НЕОНАТОЛОГІЯ, ХІРУРГІЯ ТА ПЕРИНАТАЛЬНА МЕДИЦИНА Т. XIII, № 2(48), 2023
NEONATOLOGY, SURGERY AND PERINATAL MEDICINE VOL. XIII, № 2(48), 2023
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)
KEY TITLE: NEONATOLOGIÂ, HÌRURGIÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)

АНАЛІТИЧНІ ОГЛЯДИ / ANALYTICAL REVIEWS

UDC: 618.3-06:616.98:578.834
DOI: 10.24061/2413-4260.XIII.2.48.2023.16

PECULIARITIES OF THE COURSE OF THE DISEASE IN WOMEN WITH COVID-19

V.D. Moskaliuk, O.M. Yuzko, L.V. Dubyk, N.V. Chernetska

Bukovinian State Medical University
(Chernivtsi, Ukraine)

Summary

One of the most crucial topics at the moment is the viral infection caused by the SARS-CoV-2 coronavirus, which has acquired not only medical, but also, of course, social significance. The COVID-19 pandemic has challenged healthcare systems around the world.

Pregnant women are the most vulnerable category of people, along with the elderly. Due to low immune reactivity, they are more susceptible to severe complications than others, which makes the problem of pregnancy in patients with COVID-19 a pressing issue.

A successful pregnancy requires changes in the immune system of the pregnant woman to tolerate a genetically foreign fetus. These changes in the immune system, as well as in the cardiac, pulmonary, and other systems, can lead to increased susceptibility or increased morbidity and mortality due to infection during pregnancy. Considering the physiological adaptations associated with pregnancy, we found that the high metabolic demand to maintain normal intrauterine development increases the burden of oxidative stress during pregnancy. Intracellular redox changes associated with acute phase reactions at the maternal-fetal interface may be enhanced during pregnancy. Notably, mother-to-fetal transmission of SARS-CoV-2 has not been detected in most COVID-19 pregnancies. This relative absence of vertical transmission may be due to the presence of lactoferrin in the placenta, amniotic fluid, and breast secretions. However, the cytokine storm induced during COVID-19-associated pregnancies can cause severe inflammatory damage to the fetus and, if left uncontrolled, can subsequently lead to autism spectrum disorders and brain developmental abnormalities in newborns. Given this serious health threat to a child's growth and development, preventing COVID-19 during pregnancy should be a priority.

We aimed to study risk factors and assess the course of pregnancy in women with COVID-19.

The study was carried out within the framework of the research work "Clinical and pathogenetic substantiation of differentiated treatment of combined pathology of internal organs" (№0122U002209).

Key words: *Pregnancy; COVID-19; SARS-CoV-2; SARS-CoV-2 Vaccine; Intrauterine Transmission; Lactoferrin; D-dimer; Cytokine Storm; Coagulopathy; Coagulation; Thrombosis.*

Coronavirus disease (COVID-19), caused by the SARS-CoV-2 coronavirus, was declared a pandemic by the WHO on March 11, 2020 [1]. In 2020, the number of cases of severe acute respiratory syndrome increased exponentially. As of December 2022, about 650 million cases and more than 6 million deaths caused by COVID-19 have been reported [2].

It has become clear that this virus poses a particular threat to vulnerable individuals, including the elderly, immunocompromised, those with certain comorbidities, and pregnant women, especially in the third trimester [3]. In general, pregnant women are particularly susceptible to respiratory pathogens due to immunological and physical changes that include changes in T-cell immunity, reduced lung capacity, and reduced functional residual capacity [4]. The high metabolic demand to maintain normal fetal development increases the burden of oxidative stress during pregnancy.

Interpreting susceptibility to infection during pregnancy is complex, given that the number of infections observed depends not only on susceptibility but also on the level of exposure to the pathogen. Pregnant women may be more cautious about risk, leading to lower exposure levels, which may appear as a decrease in susceptibility. To adequately address this issue, it is necessary to compare the incidence of cases between pregnant individuals and women of the same age with the same levels of exposure to SARS-CoV-2 [5].

It is currently known that most pregnant women infected with SARS-CoV-2 are asymptomatic. However, symptoms of COVID-19 during pregnancy can range from mild to severe and critical illnesses that cause acute respiratory distress syndrome and other complications such as pulmonary embolism and acute coronary syndrome. The severe illnesses caused by COVID-19 are reflected in the increased hospitalization of pregnant women. In June 2020, the Centers for Disease Control and Prevention (CDC) reported that among COVID-19 patients, 31.5% of pregnant women required hospitalization compared to 5.8% of non-pregnant women [6]. However, it is possible that this indicates greater caution in the management of pregnant women rather than more serious illnesses.

The PregCOV-19 Living Systematic Review Consortium reported that pregnant women with COVID-19 are more likely to be admitted to intensive care units and require invasive ventilation compared to non-pregnant women with COVID-19.

When assessing the impact of COVID-19 during pregnancy, it is important to distinguish between studies comparing pregnant women with COVID-19

and non-pregnant women with COVID-19 and studies comparing pregnant women with and without COVID-19. The former address the question of whether pregnancy increases the risk of adverse outcomes in women with the disease. The latter concerns the idea of whether contracting the disease during pregnancy increases the risk of adverse outcomes.

Initial reports from China, the epicenter of the pandemic, originally suggested that pregnant women were not at increased risk of COVID-19-related complications compared to the general population [7]. Subsequent studies have suggested that pregnant women are particularly susceptible to SARS-CoV-2 infection and that COVID-19 may increase health risks to mothers and infants during pregnancy [8]. It has also been found that the clinical outcomes of SARS-CoV-2 infections in pregnant women may differ from those in the general population, and pregnancy is considered a potential risk factor for susceptibility to COVID-19, as well as illness and death [9].

The placenta is a single organ consisting of cells from two different individuals - the mother and the fetus - intended for interaction between them. The main functional units of the placenta are fetal chorionic villi with fetal-placental vessels. The maternal part of the placenta is the decidual membrane with maternal vessels. Between these two areas is an interstitial space filled with maternal blood, which is enriched with "maternal lactoferrin" (LF). The expression of LF during pregnancy is regulated by several transcription factors and steroid hormones present during pregnancy, such as progesterone, estrogen, and corticosteroids [10].

