

PREDICTION OF PLACENTAL INSUFFICIENCY IN PREGNANT WOMEN WITH CORONAVIRUS INFECTION IN ANAMNESIS**N. K. Dustova**

Bukhara state medical institute, Bukhara, Uzbekistan

Key words: pregnancy, placenta, coronavirus infection, COVID-19.**Tayanch soʻzlar:** yangi koronavirus infeksiyasi, COVID-19, fetoplatsentar tizim yetishmovchiligi.**Ключевые слова:** беременность, плацента, коронавирусная инфекция, COVID-19.

The 2019 coronavirus disease (COVID-19) caused by SARS coronavirus 2 (SARS-CoV-2) has turned into a worldwide pandemic within months of its first documented appearance. Since the outbreak of coronavirus disease, there has been debate about whether pregnant women are at some risk of COVID-19 and whether it can be transmitted vertically across the placenta. A detailed histopathological description of circulatory disorders of the fetoplacental complex and morphological changes in the placental tissue is provided in current article. The results provide data for further in-depth study of COVID-19 on the impact of pregnancy and childbirth, as well as on the condition of newborns, which may well contribute to the development of fetoplacental insufficiency.

KORONAVIRUS INFEKSIYASINI OʻTKAZGAN HOMILADOR AYOLLARDA FETOPLATSENTAR TIZIM YETISHMOVCHILIGINI PROGNOZLASH**N. K. Dustova**

Buxoro davlat tibbiyot instituti, Buxoro, Oʻzbekiston

Koronavirus infeksiyasi (SARS-CoV-2) sabab boʻlgan 2019 yilgi koronavirus kasalligi (COVID-19) birinchi hujjatlashtirilganidan keyin bir necha oy ichida butun dunyo boʻylab pandemiyaga aylandi. Shuningdek, u koronavirus infeksiyasining ogʻirligi va fetoplatsentar tizimdagi qon oqimining buzilishi bilan bevosita bogʻliqdir. Koronavirus infeksiyasining yengil darajasi boʻlgan homilador ayollarda platsentar tizim qon oqimidagi buzilishlar aniqlanmaydi; koronavirus infeksiyasining oʻrtacha va ogʻir darajalari mavjud boʻlganda, fetoplatsentar tizimda sezilarli oʻzgarishlar aniqlanadi. Yangi koronavirus infeksiyasi bilan kasallangan homilador ayollarda giperkoagulyatsiya, shuningdek fetoplatsentar tizim qon oqimining buzilishi qayd etilgan.

ПРОГНОЗИРОВАНИЕ ФЕТОПЛАЦЕНТАРНОЙ НЕДОСТАТОЧНОСТИ У БЕРЕМЕННЫХ, ПЕРЕНЕСШИХ КОРОНАВИРУСНУЮ ИНФЕКЦИЮ**Н. К. Дустова**

Бухарский государственный медицинский институт, Бухара, Узбекистан

Коронавирусное заболевание 2019 года (COVID-19), вызванное SARS coronavirus 2 (SARS-CoV-2), превратилось во всемирную пандемию в течение нескольких месяцев с момента своего первого задокументированного появления. После вспышки коронавирусной болезни ведутся споры о том, подвергаются ли беременные женщины определенному риску COVID-19 и может ли он передаваться вертикально через плаценту. В статье предоставлено подробное гистопатологическое описание нарушения кровообращения фетоплацентарного комплекса и морфологических изменений в ткани плаценты. Полученные результаты дают основания для дальнейшего углубленного изучения COVID-19 на влияние течения беременности и родов, на состояние новорожденных, а также развитие фетоплацентарной недостаточности.

Introduction. The 2019 coronavirus disease (COVID-19) caused by SARS coronavirus 2 (SARS-CoV-2) has turned into a worldwide pandemic within months of its first documented appearance. Although severe courses and fatal outcomes are mainly observed in elderly patients with relevant comorbidities, there are also younger patients with an unfavorable disease outcome [1, 2]. We cannot know if pregnant women are at higher risk of developing more serious complications than the general population, as comparisons with appropriate controls are still lacking. Several studies, such as national cohort studies from France or the UK, concluded that the severity of COVID-19 in pregnant women depends on comorbidities, such as age over 35, body mass index (BMI) over 35, gestational diabetes, etc. arterial hypertension [3, 4]. Since its inception, there have also been discussions about whether this disease, like other viral infections, can affect fetal growth and be transmitted vertically through the placenta [5, 6].

