

# Factors Affecting the Severity of RH Incompatibility Newborn

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## Abstract

Rh incompatibility is a not common pediatric problem, that cause morbidity and mortality in children, and it is an important cause of hemolysis, anemia and jaundice in newborn. To study Rhesus hemolytic disease, its severity, its complications; to evaluate if ABO incompatibility is protective or not, so to find out the efficacy of anti-D globulin ; to evaluate the efficacy of phototherapy and exchange transfusion as a treatment.

This study was done on neonates with jaundice, seventy five patients (1-10 days old) who had Rh incompatibility were studied during period from the first of January 2008 to the 30<sup>th</sup> of June 2008.

History was taken about age, gender and gestational age of the patients, determination of gestational age and hepatosplenomegally as a cause of extramedullary hematopoiesis. Investigations done for patients were hemoglobin, total serum bilirubin, reticulocyte count, blood group and Rh, and direct coombs test. From 75 patients studied, 55 patients (73%) required treatment for jaundice;25 of them (46%) required only phototherapy due to mild degree of hemolysis, and 30 of them (54%) required exchange transfusion with phototherapy due to severe degree of hemolytic. The remaining 20 patients (27%) required observation alone.

Family history of previous hemolysis was positive in 44 patients and it was a risk factor for having hemolysis in present pregnancy. Early evaluation of patients for jaundice was useful in early recovery. ABO incompatibility in association with Rh incompatibility was not necessarily protective against hemolysis. The administration of anti-D globulin to the mother within first 72 hours after delivery was protective against sensitization.

Early and proper management of of Rh incompatibility may reduce need for exchange transfusion. ABO incompatibility was not necessarily protective against hemolysis. Anti-D globulin administered to mothers within 3 days after delivery was protective against sensitization, History of hemolytic in previous siblings is considered as a risk factor for present hemolytic in neonates with Rh incompatibility.

**Keywords:** RH Incompatibility; newborn; hemolytic disease

## Introduction

Hemolytic disease of newborn due to Rh-incompatibility is an isoimmune hemolytic disease results from transplacental passage of RH(-ve) maternal blood containing antibodies active against RH(+ve) red blood cells antigenes of the infant and is characterized by an increased rate of RBC destruction<sup>(1)</sup>, When Rh-

positive blood is infused into an Rh-negatives woman through error or when small quantities(usually more than 1ml) of Rh-positive fetal blood containing D antigene inherited from an RH-positive father enter the maternal circulation during pregnancy, with spontaneous or induced abortion ,or at delivery, antibody formation against D antigene may be induced in the unsensitized RH-negative recipient mother.<sup>(1)</sup>

Hemolytic disease rarely occurs during first pregnancy because transfusion of RH-positive fetal blood into an RH- negative mother occurs near the time of delivery, too late for the mother to become sensitized and transmit antibodies to her infant before delivery. <sup>(1)</sup>

When the mother and fetus are also incompatible with respect to group A or B, the mother is partially protected against sensitization by the rapid removal of RH- positive cells from her circulation by her preexisting anti- A and anti-B, which are IgM antibodies and not cross the placenta. <sup>(2)</sup> In the fetus, anemia and heart failure are associated with hyperdynamic Circulation in both arterial and venous vessels. <sup>(3)</sup> Fetal anemia in RH isoimmunization is the reduced life span of erythrocytes coated with antibodies, presumably from phagocytosis by reticuloendothelial cells. <sup>(4)</sup> In severe cases of RH isoimmunization (erythroblastosis fetalis), hydrops and heart failure related to severe anemia in the fetus occur. <sup>(5)</sup> Hydrops is often resulting in fetal or neonatal death without appropriate antenatal intervention. <sup>(5)</sup>

Laboratory evaluation include blood typing, coombs test, complete blood picture with blood film. <sup>(5)</sup> Reduced hemoglobin levels, reticulocytosis and blood film characterized by polychromasia and anisocytosis are expected with isoimmune hemolysis. <sup>(7)</sup>

In Rh-negative women, a history of previous transfusion, abortion ,or pregnancy should suggest the possibility of sensitization <sup>(1)</sup>.