LF levels change during pathological pregnancy (preterm pregnancy, preeclampsia, growth retardation, and infection). Immunohistologic studies of normal placentas have shown LF-positive cells in the interstitial spaces and fetal stem vessels. Placental cytotrophoblasts express unique LF epitopes, and such expression is enhanced in the presence of activated macrophages. This expression may be an extraembryonic response to inflammation and maternal allogeneic recognition, as an attempt to protect trophoblastic cells. LF appears to play a role in placental inflammation and the immune pathology of infections during pregnancy [11].

Due to the physiological and anatomical changes associated with pregnancy, women are susceptible to microbial infections. In addition, maternal lactoferrin and other amniotic protective factors are aimed at protecting the fetus and make the mother vulnerable to viral infections. Cytokines produced by T helper (Th) lymphocytes regulate both immune and inflammatory responses. Th1 cytokines are pro-inflammatory mediators that include interferon gamma (IFN-γ), interleukins IL-1α, IL-1β, IL-6, and IL-12. Conversely, Th2 cytokines are anti-inflammatory factors consisting of IL-4, IL-10, IL-13, and transforming growth factor-β (TGF-β). During pregnancy, the suppression of pro-inflammatory Th1 cells changes the physiological environment to a dominant anti-inflammatory Th2 phase to protect the fetus. This shift in the inflammatory cell cascade contributes to overall infectious morbidity by increasing the susceptibility of the mother to viral pathogens such as SARS-CoV-2 [12].

Despite this strong barrier, some viral pathogens are able to overcome host defenses; these include Zika virus, Varicella Zoster virus (VZV), human immunodeficiency virus (HIV), rubella virus, cytomegalovirus (HCMV), and herpes simplex virus (HSV). In contrast, and especially in the context of COVID-19 pregnancy, vertical transmission of SARS-CoV-2 does not occur with any clinically relevant frequency. Given the role of LF in placental barrier function, we analyzed the interaction between mother and fetus to understand the potential interaction of innate defense factors to prevent and control pregnancy in the context of COVID-19.

A series of 68 cases of SARS-CoV-2 placentitis associated with stillbirth or neonatal death found that the cause of death was most likely hypoxic-ischemic fetal injury due to severe placental damage rather than fetal SARS-CoV-2 infection. Indeed, placental SARS-CoV-2 infection does not necessarily equate to intrauterine infection; in this case series, fetal infection was confirmed in only 2 of 68 cases [13].

The difference in cytokine profiles between SARS and COVID-19 infections in non-pregnant patients is the basis for assessing and extrapolating disease progression and severity in sick pregnant women. Patients with SARS demonstrate predominant activation of Th1 immunity, leading to markedly elevated levels of proinflammatory cytokines (IFN-γ, IL-1β, IL-6, and IL-12) for at least two weeks after disease onset, resulting in significant lung damage [14]. In contrast, patients with COVID-19 demonstrate activation of both Th1 and Th2 immunity during the same period of the disease, culminating in the presence of IFN-γ and IL-1β in addition to IL-4 and IL-10 [15]. In addition, elevated levels of IL-6 (the predominant Th1 responder) are associated with an increased risk of mortality in patients with COVID-19 [16].

However, in COVID-19, an early adaptive immune response is predictive of a less severe outcome of the disease [17]. Changes in hormonal status during pregnancy can affect immune responses against viral pathogens [18]. Therefore, in combination, the shift to Th2 expression with anti-inflammatory cytokines (IL-4 and IL-10) and other immune adaptations may serve as an immune response to SARS-CoV-2, which may lead to a milder course of COVID-19 compared to non-pregnant individuals [19].

Pregnancy is a physiological state accompanied by a high energy requirement for many physiological functions with increased oxygen demand and increased oxidative stress. Placental oxidative stress with subsequent syncytiotrophoblast damage secondary to the early onset of maternal circulation causes miscarriages.

Infection-induced inflammation and other risk factors can cause redox imbalances, increase the release of free radicals and other oxidants, and rapidly weaken antioxidant defenses. In turn, oxidative stress can initiate intracellular signaling cascades that increase the production of pro-inflammatory mediators. Oxidative stress causes placental dysfunction and leads to fetal malformation. Prevention of placental oxidative

KEY TITLE: NEONATOLOGIÂ, HÌRURGIÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

stress is important to ensure positive birth outcomes. Oxidative stress and a strong inflammatory response ("cytokine storm") are involved in the pathogenesis of COVID-19 [20]. Thus, monitoring redox activity during COVID-19 pregnancy may provide a quick prognostic advantage.

Viral infections during pregnancy can lead to unfavorable clinical outcomes. Viral pathogens at the mother-fetus interface can affect placental function and cause pregnancy complications such as miscarriage, intrauterine growth retardation, or premature birth. The placenta functions as a physiological and immunological barrier to prevent transmission of the virus from mother to fetus. However, the immunologic response to infection can adversely affect fetal circulation or predispose the mother to an abnormal response. Viral infection of the decidual membrane and/or placenta can lead to the production of soluble immune factors that can reach the fetus and affect its development. Viruses rarely penetrate the placental barrier; however, when a pathogen does, it can cause serious birth defects such as microcephaly or even death.

Recent studies have examined the placentas of pregnant women with SARS-CoV-2 and compared the histopathological findings with the control group. Placentas from mothers with COVID-19 were significantly more likely to show abnormal or damaged maternal vessels and interventricular thrombi. It is worth noting that all analyzes of amniotic fluid, umbilical cord blood, and throat swab samples of newborns at birth were negative for SARS-CoV-2. Criteria have been developed to assess intrauterine transmission, including documentation of maternal infection, identification of SARS-CoV-2 in the first 24 hours of life, and evidence of persistent infection in the newborn [21]. Initial results have shown that although viral infections are common during pregnancy, the transplacental route of fetal infection is the exception rather than the rule [22].

Numerous studies have examined umbilical cord blood to more accurately identify newborns infected through vertical transmission. Although the fetus begins to produce both IgG and IgM between 12 and 20 weeks of gestation, maternal IgG can cross the placenta, so only the presence of IgM signals fetal exposure to the antigen. During pregnancies affected by SARS-CoV-2 infection, the detection of Spike-specific IgM in umbilical cord blood was reported in 0 to 7.7% of cases [23].

