REVIEW OF LITERATURE ON THE SPECIFICITY OF GENERAL PATHOMORPHOLOGICAL CHANGES IN SATELLITE STRUCTURES UNDER THE INFLUENCE OF CORONAVIRUS

Hamidulla A. Rasulov - D.M.Sc., professor
Tashkent Pediatric Medical Institute (Tashkent, Uzbekistan)
Khushvakt J. Beknazarov - Ph.D.
Republican Specialized Scientific-Practical Medical Center of Neurosurgery
Ulugbek O. Mavlonov - independent researcher
Tashkent Pediatric Medical Institute (Tashkent, Uzbekistan)
mavlonovu026@gmail.com

Abstract: *Viral infections observed during pregnancy can have a specific impact on the body, leading to various negative outcomes at different stages of pregnancy. This necessitates an understanding of the pathological processes occurring in the placenta (maternal-placental system). Women suffering from viral infections such as herpes, hepatitis, rubella, and measles experience changes in the placenta, which have been studied in this context. In our study, special attention is given to the morphological changes in the placenta resulting from the coronavirus infection (SARS-CoV-2), which has shocked the entire world. The main morphological changes observed in the placenta during COVID-19 infection are presented.*

Keywords: *placenta (maternal-placental system), stem villi, pregnancy, viral infections, SARS-CoV-2.*

Relevance of the Topic: The rapid spread of the coronavirus infection at the end of 2019 triggered a global pandemic, significantly impacting healthcare systems worldwide. Even today, information regarding the effects of this infection on the human body, particularly the health of pregnant women, remains highly relevant. Pregnancy is characterized by specific physiological changes in the immune system, making pregnant women more susceptible to viral infections, including SARS-CoV-2. Among viral infections, tropism is a key feature, with the upper respiratory tract serving as the primary entry point in most viral pathogenesis, with coronaviruses being a prime example. These viruses belong to the zoonotic group, with approximately 20% causing various respiratory diseases in humans. Examples include SARS in 2003 and MERS in 2012. During the early months of the pandemic, infection rates surged rapidly, with millions and billions affected, and an increase in mortality rates and subsequent complications has been observed to this day. Retrospective epidemiological analysis indicates that the highest incidence rate in the republic was recorded in Tashkent city, with an average of 28.8 cases per 100,000 population (Khamzaeva N.T., 2024). Observations show that 80% of COVID-19 patients experienced mild to moderate disease severity, with higher mortality rates observed among patients with underlying cardiovascular conditions (Svarovskaya A.V., 2025). The SARS-CoV-2 virus primarily targets type 2 pneumocytes, alveolar macrophages, and dendritic cells in lung tissue, as well as vascular endothelium, upper respiratory tract apical epithelial cells, intestinal epithelium, cardiac pericytes, proximal renal tubule epithelium, reticuloendothelial system, hepatocytes, and even certain nervous system cells, indicating the complexity of its pathogenesis (Parakhina M.V., et al.). Analysis of samples from organs of patients infected with the coronavirus primarily highlighted changes in the respiratory system, but the subsequent discovery of the virus in other organs necessitated a deeper study of its pathogenesis mechanisms. Key pathological changes in lung tissue include diffuse alveolar damage, capillary hyperemia, hyperplasia of type 2 pneumocytes with giant cell formation, and the appearance of hyaline membranes. Immunohistochemical studies indicate a high positivity rate for TTF1 in lung tissue, suggesting pneumocyte damage (A.R. Bourgonje et al.). Some researchers associate

