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RH INCOMPATIBILITY AS A CURRENT PROBLEM IN MODERN OBSTETRICS

Abstract

Rh incompatibility remains one of the current challenges in modern obstetrics and perinatology, as it may lead to the development of Hemolytic disease of the fetus and newborn, intrauterine hypoxia, hydrops fetalis, and severe perinatal complications, including fetal death. Despite significant progress in the prevention of Rh alloimmunization, this condition continues to be clinically relevant due to delayed diagnosis, insufficient prophylactic coverage, and the complexity of managing sensitized pregnancies.

The article analyzes contemporary approaches to the prevention, diagnosis, and management of pregnant women at risk of Rh alloimmunization. The main pathogenetic mechanisms of Rh incompatibility, risk factors for maternal sensitization, and the role of the maternal immune response in the development of fetal hemolytic anemia are discussed. Particular attention is paid to modern methods of prenatal diagnosis, including determination of anti-D antibody titers, ultrasonography, Doppler assessment of the fetal middle cerebral artery, and noninvasive fetal RhD genotyping using analysis of cell-free fetal DNA in maternal blood.

The study emphasizes the importance of timely fetal monitoring for early detection of hemolytic anemia and prevention of severe forms of fetal hemolytic

disease. It is highlighted that the timely administration of anti-D immunoglobulin during pregnancy and after delivery remains the most effective method for preventing Rh alloimmunization. The implementation of modern preventive protocols, improvement of molecular genetic diagnostic methods, and a personalized approach to pregnancy management contribute to reducing severe perinatal complications and improving perinatal outcomes.

Keywords: Rh incompatibility, Rh alloimmunization, Hemolytic disease of the fetus and newborn, anti-D immunoglobulin, prenatal diagnosis, Doppler assessment, pregnancy.

Problem statement. Rh incompatibility is one of the most important causes of Hemolytic disease of the fetus and newborn, which may lead to severe perinatal complications, including intrauterine fetal death. Despite significant advances in the prevention of Rh alloimmunization, this issue remains relevant due to insufficient coverage of preventive measures, delayed diagnosis, and the complexity of managing sensitized pregnant women.

Rh alloimmunization remains a serious medical and social problem because severe forms of hemolytic disease may result in fetal anemia, hydrops fetalis, preterm birth, neurological complications, and increased perinatal mortality. In many cases, the disease develops progressively and may remain asymptomatic until significant fetal impairment occurs. Therefore, timely identification of women at risk and regular prenatal monitoring are essential components of effective obstetric care.

Modern obstetrics is focused on the early identification of women at risk of developing Rh incompatibility, the implementation of timely preventive measures, and careful monitoring of fetal condition. Particular importance is given to the use of advanced diagnostic methods, including antibody screening, ultrasonography, Doppler assessment, and molecular genetic technologies for fetal RhD genotyping.

The improvement of diagnostic technologies and the standardization of preventive protocols are key strategies for reducing the incidence of hemolytic disease of the fetus and newborn.

In addition, the widespread use of anti-D immunoglobulin prophylaxis has significantly decreased the frequency of Rh sensitization and improved perinatal outcomes worldwide. However, further optimization of screening programs, accessibility of modern diagnostic methods, and adherence to international clinical guidelines remain important priorities in contemporary obstetric practice.

Analysis of recent research and publications. Contemporary studies indicate that Rh incompatibility remains an important issue in obstetrics and perinatology despite the significant reduction in the incidence of severe forms of Hemolytic disease of the fetus and newborn due to the implementation of anti-D prophylaxis [1, 2]. Scientific publications extensively describe the pathogenetic mechanisms of Rh alloimmunization, the role of fetomaternal transfusion, and the maternal immune response in the development of hemolytic disease of the fetus and newborn [1, 3]. It has been proven that the entry of Rh-positive fetal erythrocytes into the bloodstream of an Rh-negative mother triggers the synthesis of IgG antibodies, which cross the placenta and cause hemolysis of fetal erythrocytes [4, 7].

Modern research pays considerable attention to the risk factors for the development of Rh alloimmunization, among which previous pregnancies, abortions, invasive prenatal procedures, bleeding during pregnancy, and transfusion of incompatible blood are of primary importance [3, 8, 9]. Authors emphasize that the absence of timely prophylaxis significantly increases the risk of developing hemolytic disease of the fetus and severe perinatal complications [2, 8].