A systematic review of studies examining the presence of viral genome in cord blood found it in 2.9% of cases, although a larger case series of 64 deliveries has since failed to detect viral genome in the cord blood of any infant.

It is worth noting that increased levels of inflammatory cytokines were observed in the umbilical cord blood of newborns even in the absence of placental infection [24]. It is unclear whether these cytokines were produced locally by the fetus or reflect maternal cytokines that have passed through the placenta. However, the findings that immune cells in umbilical cord blood show greater cytokine production if the pregnancy was affected by SARS-CoV-2 infection, and that IL-8 levels tend to be higher in umbilical cord blood than in maternal blood, suggest that at least some of the cytokines may be produced by the newborn.

SARS-CoV-2 infection during pregnancy mainly affects the respiratory system, causing mild to moderate respiratory symptoms in 85.0% of cases. Cardiovascular, renal, neurologic, psychiatric, dermatologic, and gastrointestinal manifestations have also been reported [25-29].

A study of positive SARS-CoV-2 cases in pregnant women summarized the clinical signs of COVID-19 in pregnancy. The average age of pregnant women ranged from 29 to 32 years, and the disease occurred mainly in the 3rd trimester of pregnancy. 20.0% of pregnant women in the early weeks of gestation were discharged without delivery and without significant complications. The average gestational age varied, and the birth of a child before the 37th full week of pregnancy was 42.0%. These patients also had other comorbidities or complications during pregnancy, such as preeclampsia, gestational diabetes, hypothyroidism, placenta previa, previous uterine surgery, etc. [30].

Guan et al. reported fever in pregnant women (88.7%), cough (67.8%), fatigue (38.0%), sputum production (33.7%), shortness of breath (18.7%), myalgia or arthralgia (14, 9 %), sore throat (13.9 %), headache (13.6 %), chills (11.5 %), nausea or vomiting (5.0 %), nasal congestion (4.8 %) and diarrhea (3.85 %) as the leading symptoms.

In 5-30.0% of patients, the virus caused severe acute respiratory syndrome (ARDS), which led to the use of mechanical ventilation and progressed to multiorgan failure. ARDS is presented by hypoxemic respiratory failure with bilateral pulmonary infiltrates. Almost 5.0% of patients with COVID-19 developed a severe form of the disorder that required treatment in the intensive care unit [31-32].

Cesarean section accounted for 92.0% of all deliveries related to COVID-19 pregnancy, but successful vaginal deliveries were reported in 8.0% of cases. Fetal distress was a common indication for cesarean section. Lymphocytopenia (59.0%) with elevated C-reactive protein (70.0%) was noted in 91.0% of pregnant women with COVID-19 who delivered by cesarean section. Most mothers were discharged without serious complications, although two cases of hospitalization in the intensive care unit were reported.

Thus, severe maternal morbidity cannot be ruled out in COVID-19-related pregnancies [33].

We also analyzed a retrospective single-center study conducted at the Department of Obstetrics and Gynecology of the Central Clinical Hospital of the Ministry of Internal Affairs and Administration in Warsaw, Poland. The control group consisted of non-pregnant women of reproductive age who were randomly selected from among those prescribed for COVID-19 treatment in the hospital's departments. From May 15, 2020, to April 26, 2021, 52 pregnant and 53 non-pregnant women with COVID-19 infection were admitted for treatment. The inclusion criteria were body temperature > 39°C (despite the use of paracetamol), tachypnea > 30/min, SaO2 < 95%, or critical illness. The diagnosis of COVID-19 was confirmed by a positive PCR test performed no later than 13 days before hospitalization. The researchers

divided the patients into 4 groups based on the classification guidelines of the Polish Association of Epidemiologists and Infectious Diseases, determined by the severity of symptoms and test results. Mild (asymptomatic or cough, fever, shortness of breath, fatigue, headache, muscle pain, nausea, vomiting, diarrhea), moderate (clinical and radiological signs of lung damage), severe (respiratory failure, low peripheral SpO2 < 90%), or critical (ARDS, hypotensive shock, multiple organ failure, loss of consciousness). Upon hospitalization, all women underwent blood tests, urine tests, coagulation tests, blood chemistry, and computed tomography (without contrast) for suspected moderate, severe, and critical COVID-19 [34].

The following data were analyzed: patient's age, weight, height, body mass index (BMI), existing diseases (diabetes mellitus, hypertension, hypothyroidism, bronchial asthma), symptoms, physical examination results, pregnancy status, and gestational age at admission. The average gestational age was 30 weeks, with a range of 17 to 37 weeks. The average age of the patients was 31.9 ± 4.79 years, the median body weight was 77 kg, and the median body mass index was 28.36 kg/m2. The main clinical symptoms were dyspnea (92.3%), cough (90.3%), fever (63.4%), fatigue (42.3%), and muscle pain (42.3%).

Dyspnea and cough were more common in the pregnant group, and diarrhea was less common. Comorbidities included diabetes (17.6%), hypertension (10.0%), asthma (3.8%), and hypothyroidism (35.2%), the latter being more common in the pregnant cohort. Nine (17.3%) cases were classified as mild COVID-19. Moderate COVID-19 accounted for 25 (48.0%), 17 (32.6%), and 1 (1.9%) cases of COVID-19, respectively.

The average gestational age at hospitalization was 30 weeks. The average length of hospitalization was 8 days. The average percentage of lung lesions on CT scan was 20.0%. Forty-two (80.7%) pregnant women with COVID-19 required oxygen therapy. Hospitalization in the intensive care unit was required in 2 (3.8%) cases, and there were no indications for mechanical ventilation in the pregnant group. There were 6 (11.5%) cases of childbirth at 29, 32, 35, 36, and 37 weeks of pregnancy. Comparison of laboratory results of patients with those in the non-pregnant group revealed higher levels of leukocytes, neutrophils, CRP, procalcitonin, IL-6, D-dimer, and fibrinogen and significantly lower levels of hemoglobin, lymphocytes, platelets, NT, pro-BNP, calcium, ferritin, creatinine, urea, magnesium, sodium, and prothrombin time in the pregnant cohort [35].

