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Impact of Immunization Prophylaxis on the Course of Pregnancy in Rh-Negative Women

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The purpose of the work was to study the characteristics of the course of pregnancy in women who received Rh immunoprophylaxis.

Materials and methods. 64 pregnant women were examined, the average age of whom was 30.55 ± 7.0 (18–43) years. Out of 64 pregnant women, 24 (37.5%) were pre-pregnant, 40 (62.5%) were re-pregnant. The somatic and obstetric anamnesis of all pregnant women included in this study was studied. The average number of pregnancies in 40 repeat-bearing women with Rh (-) blood was 2.34 ± 0.6 (1–5). The obtained results of the study were subjected to statistical processing. At the same time, a computer program "Statgraph" was used, designed for statistical data processing in a parametric and nonparametric way. The work was carried out on the basis of the Educational and Surgical Clinic of the Azerbaijan Medical University.

Results and discussion. The study of the course of pregnancy in women with no Rh isosensitization made it possible to establish the presence in the first trimester of a high incidence of anemia (27.3%), vomiting and nausea (21.2%), asymptomatic bacteriuria (17.4%), threatened abortions (14.4%).

In the second trimester, there was also a high incidence of anemia (28.6%), asymptomatic bacteriuria (21.4%), threatened abortions (15.7%), exacerbation of chronic pyelonephritis (12.9%), mild preeclampsia (10%).

In the third trimester, a high frequency of the menace of uterine rupture along the scar was 22.6%, the threat of preterm birth was 18.5%, and acute respiratory viral infection was 16.9%. It was found that the frequency of abdominal delivery was 73.4%, the frequency of the vaginal birth was 26.6%.

A study of the condition of newborns made it possible to establish a satisfactory condition in 70%, a moderate condition in 18.8%, and a serious condition in 6.3% of infants. The severity of the condition was determined by the presence of prematurity in 15.6%, weakness of labor and labor stimulation in 6.3%, and the presence of umbilical cord pathology in 6.3%.

None of the newborns had clinical and laboratory manifestations of hemolytic disease of the newborn, which reflects the effectiveness of the prevention of Rh isosensitization, the introduction of anti-D immunoglobulin during pregnancy and after childbirth.

Conclusion. The use of anti-D immunoglobulin after previous births and at a gestational age of 27.7 ± 0.09 weeks in present pregnancy eliminates isosensitization in pregnant women with Rh-negative blood. Timely prophylaxis of anti-D immunoglobulin prevents the development of hemolytic disease of the newborn in this group of women. The use of anti-D immunoglobulin is of great importance to reduce perinatal morbidity and mortality in pregnant women with Rh-negative blood.

Keywords: Rh-positive blood factor, Rh isosensitization, immunization, isoimmunization, anti-Rh (D) immunoglobulin.

Introduction. An urgent problem of modern obstetrics is the presence of isoimmunization by Rh conflict. According to W. Sameer, et.al. [1] 15–20% of white women and 5–10% of African Americans are Rh negative.

It was found that in Asia, America, and India, the frequency of Rh-negative blood is 5% [2, 3, 4].

According to Russian authors, the frequency of Rh isosensitization ranges from 1.2%, which is explained by the high cost of antiresus immunoglobulin and, accordingly, the inability to apply it to all women in this country [4].

According to I. V. Mitra [5], a risk factor for the development of Rh isosensitization in women with Rh-negative blood is transfusion of Rh-positive donor blood. The frequency of this factor, as the cause of Rh isosensitization of women, is 2.9%. The lack of prevention of immunoglobulin antiresus is the cause of rhesus sensitization in 97.1% of pregnant women. Another reason for Rh isosensitization is the exacerbation of herpes and cytamegalovirus infection in 45.9% and the presence of fetoplacental insufficiency in 28.7%.

According to modern studies, it has been established that the use of antiresus immunoglobulin Rh (-) in women in the prevention of Rh sensitization significantly affects the course of pregnancy and the outcome of childbirth [6, 7].

