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FEATURES OF THE FETO-PLACENTAL COMPLEX IN WOMEN WITH POSITIVE HIV STATUS

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Abstract
The incidence of HIV infection in the world is steadily increasing. The total number of people infected with HIV in 2022 reached 39 million people. Of these, 37.5 million are people aged 15 years and older, and 1.5 million are younger. The majority (53%) were female [Fact sheet - Global HIV statistics, UNAIDS]. The impact of HIV infection on the occurrence and progression of various obstetric complications is a subject of debate among most researchers. Some authors associate the development of gestational complications with the level of viral load, the state of the immune system, others with the duration of the infectious process, as well as the presence of concomitant coinfection or obstetric history.

Keywords: HIV infection, pregnancy, fetoplacental complex.

Introduction

Although the adverse effect of HIV infection on the course of gestation is obvious, most authors disagree regarding the impact of the virus on the development of obstetric pathological processes. Some believe that the human immunodeficiency virus does not affect the course of gestation, while others point to a detrimental effect on perinatal pregnancy outcomes [1,2,11]. Disagreements in the positions taken are associated with concomitant factors that are typical for most pregnant HIV-infected women, although not directly related to them. These factors can have a significant impact on the outcome of pregnancy and childbirth, which leads to ambiguous research results. Researchers face difficulties in

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establishing a clear link between infection and obstetric problems, since these factors can not only aggravate the situation, but also create false conclusions. Thus, the complexity of the situation requires careful analysis and consideration of all possible variables, which causes contradictions in assessing the impact of HIV on the health of pregnant women [9,15]. This situation contributes to the emergence of additional disputes among obstetricians and gynecologists, neonatologists, and infectious disease specialists, due to disagreements regarding the appropriateness of certain tactics for managing such pregnant women.

If we consider the pathogenesis of HIV infection, the main mechanism of infection in the antenatal period is intranatal, i.e. occurring during childbirth, followed by the transplacental mechanism. In the transplacental route of HIV infection, the risk factor is the occurrence of changes in the placenta by the type of inflammation, in particular chorioamnionitis and placentitis, as well as directly, violations of the integrity of the placenta that occur during its detachment [6,10,14].

An increased risk of vertical transmission of infection is associated with a high content of HIV RNA copies in 1 ml of blood, a reduced state of cellular immunity (CD4 cells), and later stages of the process.

Thus, according to Kravchenko E.N. (2019) et al., among HIV-positive pregnant women with perinatal transmission of the virus, more than 50% had a high viral load [7].

According to Makatsaria A.D. et al. (2016), the metamorphosis of giant cells and the death of endothelial cells, virus replication in macrophages with their subsequent elimination, as well as an increase in the expression of the antiangiogenic factor TGFβ underlie pathological changes in the syncytiocapillary membrane in HIV-infected pregnant women [8].

According to the results of the work of Belokoneva T.S. et al. (2018), it was found that newborns who had vertical transmission of the virus had hypotrophy compared to newborns in whom preventive measures to prevent perinatal transmission of the virus were successful, while HIV-positive mothers did not differ significantly in gestational age at delivery [5]. This, according to the authors, is associated with the occurrence of morphofunctional changes in the

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fetoplacental system, which led to inadequate maintenance of exchange between the mother and the fetus with the subsequent occurrence of low weight and growth of the newborn.

Features of the course of pregnancy in women with seropositive HIV infection are impaired fetoplacental circulation due to pathological changes in capillary blood flow, which can lead to the development of intrauterine fetal hypotrophy, antenatal death as a result of premature aging of the placenta [5,6,9].

The risk of developing obstetric complications in pregnant women with HIV as a result of increasing immunodeficiency is associated with an increase in the viral load, which is the main cause of the development of various obstetric complications. Compared with HIV-negative women, the risk of developing a complicated pregnancy in women with HIV infection is higher.

The role of HIV infection in the development of the pathological course of pregnancy seems to be a complex process. Since during pregnancy, exacerbations of other diseases (extragenital diseases, hepatitis, endocrine diseases, etc.), opportunistic infections (tuberculosis) are more often observed [6, 13].

Dissociated maturation of the villous chorion, which results in chronic placental insufficiency in patients infected with HIV, develops as a result of an imbalance of proangiogenic (VEGF, bFGF, CD31) and antiangiogenic (TGF-b1, Tsp-1) factors. When studying the placental tissues during transplacental transmission of HIV, a marked decrease in CD68+ and CD14+ macrophages is found. Of course, a defect in the placental barrier facilitates fetal infection. In this regard, therapy for placental dysfunction, along with specific chemoprophylaxis with antiretroviral drugs and treatment of opportunistic infections, are pathogenetically justified in reducing perinatal infection [1,5,11].