According to available data, the severe and critical course of COVID-19 is mainly a hyperinflammatory, immune-mediated disorder caused by the virus. Due to their immunological characteristics, pregnant women are particularly susceptible to intracellular infections and immunological disorders, especially at the end of the second and third trimester. During the second trimester, these changes are characterized mainly by an increase in humoral immune responses and a suppression of cell-mediated immunity, called the T helper lymphocyte shift (Th1-Th2).

Thus, Th1 cell-mediated immunity is impaired, which increases the susceptibility of pregnant women to viral and intracellular bacterial infections. During the third trimester, an increased number of monocytes and granulocytes are detected in the mother's blood compared to non-pregnant women, which releases inflammatory cytokines, such as IL-8, TNF-a, and IL-6. In addition, the pathophysiological processes responsible for the development of hypertension, diabetes, or cardiovascular disease are aggravated during the 3rd trimester, and pregnant women with comorbidities and elderly pregnant women are at particularly increased risk of adverse maternal outcomes [36].

Pregnancy is a complex state of immunological dichotomy. The maternal-fetal interface of the decidual membrane provides immune tolerance to the "foreign" allogeneic fetus while maintaining the immune capacity to fight off invading pathogens. The interface also facilitates the transfer of O2, CO2, and nutrients to support the synthesis of various hormones, enzymes, and cytokines [37]. This unique immune dichotomy during pregnancy is achieved through a programmed switch of cytokines from Th1 to Th2. Progesterone, estradiol, prostaglandin D2, and leukemia inhibitory factor during pregnancy enhance the Th2 cytokine profile and are responsible for the Th2 shift associated with normal pregnancy. This Th2-related immune change is a major factor in susceptibility to COVID-19 infection in pregnant women. Hypersensitivity causes suppression of cell-mediated immunity as pregnancy shifts from a pro-inflammatory Th1 to Th2 immune environment [38].

Pregnancy immunology is a combination of signals and responses from the maternal immune system and the fetal-placental immune system. Signals originating in the placenta modulate the maternal immune response in the presence of a potential pathogen. The trophoblast, a cellular unit of the placenta, releases antimicrobial peptides such as human β-defensins, leukocyte secretory protease inhibitor (SLPI) and expresses toll-like receptors (TLR-3, TLR-7, TLR-8 and TLR-9). Placental syncytiotrophoblasts express "maternal lactoferrin" (LF), an extraembryonic response to inflammation and maternal allogeneic recognition to protect trophoblastic cells. Placental-LF, IFN-β and SLP. The production of trophoblast I by trophoblast cells in response to viral infection at the maternal-fetal junction may represent a potential mechanism by which the placenta markedly inhibits the transmission of viral infection to the fetus during pregnancy. Together with trophoblast factors in the placenta, LF may be critical in providing a first line of defense against viral infections [39].

The maternal-fetal interface is an immunologically unique site designed to promote tolerance to the allogeneic fetus and maintain host defense against a diverse range of possible pathogens. Innate immune responses to viruses at the maternal-fetal interface can have a significant impact on pregnancy outcomes. Cytotoxic adaptive immune responses are reduced, bypassed, or even suppressed, while regulatory adaptive immunity is enhanced during pregnancy. In contrast, innate (natural) immunity remains intact, serving two purposes: 1) to continue to protect the

KEY TITLE: NEONATOLOGIÂ, HÌRURGIÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

body against infection and 2) to interact with fetal tissues to promote successful placentation and pregnancy.

It is currently known that many factors can influence the incidence, duration, and severity of viral infection at the mother-fetus interface. Viruses gain access to the cells of the decidual membrane and placenta by ascending from the lower reproductive tract or by hematogenous route [40].

After access to the upper reproductive tract, viral tropism to the decidual membrane and/or placenta depends on both the expression of the viral entry receptor by these tissues and the specific immune response of the mother against the virus. These factors vary with cell type and gestational age and are influenced by changes in the intrauterine environment and maternal immunity. Virus-host interactions during pregnancy are complex and highly variable. Innate immune cells, including NK cells, DCs, macrophages, and the maternal humoral response, play a crucial role in the infection, which, therefore, determines the severity of COVID-19. In contrast to non-pregnant women, the function of the innate immune system during pregnancy is affected by the fetal/placental unit [41].

Severe cases of COVID-19 include a "cytokine storm" with elevated levels of IL-2, IL-7, IL-10, G-CSF, IFN-γ-inducible protein-10, monocyte chemoattractant protein-1, macrophage inflammatory protein-1α, and TNF-α, which is a result of ADE [42]. Since pregnant women are in a Th2 state during the 1st and 3rd trimester, the cytokine storm caused by SARS-CoV-2 can lead to severe inflammatory damage. Increased cytokine responses to viral infections during pregnancy can later cause autism spectrum disorders and brain developmental abnormalities in children.

In a meta-analysis conducted by Zambrano et al. that included more than 23,000 pregnant women and more than 386,000 non-pregnant women of reproductive age with symptomatic laboratory-confirmed SARS-CoV-2 infection, pregnant patients were at higher risk of intensive care unit admission, invasive ventilation, and death. The results of laboratory tests performed in the pregnant group on admission, comparing inflammatory markers with the non-pregnant group, showed that white blood cell counts, neutrophil counts, CRP levels, procalcitonin and IL-6 levels were higher, except for ferritin levels.

Some findings are consistent with similar studies and can be explained by the hyperinduction of the immune system caused by pregnancy and SARS-CoV-2 infection [43]. Nevertheless, the analysis of the data presented by Liu et al. shows that the number of leukocytes is at the upper limit of the normal range of values for pregnant women. In addition, mild leukocytosis physiologically occurs in the third trimester. Serum ferritin levels were not significantly higher, probably due to the higher incidence of iron deficiency anemia in the pregnant group [44].

When examining the state of hypercoagulability, which is manifested by increased levels of D-dimer and fibrinogen and decreased prothrombin time, could be partially caused by pregnancy. This suggests an increased risk of venous thromboembolism associated with COVID-19 in infected pregnant patients compared to uninfected pregnant patients [45].

Lower levels of hemoglobin, platelets, creatinine, and urea are typical in pregnancy due to hemodilution, increased renal blood flow, and pregnancy-related thrombocytopenia.

