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Hemolytic disease by isoimmunization in Rh and ABO systems in newborns. A clinical study

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Abstract

The following study aims are to establish the incidence of the hemolytic disease, the risk factors, clinical forms and the main therapeutic measures in the newborns of Constanta County Emergency Hospital over a period of two years, on a group of 76 newborn infants diagnosed with the Rh and ABO hemolytic disease incompatibility. Out of the76 cases of maternal-fetal incompatibility, 39 newborn infants presented Rh isoimmunization, 20 cases presented ABO isoimmunization, and 17 cases presented group and Rh double isoimmunization. Pathological jaundice was presented in all cases, occurred within 24 hours since birth. Based on the classification of clinical signs and laboratory investigations, patients could be divided in two clinical forms of neonatal hemolytic disease: 9 cases with severe anemia at birth and 67 with severe jaundice and moderate anemia. In this cases, we recommend the use of the guide regarding Rh incompatibility in pregnancy which represents a modern and uniform approach of this pathology at national level, decreasing in this way the number of immunized patients during pregnancy.

Keywords: *hemolityc disease, newborn*

Introduction

Hemolytic disease of the newborn (HDN) is known as a blood disorder in a fetus or newborn. The first infants are usually not affected by this disorder, unless the mother had an abortion in the past. Therefore, all the infants which will have later positive Rh could be affected[1,2]. The antibodies which are involved in the transfer to the placenta could attack the antigens in time, destroying the cells and achieving the hemolysis. In this case, the infant could develop further reticulocytosis and sudden death could occur from heart failure (i.e. hydrops fatalis). Moreover, many erythroblasts could be present in the fetal blood and this form is known as erythroblastosis fetalis[3,4].

In the present paper our main objectives were to:

- determining the incidence of HDN due to incompatibility in Rh and ABO systems in newborn infants at the Maternity of Constanta County EmergencyHospital;
- analysis the risk factors in the occurrence of disease;
- analysis the main clinical manifestations; and
- positive diagnosis and the main therapeutic measures.

Methods

The study is a retrospective clinical type. It was conducted in the Neonatology Clinical and Premature Baby Department on a group of 76 newborn infants diagnosed with the Rh and ABO hemolytic disease incompatibility, respectively Rh and group double incompatibility, over a period of 2 years, from 01 January 2012 till 31 December 2013.

We analyzed the following parameters: historical data related to mother (age, address, educational background, pregnancy and childbirth status, pregnancy monitoring), gestational age at birth, newborn sex, anthropometric data of the newborn (weight and waist parameters), Apgar score, clinical manifestations at birth or in progress and the treatment applied.

Results

The repartition of newborn hemolytic disease cases on years shows a decrease in disease incidence, practically the number of cases halved from year to year in all three categories of maternal-fetal incompatibility (Figure 1, A and B).

The distribution by sex showed that from the total consignment of 76 cases of incompatibility, the frequency between the 2 sexes was equal (38 male cases versus 38 female cases), but with an unequal distribution among the three types of incompatibility (Table 1).

The newborns came mainly from urban areas, 40 cases of the cohort, compared to 36 cases from rural areas, the explanation being the possibility of establishing risk pregnancy with Rh or group incompatibility during prenatal period and the fact that mothers were guided to enroll to specialized maternities to care newborn suffering from this disease (Figure 2).

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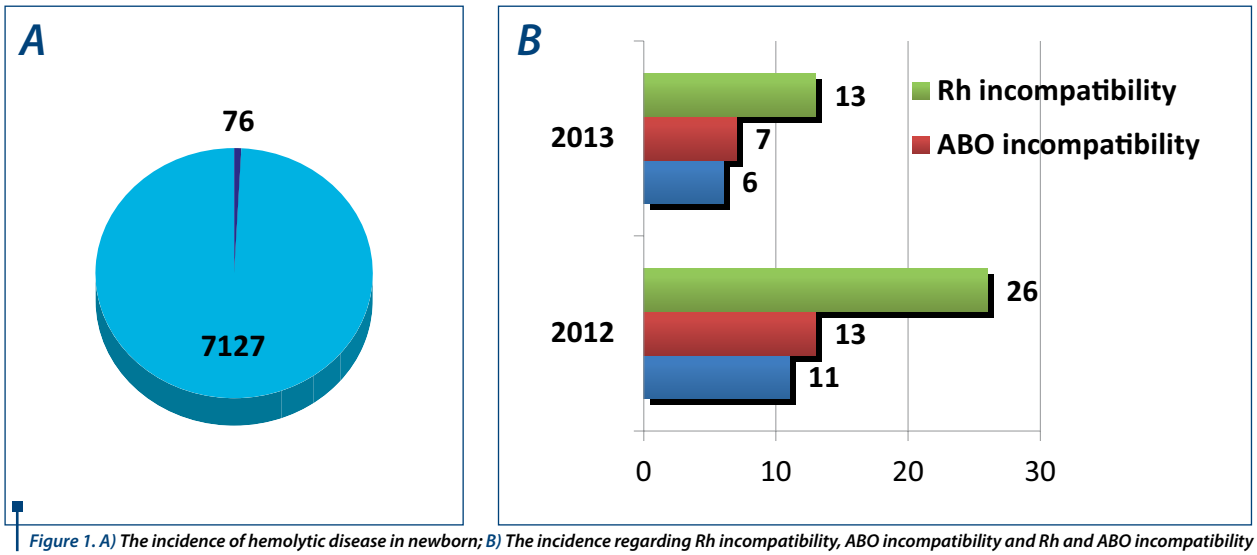