Parents blood types should be tested , and maternal titer of IgG antibodies to D antigene should be assayed at 12-16 ,28-32 ,and 36wk ; the presence of elevated antibody titers at beginning of pregnancy, or rapid rise in titer, or titer of 1:64 or greater suggests significant hemolytic disease<sup>(1)</sup> . Immediately after birth of any infant to Rh negative woman, blood from the umbilical cord or from infant should be examined for blood group, Rh type, hematocrit and hemoglobin, and reaction of the direct coombs test; if the coombs test is positive, baseline serum bilirubin should be measured being done not only to establish the diagnosis but also to ensure the selection of the most compatible blood for exchange transfusion. <sup>(1)</sup>

**Aim of current study :** To determine the severity of Rh hemolytic disease and its subsequent complications. and determine the protective effect of ABO incompatibility , so to find out the efficacy of anti-D globulin and effect of treatment of Rh incompatibility with phototherapy and exchange transfusion.

#### **Patients and methods:**

About 75 neonates with jaundice and Rh incompatibility admitted to Central Child Teaching Hospital and Al-Yarmook Teaching Hospital were studied during the period from the first of January 2008 to the 30th of June 2008. Forty six patients were males and twenty nine were females and their age range from 1-10 days.

**Clinical information collected** include: gestational age, gender, parity of the mothers, the presence of previous hemolysis or previous abortions, administration of anti-D antibody to the mothers, previous blood transfusion to the mother, presence of jaundice and its time of onset, and presence of pallor. So all the neonates were examined thoroughly for the presence of jaundice determination of gestational age, hepatosplenomegaly and ascitis. the pallor, in addition to investigations were done: **for neonates** = hemoglobin, reticulocyte count, blood group and Rh, total serum bilirubin, and direct coombs test (the method of direct coombs test in hospitals mentioned above is by putting on drop of whole blood and wash it 4 times with normal saline then remove supernatant and add 2 drops of antihuman globulin then test for agglutination by naked eye); **for mothers** = blood group and Rh. With regards to treatment, we found that = -20 patients need no specific treatment. -25 patients need treatment with phototherapy alone (Group A).30 patients need treatment with phototherapy and exchange transfusion(Group B).

#### **Results**

The frequency of severe Rhesus hemolytic disease and the need for exchange transfusion were more in those with multiparous mothers, as shown in table (1):

**Table (1): Relationship between hemolysis in neonates and parity of their mothers.**

Study Groups		Gravida 5<		Gravida 5≤		Total No.
		No.	%	No.	%	
Group B	Exchange transfusion and phototherapy	19	63	11	37	30
Group A	Phototherapy alone	12	48	13	52	25

**P value=0.05 (significant).**

Results showed in table (2) blood group in mothers and their neonates is shown in table (2) , There were No.= 58(78%) and No.= 27(36%) for both mothers and neonates patients with type O ,whilst about No.= 4(5%) and No.= 25(33%) for both mothers and neonates patients with type A.

**Table (2): The distribution of different blood groups in the mothers and babies with Rh incompatibility**

Blood groups	mothers with Rh incompatibility	babies with Rh incompatibility	
	No.(%)	No.(%)	
A	4(5)	25 (33)	
B	10(13)	12 (16)	
AB	3 (4)	11(15)	
O	58(78)	27 (36)	

History of previous hemolysis was present in 44 babies who need treatment and no one in neonates who not need treatment as shown in table(3):

**Table (3): The incidence of previous hemolysis in Rh incompatibility neonates**

History of previous hemolysis in neonates siblings	Patients who need treatment		Patients who not need treatment	
	No.	%	No.	%
Not present	11	20	20	100
Present	44	80	0	0
Total no.	55(100)		20(100)	

P-value =0.0001 ( very significant).

History of previous hemolysis was present in 17 of 25 neonates treated with phototherapy and in 27 of 30 neonates treated with exchange transfusion, as shown in table (4), so only five neonates(9%) of those who need treatment (55 neonates), their mothers had history of regular administration of anti-D following every pregnancy.

**Table(4): The frequency of previous hemolysis in phototherapy and exchange transfusion groups.**

History of previous hemolysis in babies siblings	Phototherapy alone Group(A)		Exchange transfusion Group(B)	
	No.	%	No.	%
Not present	8	32	3	10
Present	17	68	27	90
Total no.	25		30	

**P-value =0.002( significant).**

Table (5) showed about fifteen neonates(75%) of those did not need treatment (20 patients), their mothers had history of regular administration of anti-D following every pregnancy.which means that administration of anti-D was protective against hemolysis.

**Table(5): The frequency of anti-D administration among treated and untreated neonates with Rh incompatibility.**

Anti D administration	Hemolysis			
	Present		Absent	
	No.	%	No.	%
Not given	50	91	5	25
Given	5	9	15	75
Total no.	55 neonates need treatment		20 neonates need no treatment	

**P-value = 0.0001 (very significant).**

From data collected, ABO incompatibility presence with Rh incompatibility was not protective ,and the incidence of ABO incompatibility in treated and untreated neonates is shown in table(6).

