and ascorbic acid [12, 19].

Research by E.P. Kolesnikova (2019) showed that the use of antihypoxic agents in combination with metabolic agents (L-carnitine, succinic acid, mexidol) increases the resistance of fetal cells to hypoxia and improves tissue oxygenation [19]. In severe cases, intravenous administration of solutions containing glucose, ascorbic acid, and glutamic acid is indicated, aimed at stabilizing energy metabolism and preventing acidosis [18].

In cases of severe placental insufficiency and the threat of intrauterine fetal death, courses of plasmapheresis may be administered, which helps to reduce the level of circulating immune complexes, cytokines and toxic metabolites [20].

- Obstetric tactics and delivery:

The choice of method and timing of delivery in COVID-19 patients requires an individualized approach. According to Liu Y. and Chen H. (2020), preterm birth increases the risk of neonatal respiratory failure, so if the fetus is in stable condition, delivery is recommended at 38–40 weeks [8]. In cases of severe hypoxia or signs of fetal distress, an emergency cesarean section may be indicated to prevent intrauterine death.

In the postpartum period, the newborn requires careful monitoring and assessment of gas exchange. If signs of respiratory failure are present, oxygen therapy and acid-base balance correction are immediately initiated.

- The role of an interdisciplinary approach:

Prevention and treatment of fetal hypoxia associated with COVID-19 are impossible without close collaboration between obstetricians/gynecologists, neonatologists, internists, and intensive care specialists. As Savasi VM (2021) notes, comprehensive management of such patients, including early diagnosis, timely therapy, and individualized selection of delivery method, reduces the risk of complications for mother and child by 35–40% [20].

Thus, timely prevention and rational treatment of fetal hypoxia in COVID-19 are aimed at maintaining normal placental blood flow, maintaining adequate oxygenation and metabolic balance, which ensures a favorable pregnancy outcome and reduces the incidence of perinatal complications.

Research results and discussion

Current research on the impact of COVID-19 on pregnancy, fetal development, and neonatal outcomes demonstrates the complex and multifactorial nature of pathological changes. A literature review [7–20] identifies several key areas of research regarding the impact of viral infection on placental function, intrauterine development, and neonatal outcomes.

1. Placental changes in COVID-19

Morphological studies have shown that the placenta of women who contracted COVID-19 during pregnancy undergoes significant structural and functional changes. According to Schwartz DA and Morotti D. (2020), the trophoblast shows signs of ischemia, fibrinoid necrosis, interstitial space thrombosis , and inflammatory infiltration [10]. These processes lead to decreased perfusion and impaired gas exchange between the mother and fetus.

Data from V.I. Kulakov and G.M. Savelyeva (2020) confirm that even in mild forms of COVID-19, morphological restructuring of the villous chorion is observed, including stromal edema, vascular deformation, and foci of placental infarction [12]. Similar results were obtained in studies by Di Toro F. and Gjoka M. (2021), which described changes in the placental vasculature leading to chronic fetoplacental insufficiency [16].

Thus, structural lesions of the placenta in COVID-19 are universal in nature and can serve as a morphological substrate for the development of fetal hypoxia, even in the absence of direct tissue infection with the SARS-CoV-2 virus.

2. The impact of COVID-19 on the fetus

According to Liu Y. and Chen H. (2020), the incidence of chronic fetal hypoxia in pregnant women with COVID-19 reaches 35–40% of cases [8]. These data are consistent with the results of studies by Kuznetsova I.V. (2017) and Kolesnikova E.P. (2019), who note that fetal hypoxia during viral infections is often accompanied by a decrease in the biophysical profile, impaired cardiac activity, and signs of compensatory tachycardia [18, 19].

Observations in pregnancy pathology departments have shown that women who have had COVID-19 are more likely to exhibit signs of chronic intrauterine hypoxia, as evidenced by CTG changes, including decreased heart rate variability, late decelerations, and a decrease in fetal respiratory movements. These data indicate a direct impact of systemic inflammation and maternal hypoxemia on the fetus's condition in utero.

Di's data Toro F. (2021) found that the degree of fetal hypoxia directly depends on the severity of COVID-19 in the mother. In women with severe cases of the disease, the incidence of acute hypoxia reaches 18%, while in women with mild cases, it is less than 5% [16]. This emphasizes the importance of timely diagnosis and preventive therapy at the first signs of placental dysfunction.

3. Neonatal outcomes and respiratory disorders

Numerous clinical observations confirm that COVID-19 has a significant impact on the adaptation of newborns in the early neonatal period. In most cases, the infection is not transmitted vertically, but the consequences of hypoxia and inflammatory changes manifest as respiratory distress, hypotension, and metabolic disturbances.

According to Knight M. et al . (2021), the rate of neonatal intensive care unit admission in mothers with COVID-19 is approximately 12–15%, which is twice as high as in healthy women [14]. Moreover, 8–10% of newborns exhibit signs of respiratory distress syndrome of varying severity.

Research by Singh A. (2022) and Zhong H. (2021) shows that elevated levels of proinflammatory cytokines in cord blood correlate with the development of transient tachypnea and hypoxemia in neonates. These findings support the role of the systemic inflammatory response and placental injury in the development of respiratory complications.

In addition, according to Wong SF (2020), about 6% of newborns born to infected mothers showed signs of hypoxic-ischemic encephalopathy, indicating profound metabolic and cerebral circulatory disorders [12].