A separate area of contemporary research is devoted to improving methods of prenatal diagnosis and fetal monitoring. Scientific studies confirm the high

diagnostic value of determining anti-D antibody titers, ultrasonography, and Doppler assessment of the fetal middle cerebral artery for the early detection of hemolytic anemia [7, 11, 14]. Significant progress in the management of Rh-incompatible pregnancy is associated with the introduction of noninvasive fetal RhD genotyping using analysis of cell-free fetal DNA in maternal blood, which allows the personalization of prophylactic strategies and helps avoid unnecessary administration of anti-D immunoglobulin [12].

Modern literature also actively investigates the effectiveness of anti-D immunoglobulin as the primary method for preventing Rh alloimmunization. It has been demonstrated that timely administration of anti-D immunoglobulin during pregnancy and after delivery significantly reduces the risk of sensitization and the development of hemolytic disease of the fetus [2, 8]. At the same time, authors emphasize the need to improve monitoring algorithms for sensitized pregnant women and to enhance access to modern diagnostic and preventive methods [7, 13].

Purpose of the study. To analyze contemporary approaches to the prevention of Rh incompatibility and Hemolytic disease of the fetus and newborn, and to determine the effectiveness of modern methods of diagnosis, monitoring, and preventive management of pregnant women at risk of Rh alloimmunization.

Presentation of the main material. Rh incompatibility is one of the most important immunological complications of pregnancy that occurs due to incompatibility between maternal and fetal blood according to the Rh factor. The condition most commonly develops when a pregnant woman has Rh-negative blood and the fetus inherits the Rh-positive antigen from the father. According to epidemiological studies, approximately 10–15% of the population is Rh-negative, while the risk of delivering an Rh-positive child in Rh-negative mothers is about 60–70%, depending on the paternal genotype [1].

Before the introduction of specific immunoprophylaxis, hemolytic disease of the fetus and newborn was one of the leading causes of perinatal mortality. In the mid-20th century, the rate of sensitization among Rh-negative women after pregnancy with an Rh-positive fetus reached 13–16%, whereas the modern use of anti-D immunoglobulin has reduced this rate to less than 1% [2].

Pathogenetically, Rh incompatibility develops as a result of the entry of Rh-positive fetal erythrocytes into the maternal bloodstream. Even a minimal volume of fetomaternal transfusion, approximately 0.1 mL of fetal blood, may trigger a maternal immune response [3].

During the initial exposure, the immune system predominantly produces IgM antibodies, which are unable to cross the placental barrier. However, immunological memory subsequently develops, and upon repeated exposure to the Rh antigen, IgG antibodies are rapidly synthesized. These antibodies can cross the placenta and induce hemolysis of fetal erythrocytes [4]. As a result of massive erythrocyte destruction, anemia, tissue hypoxia, and impairment of fetal hepatic and cardiovascular function develop. With progression of the hemolytic process, extramedullary hematopoiesis is activated, the fetal liver and spleen enlarge, and decreased oncotic pressure leads to generalized edema and the development of hydrops fetalis [5].

One of the most severe consequences of Rh incompatibility is Hemolytic disease of the fetus and newborn. The severity of the condition depends on the concentration of maternal antibodies and the intensity of hemolysis. Mild forms are characterized by moderate hyperbilirubinemia after birth, whereas severe forms are accompanied by hydrops fetalis, generalized edema, heart failure, and multiple organ dysfunction [6].

Hydrops fetalis is a critical condition in which mortality without treatment may exceed 50–80%. According to contemporary studies, severe forms of alloimmunization remain associated with a high risk of preterm birth, the need for

intrauterine transfusions, and perinatal complications [15]. As a consequence of chronic hypoxia and hyperbilirubinemia, newborns may develop central nervous system damage, including bilirubin encephalopathy, hearing impairment, seizure syndrome, and persistent neurological disorders [7].

The risk of Rh alloimmunization significantly increases in the presence of factors associated with fetomaternal transfusion. Sensitization most commonly occurs after delivery of an Rh-positive fetus; however, spontaneous and induced abortions, ectopic pregnancy, invasive procedures, bleeding during pregnancy, placental abruption, and abdominal trauma are also important contributing factors [8].