According to L. V. Tkachenko et al., [8] it was found that the management of pregnant women with Rh-negative blood, starting from the early stages of pregnancy (from 8–10 weeks) involves the determination of the antibody titer at least once a month. It is

also important to determine the rhesus and blood type of the spouse of a pregnant woman. In the presence of Rh (-) blood of a Rhesus spouse, immunization is not indicated. With Rh (+) of the spouse's blood, it is important to determine the antibody titer every 4 weeks until 28 weeks of gestation. In the absence of an antibody titer, a pregnant woman is shown to undergo Rh isoimmunization with anti-Rh (D) immunoglobulin at a dose of 1250–1500 IU (250–300 mcg). In the absence of prophylaxis at 28 weeks of pregnancy, the administration of antiresus immunoglobulin is possible in the near term of gestation against the background of the absence of Rh antibodies.

According to scientific research, the use of invasive diagnostic methods, including chorionic villus biopsy, amniocentesis, cerclage, embryo reduction in multiple pregnancies are indications for additional immunoprophylaxis [9, 10].

Prevention of rhesus isoimmunization in the first trimester of pregnancy is carried out by anti-Rh (D) immunoglobulin at a dose of 625 IU (125 mcg), in the second trimester at a dose of 1250–1500 IU (250–300 mcg). It is mandatory to carry out the prevention of Rh immunization in the first trimester after a medical abortion, in the second trimester after spontaneous miscarriage and termination of pregnancy for medical reasons. The effectiveness of Rh immunization prevention is determined 6–12 months after delivery by the presence of antibodies [11, 12].

It has been established that combined, antenatal and postnatal antiresus immunoglobulin prophylaxis reduces the frequency of isosensitization by 100 times [11, 13].

It should be noted that there is no data on the peculiarities of the course of pregnancy in women against the background of the prevention of Rh isosensitization.

The purpose of the work was to study the peculiarities of the course of pregnancy in women who received Rh immunoprophylaxis.

Materials and methods. 64 pregnant women were examined, the average age of whom was 30.55 ± 7.0 (18–43) years.

The study was carried out in compliance with the basic provisions of the "Rules of ethical principles of scientific medical research with human participation", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEC Directive No. 609 (dated 24.11.1986), Orders of the Ministry of Health of Ukraine No. 690 (dated 23.09.2009), No. 944 (dated 14.12.2009), No. 616 (dated 03.08.2012). All the participants were informed about the goals, organization, methods of examination and signed an informed consent to participate in the completely anonymous study.

Out of 64 pregnant women, 24 (37.5%) were pre-pregnant, 40 (62.5%) were re-pregnant. The somatic and obstetric anamnesis of all pregnant women included in this study was studied.

The average number of pregnancies in 40 repeat-bearing women with Rh (-) blood was 2.34 ± 0.6 (1–5).

The obtained results of the study were subjected to statistical processing. At the same time, a computer program "Statgraph" was used, designed for statistical data processing in a parametric and nonparametric way.

The work was carried out on the basis of the Educational and Surgical Clinic of the Azerbaijan Medical University.

Results and discussion. As a result of the study, the obstetric history of pregnant women with Rh (-) blood was studied. The results of the study were presented in **Table 1**.

Table 1 – Outcomes of previous pregnancies in women with Rh (-) blood and absence of Rh isosensitization (according to obstetric history)

Outcomes of previous pregnancies	Abs.	%
Births	41	55.4
Non-developing pregnancy	19	25.7
Medical abortion	7	9.5
Impaired ectopic pregnancy	2	2.7
Spontaneous miscarriage	5	6.8

Note: The total number of pregnancies is taken as 100%.

As can be seen from **Table 1**, 40 repeat births with Rh (-) blood had childbirth in 55.4% of cases, non-developing pregnancy in 25.7%, medical abortion in 9.5%, spontaneous miscarriage in 6.8%, ectopic pregnancy disorder in 2.7%.

It should be noted that all pregnant women after previous childbirth and termination of pregnancy were injected with anti-D immunoglobulin within 72 hours.

A study of the course of a real pregnancy in 64 women with Rh (-) blood and the absence of Rh isosensitization is presented in **Tables 2, 3, 4**.

Table 2 - Frequency of complications in the first trimester of pregnancy in the absence of Rh isosensitization

Complications of pregnancy	Abs.	%
Early toxicosis	28	21.2
Threat of miscarriage	19	14.4
Acute respiratory viral infection	11	8.3
Anemia	36	27.3
Acute cystitis	12	9.1
Exacerbation of chronic cystitis	3	2.3
Asymptomatic bacteriuria	23	17.4

Note: The total number of pregnancies is taken as 100%.

