

Occurrence of ABO And RhD Incompatibility with Rh Negative Mothers

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ABSTRACT

Introduction: Hemolytic disease of the newborn was first described in the medical literature 1609, when it was diagnosed in one French housewife. In 1932 Diamond and colleagues described the mutual relationship of fetal hydrops, jaundice, anemia and erythroblastosis, which was later called fetal erythroblastosis. Hemolytic disease of the newborn (HDN) in the strict sense is considered disease whose basis is accelerated immune destruction of fetal/child erythrocytes that are bound to IgG antibodies of maternal origin. These antibodies are directed against antigens of father's origin, which are present in the fetal/children's erythrocytes and that the mother's immune system recognizes them as foreign antigens. **Goal:** The goal is that in the period from January 1st 2011 to October 23rd 2013 determine the frequency of ABO and Rh D incompatibilities in our sample of pregnant women/mothers, and to underscore the importance of regular check of ABO Rh D negative pregnant women and application specific Rh D protection. **Material and methods:** In the General Hospital "Prim. Dr. Abdulah Nakas" in Sarajevo by retrospective study are followed several relevant variables. Immune alloantibodies were detected in vivo by indirect Coombs test (ICT) with serum mother and O test erythrocytes, by direct Coombs test (DCT) with erythrocytes of a newborn. **Results:** The total number of births ABO Rh D negative was 596 (14%) and ABO Rh D positive mothers 4261 (86%). Of the total number of Rh D negative mothers there was A Rh D: negative mothers 42%; O Rh D negative 33%; B Rh D: negative 17% and AB Rh D: negative 8%. Most of immune antibodies appear in mothers with O Rh D: negative blood type. The emergence of immune antibodies in the Rh D negative mothers was 1%, the appearance of ABO incompatibilities amounted to 2.3% of our sample. **Conclusion:** In order to reduce the occurrence of alloimmunization of the mother to erythrocyte antigens of the newborn that can lead to major complications in subsequent pregnancies of Rh D: negative mothers and HDN constant monitoring in order to prevent them is necessary. Prevention is essential because once immunized mother will remain immunized for life.

Key words: ABO and RhD incompatibility, Rh negative mothers, incidence, Bosnia and Herzegovina.

1. INTRODUCTION

Hemolytic disease of the newborn was first described in the medical literature 1609, when it was diagnosed in one French housewife. In 1932 Diamond and colleagues described the mutual relationship of fetal hydrops, jaundice, anemia and erythroblastosis, which was later called fetal erythroblastosis. In 1940s Landsteiner and Weiner also made discovery of the blood Rh factor within the blood type and in 1953 Chown confirmed that the pathogenesis of Rh alloimmunization is the result of the passage of Rh-positive red blood cells of the fetus, after or during transplacental hemorrhage which are antigens in the mother's circulation (1, 2).

According to the U.S. Center for Disease Control and Prevention, during the 1996 in the United States were recorded 21 deaths of children which can be attributed to hemolytic disease (erythroblastosis fetalis) and jaundice. Determination of blood type in ABO Rh D negative pregnant women allows reasonable precautions which limit the risk to fetus. Erythroblastosis is a very serious medical condition for about 4000 babies a year. In

15% of cases of babies die before birth. Those who survive may suffer from jaundice, which leads to the deaf-muteness, speech disturbances, cerebral palsy and mental retardation (1, 2).

Rh antigens are lipoprotein molecules, which are sparsely located at the erythrocyte surface. About 50 of them can be identified, which indicates the specific complexity of the Rh antigen. D antigen is the most immunogenic and therefore the most important antigen. It causes the formation of antibodies 50 times more often than the C and E antigens. Rh D negative people do not have the D antigen in the Caucasian population, 85% of people are Rh positive and 15% Rh negative (2, 4). The frequency of Rh negative women than is more common for Caucasian women (15%) than African American (5%) and is less common in Asian women (2, 3, 7, 8, 9).

Antibodies from Rh system are almost always immune, predominantly in the IgG class, passing due to its size through the umbilical cord and cause hemolytic disease of the newborn (HDN). Under HDN in the strict sense is considered disease whose basis is accelerated immune destruction of fetal/child

erythrocytes that are bound to IgG antibodies of maternal origin. These antibodies are directed against antigens of father's origin, which are present in the fetal/children's erythrocytes and that the mother's immune system recognizes them as foreign antigens. This happens if the fetal red blood cells enter mother's circulation (3, 5). Sensitization occurs during childbirth when the mother's bloodstream penetrates certain amount of Rh positive child erythrocytes. Erythrocytes, as foreign substance to the mother, encouraged her body to begin to produce Rh antibodies. Therefore, the second and other pregnancy can have complications related to maternal Rh antibodies to Rh positive fetal red blood cells (1, 2, 3, 5, 6, 7, 8, 9).