Changes in ion levels occur due to physiological changes during pregnancy, namely decreased levels of magnesium, calcium, and sodium.

A systematic review and meta-analysis showed increased risks of intensive care unit admission, need for invasive ventilation, and need for extracorporeal membrane oxygenation for pregnant and recently pregnant women compared to non-pregnant women of reproductive age [46]. Several studies have shown that SARS-CoV-2 infection during pregnancy increases the risk of pregnancy complications. In a systematic review and meta-analysis that included 42 studies involving 438,548 pregnant women, COVID-19 was associated with an increased risk of pre-eclampsia, preterm birth, and stillbirth compared to no SARS-CoV-2 infection during pregnancy. Severe COVID-19 was associated with pre-eclampsia, gestational diabetes, cesarean section, preterm birth, low birth weight, and admission to the neonatal intensive care unit compared to mild COVID-19 (defined as a positive SARS-CoV-2 test without serious symptoms) [47].

A study carried out in Colombia also showed a significantly increased risk of death among pregnant women compared to non-pregnant women of reproductive age. It was found that the risk of postpartum complications (fever, hypoxia, or the need for re-hospitalization) was higher among patients with COVID-19 (12.9%) compared to those without COVID-19. In addition, several risk factors for serious illness during pregnancy have been identified, including older maternal age, high body mass index, and preexisting extragenital diseases such as diabetes and hypertension [48, 49].

Analyses focusing on the impact of SARS-CoV-2 infection during pregnancy and pre-eclampsia showed increased risks of pre-eclampsia, eclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome (HELLP syndrome) in pregnant women with SARS-CoV-2 infection compared to those without SARS-CoV-2 infection. An increased probability of pre-eclampsia was observed in patients with both asymptomatic and symptomatic SARS-CoV-2 infection, but the odds were higher among patients with COVID-19 symptoms [50]. Various studies have identified risk factors associated with COVID-19 prevalence and severe illness in pregnant women [51].

The results of the study demonstrate the association of COVID-19 with hemostatic and thromboembolic complications. Pregnancy is a prothrombotic condition. It is likely that COVID-19 exacerbates the already increased risk of thromboembolic complications during pregnancy. A recent review of 1630 pregnant women with confirmed COVID-19 found that 15 women were diagnosed with coagulopathy, thromboembolism, deep vein thrombosis, or disseminated intravascular coagulopathy, suggesting that COVID-19 increases the risk of these pathologies [52].

Another study showed that the rate of venous

thromboembolism and myocardial infarction was higher in pregnant women with COVID-19 than in pregnant women without COVID-19 [53]. This may explain the possible increase in maternal mortality associated with COVID-19 and emphasizes the importance of early thromboprophylaxis.

A study comparing bleeding-related outcomes in pregnant women with and without COVID-19 found that blood loss and obstetric hemorrhage rates were not higher in pregnant women with COVID-19 [54].

A study in Wuhan comparing pregnant women with confirmed COVID-19 and pregnant women without COVID-19 found that there is an increased risk of cesarean section in pregnant women with COVID-19. Indications for cesarean section included worsening COVID-19 symptoms, such as maternal shortness of breath [55].

The increase in cesarean section rates can be explained by the direct impact of COVID-19 on maternal health, as well as an increase in the incidence of pathologies indirectly caused by COVID-19 [53]. The results of the study show that the incidence of cesarean section is higher in women with confirmed COVID-19, but these rates vary significantly from country to country. This may be due to the time period during which these studies were conducted, especially if data collection took place during the peak of the pandemic or at the beginning of the pandemic, when midwives who were rapidly trained may have had a lower threshold for cesarean delivery. Although absolute preterm birth rates vary by country, with US studies showing lower rates (12.0%) than European (19.0%) and Chinese studies (17.0%), the impact of COVID-19 is consistent [56].

Conclusions

Pregnant women's susceptibility to infections and hypercoagulability puts them at risk for COVID-19 infection and increased risk of pregnancy-related complications, such as miscarriages, preterm birth, preeclampsia, and fetal growth retardation.

Pregnant women are especially susceptible to respiratory infections due to physiological adaptation to pregnancy (high diaphragm position, increased oxygen demand, airway edema, hypoxemia intolerance) and immunological modulation from a pro-inflammatory state (favorable for cell clearance, angiogenesis and fetal growth) during the first trimester to an anti-inflammatory state, combined with a shift towards humoral immunity (favorable for fetal growth) in the second trimester, and finally reaching a second pro-inflammatory state during the third trimester (the onset of labor).

Maternal lactoferrin is an innate regulator of immune-restorative transitions at the maternal-fetal interface with multifunctional importance in antiviral protection, immunomodulation, inflammation regulation, and redox control of metabolic syndromes. Thus, it may serve as a powerful innate defense factor against COVID-19 during pregnancy and the postpartum period.

Laboratory and imaging findings are generally similar in both pregnant and non-pregnant groups. Coagulation test results, morphology, or serum ion levels can be explained by normal physiologic processes associated with pregnancy. Moderate and severe clinical course of COVID-19 in pregnant women is associated with higher levels of inflammatory markers, except for serum ferritin, than in non-pregnant women.

Early detection and treatment of COVID-19 in pregnant women can help prevent negative outcomes for newborns and reduce potential obstetric complications such as abortion and preterm birth.

It is important to take a multidisciplinary approach to the care of pregnant and postpartum women with COVID-19 and provide specific advice to reduce the risk of complications and intensive care unit admission.

The study was carried out within the framework of the research work "Clinical and pathogenetic substantiation of differentiated treatment of combined pathology of internal organs" (№0122U002209).