As can be seen from **Table 2**, in the first trimester of pregnancy, against the background of the absence of Rh isosensitization, there was a high incidence of anemia (27.3%), early toxicosis (21.2%), asymptomatic bacteriuria (17.4%), the threat of miscarriage (14.4%).

The frequency of complications observed in the second trimester in pregnant women with the absence of Rh isosensitization is shown in **Table 3**.

Table 3 – Frequency of complications in the second trimester of pregnancy in the absence of Rh isosensitization

Complications in the second trimester of pregnancy	Abs.	%
Risk of miscarriage	11	15.7
Premature discharge of amniotic fluid	2	2.9
Partial detachment of a normally located placenta	3	4.3
Exacerbation of chronic pyelonephritis	9	12.9
Isthmic-cervical insufficiency	3	4.3
Mild preeclampsia	7	10
Asymptomatic bacteriuria	15	21.4
Anemia	20	28.6

As can be seen from **Table 3**, pregnant women with the absence of Rh isosensitization have a high incidence of anemia (28.6%), asymptomatic bacteriuria (21.4%), the threat of miscarriage (15.7%), exacerbation of chronic pyelonephritis (12.9%), mild preeclampsia (10%).

The frequency of complications in the third trimester of pregnancy is shown in **Table 4**.

Table 4 – Frequency of complications in the third trimester of pregnancy in the absence of Rh isosensitization

Frequency of complications in the third trimester of pregnancy	Abs.	%
Threat of premature birth	23	18.5
Premature birth	8	6.5
Chronic fetal hypoxia	8	6.5
Premature discharge of amniotic fluid	2	1.6
Threat of uterine rupture along the scar	28	22.6
Partial premature detachment	2	1.6
Normally located placenta	5	4.0
Pelvic presentation of the fetus	9	7.3
Mild preeclampsia	4	3.2
Lack of water	6	4.8
Acute respiratory viral infection	21	16.9
Gestational pyelonephritis	8	6.5

As can be seen from **Table 4**, pregnant women with no rhesus isosensitization in the third trimester of pregnancy had a high frequency of threat of uterine rupture along the scar (22.6%), threat of premature birth (18.5%), acute respiratory viral infection (16.9%).

Preterm labor (6.5%), chronic fetal hypoxia (6.5%), gestational pyelonephritis (6.5%), mild preeclampsia (6.5%) were noted with a slightly lower frequency.

All pregnant women with Rh (-) blood had a Coombs reaction during pregnancy. Ultrasound and Doppler studies were performed to assess the condition of the fetus, placenta, as well as to determine the state of uteroplacental blood flow.

As a result of the study, the absence of clinical, functional, laboratory manifestations of Rh isosensitization was established.

All pregnant women at 28.7 ± 0.09 weeks of gestation were immunized with anti-D immunoglobulin. The absence of Rh isosensitization is shown in **Table 5**.

Table 5 – Outcome of childbirth in women in labor with the absence of Rh isosensitization

Features of childbirth	Abs	%
Premature birth through the natural birth canal	15	23.4
Premature birth by caesarean section	39	60.9
Timely delivery through the natural birth canal	2	3.12
Timely delivery by caesarean section	8	12.5

As can be seen from **Table 5**, 73.4% of women (n = 47) underwent cesarean section at 38.9 ± 1.8 weeks, 26.6% (n = 17) had childbirth through the natural birth canal.

64 newborns were born from 64 women with no rhesus isosensitization, while 48 newborns (75%) were in satisfactory condition, 12 (18.8%) were in moderate condition, 4 children (6.3%) were in serious condition.

There were no stillbirths among the examined women.

The severity of the condition of newborns was determined by the presence of premature labor (n = 10), weakness of labor activity and the need for stimulation of labor activity (n = 4) and pathology of the umbilical cord (n = 2).

The features of the course of the early neonatal period in newborns born to mothers with rhesus isosensitization are presented in **Table 6**.

As can be seen from **Table 6**, 62.3% of newborns had an uncomplicated course of the early neonatal period. The condition after chronic hypoxia was noted in 10.4% (n = 8), respiratory distress syndrome in 14.3%, morphofunctional immaturity in 5.2%, cerebrovascular accident of the I and II degree in 5.2%, manifestation of intrauterine infection in 2.6% of cases.