Figure 1. A) The incidence of hemolytic disease in newborn; B) The incidence regarding Rh incompatibility, ABO incompatibility and Rh and ABO incompatibility

Table 1 The distribution of cases by sex

	Male	Female
Rh incompatibility	27	12
ABO incompatibility	7	13
Rh and ABO incompatibility	4	13
Total	38	38

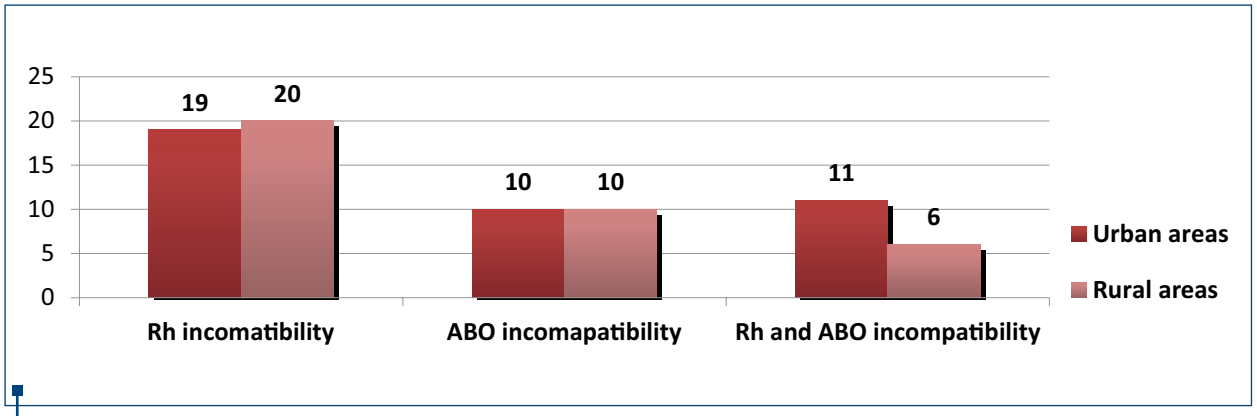

Figure 2. The distribution of cases according to rural and urban areas

In the present study we note a higher rate of HDN from mothers aged between 21 and 30 (44 cases in total, 20 with Rh incompatibility, 14 with ABO incompatibility and 10 cases with double incompatibility). About 9 cases were observed in the age group from 15 to 20 years old (5 cases with Rh incompatibility, 3 with ABO incompatibility and 1 case with group and Rh double incompatibility), as well as 2 cases in the age group over 40 years old (1 case with Rh incompatibility and 1 case with ABO incompatibility).

Most probably, isoimmunization cause is given by previous births in 50 cases, miscarriages and abortions

Table 2 The distribution of cases based on birth rank

Birth rank	1	2	3	≥4
Rh incompatibility	11	21	4	3
ABO incompatibility	6	11	1	2
Rh and ABO incompatibility	9	6	1	1
Total	26	38	6	6

history in 26 cases. The major of the cases with incompatibility occurred in the second birth, but isoimmunization occurred in the case of the third, or after more than 4 births (Table 2).

A total of 56 births were monitored during pregnancy while 20 births have not been followed.

The distribution depending on the educational level of the mothers was 5 illiterate mothers, 22 mothers with gymnasium graduation, 12 mothers with high-school graduation, and 11 mothers with collage graduation. The mothers had regular checks of pregnancy graduated high-school or college.

Gestational age was below 37 weeks in 20 cases of incompatibility, and 56 infants were born at full-term. About 32 births were by cesarean surgery while 44 births were by spontaneous birth. The distribution of newborn can be seen in Table 3.

Pathological jaundice occurred within 24 hours since birth and was presented in 100% of cases.

Patients were divided in two clinical forms of neonatal hemolytic disease (Table 4).

We noted that during this study no case of feto-placental anasarca was observed, and presented features like pallor, jaundice, hepatospenomegaly, ascites or edema (Table 5).

The investigations regarding serum bilirubin within the first 24 hours, bilirubin in umbilical cord and hemoglobin can be seen in Table 6.

Rh and ABO incompatibility hemolytic disease was correlated with an average rate of prematurity (20/76 cases) and perinatal complications of prematurity as it is shown below (Table 7).