After spontaneous abortion, the risk of sensitization is approximately 1.5–2%; after invasive procedures, up to 5%; and after delivery without prophylaxis, it may exceed 15%. Particularly high risk is observed in women with repeated pregnancies and a complicated obstetric history. In addition, the risk of sensitization increases after cesarean section, manual removal of the placenta, and obstetric manipulations associated with disruption of the placental barrier [8].

Modern approaches to the diagnosis of Rh incompatibility are based on the early identification of women at risk. All pregnant women undergo determination of blood group and Rh status during their first prenatal visit [10]. Rh-negative women are обязательно tested for anti-D antibody titers. In the absence of sensitization, antibody screening is repeated at 18–20 weeks, 28 weeks, and before delivery. An antibody titer of 1:16 or higher is considered critical, as it is associated with a high risk of severe Hemolytic disease of the fetus and newborn. An increase in antibody titers requires more frequent monitoring and comprehensive examination. Contemporary practice also includes the determination of IgG antibody subclasses, since IgG1 and IgG3 possess the highest hemolytic activity [11].

An important achievement of modern perinatology has been the introduction of noninvasive fetal RhD genotyping through analysis of cell-free fetal DNA in maternal blood [9]. This method has a sensitivity exceeding 99% and allows determination of fetal Rh status as early as the 10th week of pregnancy [13]. This approach helps avoid unnecessary administration of anti-D immunoglobulin in cases where the fetus is also Rh-negative. The use of this technology significantly reduces the number of invasive procedures and contributes to personalized pregnancy management. Furthermore, the application of molecular genetic methods enables timely prediction of the risk of severe hemolytic disease of the fetus and optimization of monitoring strategies [13].

Ultrasonography remains the primary method for assessing fetal condition in Rh incompatibility. It allows evaluation of fetal size, placental thickness, amniotic fluid volume, and the presence of signs of hydrops fetalis [14].

Characteristic ultrasound signs of severe hemolytic disease include ascites, pleural effusion, subcutaneous edema greater than 5 mm, cardiomegaly, and hepatosplenomegaly. Significant placental thickening also indicates fetal decompensation and severe disease progression. In cases of progressive anemia, signs of heart failure and impaired placental circulation may be observed, requiring immediate adjustment of pregnancy management strategies.

The most effective method for preventing hemolytic disease of the fetus is the timely administration of Rh(D) anti-D immunoglobulin. Current recommendations include routine antenatal prophylaxis for Rh-negative women, as well as administration of the drug after delivery, invasive procedures, abortions, bleeding episodes, and other situations associated with the risk of fetomaternal transfusion. The use of anti-D immunoglobulin after delivery and during pregnancy significantly reduces the risk of Rh alloimmunization and the development of hemolytic disease of the fetus [12].

Due to the implementation of modern preventive methods, molecular genetic diagnostics, and careful fetal monitoring, the incidence of severe forms of Hemolytic disease of the fetus and newborn has significantly decreased, leading to improved perinatal outcomes.

Conclusions. Rh incompatibility remains one of the most significant immunological complications in modern obstetrics, as it may lead to the development of Hemolytic disease of the fetus and newborn, intrauterine hypoxia, hydrops fetalis, and severe perinatal complications, including fetal death. Despite considerable progress in preventive strategies, the problem continues to be clinically relevant due to the risk of maternal sensitization and the complexity of managing alloimmunized pregnancies.

Contemporary diagnostic approaches, including determination of anti-D antibody titers, ultrasonography, Doppler assessment of the fetal middle cerebral artery, and noninvasive fetal RhD genotyping using cell-free fetal DNA, enable early identification of pathological changes and accurate evaluation of fetal condition. These methods contribute to timely risk stratification, optimization of pregnancy management, and reduction in the incidence of severe fetal complications.

The timely administration of Rh(D) anti-D immunoglobulin remains the most effective method for preventing Rh alloimmunization. Routine antenatal and postnatal prophylaxis significantly decreases the risk of maternal sensitization and improves perinatal outcomes. Therefore, further improvement of screening programs, accessibility of modern diagnostic technologies, and adherence to standardized preventive protocols are essential for reducing the incidence of hemolytic disease of the fetus and newborn and improving maternal and neonatal health outcomes.

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