pathological changes in lung tissue with pulmonary edema, alveolar hemorrhage, and thromboembolism. Thrombi and thromboembolism have been identified in central or peripheral parts of lung tissue, with coagulopathies playing a significant role in thrombus formation. Focal pneumonia indicates superinfection or viral-bacterial etiology. In the heart, the mechanisms of coronavirus infection include non-coronary infarctions and dystrophic changes in cardiomyocytes, with some studies reporting myocarditis prevalence rates exceeding 7% (Su S, et al.). In the kidneys, acute tubular damage, interstitial edema, necrosis of some tubular epithelial cells, and accumulation of viral particles in podocytes have been observed (Nabil et al.). In the gastrointestinal system, key pathological features include necrosis of endothelial cells in the submucosal blood vessels and the presence of viral inclusions in epithelial cells. In the liver, non-specific changes such as parenchymal fatty dystrophy and inflammation of portal tracts are typical. In bone marrow, reactive erythropoiesis, a left shift in myelopoiesis, cytotoxic hyperplasia of CD8-positive T cells, and hemophagocytosis are observed. Morphological changes in lymph nodes include significant hyperemia, reduced lymphocyte size, and an increase in reactive plasmablasts, indicating immune system activation. During pregnancy, infection with the coronavirus during the pandemic was challenging due to the unknown mechanisms of disease progression, resulting in relatively low effectiveness of treatment measures. The cytokine storm or disruption of blood rheology caused by this virus leads to severe, irreversible complications in the maternal body and various adverse outcomes in the fetus, including mortality. Viral infections during pregnancy primarily disrupt the morphofunctional state of the fetus and mother, manifesting in diverse clinical symptoms and disease progression. Compared to non-pregnant women, pregnant women with influenza, Ebola, Zika, hepatitis E, and smallpox viruses experience more severe clinical courses, increased complications, and higher mortality rates (Yakimova A.V., et al.). In cytomegalovirus infections, placental changes include lymphoplasmacytic infiltration in the villous stroma, hemosiderin granules around blood vessels, villous necrosis, and focal or diffuse villitis and intervillitis (Lindholm K et al.). In pregnant women with SARS, fibrin deposits in perivillous and subchorial areas, large-scale avascularization of villi, and infarctions are observed (W. Ng et al.). Knowledge of pathological changes in the placenta is crucial for the proper application of treatment measures at various stages of pregnancy to prevent complications. Studying the pathological changes in the placenta of pregnant women infected with the coronavirus is vital for both maternal and fetal health, holding particular significance due to its relevance. Investigating the significance of morphological changes in the placenta of pregnant women infected with SARS-CoV-2 and linking adverse fetal outcomes to this pathogen helps develop morphological criteria and select treatment measures to prevent complications during pregnancy, prenatal, and postnatal periods, addressing one of the most pressing issues today. Current data indicate frequent occurrences of thrombosis, infarction, villous fibrosis, fibrinoid exudate, and chorioamnionitis in the placenta during coronavirus infection. However, scientific opinions differ on whether these changes are specific to the coronavirus or represent a general infectious response. Therefore, a thorough and systematic analysis of placental morphology under the influence of COVID-19 is of significant importance in clinical practice, perinatology, and pathomorphology.

Role of the Placenta in Fetal Development: Briefly addressing the morphofunctional role of the placenta in fetal development, this organ begins its functional activity rapidly from the third week of pregnancy. The placenta, formed from chorionic villi, plays a critical role in ensuring fetal viability, development, immunological protection, and hormonal and metabolic stability, managing physiological mechanisms vital for the fetus's adaptation to the external environment. Oxygen exchange occurs through highly specialized tissues between fine capillaries and villi, facilitating fetal respiration. Nutrients and metabolites, such as glucose, amino acids, fatty acids, and trace elements, pass from maternal blood to the fetus via the placenta, while fetal metabolic waste is returned to the maternal body. This bidirectional exchange ensures metabolic stability. The placenta produces essential hormones, including human chorionic gonadotropin (hCG), progesterone, estrogens,

placental lactogen, and other bioactive substances, which are crucial for maintaining pregnancy, regulating uterine tissue changes, and preparing mammary glands. The placenta also contributes to the fetus's immune system by providing initial immunological cues, shaping lifelong immunity, and protecting the fetus from potential maternal immune attacks. Placental cells produce immune-modulating molecules, safeguarding the fetus despite its "foreign" antigens. Immunoglobulin G (IgG) antibodies also pass through the placenta, forming the fetus's passive immunity. The placental barrier prevents direct mixing of maternal and fetal blood, protecting the fetus from infections, toxins, and certain medications. However, this barrier is not always effective, as some viruses (e.g., cytomegalovirus, toxoplasmosis, and possibly coronavirus) can breach it, causing vertical transmission. The placenta's morphological structures, including microvessels, chorionic villi, and stromal tissues, continuously adapt to the fetus's gestational age and needs, ensuring oxygen and nutrient supply through flexible adaptation. Normal fetal development requires proportional formation of placental morphology and function. Any placental pathology—hypoplasia, thrombosis, infarction, inflammation, or dystrophic changes—can pose life-threatening risks to the fetus. Thus, studying the placenta at microscopic and macroscopic levels is a critical diagnostic method for assessing fetal health.

Objective: To study the specific morphological changes in the placental structures of pregnant women infected with the coronavirus.

Research Objects and Methods: Between 2020 and 2025, medical scientific articles related to coronavirus infection were reviewed, focusing on observational, statistical, and clinical morphological research methods. Most articles were sourced from foreign databases such as Google Scholar, eLIBRARY.RU, CrossRef, ResearchGate, and PubMed. Local articles' research methods and statistical data were partially utilized.

Results Obtained: Based on the data from scientific articles, a brief discussion of the results follows. The coronavirus (SARS-CoV-2) is an RNA-containing virus belonging to the Coronaviridae family, specifically the Betacoronavirus genus. Its genomic structure, including spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins, makes it highly pathogenic (Zhu, N. et al.). The virus primarily spreads via the air-droplet route. Upon entering the body, it initially affects respiratory epithelial cells, starting in the upper respiratory tract and potentially spreading throughout the body. SARS-CoV-2 affects not only the respiratory system but also other organs, including the heart, kidneys, central nervous system, and reproductive system. The infection spreads through viremia and, in some cases, reaches placental tissues. COVID-19 poses a high risk to pregnant women due to factors such as natural immune suppression during pregnancy, physiological changes in the respiratory system, and increased blood volume, which increase the likelihood of severe disease progression.