Prophylaxis and treatment

a) AntiRh Immunoprophylaxis

A number of 9 pregnant women received prophylaxis with anti-D immunoglobulin at 28 weeks of pregnancy, according to the current protocol. In the first 72 hours postpartum prophylaxis with anti-D immunoglobulin was performed in 15 cases.

b) Treatment of Rh and ABO isoimmunization hemolytic disease

The treatment was applied according to weight and age of the newborn and serum bilirubin values in peripheral blood which included phototherapy and exchange transfusion (EST) can be seen below (Table 8).

Phenobarbital at a dose of 5 mg/kg/day was used as an adjuvant treatment in 19 cases. In the present study no Rh or ABO incompatibility-related death was registered.

Post-hospitalization care plan consisted in informing the parents. The newborn had a higher risk to develop clinically significant anemia in the first 3-4 months of life. They were recommended weekly determinations of hematocrit, hemoglobin and reticulocytes.

In the cases were hemoglobin would present a valuew below 7 g/dl, the miniaturized extracorporeal circuits transfusion should be reccomended.

Discussion

The disease represents the most important cause of mortality among newborns. Nowadays, due to tests and screenings, this disease can be treated and even entirely prevented[5,6,7]. This indicates that despite the availability of an effective preventive measure, Rh HDN continues to

Table 3 The distribution of cases based on Apgar score

Parameters	Apgar 8 - 10	Apgar 5 - 7	Apgar 1 - 4
Rh incompatibility	34	4	1
ABO incompatibility	17	2	1
Rh și ABO incompatibility	14	3	0
Total	65	9	2

Table 4 The distribution of patients by severe anemia and severe jaundice with moderate anemia

Parameters	Severe anemia	Severe jaundice with moderate anemia
Rh Incompatibility	6	33
ABO Incompatibility	2	18
Rh and ABO Incompatibility	1	16
Total	9	67

Table 5 The major signs of cases observed during the study

Signs	Severe anemia a	Severe jaundice with moderate anemia
Pallor	++	+
Jaundice	+	++
Hepatosplenomegaly	++	+/-
Ascites	-	-
Edema	+	-
No. of cases	9	67

Table 6 The main characteristics of the cases based on severe anemia and severe jaundice with moderate anemia

Characteristics	Severe anemia	Severe jaundice with moderate anemia
Serum bilirubin within the first 24 hours of birth	<10 mg/dl	10-18 mg/dl
Bilirubin in umbilical cord	3-5 mg/dl	<3 mg/dl
Hemoglobin	<12 g/dl	>12 g/dl
No. of cases	9	67

Table 7 The main perinatal complications of cases

Idiopathic respiratory distress syndrome	5
Neonatal sepsis	13
Perinatal hypoxia	12
Fetal distress (green amniotic fluid)	10
Intrauterine growth restriction	4

Table 8 The results of serum bilirubin values in peripheral blood which included phototherapy and exchange transfusion

Serum Bilirubin (mg/dl)	G birth	<24 hours	24-48 hours	49-72 hours	>72 hours	No. of cases
5-9	Regardless of weight	Phototherapy				43
10-14	<2500g >2500g	EST*	Phototherapy			16
15-19	<2500g >2500g	EST*	EST*	EST* Phototherapy		17

**EST= exchange transfusion*

contribute significantly to infant morbidity and mortality in the United States[8]. Before the introduction of anti-D immunoglobulin for isoimmunization prophylaxis during pregnancy, HDN by Rh incompatibility affected 9-10% of pregnancies and represented a major cause of perinatal mortality and morbidity. Nevertheless, Rh isoimmunization remains a serious issue, continuing to affect about 2% of pregnancies in Romania[9,10,11].

Out of 7127 newborn infants in the Neonatal Premature Baby Department over a period of 2 years (1 January 2012 till 31 December 2013), a number of 76 newborn infants were diagnosed with hemolytic disease by isoimmunization.

The study showed that from the 76 children born with maternal-fetal incompatibility, 39 newborn infants presented Rh isoimmunization, 20 cases presented ABO isoimmunization, and 17 cases presented group and Rh double isoimmunization.

Although the national level of isoimmunization affects around 2% of newborn, in our study it showed a lower level of isoimmunization, mainly 1.065%.

Furthermore, the cases presented two clinical forms of neonatal hemolytic disease, 9 cases with severe anemia at birth and 67 with severe jaundice with moderate anemia. Pathological jaundice occurred within 24 hours since birth, was presenting 100% of cases. There was no case of reported feto-placental anasarca.

Isoimmunization cause is given by previous births implying miscarriages and abortions history. Most cases of incompatibility occurred in the second birth and approximately 75% of births (56 cases) have been monitored by a physician.

Conclusions

Hemolytic disease by isoimmunization in Rh and ABO was correlated with prematurity in approximately one quarter of the cases (20 cases from 76). It was also associated with perinatal complication like infectious or idiopathic pulmonary distress. Phototherapy represented the most common method used in jaundice treatment by medium intensity. Therefore we recommend the use of the guide regarding Rh incompatibility in pregnancy which represents a modern and uniform approach of this pathology at national level, helping to decrease the number of immunized patients during pregnancy as well as mortality. ■

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