Their appearance in the circulation is also possible after amniocentesis, spontaneous or induced abortion, cardiocentesis, chorionic villus sampling, ruptured ectopic pregnancy and a blunt trauma to the abdomen (5).

In the case of specific antigen immune stimuli that person does not have, can occur the creation of IgG anti-A and anti-B antibodies, which can pass the placenta and cause destruction of fetal red blood cells (1, 2, 3, 4, 5).

2. GOAL

The goal is that in the period from January 1st 2011 to October 23rd 2013 determine the frequency of ABO and Rh D incompatibilities in our sample of pregnant women/mothers, and to underscore the importance of regular check of ABO Rh D negative pregnant women and application specific Rh D protection.

3. MATERIAL AND METHODS

Testing was performed on selected samples that comprised pregnant women at different fertile and gestational age. In the General Hospital "Prim. Dr. Abdulah Nakas" in Sarajevo by retrospective study which covered a period of three years from January 1st 2011 to October 23rd 2013. Followed are several relevant variables (which and how immune antibodies appear in the serum of ABO Rh D negative pregnant women and the emergence of immune antibodies to the erythrocytes of a newborn). Immune alloantibodies were detected in vivo by indirect Coombs test (ICT) with serum mother and O test erythrocytes, by direct Coombs test (DCT) with erythrocytes of a newborn. DCT measures the level of maternal antibodies that attack the fetus red blood cells (2).

ICT is performed so that the serum is incubated with test erythrocytes and antibodies from the serum react with the corresponding erythrocyte antigens. Erythrocytes coated with antibody are incubated by Coombs anti-human globulin and with the presence of antibodies it leads to agglutination of erythrocytes. Identification of anti-D antibodies was performed in the Department of Transfusion Medicine in Sarajevo.

Inclusion criteria:

- ABO Rh D: negative mother and newborn Rh D: negative mothers

Exclusion criteria:

- ABO Rh D: positive mother and newborn Rh D: positive mothers without ABO incompatibility

4. RESULTS

We analyzed several important indicators on which it is possible to assess the health care of pregnant women treated in the

General Hospital "Prim. Dr. Abdulah Nakas" in Sarajevo. In our sample, the occurrence of immune Rh D antibodies during the period from January 1st 2011 to October 23rd 2013 range in percentage of 1% of cases. ABO Incompatibilities in our sample ranged up to 2.3%. The results are shown in tables and charts and compared with similar from the literature. (Table 1, Figure 1)

Total No- of deliveries	4261	Rh D neg	Rh D pos	Rh D neg%	Rh D pos%
2011	1583	201	1382	13%	87%
2012	1747	252	1495	14%	86%
2013	931	143	788	15%	85%

Table 1. Total number of births in the 2011, 2012 and 2013 (January 1st 2013 – October 23rd 2013), the number of Rh D negative mothers in the General Hospital, Sarajevo

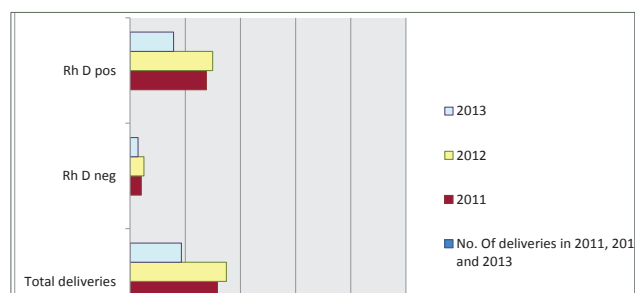


Figure 1. Total number of births in the 2011, 2012 and 2013 (January 1st 2013 – October 23rd 2013), the number of Rh D negative mothers and Rh D positive mothers

The total number of births ABO Rh D negative was 596 (14%) and ABO Rh D positive mothers 4261 (86%). (Figure 2)

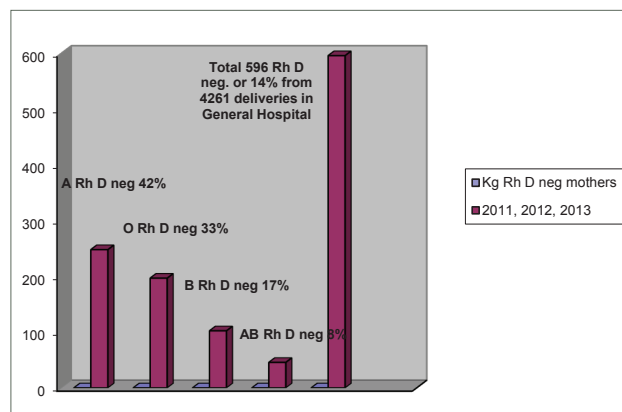


Figure 2. Blood types of ABO Rh D negative mothers

Of the total number of Rh D negative mothers there was A Rh D: negative mothers 42%; O Rh D negative 33%; B Rh D: negative 17% and AB Rh D: negative 8%.

