ABO incompatibility in newborn babies

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Abstract:

Background: Hemolytic disease of the newborn due to ABO incompatibility (HDN-ABO) is the most common cause of hemolytic disease of the newborn. The spectrum of disease that results is extremely broad, with relatively small percentage of infants requiring intervention for control of hyperbilirubinemia or anemia. In Iraq, significant neonatal hyperbilirubinemia including ABO incompatibility is still common cause of morbidities and mortalities.

Objectives: To know the severity of the Hemolytic disease of the newborn due to ABO incompatibility, it's relation to the age, sex, gestational age, birth weight, parity of the mother and effectiveness of phototherapy in treating neonatal jaundice and preventing exchange transfusion.

Patients and methods: This Descriptive study was done in Children Welfare Teaching Hospital from the first of April t 2010 to the end of September 2010. A total of 100 neonates admitted to NCU of this hospital with blood group A, B or AB Rh+ve ,whose mothers were blood group O Rh +ve, were included in the study .The data were collected from the patient's mothers , the patient's relatives and case sheets. All patients were examined and their blood samples were tested for blood group and Rh, TSB, Direct coomb's test (DCT), hematocrit (Hct) and reticulocyte percentage. The data were observed and analysis was carried out using the Statistical Package for Social Sciences-Version 17 (SPSS.v17).

Results: The total number of patients were 100 with age range from 1-12 days. Fifty three percent were males and 47% were females.85 % were term , 13% were preterm and 2% were post term. Family history of neonatal jaundice ,history of jaundice 's treatment is negative in 54% .Seventy six percent presented during the second and third day of life and the jaundice was the hallmark of the disease in 100%. TSB was 322±76mmol/l. The Hct was 40-75% in (89%) and less than 40% in (11%). Reticulocyte percentage was less than 5% in 81 % patients and more than 5% in 19% patients . Direct coomb's test (DCT) was negative in all patients. Seventy - seven percentage of patients treated with phototherapy ,and in 46% of them the duration of phototherapy was 24-48hr, while 23% of patients treated with exchange transfusion and phototherapy.

Conclusions: HDN-ABO incompatibility is important cause of bilirubin encephalopathy (kernicterus). The age of neonate, gestational age , birth weight, parity of the mother has relation to the severity of the disease .The phototherapy is effective in treating neonatal hyperbilirubinemia and in preventing the need for exchange transfusion. The outcome is not good.

Keywords: Hemolytic disease, newborn, ABO incompatibility, neonatal jaundice

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Introduction:

ABO incompatibility is the most common cause of hemolytic disease of the newborn. Approximately 15% of live births are at risk, but manifestations of disease occur in only 0.3-2.2%. Major blood group incompatibility between the mother and fetus generally results in milder disease than Rh incompatibility does. Maternal antibody may be formed against B cells if the mother is type A or against A cells if the mother is type B. However, usually, the mother is type O and the infant is type A or B.(1)

Most cases are mild, with jaundice being the only clinical manifestation. Neonates with blood group incompatibility often develop early-onset, hemolysis-mediated hyperbilirubinemia. The infant is not generally affected at birth; pallor is not present, and hydrops fetalis is extremely rare. The liver and spleen are not greatly enlarged, if at all. Jaundice usually appears during the 1st 24 hr. Rarely, it may become severe, and symptoms and signs of kernicterus develop rapidly.(1) There is no need for prenatal diagnosis or treatment and no need for early delivery. (2)

A presumptive diagnosis is based on the presence of ABO incompatibility, a weakly to moderately positive direct Coombs test result, and spherocytes in the blood smear, which may at times suggest the presence of hereditary spherocytosis. Hyperbilirubinemia is often the only other laboratory abnormality. The hemoglobin level is usually normal but may

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be as low as 10-12 g/dL (100-120 g/L). Reticulocytes may be increased to 10-15%, with extensive polychromasia and increased numbers of nucleated RBCs. In 10-20% of affected infants, the unconjugated serum bilirubin level may reach 20 mg/dL or more unless phototherapy is administered. (1)The reticulocyte count, a positive direct antiglobulin test, and the presence of a sibling with neonatal jaundice were determined to be the good predictors for the development of significant hyperbilirubinemia and severe hemolytic disease of the newborn. (3)