Conflict of interest: none
Sources of funding: self-financing

References:

1. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. 11 March 2020 [Internet]. Geneva: WHO; 2020[cited 2023 Feb 10]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

2. World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. Geneva: WHO; 2023[cited 2023 Feb 13]. Available from: https://covid19.who.int

3. Wenling Y, Junchao Q, Xiao Z, Ouyang S. Pregnancy and COVID-19: management and challenges. Rev Inst Med Trop São Paulo [Internet]. 2020[cited 2023 Feb 07];62:e62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7458076/pdf/1678-9946-rimtsp-62-S1678-9946202062062.pdf doi: 10.1590/s1678-9946202062062

4. Tang P, Wang J, Song Y. Characteristics and pregnancy outcomes of patients with severe pneumonia complicating pregnancy: a retrospective study of 12 cases and a literature review. BMC Pregnancy Childbirth [Internet]. 2018[cited 2023 Feb 10];18(1):434. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6215647/pdf/12884_2018_Article_2070.pdf doi: 10.1186/s12884-018-2070-0

5. Dawood FS, Varner M, Tita A, Newes-Adeyi G, Gyamfi-Bannerman C, Battarbee A, et al. Incidence, clinical characteristics, and risk factors of SARS-CoV-2 infection among pregnant individuals in the United States. Clin Infect Dis. 2022;74(12):2218-26. doi: 10.1093/cid/ciab713

6. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status-United States, 22 January-3 October 2020. MMWR Morb Mortal Wkly Rep. 2020;69(44):1641-7. doi: 10.15585/mmwr.mm6944e3

7. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ [Internet]. 2020[cited 2023 Feb 10];370:m3320. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7459193/pdf/bmj.m3320.pdf doi: 10.1136/bmj.m3320

8. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand. 2020; 99(7):823-9. doi: 10.1111/aogs.13867

9. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. Am J Obstet Gynecol. 2020;222(6):521-31. doi: 10.1016/j.ajog.2020.03.021

10. Xu J, Zhao S, Teng T, Abdalla AE, Zhu W, Xie L, et al. Systematic comparison of two animal-to-human transmitted human coronaviruses: SARS-CoV-2 and SARS-CoV. Viruses [Internet]. 2020[cited 2023 Feb 07];12(2):244. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7077191/pdf/viruses-12-00244.pdf doi: 10.3390/v12020244

11. Naidu SAG, Clemens RA, Pressman P, Zaigham M, Davies KJA, Naidu AS. COVID-19 during Pregnancy and Postpartum. J Diet Suppl. 2022;19(1):78-114. doi: 10.1080/19390211.2020.1834049

12. Schwartz DA, Avvad-Portari E, Babál P, Baldewijns M, Blomberg M, Bouachba A, et al. Placental tissue destruction and insufficiency from COVID-19 causes stillbirth and neonatal death from hypoxic-ischemic injury: a study of 68 cases with SARS-CoV-2 placentitis from 12 countries. Arch Pathol Lab Med. 2022;146(6):660-6. doi: 10.5858/arpa.2022-0029-sa

13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. doi: 10.1016/s0140-6736(20)30183-5

14. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intense Care Med. 2020;46(5):846-8. doi: 10.1007/s00134-020-05991-x

15. Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, van de Sandt CE, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nat Med. 2020;26(4):453-5. doi: 10.1038/s41591-020-0819-2

16. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases. Zhonghua Bing Li Xue Za Zhi. 2020;49(5):418-23. doi: 10.3760/cma.j.cn112151-20200225-00138

17. Delgado-Roche L, Mesta F. Oxidative stress as key player in Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) Infection. Arch Med Res. 2020;51(5):384-7. doi: 10.1016/j.arcmed.2020.04.019

18. Blumberg DA, Underwood MA, Hedriana HL, Lakshminrusimha S. Vertical transmission of SARS-CoV-2: what is the optimal definition? Am J Perinatol. 2020;37(8):769-72. doi: 10.1055/s-0040-1712457

19. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental pathology in COVID-19. Am J Clin Pathol. 2020;154(1):23-32. doi: 10.1093/ajcp/aqaa089

20. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol. 2021;224(1):35-53. doi: 10.1016/j.ajog.2020.07.049

21. Gee S, Chandiramani M, Seow J, Pollock E, Modestini C, Das A, et al. The legacy of maternal SARS-CoV-2 infection on the immunology of the neonate. Nat Immunol. 2021;22(12):1490-502. doi: 10.1038/s41590-021-01049-2

22. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20. doi: 10.1056/NEJMoa2002032

23. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. doi: 10.1001/jama.2020.1585

24. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. PLoS One [Internet]. 2020[cited 2023 Feb 10];15(6):e0234765. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7310678/pdf/pone.0234765.pdf doi: 10.1371/journal.pone.0234765

25. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiatry. 2020;7:611-27. doi: 10.1016/S2215-0366(20)30203-0

26. Vittori A, Lerman J, Cascella M, Gomez-Morad AD, Marchetti G, Marinangeli F, et al. COVID-19 pandemic acute respiratory distress syndrome survivors: Pain after the storm? Anesth Analg. 2020;131(1):117-9. doi: 10.1213/ane.0000000000004914

27. Ñamendys-Silva SA. ECMO for ARDS due to COVID-19. Heart Lung. 2020;49(4):348-9. doi: 10.1016/j.hrtlng.2020.03.012

28. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARSCoV-2 pneumonia in Wuhan, China: A singlecentered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81. doi: 10.1016/s2213-2600(20)30079-5

29. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Ann Intern Med. 2020;172(9):577–82. doi: 10.7326/m20-0504

30. Flisiak R, Horban A, Jaroszewicz J, Kozielewicz D, Pawłowska M, Parczewski M, et al. Management of SARS-CoV-2 infection: Recommendations of the Polish Association of Epidemiologists and Infectiologists as of March 31, 2020. Pol Arch Intern Med. 2020;130(4):352-7. doi: 10.20452/pamw.15270

31. López M, Gonce A, Meler E, Plaza A, Hernández S, Martinez-Portilla RJ, et al. Coronavirus Disease 2019 in Pregnancy: A Clinical Management Protocol and Considerations for Practice. Fetal Diagn Ther. 2020;47(7):519-28. doi: 10.1159/000508487

32. Yang F, Zheng Q, Jin L. Dynamic function and composition changes of immune cells during normal and pathological pregnancy at the maternal-fetal interface. Front Immunol [Internet]. 2019[cited 2023 Feb 13];10:2317. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6813251/pdf/fimmu-10-02317.pdf doi: 10.3389/fimmu.2019.02317

33. Gedeon C, Koren G. Designing pregnancy centered medications: drugs which do not cross the human placenta. Placenta. 2006;27(8):861–8. doi: 10.1016/j.placenta.2005.09.001