Presentation in% of ABO Rh D blood types of the newborns.

O Rh D neg blood type in 5 cases was sensitized to the Rh D antigen and in one case B Rh D negative. (Table 2).

Mothers blood type	Rh D-antibodies ICT-pos	Rh D-antibodies%	Newborn blood type	DCT-pos	%
O Rh D neg	5	1%	O Rh D pos	4	0.7%
B Rh D neg	1	0.2%	B Rh D pos	2	0.3%
Total	6	1%	Total	6	1%

Table 2. The emergence of Rh D antibodies in the period from January 1st 2011 – October 23rd 2013 at the General Hospital, Sarajevo

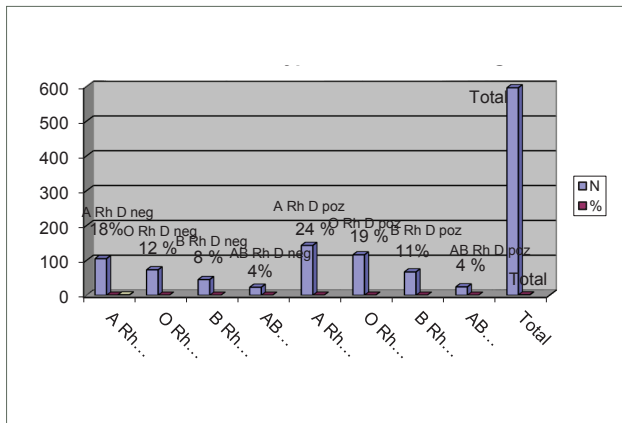


Figure 3. Blood types of newborns

ABO/ mother	ABO ICT- neg	%	ABO/ newborn	DCT-pos	ABO%
O Rh D neg	10	1.8%	A	9	1.5%
O Rh D pos	2	0.3%	B	6	1%
AB Rh D neg	1	0.2%	Total		
Total	14	2.3%			

Table 3. Appearance of ABO incompatibilities in the period from January 1st 2011 – October 23rd 2013 at the General Hospital in Sarajevo

Although ABO incompatibilities usually occur in O Rh D neg blood type here we have also two O Rh D positive and one AB Rh D negative blood type where there is sensitivity to the ABO antigen, indicating a positive DCT in newborn erythrocytes. (Figure 3, Table 3, Figure 4).

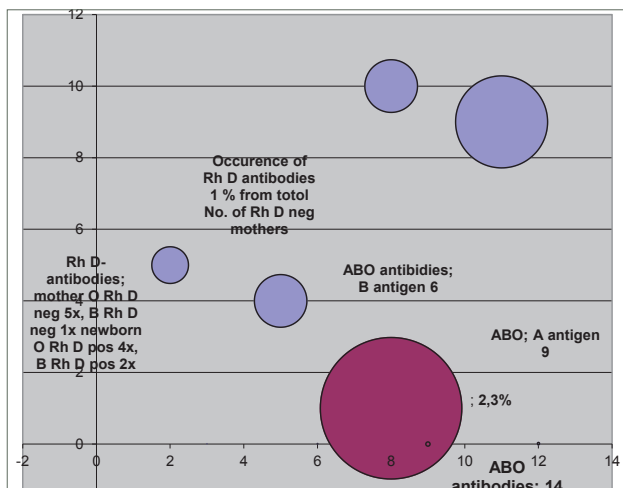


Figure 4. The emergence of ABO and Rh D Incompatibilities

Most of immune antibodies appear in mothers with O Rh D: negative blood type. The emergence of immune antibodies in the Rh D negative mothers was 1%, the appearance of ABO incompatibilities amounted to 2.3% of our sample.

5. DISCUSSION

In the sample examined ABO Rh D negative mothers we found that in a three years period of in 1% of cases occurred Rh D immune antibodies. It is important to emphasize that they most often occur in mothers with O Rh D: negative blood type, where Rh D immunization is higher. ABO immunization is more common in alloimmunization with antigen A pregnant O Rh D negative blood type. In our sample of Rh D incompat-

ibilities occurring mostly in O blood type mothers. All pregnant women in our sample did not have test to immune antibodies in the serum during follow up in our hospital pregnancy is managed in other institutions while they first come for delivery.