Phototherapy may be effective in lowering serum bilirubin levels. In rare severe cases, treatment is directed at correcting dangerous degrees of anemia or hyperbilirubinemia by exchange transfusions with type O blood of the same Rh type as the infant. Some infants with ABO hemolytic disease may require transfusion of packed RBC's at several weeks of age because of slowly progressive anemia. Post-discharge monitoring of hemoglobin/ Hct is essential in newborns with ABO hemolytic disease. (1)

In Iraq, significant neonatal hyperbilirubinemia including ABO incompatibility is a common cause of morbidities and mortalities. Risks of mortality and irreversible brain injury among healthy infants admitted for newborn jaundice are urgent reminders to promote education of communities, families and primary health care providers, especially in a poor health system. Known risk factors for severe hyperbilirubinemia were signified by the effect of advanced acute bilirubin encephalopathy(ABE.) (4)

This study aimed to know the severity of the hemolysis due to ABO -incompatibility in the neonates, the incidence in relation to age, sex, gestational age, birth weight and the parity of the mother, and to know whether phototherapy is effective in preventing exchange transfusion or not.

Patients & Method

This descriptive study was done on 100 neonates with blood groups A , B and AB, Rh +ve whose mothers were blood group O +ve, who were admitted to the neonate care unit(NCU) of Children Welfare Teaching Hospital(CWTH) over a period of six months from first of April to the end of September 2010. The clinical data were collected from the patient's relatives and from their case sheets , and included age, sex, gestational age, birth weight, parity of the mother , previous family history of neonatal jaundice, the time of onset of jaundice, the feeding of the baby, and activity of the baby.

Physical examination was done for all the babies including pallor, jaundice, hepatosplenomegally and neurological signs .

Blood samples were taken from all the babies and sent for blood group and Rh, total serum bilirubin(TSB), reticulocyte count, hematocrit and direct coomb's test (DCT). Reticulocyte count was done by the laboratory for only 58 patients.

All the babies were treated by phototherapy and/or exchange transfusion depending on an age –specific(by-hour) nomogram.(5)

Babies with features of sepsis were excluded from the study but one case developed sepsis in the hospital.

The statistical Package for Social Sciences –Version 17(SPSS. v17) was used for data input and analysis. Continuous variables are expressed as means and standard deviations and discrete variables expressed as numbers and percentages. Chi square test for goodness of fit used to test the distribution of discrete variables .Pearson chi square test of independence used to test the association(relationship) between discrete variables. t test for independent samples used to test the difference between two independent normally distributed continuous variables, and whenever distribution normality was questioned we shifted to Mann-Whiney t est. Finding with P value of less than 0.05 were considered significant.

Results:

The total number of patients was 100 with age range from 1-12 days,76% of the patients developed jaundice between the age of 1-3 days,13% of patients developed jaundice after the 3rd day and 11% of patients develop jaundice during the first 24hrs. (table 1)

Fifty three percent were males and 47% were females.(table 1)

There was significant value regarding weight of the patients,79% of the patients had weights more than 2.5kg while 21% of the patients had weights less than 2.5kg. (table 1)

Fifty five percent of the patients have blood group A Rh+ve , while 45% of patients were blood group B Rh +ve .(table 1)

Eighty five percentage were term 13% were preterm and 2% were post term. (table 1)

Thirty seven percentage were admitted at the age of less than 3 days and 63% of the patients admitted at the age of more than 3 days.(table 1)

The mothers of (37%) of patients were primigravida , while (63%) were multigravida. (Table 2)

Forty six percent of patients had positive family history of previous neonatal jaundice. Thirteen percent had family history of phototherapy ,while (3%) had previous history of exchange transfusion.(table 2)

One hundred percent of patients presented with jaundice,15% had pallor, (4%) had organomegaly.(table 2)

Thirty five percent of patients had lethargy. Forty three percentage of patients had poor feeding .Three percent had opsithotonos. (Table 2)

The total serum bilirubin after 6hrs of phototherapy were decreased (mean±SD,20.3±10.8) ,there was significant association between the use of phototherapy and the decrease in TSB(p value=0.000).(table 3)