In the early neonatal period, all newborns were determined by the Rh and blood type of the newborn from mothers with no Rh isosensitization.

Table 6 – Features of the course of the early neonatal period of newborns born from mothers with the absence of Rh isosensitization

Course of the early neonatal period	Abs.	%
Uncomplicated flow	48	62.3
Condition after chronic intrauterine fetal hypoxia	8	10.4
Respiratory distress syndrome	11	14.3
Morphofunctional immaturity	4	5.2
Violation of cerebral circulation of the III degree	4	5.2
Clinical and laboratory manifestations of intrauterine infection	2	2.6

As can be seen from **Table 7**, 58 (90.6%) newborns had Rh (+) blood factor, 6 newborns (9.4%) had Rh (-) blood factor.

Table 7 – Frequency of occurrence of Rh factor and blood group in a newborn from a mother with no Rh isosensitization

Rh and newborn blood group	Abs.	%
O (I), Rh (+) positive	20	31.3
A (II), Rh (+) positive	24	37.5
B (III), Rh (+) positive	10	15.6
AB(IV), Rh (+) positive	4	6.25
O (I), Rh (-) negative	2	3.1
A (II), Rh (-) negative	2	3.1
B (III), Rh (-) negative	1	1.6
AB (IV), Rh (-) negative	1	1.6

All maternity women with Rh-positive blood factor underwent repeated prevention of Rh isosensitization by administration of anti-D immunoglobulin.

It should be noted that, despite the numerous scientific studies of the pathogenesis and clinic of Rh-conflict pregnancy, the frequency of Rh-sensitized women remains high.

The use of anti-Rh immunoglobulin in pregnant women significantly reduces the risk of Rh isosensitization, reduces the frequency of complications during pregnancy and childbirth.

According to the Cochrane Guidelines, the administration of anti-D immunoglobulin during first 72 hours after delivery significantly reduces the risk of Rh-D immunization in women with Rh-negative, and, accordingly, the frequency of hemolytic disease of the fetus (HDF) and newborn (HDN).

To date, there are no specific data on the dose of the immunoglobulin antidote used. The authors believe that the use of one dose (300 mcg) of the drug is sufficient to prevent sensitization by the Rh factor [3, 4, 6].

There is also no consensus on the timing of immunization of pregnant women.

The authors recommend at 28 weeks of pregnancy, during which isoimmunization should be carried out, while the process of transition of erythrocytes of Rh-positive fetal blood may occur at an earlier date.

In our study, immunization was also carried out with anti-D immunoglobulin at 28.7 ± 0.09 weeks at a dose of 300 mcg (1500 IU), which affected the peculiarities of the course of pregnancy and childbirth and the absence of Rh-positive blood in HDF and HDN fetuses.

It should be noted that the prevention of rhesus isosensitization in the UK was carried out in the 50s of the last century, which significantly reduced the mortality from HDN.

It was found that the frequency of HDN for 2180 births was 1 case.

The improvement of neonatal care and preventive measures currently has allowed to significantly reduce the mortality rate from HDN [7, 12].

It has been established that in economically developed countries, the prevention of Rh sensitization by the introduction of anti-Rh immunoglobulin forms the basis of existing protocols [9].

The study made it possible to establish the effectiveness of both intravenous and intramuscular anti-D immunoglobulin [23].

There are also data on the effectiveness of a single administration of immunoglobulin (1500 IU) at 28–37 weeks of pregnancy.

The effectiveness of the prevention of isosensitization is 76%.

The conducted study allows us to establish that the use of a single dose of immunoglobulin prevents sensitization during subsequent pregnancies.

Our prevention before the present pregnancy and the use of immunoglobulin in the dynamics of pregnancy is effective, has no local and systemic allergic reactions and significantly reduces perinatal morbidity and mortality in pregnant women with Rh-negative blood.

Thus, the study of the peculiarities of the course of pregnancy in women without Rh isosensitization allowed us to establish the presence in the first trimester of a high frequency of anemia (27.3%), early toxicosis (21.2%), asymptomatic bacteriuria (17.4%), the threat of miscarriage (14.4%).

In the second trimester, a high frequency of anemia (28.6%) was also noted, asymptomatic bacteriuria (21.4%), threat of miscarriage (15.7%), exacerbation of chronic pyelonephritis (12.9%), mild preeclampsia (10%).