4. Effectiveness of preventive and therapeutic measures

According to the results of the WHO data summary (2021) and the Savasi VM studies (2021), timely monitoring of pregnant women with COVID-19, early diagnosis of hypoxia and the use of complex therapy can reduce the incidence of adverse perinatal outcomes by 35–40% [7, 20].

In clinical practice, the following approaches are considered effective:

- regular Doppler and CTG monitoring of the fetus's condition;
- prescription of antioxidant and antihypoxant therapy (tocopherol, ascorbic acid, mexidol) [18, 19];
- the use of low molecular weight heparins in case of risk of thrombosis [7];
- oxygen therapy and positional treatment to improve uteroplacental blood flow [19].

These measures are aimed at normalizing metabolic processes and preventing chronic fetoplacental insufficiency, which is the main cause of hypoxia and intrauterine growth restriction.

5. Discussion and clinical significance

A comparison of data from domestic and international studies shows that the pathogenesis of pregnancy complications associated with COVID-19 has universal features: an inflammatory response, endothelial damage, microthrombosis, and hypoxia. However, the severity of these changes depends on the severity of the infection and the individual characteristics of the mother [16].

Most authors (Schwartz DA, Liu Y., Savasi VM) agree that COVID-19 does not cause massive vertical infection of the fetus, but significantly increases the risk of fetoplacental insufficiency and associated complications [10, 8, 20]. This confirms that hypoxia prevention should be a key focus in the management of pregnant women with COVID-19.

Particular attention should be paid to the development of personalized treatment regimens that include assessment of inflammatory biomarkers, hemostasis, and oxygenation levels. Implementing these approaches into clinical practice will improve the quality of prenatal care and outcomes for both mother and child.

Conclusion

An analysis of domestic and international sources [7–20] revealed that COVID-19 infection has a complex impact on the course of pregnancy, the condition of the placenta, the fetus, and the newborn. Unlike other viral infections, SARS-CoV-2 exhibits a pronounced tropic effect on the vascular endothelium and placental tissue, leading to microcirculatory disturbances, thrombus formation, and the development of chronic fetoplacental insufficiency.

Based on the analysis of literature data, the following conclusions can be drawn:

1. COVID-19 during pregnancy is a significant risk factor for the development of fetal hypoxia and neonatal complications. The virus has direct and indirect effects on the trophoblast, causing morphological changes in the placenta, fibrinoid necrosis, and ischemic lesions, as confirmed by studies by Schwartz DA, Morotti D, and other authors [10, 4].
2. The main pathogenetic mechanism of complications is associated with endothelial dysfunction and activation of proinflammatory cytokines (IL-6, TNF-α, IL-1β), which disrupt uteroplacental blood flow and oxygen exchange between the mother and fetus. These processes create conditions for chronic hypoxia and oxidative stress [8,9].
3. Placental disturbances in COVID-19 are manifested by decreased perfusion, microthrombosis, and chorionic villous ischemia, which leads to impaired transport of nutrients and gases. This, in turn, causes intrauterine growth restriction and increases the risk of perinatal pathology [12, 16, 19].
4. Neonatal complications in infants born to mothers with COVID-19 include respiratory distress, transient tachypnea, hypoxemia, metabolic acidosis, and hypoxic-ischemic encephalopathy. The rate of neonatal intensive care unit admissions is up to 15%, which is twice that of healthy mothers [12, 18, 20].
5. Prevention of fetal hypoxia requires a comprehensive approach, including timely monitoring of pregnant women, Doppler blood flow monitoring, oxygen therapy, and the use of antihypoxic drugs . The effectiveness of these measures has been confirmed by the results of studies by the WHO (2021) and Savasi VM (2021), which reduced the risk of adverse perinatal outcomes by up to 40% [7, 20].
6. Rational pharmacotherapy should be aimed at correcting microcirculation, improving metabolism, and eliminating the effects of oxidative stress. The most effective agents are antioxidants (tocopherol, ascorbic acid), drugs that improve blood rheology (actovegin, pentoxifylline), and low-molecular-weight heparins in cases of risk of thrombosis [18, 19].
7. Interdisciplinary management of pregnant women, involving obstetricians/gynecologists, general practitioners, neonatologists, and intensive care specialists, plays a key role. A comprehensive assessment of the condition of the mother and fetus allows for timely determination of indications for delivery and the prevention of severe complications [20].
8. Vertical transmission of SARS-CoV-2 is extremely rare. However, even in the absence of direct fetal infection, systemic inflammation and placental disturbances create conditions for chronic hypoxia and impaired postnatal adaptation [8, 17].

Overall, COVID-19 should not be considered a direct threat of intrauterine infection. However, its impact on the fetoplacental system requires special attention and early prevention. Prenatal monitoring, including mandatory ultrasound, Doppler ultrasound , and CTG, is recommended, especially in pregnant women with signs of hypoxemia and vascular complications.

To reduce the risk of adverse outcomes, it is necessary:

- maintaining normal saturation levels in the mother ($SpO_2 \geq 95\%$);
- monitoring of coagulation and prevention of thrombus formation;
- the use of antihypoxic agents and antioxidants in therapeutic doses;
- early delivery with signs of decompensated hypoxia.

Thus, the analysis results demonstrate that timely detection and correction of placental abnormalities associated with COVID-19 are crucial for maintaining the health of mother and child. The introduction of standards for early screening, hypoxia prevention, and interdisciplinary monitoring will reduce perinatal mortality and improve the quality of medical care for pregnant women in infectious disease-risk settings.

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