The hematocrit (PCV) of (89%) was 40-75% while (11%)

patients had PCV less than 40%. One hundred patients had negative coomb's test. Reticulocyte percent was done by the laboratory for only (58%) of patients,81% of them had reticulocyte percent of less than 5% while 19% patients had reticulocyte percent of more than 5%. (table 3)

Seventy seven percentage of patients were treated by phototherapy while (23%) were treated by combined phototherapy and exchange transfusion) ,there was highly significant association(P value=0.000) . (table 4)

Forty six percentage of patients needed 48hrs phototherapy while (54%) of patients needed more than 48hrs phototherapy .Eighteen percentage of patients needed single exchange transfusion , while (5%) of patients needed twice exchange transfusion.(table 4)

Eighty seven percentage of patients were discharged well, (9%) of patients had kernicterus, one patient died , while (3%)of patients discharged on the responsibility of their families. (table 4)

Table 1 : General description of 100 neonates with ABO incompatibility

Variables	Statistic	X2	P
Age at Onset of Jaundice			
Mean ± SD	2.44 ± 0.9		
< 1 day, n (%)	11 (11.0)		
1-3 days, n (%)	76 (76.0)	81.98	0.000
> 3 days, n (%)	13 (13.0)		
Sex			
Male, n (%)	53 (53.0)	0.360	0.549
Female, n (%)	47 (47.0)		
Birth Weight (Kg)			
Mean ± SD	2.8 ± 0.6		
< 2.5, n (%)	21 (21.0)		
2.5 –< 4, n (%)	76 (76.0)	86.78	0.000
≥ 4.0, n (%)	3 (3.0)		
Fetal Maturity at Birth			
Term, n (%)	85 (85.0)		
Preterm, n (%)	13 (13.0)	121.94	0.000
Post term, n (%)	2 (2.0)		
Blood Group			
A,n(%)	55(55.o)	1.00	0.317
B,n(%)	45(45.o)		
Age at Admission (days)			
Mean ± SD	4.5 ± 2.0		
0-3 days, n (%)	37 (37.0)		
3-<7days, n (%)	47 (47.0)	50.24	0.000
7-<10 days, n (%)	13 (13.0)		
10-11 days,n(%)	3 (3.0)		

Table 2: Distribution of obstetric history, family history, general examination, and features of kernicterus.

Variables	Statistic	X2	P
Maternal (Obstetric) Conditions			
Gravida,		---	---
Pimigravida,n(%)	37(37.0)	---	---
Multigravida,n(%)	63(63.0)	---	---
Positive Family History			
Jaundice, n (%)	46 (46.0)	0.495	0.482
Phototherapy, n (%)	13 (13.0)	45.76	0.000
Exchange Transfusion, n (%)	3 (3.0)	88.63	0.000
Positive Findings of General Examination:			
Jaundice, n (%)	100 (100.0)	---	---
Pallor, n (%)	15 (15.0)	49.00	0.000
Organomegaly, n (%)	4 (4.0)	84.64	0.000
Hydrops Fetalis, n (%)	0 (0.0)	---	---
	0 (0.0)	---	---
Presence of Features of Kernicterus:			
Lethargy, n (%)	35 (35.0)	9.0	0.003
Poor Feeding, n (%)	43 (43.0)	1.96	0.162
Opisthotonos, n (%)	3 (3.0)	88.36	0.000
Seizure	0(0.0)		

Table 3: Laboratory investigations:

Variables	Statistic	T	P
T.S.B (mmol/L)*			
On admission, Mean ± SD	322 ± 76		
After 6 hours, Mean ± SD	252 ± 47	12.93	0.000
Percent decrease after 6 hr (%), Mean ± SD	20.3 ± 10.8		
PCV (%)			
On admission, Mean ± SD	51.1 ± 9.2		
After 12 hours, Mean ± SD	51.2 ± 8.8	- 0.0.68	0.946
PCV<40% , n(%)	11(11.0)		
40-75%, n(%)	89(89.0)		
Positive Direct Coomb>s Test, n (%)	0 (0.0)	--	--
Retic Count (%), <5%	81(81.0)	--	--
>5%	19(19.0)		

* 1mg = 17 mmo

Table 4: Description of interventions and their impact.