The risk of Rh D alloimmunization after first birth is 16 % if the fetus is ABO compatible with the mother, 2 % if it is not compatible and 2 % after termination of pregnancy. Rh sensitization refers to the level fetomaternal hemorrhage (3 % < 0.1 ml and 22 % > 0.1 ml) (1, 2, 8, 9). When a mother produces antibodies against the blood of unborn fetus, pregnancy is carefully monitored. If the fetus is in danger in pregnancy of at least 32-34 weeks, delivery is induced. Below 32 weeks of pregnancy to the fetus is given a blood transfusion while still in the uterus. There are two techniques that are used to perform a blood transfusion before the birth. Firstly needle is inserted through the mother's abdomen and uterus to fetus abdomen. Erythrocytes are injected/inserted into the fetus's abdominal cavity which is further absorbed into the bloodstream. In early pregnancy, or if the bilirubin level is extremely high cardiocentesis is performed. This procedure is based on placing a thin needle through the mother's abdomen, guided by ultrasound in the umbilical vein and erythrocytes are injected directly into the fetus's bloodstream (2). After birth is estimated the severity of symptoms shown by the newborn. One or more transfusions may be necessary to prevent anemia, hyperbilirubinemia and hemorrhage. Hyperbilirubinemia is also treated with phototherapy (2, 8, 9).

Before the introduction of immunoprophylaxis the immunization incidence of Rh D negative multiparas with Rh D positive child to Rh D antigen was approximately 18%. Introducing postnatal Rh D immunization of pregnant women (Rhogam) reduced the incidence of immunization to less than 1%. The introduction of combined antenatal (at 28th week of gestation) and postnatal Rh D immunization of pregnant women the incidence of immunization is reduced to less than 0.1% (5,7). With or without antenatal immunoprophylaxis all Rh D negative pregnant women who gave birth to Rh D positive fetus and not immunized with the D antigen, should receive 100-300 mg (500-1500 IU) Rh Ig IM within the first 72 hours after delivery. Rh Ig dose should be adjusted to the size of fetus-maternal hemorrhage. It is estimated by Kleihauer-Betke gel agglutination or other testing of maternal blood sample taken up to 1 hour after birth. Significant fetal-maternal hemorrhage requiring Rh D immunoprophylaxis in doses higher than the standard usually occurs during the traumatic delivery (including caesarean section), the manual removal of the placenta, intrauterine fetal death, stillborn, abdominal trauma in the third trimester of pregnancy, simultaneous delivery of two or more children and/or unexplained fetal hydrops. Rh Ig should receive Rh D negative women not immunized after each "event" that could lead to the entry of fetal blood in their circulation (amniocentesis, ectopic pregnancy, spontaneous abortion after 12 weeks, induced abortion, cardiocentesis, bleeding before birth, fetal death...) (5, 7, 8, 9). Prevention of HBN is successful when hyperimmune Rh D gammaglobulin is used in 28/29 and 32/34 week of pregnancy (6, 7).

In our case, we do not differs according to the emergence of immune antibodies from other mentioned in the literature, however, we assume that some pregnant women cannot, because of their social status, buy Rh D immunoprophylaxis which costs

128 KM and all women who have given birth to Rh D positive infant must buy Rhogam given to Rh D immunoprophylaxis which can lead to an increase in the number of pregnant women sensitized to the Rh D antigen. The only option is to provide to Rh D negative pregnant women, new mothers free and mandatory Rh D immunoprophylaxis.

In case of ABO incompatibilities in 15% of pregnancies mother with O blood type give birth to a child with A or B blood type antigen, the incidence of ABO HDN is rare and occurs 1/150 pregnancies. ABO HDN can occur in any pregnancy, including the first. Its symptoms are usually mild and usually manifest in the neonatal period. Usually within the first 36 hours after birth in the newborn is observed increase of indirect bilirubin levels and mild anemia. Newborns with ABO HDN are usually treated with phototherapy. Less than 2% of newborns needs blood transfusion (5, 7, 8).

6. CONCLUSION

The emergence of Rh D immune antibodies in the serum of our sample is 1% and ABO incompatibilities 2.3% during the period from January 1st 2011 – October 23rd 2013. In order to reduce the occurrence of alloimmunization of the mother to erythrocyte antigens of the newborn that can lead to major complications in subsequent pregnancies of Rh D: negative mothers and HDN constant monitoring in order to prevent them is necessary. Prevention is essential because once immunized mother will remain immunized for life. Because the social status in Bosnia and Herzegovina is low, the possibility of increased sensitization of pregnant women could be on the rise.

Therefore, one recommendation would be to make the preparation of anti-IgG. (Rhogam) free of charge. Immunization of mothers on erythrocyte antigens is rare but the disease

HDN erythroblastosis is a very serious medical condition and the in socially vulnerable population it could have a tendency to increase due to the inability to purchase anti-IgG products.

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