As a result of the resulting dysfunction of the fetoplacental system, various perinatal complications are naturally observed in HIV-positive pregnant women. In particular, in the studies of scientists, a high proportion of complications such as intrauterine infection of the fetus, respiratory failure syndrome, limitation of weight and height indicators, damage to the central and peripheral nervous systems in the fetus are noted [1, 7, 15]. As is known, the main etiological component of the occurrence of intrauterine fetal hypoxia, the appearance of fetal

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growth restriction syndrome is considered to be the development of chronic placental insufficiency. According to Belotserkovtseva L.D. (2014), HIV transmission to the fetus can be carried out hematogenously with damage to the stromal cells of the villi or the transition of HIV from the basal plate to trophoblastic cells. These changes are characteristic of an earlier stage of pregnancy. In the late stages of gestation, infection occurs as a result of the passage of the virus into the amniotic fluid through the chorionic plate. The study indicates the presence of morphological changes in all placentas of HIV-infected women. Moreover, the detected changes are characteristic of most viral infections. The main morphological features of the placentas of HIV-infected women were the formation of symplast in decidual cells, the presence of pathological changes in trophoblast cells, as well as sclerotic changes in the endothelium and stroma of the villi. Microscopic examination revealed changes in the endothelium, stromal fibroblasts of the villi, and decidual trophoblast cells, in particular an increase and clearing of their nuclei. Signs of acute chorioamnionitis were most frequently observed in the placentas of HIV-infected women [6]. According to E.K. Aylamazyan et al. [3], compensatory reactions to morphologically conditioned adaptation of the placenta. Hyperplasia of the chorionic capillaries may include hypervascularization, reaction of cells with low acidity, hyperplasia, dilation of the vessels of synthetotrophoblasts, terminal villi. The severity of these symptoms and the area of placental damage depends on the degree of compensatory and adaptive reactions, morphological bases of compensatory and adaptive reactions. Compensatory-adaptive reactions reach their peak activity during physiological pregnancy, while a decrease in compensatory-adaptive activity is noted in chronic placental insufficiency. It is known that the course of gestation in patients infected with HIV is aggravated by the development of fetoplacental insufficiency. This may occur as a result of both the influence of the HIV infection itself and the low level of health in this contingent of women. HIV-seropositive women more often give birth to newborns with growth-weight deficit. According to the results of the study by Bogadejnikov I.V. et al. (2014), in addition to growth and weight deficit, newborns of women with HIV without perinatal HIV transmission showed signs

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of anemia, protein-energy spectrum disorders, and idiopathic suppression of the immune system. At the same time, the immune response to vaccination in such children is similar to that in HIV-infected infants [4]. Opruzhnikov A.V. (2011) notes a sixfold increase in the development of hyporeflexia and muscle hypotonia in newborns from women with HIV compared to the control group [8].

As a consequence of immunodeficiency in pregnant women with HIV, which increases with the progression of pregnancy, intrauterine infection of the fetus occurs significantly more often, especially in women without pre-pregnancy preparation. In this case, perinatal transmission of HIV, when preventive measures are taken, in particular timely and full use of antiretroviral drugs, operative delivery and refusal of breastfeeding, reaches minimal levels [2,10,15]. Analysis of Doppler data of the uteroplacental-fetal blood flow in the works of Shteiman A.A. (2016) established the presence of hemodynamic disturbances in the arteries, both in the umbilical and uterine arteries in pregnant women with HIV. At the same time, an inverse relationship is noted between the hemodynamics of the uteroplacental-fetal complex and the anthropometric parameters of the newborn and its condition on the Apgar scale at 5 minutes [13]. Summarizing the above, a review of domestic and foreign literature showed that there are quite a few research papers on the impact of HIV infection on the course and outcome of pregnancy.

There are works devoted directly to the occurrence of gestational disorders in women with HIV, separate works related to the discrepancy between the anthropometric parameters of newborns born to HIV-seronegative women. Rare cases of pathomorphological and immunohistochemical analysis of placentas obtained from HIV-infected women are described. Although the incidence continues to grow throughout the world, successful preventive measures to prevent vertical transmission of HIV do not remove the relevance of the problem of pregnancy complications and subsequent perinatal disorders in newborns. Research studies related to the solution of the listed problems have not only practical, but also scientific significance.

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