The placenta is an immunoprivileged organ with a weakened immune response and a target for several viral infections [7]. Viruses such as cytomegalovirus (CMV), herpes simplex virus 1 and 2 (HSV), rubella virus, human immunodeficiency virus (HIV), and recently Zika virus has been shown to be able to cross the placental barrier and may be associated with severe malformations fetal development [8, 9]. The morphological response to viral infections differs: while CMV and HSV classically cause chronic lymphoplasmacytic villitis, there is no inflammatory response in Zika virus infection, but proliferation of Hofbauer cells (specialized placental macro-

phages) can be observed [10].

Pregnant women infected with other coronaviruses, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), have already been investigated in small case series. ICU hospitalization and maternal mortality rates were significantly higher among SARS-infected pregnant women than in the general population, and regardless of the trimester of infection. Fetal outcome was characterized by higher rates of miscarriage, intrauterine fetal death, and preterm birth [11]. Placental weight was below the 5th percentile in a series of seven patients, two of whom had abnormal pathology findings (thrombotic vasculopathy with avascular fibrous villi and/or placental infarction) [12]. When infection occurred within a week before birth, there was no restriction of fetal growth. When infection occurred 1 month or more before birth, two fetuses (2/3, 33 %) had fetal growth restriction with oligohydramnios associated with the abnormal placenta presented above. In the group of patients who gave birth in the acute phase of the disease, the placental test showed pronounced signs of fetal and maternal malperfusion, but there was no increase in inflammatory infiltrates or signs of villitis. Pooled information on pregnancy outcome in women infected with MERS showed no risk of miscarriage, but showed a higher risk of preterm birth and preeclampsia. None of the SARS or MERS studies showed signs of vertical transmission during the follow-up period [13]. So far, no morphological assessments of the placenta have been published in MERS-positive patients [14, 15]. two fetuses (2/3, 33 %) had fetal growth restriction with oligohydramnios associated with the abnormal placenta presented above. In the group of patients who gave birth in the acute phase of the disease, the placental test showed pronounced signs of fetal and maternal malperfusion, but there was no increase in inflammatory infiltrates or signs of villitis. Pooled information on pregnancy outcome in women infected with MERS showed no risk of miscarriage, but showed a higher risk of preterm birth and preeclampsia. None of the SARS or MERS studies showed signs of vertical transmission during the follow-up period [13]. So far, no morphological assessments of the placenta have been published in MERS-positive patients [14, 15]. In the group of patients who gave birth in the acute phase of the disease, the placental test showed pronounced signs of fetal and maternal malperfusion, but there was no increase in inflammatory infiltrates or signs of villitis. Pooled information on pregnancy outcome in women infected with MERS showed no risk of miscarriage, but showed a higher risk of preterm birth and preeclampsia. None of the SARS or MERS studies showed signs of vertical transmission during the follow-up period [13]. So far, no morphological assessments of the placenta have been published in MERS-positive patients [14, 15]. In the group of patients who gave birth in the acute phase of the disease, the placental test showed pronounced signs of fetal and maternal malperfusion, but there was no increase in inflammatory infiltrates or signs of villitis. Pooled information on pregnancy outcome in women infected with MERS showed no risk of miscarriage, but showed a higher risk of preterm birth and preeclampsia. None of the SARS or MERS studies showed signs of vertical transmission during the follow-up period [13]. So far, no morphological assessments of the placenta have been published in MERS-positive patients [14, 15].

The aim: examine pathological placental changes in pregnant women infected with the

new coronavirus COVID-19

Materials and methods: On September 4, 2020, placental tissues of pregnant women diagnosed with COVID-19 were collected from the Kagan maternity complex in the Bukhara region and sent to the pathological and anatomical bureau of the Bukhara region. Relevant clinical data, laboratory results from medical records were collected.

According to guidelines for fixing a COVID-19 surgical specimen, placental tissue was completely fixed with 3.7 % formaldehyde solution within 48 hours [12, 14, 17]. Then the procedures recommended in the literature for a general examination of the placenta were performed [13, 15]. Materials were carefully checked and fully sampled and normal cuts were made after paraffin embedding. Each slice is 4 μm thick. All sections were observed and reviewed by the pathologist and the attending physician.

Research results. All 19 patients were hospitalized in the third trimester of pregnancy for treatment and monitoring of the condition of the patients. All patients were found to have positive throat swab test result for COVID-19 virus nucleic acid, and one had a confirmed clinical result. The age of the patients was from 21 to 36 years, the average age was 28.5 ± 1.5 years.