34. -Tetro JA. Is COVID-19 receiving ADE from other coronaviruses? Microbes Infect. 2020;22(2):72-3. doi: 10.1016/j.micinf.2020.02.006

35. Stewart T, Lambourne J, Thorp-Jones D, Thomas D. Implementation of early management of iron deficiency in pregnancy during the SARS-CoV-2 pandemic. Eur J Obstet Gynecol Reprod Biol. 2021;258:60-2. doi: 10.1016/j.ejogrb.2020.12.055

36. Servante J, Swallow G, Thornton JG, Myers B, Munireddy S, Malinowski AK, et al. Haemostatic and thrombo-embolic complications in pregnant women with COVID-19: A systematic review and critical analysis. BMC Pregnancy Childbirth [Internet]. 2021[cited 2023 Feb 07];21:108. Available from: https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-021-03568-0 doi: 10.1186/s12884-021-03568-0

37. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. CMAJ [Internet]. 2021[cited 2023 Feb 07];193(16):E540-8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8084555/pdf/193e540.pdf doi: 10.1503/cmaj.202604

38. Jamieson DJ, Rasmussen SA. An update on COVID-19 and pregnancy. Am J Obstet Gynecol. 2022;226(2):177-86. doi: 10.1016/j.ajog.2021.08.054

39. Conde-Agudelo A, Romero R. SARS-CoV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. Am J Obstet Gynecol. 2022;226(1):68-89. doi: 10.1016/j.ajog.2021.07.009

40. Gold S, Saeed H, Mokhtari N, Chornock RL, Fries M, Overcash R, et al. 564 Comparison of clinical outcomes in pregnant women with and without COVID-19 based on disease severity. Am J Obstet Gynecol [Internet]. 2021[cited 2023 Feb 10];224(2):S357. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7848487/ doi: 10.1016/j.ajog.2020.12.585

41. Mendoza M, Garcia-Ruiz I, Maiz N, Rodo C, Garcia-Manau P, Serrano B, et al. Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study. Br J Obstet Gynaecol. 2020;127(11):1374-80. doi: 10.1111/1471-0528.16339

42. Jering KS, Claggett BL, Cunningham JW, Rosenthal N, Vardeny O, Greene MF, et al. Clinical characteristics and outcomes of hospitalized women giving birth with and without COVID-19. JAMA Intern Med. 2021;181(5):714-7. doi: 10.1001/jamainternmed.2020.9241

43. Wang MJ, Schapero M, Iverson R, Yarrington CD. Obstetric hemorrhage risk associated with novel COVID-19 diagnosis from a single-institution cohort in the United States. Am J Perinatol. 2020;37(14):1411-6. doi: 10.1055/s-0040-1718403

44. Society for Maternal-Fetal Medicine. Management considerations for pregnant patients with COVID-19 [Internet]. Society for Maternal-Fetal Medicine; 2021[cited 2023 Feb 07]. 33 p. Available from: https://s3.amazonaws.com/cdn.smfm.org/media/2734/SMFM_COVID_Management_of_COVID_pos_preg_patients_2-2-21_(final).pdf

45. Pineles BL, Stephens A, Narendran LM, Tigner MA, Leidlein C, Pedroza C, et al. The relationship between delivery and the PaO2/FiO2 ratio in COVID-19: a cohort study. BJOG. 2021;129(3):493-9. doi: 10.1111/1471-0528.16858

46. Yang R, Mei H, Zheng T, Fu Q, Zhang Y, Buka S, et al. Pregnant women with COVID-19 and risk of adverse birth outcomes and maternal-fetal vertical transmission: a population-based cohort study in Wuhan, China. BMC Med [Internet]. 2020[cited 2023 Feb 13];18(1):330. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7568966/pdf/12916_2020_Article_1798.pdf doi: 10.1186/s12916-020-01798-1

47. Zhang J, Zhang Y, Ma Y, Ke Y, Huo S, He L, et al. The associated factors of cesarean section during COVID-19 pandemic: a cross-sectional study in nine cities of China. Environ Health Prev Med [Internet]. 2020[cited 2023 Feb 10];25(1):60. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7547292/pdf/12199_2020_Article_899.pdf doi: 10.1186/s12199-020-00899-w

48. Dubey P, Reddy SY, Manuel S, Dwivedi AK. Maternal and neonatal characteristics and outcomes among COVID-19 infected women: an updated systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2020;252:490–501. doi: 10.1016/j.ejogrb.2020.07.034

49. Viana J, van Dorp CH, Nunes A, Gomes MC, van Boven M, Kretzschmar ME, et al. Controlling the pandemic during the SARS-CoV-2 vaccination rollout. Nat Commun [Internet]. 2021[cited 2023 Feb 07];12:3674. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8209021/pdf/41467_2021_Article_23938.pdf doi: 10.1038/s41467-021-23938-8

50. Royal College of Obstetricians and Gynaecologists. Maternity Royal Colleges welcome increased COVID-19 vaccine uptake in pregnant women [Internet]. Royal College of Obstetricians and Gynaecologists; 2022[cited 2023 Feb 13]. Available from: https://www.rcog.org.uk/news/maternity-royal-colleges-welcome-increased-covid-19-vaccine-uptake-in-pregnant-women/

51. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) Infection in Pregnancy. Information for healthcare professionals. Version 16 [Internet]. Royal College of Obstetricians and Gynaecologists; 2022[cited 2023 Feb 13]. Available from: https://www.rcog.org.uk/media/ftzilsfj/2022-12-15-coronavirus-covid-19-infection-in-pregnancy-v16.pdf

52. Mithal LB, Otero S, Shanes ED, Goldstein JA, Miller ES. Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy. Am J Obstet Gynecol. 2021;225(2):192-94. doi: 10.1016/j.ajog.2021.03.035

53. Prahl M, Golan Y, Cassidy AG, Matsui Y, Li L, Alvarenga B, et al. Evaluation of transplacental transfer of mRNA vaccine products and functional antibodies during pregnancy and early infancy. medRxiv [Internet]. 2021[cited 2023 Feb 07];2021.12.09.21267423. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8687468/ doi: 10.1101/2021.12.09.21267423