Meta-analyses from studies conducted in several developed countries revealed the following:

1. Pregnant women infected with the coronavirus were three times more likely to require intensive care compared to uninfected pregnant women.
2. Infection during the first trimester led to intrauterine hypoxia and spontaneous abortion.
3. Severe disease in pregnant women with coronavirus was associated with increased rates of preeclampsia, thromboembolism, amniotic fluid deficiency, and cesarean sections (Allotey, J. et al., Knight, M. et al.).

Additionally, the infection was more severe in cases of multiple pregnancies or in women with endocrine or autoimmune disorders.

Although the placental barrier plays a crucial role in protecting the fetus from external infections, some studies indicate that SARS-CoV-2 can bypass this barrier. The virus can infiltrate villous tissues, syncytiotrophoblasts, and cytotrophoblasts, triggering inflammatory processes and affecting blood circulation (Schwartz, D.A., Hosier, H. et al.). Pathomorphological changes such as chorioamnionitis, fibrinoid necrosis, villous infarction, and microthrombosis have been noted, posing

significant risks to fetal oxygen supply, growth, and viability. SARS-CoV-2 primarily uses angiotensin-converting enzyme 2 (ACE2) receptors and transmembrane serine protease 2 (TMPRSS2) enzymes to enter human cells. The viral spike (S) protein binds to ACE2, and TMPRSS2 activates it, facilitating viral entry into the cell cytoplasm (Hoffmann, M. et al.). ACE2 receptors are expressed not only in lung tissues but also in placental trophoblasts, enabling the virus to affect placental tissues. Some studies suggest that ACE2 and TMPRSS2 expression in the placenta varies across pregnancy stages (Li, M. et al., Bloise, E. et al.), which is critical for understanding vertical transmission risks and developing prevention and treatment strategies.

The mechanism of viral entry into the placenta involves ACE2 and TMPRSS2 receptors in syncytiotrophoblast and cytotrophoblast layers, allowing the virus to reach villous tissues. This results in intervillous inflammation (intervillitis), fibrinoid infiltration, villous infarction, and vascular thrombosis. Although most studies found no viral presence in newborns via PCR, SARS-CoV-2 was detected in amniotic fluid, vaginal secretions, and placental structures in some cases between 2020 and 2021. Vertical transmission is less likely, but in late pregnancy, particularly the third trimester, the placental barrier's function may weaken, increasing the risk of infection transmission. Morphological changes in the placenta under coronavirus influence include decidual vasculopathy, microthrombosis, villous dystrophy, syncytiotrophoblast necrosis, and inflammation. Increased activity of CD68+ macrophages (Hofbauer cells), CD3+ T-lymphocytes, and interleukins (IL-6, IL-1β, TNF-α) has been noted in the placenta of infected pregnant women, exacerbating pathological processes in the inflammatory context.

Comparison of Pathomorphological Changes in the Placenta of Pregnant Women Infected with Coronavirus to Other Viral Infections:

When considering the role of physiological and pathological factors in placental structural changes, pathological factors primarily affect the mother and fetus through the placenta as an intermediary. Consequently, primary changes occur, with outcomes depending on the duration and impact of these changes, which can be positive or negative. Among pathological factors, infections are particularly significant, with viral infections causing numerous placental changes, including villitis, trophoblastic dysfunction, vasculitis and microangiopathy in blood vessels, fibrin accumulation in villi and intervillous spaces, and infarctions of varying degrees. In coronavirus infection, placental structures undergo specific changes, particularly in trophoblast structures and villous microvessels, which are of significant importance.

When comparing the pathomorphological changes in the placenta caused by coronavirus and other infections, the following differences were observed:

Placental Pathomorphological Changes	In Coronavirus Infection	In Other Viral Infections (CMV, Zika, Herpes)
Placental infarctions	Common	Rare
Microthrombosis	High risk	Rare
Villositis	Rare	Common in CMV
Chorioamnionitis	Rare	Common in herpes and bacterial infections
ACE2 expression	Specific to COVID-19	Less significant in others
Risk of fetal infection	5–10%	High in Zika and CMV

From the results of the above-mentioned scientific studies, it can be seen that COVID-19 primarily causes vascular changes in the placental structures, while infectious villositis and chorioamnionitis are relatively rare. This is one of the distinguishing features of coronavirus infection compared to other viral infections.

Conclusion. The placenta is normally a complex morphofunctional structure that performs vital physiological functions necessary for the life of the fetus. During each trimester, the placenta undergoes morphological and functional changes that adapt to the needs of the fetus. In pathological conditions—especially in COVID-19 infections—pregnancy and placental function are affected in a complex manner. The ACE2 and TMPRSS2 receptors in placental tissues serve as entry points for the virus. In such cases, pathomorphological analysis and monitoring of the placenta are of great importance for the comprehensive assessment of pregnant women with COVID-19. Structural damage to the placenta can have a serious impact on fetal development. Therefore, a thorough study of placental morphology and its pathomorphological state is of significant importance in medical practice and in the field of perinatal pathology.

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