Three patients had mild symptoms of COVID-19 pneumonia. 1 case of prenatal fever with chest tightness, 2 cases of puerperal fever, 3 patients had no clinical symptoms such as sore throat, chest pain, shortness of breath and fatigue.

The results of laboratory studies showed that C-reactive protein and hemostatic system parameters were significantly increased, in 3 patients it exceeded the upper limits of the norm, there was no significant leukopenia and lymphopenia, transaminase was normal, not a single case in pregnant women progressed to severe illness and all were cured and discharged after treatment. There were no serious adverse outcomes for mother and child.

When studying the hemostatic system, some deviations were revealed: in pregnant women with COVID-19 more pronounced disorders of the coagulation link of hemostasis were observed. Despite the mild course of the disease, changes in the hemostasis system were significantly higher ($P < 0.05$). The increase in fibrinogen is of clinical importance. The level of D-dimer is significantly increased in severe cases, which is their potential risk factor and the basis for a poor prognosis. In patients receiving anticoagulant therapy, the levels of APTT, D-dimer, and VSC were monitored. The issue of stopping anticoagulant therapy was decided on the basis of coagulogram and D-dimer parameters. An increase in the level of ferritin and C-reactive protein by 2-3 times indicated bacterial infections, which were started on antibiotic therapy from the moment of admission.

When examining the morphological features of the placenta, several deviations were revealed. When studying the morphological features of the placenta, it was revealed that the weight of the placenta in pregnant women with COVID-19 was slightly larger (from 350.0 to 690.0 ± 0.2 g, on average 589.0 ± 0.5 g). Placental volume ranged from 420 to 655 cm^3 (mean 503 cm^3). Basically, at the birth of children with hypoxic syndrome, foci of hemorrhages and necrosis were found in the placenta of mothers.

The remaining tissues, including the fetal membranes and umbilical cord, do not have obvious anomalies. Microscopic observation: the area of the gray nodule in Example 1 consists of a large number of small capillary-like blood vessels with a small amount of loose interstitium between the blood vessels, in the rest of the placental tissue, fibrin deposits in the interstitium of the villi and around the villi are increased, and local syncytial nodules increase.

The most significant change is a multifocal infarction of the placental tissue, which shows collapse of the villous space with fibrin deposition under the microscope and finally forms ghostly after-images of the villous (rice one). Fibrin deposits in the interstitium around the villi can be seen in placental tissue, and localized syncytial nodules are enlarged (Figure 1).

It was also revealed an increase in vascularization due to hyperplasia (expansion) of capillaries, which, as you know, is a characteristic compensatory mechanism that ensures the development of the fetus. In all cases, there was no obvious chorioamnionitis,

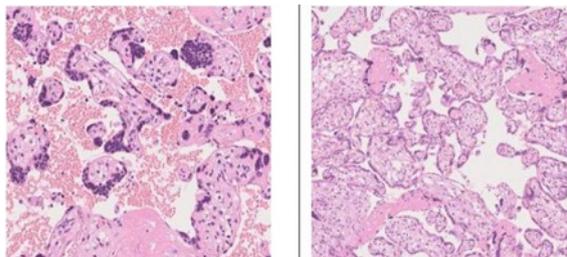


Fig. 1. Microscopic picture of fibrin deposits in the interstitium around the villi of the placenta of pregnant women with COVID-19

there was no clear formation of virus inclusion bodies; no abnormalities in the umbilical cord and membranes under the microscope, other than a slight thrombosis in the blood vessels of the umbilical cord, and no clear nucleated red blood cells in the vessels of the villi were found in our cases.

After analyzing the clinical characteristics of 19 pregnant women infected with COVID-19 in the third trimester. Limited data showed that the clinical manifestations of pregnant women infected with COVID-19 were similar to those of normally infected women, and there were no serious adverse maternal and child outcomes. Under the microscope, no specific pathological changes indicative of a placental infection were found; placental tissue nucleic acid tests and neonatal throat swabs were negative, suggesting that there is no direct evidence of vertical transmission of COVID-19 infection from mother to fetus in late pregnancy. This study provides important clues to understanding the clinical features of third trimester COVID-19 infection.

Conclusions. Thus, 19 cases of placental pathology with COVID-19 infection were reported in the third trimester of pregnancy in Bukhara region. Currently, there is no direct evidence of vertical transmission of the infection from mother to fetus in the third trimester of pregnancy, since the children were born in a relatively satisfactory condition, respectively, after treatment according to the COVID-19 clinical protocol. At the same time, current data and information on motherhood related to COVID-19 is still very lacking and the clinical sample size needs to be increased for further analysis.