54. Shimabukuro TT, Shin YK, Tanya RM, Pedro LM, Titilope O, Lakshmi P, et al. Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons. N Engl J Med. 2021;384:2273-82. doi: 10.1056/NEJMoa2104983

55. Goldshtein I, Nevo D, Steinberg DM, Rotem RS, Gorfine M, Chodick G, et al. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. JAMA. 2021;326(8):728-35. doi: 10.1001/jama.2021.11035

56. Dagan N, Barda N, Biron-Shental T, Makov-Assif M, Key C, Kohane IS, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. Nat Med. 2021;27(10):1693-5. doi: 10.1038/s41591-021-01490-8

НЕОНАТОЛОГІЯ, ХІРУРГІЯ ТА ПЕРИНАТАЛЬНА МЕДИЦИНА Т. XIII, № 2(48), 2023
NEONATOLOGY, SURGERY AND PERINATAL MEDICINE VOL. XIII, № 2(48), 2023
KEY TITLE: NEONATOLOGIÂ, HÌRURGIÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

ОСОБЛИВОСТІ ПЕРЕБІГУ ВАГІТНОСТІ У ЖІНОК, ХВОРИХ НА COVID-19

В.Д. Москалюк, О.М. Юзько, Л.В. Дубик, Н.В. Чернецька

Буковинський державний медичний університет
(м. Чернівці, Україна)

Резюме

Однією з актуальних проблем сучасної медицини в теперішній час є вірусна інфекція, викликана коронавірусом SARS-CoV-2, яка набула не тільки медичного, а й, безумовно, соціального значення. Пандемія COVID-19 кинула виклик системам охорони здоров'я в усьому світі.

Найбільш вразлива категорія людей, поряд з особами старшого віку, − вагітні жінки. Через низьку імунну реактивність вони більше за інших схильні до тяжких ускладнень, що зумовлює актуальність проблеми перебігу вагітності у хворих на COVID-19.

Успішна вагітність вимагає змін в імунній системі вагітної жінки, щоб переносити генетично чужорідний плід. Ці зміни в імунній, а також в серцевій, легеневій та інших системах можуть призвести до підвищеної сприйнятливості або збільшення захворюваності та смертності від інфекції під час вагітності. Розглядаючи фізіологічну адаптацію, пов'язану з вагітністю, ми встановили, що високий метаболічний попит для підтримки нормального внутрішньоутробного розвитку збільшує тягар окисного стресу під час вагітності. Внутрішньоклітинні окиснювально-відновні зміни, переплетені з реакціями гострої фази на материнсько-фетальному інтерфейсі, можуть посилюватися під час вагітності. Цікаво, що передача SARS-CoV-2 від матері до плода не була виявлена у більшості випадків вагітності з COVID-19. Ця відносна відсутність вертикальної передачі може бути пов'язана з наявністю лактоферину в плаценті, амніотичній рідині та секреті молочних залоз. Однак цитокіновий шторм, викликаний під час вагітності, асоційованої з COVID-19, може спричинити серйозне запальне ураження плода, а якщо його не контролювати, згодом може призвести до розладів аутистичного спектру та аномалій розвитку мозку у новонароджених. Враховуючи цю серйозну загрозу здоров'ю для росту та розвитку дитини, профілактика COVID-19 під час вагітності має бути пріоритетною.

Ми поставили за мету вивчити фактори ризику та оцінити перебіг вагітності у жінок, хворих на COVID-19.

Робота виконана в рамках НДР «Клініко-патогенетичне обгрунтування диференційованого лікування поєднаної патології внутрішніх органів» (№0122U002209).

Ключові слова: вагітність; COVID-19; SARS-CoV-2; вакцина SARS-CoV-2; внутрішньоутробна передача; лактоферин; D-димер; цитокіновий шторм; коагулопатія; коагуляція; тромбоз.

Contact Information:
Vasyl Moskaliuk – Doctor of Medical Science, Full Professor, Head of the Department of Infectious Diseases and Epidemiology, Bukovinian State Medical University (Chernivtsi, Ukraine)
e-mail: vdmoskaliuk@ukr.net
ORCID ID: https://orcid.org/0000-0001-6206-1210

Oleksandr Yuzko – Doctor of Medical Science, Full Professor, Head of the Department of Obstetrics and Gynecology, Bukovinian State Medical University (Chernivtsi, Ukraine)
e-mail: prof.yuzko@gmail.com
ORCID ID: https://orcid.org/0000-0003-1270-9095

Ludmyla Dubyk – PhD, Assistant of the Department of Obstetrics and Gynecology, Bukovinian State Medical University (Chernivtsi, Ukraine)
e-mail: moskaljuk.ljuda@ukr.net
ORCID ID: https://orcid.org/0000-0001-8307-1733

Nataliia Chernetska – PhD, Assistant of the Department of Internal Medicine, Bukovinian State Medical University (Chernivtsi, Ukraine)
e-mail: chernetskanataliia@ukr.net
ORCID ID: https://orcid.org/0000-0002-5156-1313

Контактна інформація:
Москалюк Василь Деонізійович – доктор медичних наук, професор, завідувач кафедри інфекційних хвороб та епідеміології Буковинського державного медичного університету (м. Чернівці, Україна)
e-mail: vdmoskaliuk@ukr.net
ORCID ID: https://orcid.org/0000-0001-6206-1210

Юзько Олександр Михайлович – доктор медичних наук, професор, завідувач кафедри акушерства та гінекології Буковинського державного медичного університету (м. Чернівці, Україна)
e-mail: prof.yuzko@gmail.com
ORCID ID: https://orcid.org/0000-0003-1270-9095

Дубик Людмила Василівна – доктор філософії, асистент кафедри акушерства та гінекології Буковинського державного медичного університету (м. Чернівці, Україна)
e-mail: moskaljuk.ljuda@ukr.net
ORCID ID: https://orcid.org/0000-0001-8307-1733

Чернецька Наталія Василівна – доктор філософії, асистент кафедри внутрішньої медицини Буковинського державного медичного університету (м. Чернівці, Україна)
e-mail: chernetskanataliia@ukr.net
ORCID ID: https://orcid.org/0000-0002-5156-1313

Received for editorial office on 11/03/2023
Signed for printing on 20/05/2023