**Table(6): The incidence of ABO incompatibility in patients groups**

ABO incompatibility	Patients who need treatment		Patients who not need treatment	
	No.	%	No.	%
Not present	14	25.5	3	15
Present	41	74.5	17	85
Total no.	55		20	

**P-value = 0.34 ( not significant).**

### Discussion

In this study we found that when the parity increases, the severity of hemolysis will be more and the need for exchange transfusion will also increases as shown that exchange transfusion was needed more in those with multiparous mothers, this result was also proved by Swinhoe & Gilmore which found that Rh hemolytic disease increased with subsequent pregnancies<sup>(29)</sup> and also Joseph & Kramer who found the same results<sup>(28)</sup>; and this is because fetomaternal transfusion occur with each pregnancy and the illness will be more worse with successive pregnancies<sup>(1)</sup>.

We found that the majority of those who required exchange transfusion had a history of previous hemolysis in their siblings (27 from 30 neonates) (90%) and 17 neonates of 25 neonates (68%) who required phototherapy had history of previous hemolysis siblings and this means that the history of previous hemolysis increases the the possibility that subsequent pregnancies and babies need active treatment; while no one in the untreated group had history of previous hemolysis; and this goes with( the fact that consider previous kernicterus or severe erythro-blastosis fetalis in a sibling as a further factor to decide treatment and not only to base the decision for treatment on the degree of anemia and/or hyperbilirubinemia<sup>(1)</sup>.

Fifteen of 20 neonates (75%) who did not require treatment, their mothers received dose of anti-D immunoglobulin and it was effective in preventing

hemolysis in the successive pregnancies and that is why their neonates did not need treatment. Only 5 of 55 mothers (9%) whom their babies required treatment, received dose of anti-D. This result is similar to what was found by Swinhoe & Gilmore<sup>(29)</sup>, and also by LAD & Jane<sup>(30)</sup>; while Hundric found that prevention of Rh immunization by anti-D immunoglobulin does not comprise all the Rh negative mothers especially inadequate after abortions and multiple pregnancies<sup>(34)</sup>.

So, we found that the presence of ABO incompatibility between neonates and their mothers was not effective in protection against hemolysis; this result is similar to that found in Vox who found that ABO incompatibility has no effect on ameliorating the severity of erythroblastosis after Rh- incompatibility has developed<sup>(32)</sup>, while VOS in his study found that Rh immunization in pregnancy is significantly less in ABO incompatible matings than in ABO compatible matings<sup>(31)</sup>. The fact that ABO incompatibility is protective against Rhesus hemolysis by the rapid removal of the fetal red blood cells by the mother's natural IgM anti-A and anti-B antibodies which do not cross the placenta<sup>(1)</sup>.

Clinical features of hemolysis like jaundice and pallor were evident in 89% and 40% of the neonates respectively, this is because that Rhesus incomp atibility is a cause of hemolysis and this evidence of hemolysis was more clear in the group who required exchange transfusion than those patients treated with phototherapy alone.

We found in this study regarding the hematological findings that the difference in the hemoglobin and reticulocyte count between neonates who required exchange transfusion and those treated with phototherapy alone was highly significant (p-value less than 0.001), which means that there is lower hemoglobin level and higher reticulocyte count in the exchange transfusion group than in phototherapy group, also the TSB levels were significantly higher in the group who required exchange transfusion than those treated with phototherapy alone.

All the above findings indicate that hemolysis was more severe in the exchange group than in the phototherapy group, and this was approved by Hayde & Widness in their study when they found that among infants with severe Rh isoimmunization, high total serum bilirubin levels and low hemoglobin levels indicate continuing severe hemolysis<sup>(33)</sup>, Direct coombs test was positive in 27 from 30 neonates(90%) who required exchange transfusion due to the presence of high titer of maternal anti-bodies against the babies Rhesus positive red blood cells and it was positive in 15 from 25 neonates(60%) treated with phototherapy alone.

### Conclusion

1) Early and proper management of the Rh-incompatibility may reduce the need for exchange transfusion. So, ABO incompatibility if occur with Rh incompatibility is not necessarily protective.also Anti-D immunoglobulin was protective against Rhesus hemolytic disease.

2) History of previous hemolysis in previous siblings is considered as risk factor for present hemolysis in neonate with Rh-incompatibility.

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**Conflict of Interest:** None

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