References:

1. Д. З. Юнусова Медико-социальные аспекты материнской смертности в условиях пандемии коронавирусной инфекции (COVID-19) // Вестник врача, № 1 (102), 2022. С.105-108. DOI: 10.38095/2181-466X-20221042-95-98
2. Ж. А. Ризаев, И. Р. Агабабян, С. Ш. Солева Фенофибриновая кислота - средство для снижения инфицирования больных коронавирусом SARS-COV-2 // Вестник врача, № 4 (101), 2021. С.135-140. DOI: 10.38095/2181-466X-20211014-135-140
3. Babadzhanova G.S. et al. Clinical aspects of varicose veins in pregnant women // University science: a look into the future. - 2020. - S. 556-559.
4. Babadzhanova G.S., Dustova N.K., Aslonova M.Zh., Ikhtiyarova G.A. Clinical aspects of varicose veins in pregnant women//International scientific conference dedicated to the 85th anniversary of the Kursk State Medical University. - 2020. - No. 1. - FROM.556 - 559.
5. Bakhodirova SF, Ikhtiyarova GA, Aslonova MJ & Davlatov SS (2020). Features of perinatal outcomes in women after supporting reproductive technologies. European Journal of Molecular and Clinical Medicine, 7 (2), 6350-6356.
6. Bakhramova, S.U., Ikhtiyarova, G.A., Dustova, N.K., & Kudratova, R.R. (2021). Thrombophilic Complications in the Development of Gestational Hypertension. Annals of the Romanian Society for Cell Biology, 6198-6205.
7. Dobrokhotova Yu.E., Ikhtiyarova G.A., Dustova N.K. Features of acurrent pregnancy and delivery in pregnant women with varicose // Eurasian Bulletin of Pediatrics. - 2020. - No. 2 (5). - S. 182 - 186.
8. Dustova N.K. Features of the course of pregnancy and childbirth in patients with varicose veins of the small pelvis and lower limbs // Tibbiyotda yangi kun. - 2018. - No. 8. - S. 164 - 167.
9. Dustova N.K. Ikhtiyarova G.A. Aslonova M.Zh. The role of infectious factors in fetal loss syndrome// Tibbiyotda yangi kun. - 2020. - No. 1 (30/2) - C. 116 - 119.
10. Dustova N.K., Babadjanova G.S., Ikhtiyarova G.A. Reculiarities of pręgnanęu and lobar ręcularities in patients with varicose veins of the relvis// International Journal of Bioscience and Biotechnologu. - 2019. Vol.11. Iss.9. - P. 92 - 97.
11. Dustova N.K., Hafizova D.A. Prevention of complications of varicose veins of relvis organs in women of reproductive age// Asian Journal of Multidimensional Research. - 2018. - No. 7(11). - P. 14 - 29.
12. Ikhtiyarova G.A., Dustova N.K., Khasanova M.A., Davlatov S.S. (2021). Pathomorphological changes of the placenta in pregnant women infected with coronavirus COVID-19. International Journal of Pharmaceutical Research, 13(1), 1935-1942. doi: 10.31838/ijpr/2021.13.01.283
13. Ikhtiyarova GA, Khamidova Sh.Sh., Matrizayeva JG, Aslonova MJ, Dustova NK, Rozikova DK (2020). Uterine fibroids and endometriosis as a problemgenetic of systemic disease Egypt/Egyptology, 17(6),13931-13946
14. Ikhtiyarova G.A., Tosheva I.I., Aslonova M.J., Dustova N.K. (2020). Prenatal rupture of amnion membranes as A risk of development of obstetrics pathologies. European Journal of Molecular and Clinical Medicine, 7(7),530-535.
15. Ikhtiyarova G.A., Dustova N.K., Dobrokhotova Yu.E., Matrizayeva G.Zh., Aslonova M.Zh. Features of the course of pregnancy and childbirth in pregnant women with varicose veins // Tibbiyotda yangi kun. - 2020. - No. 1 (29). - S. 69 - 71.
16. Pulatova R.A., Dustova N.K. Varicose veins of the pelvis in women suffering from varicose veins of the lower extremities // XXI All-Russian Scientific Forum "Mother and Child". - 2015. - S. 176 - 177.
17. Tosheva I.I., Ikhtiyarova G.A. Morphological and microbiological changes in the placenta in women with premature rupture of amniotic fluid // Journal of Problems of Biology and Medicine. - 2019.- No. 4.2(115). - P.146 - 149.