In the third trimester, a high frequency of the threat of uterine rupture along the scar was determined by 22.6%, the threat of premature birth by 18.5%, acute respiratory viral infection by 16.9%.

It was found that the frequency of abdominal delivery was 73.4%, delivery through the natural birth canal 26.6%.

The study of the condition of newborns allowed to establish a satisfactory condition in 70%, a state of moderate severity in 18.8%, a serious condition in 6.3%. The severity of the condition was determined by the presence of prematurity in 15.6%, weakness of labor and stimulation of labor in 6.3% and the presence of umbilical cord pathology in 6.3%.

None of the newborns had clinical and laboratory manifestations of hemolytic disease of the newborn, which reflects the effectiveness of the prevention of rhesus isosensitization, the introduction of anti-D immunoglobulin during pregnancy.

Conclusion

1. The use of anti-D immunoglobulin after previous childbirth and at the gestation period of 27.7 ± 0.09 weeks with a non-standing pregnancy makes it possible to exclude isosensitization in pregnant women with Rh-negative blood.
2. Timely prevention of anti-D immunoglobulin prevents the development of hemolytic disease of the newborn in this contingent of women.
3. The use of anti-D immunoglobulin is of great importance for reducing perinatal morbidity and mortality in pregnant women with Rh-negative blood.

Perspectives of further research. This study will identify risk factors for the development of isosensitization and hemolytic disease of the fetus and newborn in patients with Rh-negative blood who have not received immunoglobulin prophylaxis. Further studies will reveal the effectiveness of intrauterine hemotransfusion in patients with isosensitization and clinical and laboratory manifestations of HDF.

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ВПЛИВ ПРОФІЛАКТИКИ ІМУНІЗАЦІЇ НА ПЕРЕБІГ ВАГІТНОСТІ У ЖІНОК З РЕЗУС НЕГАТИВНОЮ КРОВ'Ю

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Резюме. *Мета.* Вивчення особливостей перебігу вагітності у жінок, які отримали резус імунопрофілактику.

Матеріал та методи. Обстежено 64 вагітних, середній вік яких становив 30,55±7,0 (18-43) років. З 64 вагітних 24 (37,5%) були першовагітні, 40 (62,5%) - повторновагітні.

Результати. Вивчення особливості перебігу вагітності у жінок з відсутністю резус ізосенсибілізації дозволило встановити наявність у I триместрі високої частоти анемії (27,3%), раннього токсикозу (21,2%), безсимптомної бактеріурії (17,4%), загрози викидня (14,4%). У II триместрі також відзначалася висока частота анемії (28,6%), безсимптомної бактеріурії (21,4%), загрози викидня (15,7%), загострення хронічного пієлонефриту (12,9%), прееклампсії легкої стадії (10%). У III триместрі визначалася висока частота загрози розриву матки по рубцю 22,6%, загрози передчасних пологів 18,5%, гострої вірусної респіраторної інфекції 16,9%.

Дослідження стану новонароджених дозволило встановити задовільний стан 70%, стан середньої тяжкості 18,8%, тяжкий стан 6,3%. Тяжкість стану була визначена наявністю недоношеності у 15,6%, слабкістю пологової діяльності та проведенням стимуляції пологової діяльності у 6,3% та наявність патології пуповини у 6,3%. У новонароджених не відмічалась наявність клініко-лабораторних проявів гемолітичної хвороби новонародженого, що відображає ефективність проведення профілактики резус ізосенсибілізації введенням анти-Д імуноглобуліну при вагітності та після пологів.

Висновки. Застосування анти-Д імуноглобуліну після попередніх пологів та у терміни гестації 27,7±0,09 тижнів при несправжній вагітності дозволяє виключити ізосенсибілізацію у вагітних із резус негативною кров'ю. Своєчасна профілактика анти-Д імуноглобуліну запобігає розвитку гемолітичної хвороби новонародженого у даного контингенту жінок. Застосування анти-Д імуноглобуліну має велике значення для зниження перинатальної захворюваності та смертності у вагітних із резус негативною кров'ю.

Ключові слова: резус позитивний фактор крові, резус ізосенсибілізація, імунізація, ізоімунізація, антирезус (Д) імуноглобулін.

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