	Statistic	X2	P
Type of Treatment Phototherapy, n (%) Combined, n (%)	77 (23.0) 23 (23.0)	29.16	0.000
T.S.B (mmol/L) Immediately after exchange transfusion	286 ± 89	---	---
Duration of phototherapy (hours) Mean ± SD < 48 hours, n (%) 49-96 hours, n (%)	63.7 ± 17.9 46 (46.0) 54 (54.0)	--- 0.64	--- 0.424
Frequency of exchange transfusion Mean ± SD Once, n (%) Twice, n (%) > Twice, n (%)	1.2 ± 0.4 18 (18.0) 5 (5.0) 0 (0.0)	7.384	0.007
Condition on Discharge Well, n (%) Kernicterus, n (%) Died, n (%) Discharged on Companion>s Responsibility, n (%) Referred, n (%) Others, n (%)	87 (87.0) 9 (9.0) 1 (1.0) 3 (3.0) 0 (0.0) 0 (0.0)	54.76	0.000

Discussion:

In this study, (76%) of newborns presented with jaundice during the second and the third day of life whereas (11%) presented in the first day of life and (13%) presented after the third day. These results agree with Weng YH who found that neonates with blood group incompatibility often develop early-onset, hemolysis-mediated hyperbilirubinemia, and they are at great risk of kernicterus. (6) These results disagree with Stoll BJ.(1)

Fifty three percentage of newborns were males while (47%) were females, this study agrees with Kalakheti BK study where (54%) were males, while(46%) were females. (7)

In(21%) of patients, the body weight was less than 2.5 kg, while (79%) of patients were more than 2.5 kg. In contrast to the fact that gestational age babies developed polycythemia which lead to hyperbilirubinemia, which was reported by Kalakheti BK study where there was 1.3 times more neonates having hyperbilirubinemia in VLBW babies than in normal birth weight(BW) babies. (7) This finding is probably because very low birth weight(VLBW) usually died in our NCU and the percentage of very (VLBW) babies was lower than that of normal BW.

Fifty five percentage of patients were A Rh+ve while (45%) of patients were B Rh+ve ,while in Murat study(72%) were A Rh+ve and (28%) were B Rh+ve.(3)

Eighty five percentage of patients were term, while (13%) were preterm and (2%) were post term. In Kalakheti BK, there was 1.4 times higher chance of having hyperbilirubinemia in preterm babies than in term babies (7),this finding is probably because the percentage of preterm is only 67%- of all births and their mortality rate is high.(1)

The mothers of (37%) of patients were primigravida while(63%) were multigravida .A similar finding was reported in Kathleen study (8) ,(24.4%) were primigravida and (75.6%) were multigravida but not reported by Kalakheti study ,(95%) were primigravida and (5%) were multigravida.(7) ,this is probably because ABO incompatibility with neonatal hemolysis develops only if the mother has IgG antibodies from a previous exposure to A or B antigens(by first trimester abortion, ectopic pregnancy or normal pregnancy),also many mothers who have blood group O have IgG antibodies to A and B before pregnancy, the first born infant of A and B blood type may be affected.(9)

Fifty four percentage of patients had no previous family history of jaundice ,phototherapy or exchange transfusion while in Murat study (3) ,(21%) had previous history. This results were supported by the fact that ABO hemolytic disease does not become more severe with subsequent pregnancy.(10)

All newborns had jaundice as the hallmark of the disease .This finding was reported by Kalakheti BK study (7) , there was 2.6 times higher chance of having hyperbilirubinemia in the babies with ABO incompatibility than O positive babies. Fifteen percentage of patients developed pallor with jaundice ,this finding was reported by Murat study (3) while (4%) had jaundice with organomegally. Forty three percentage of the patients developed neurological signs as poor feeding with lethargy, while(35%) developed lethargy and only(3%) had opisthotonos ,this finding was reported by Stoll B J et al. (1)

The hematocrit (Hct) was 4075%- in (89%) of the patients at admission, while in (11%) of the patients the PCV was less than 40% .The reticulocyte percentage was done by the laboratory for only (58%) of the patients. Forty seven percentage of patients had reticulocyte percentage of less than 5% , while (11%) had reticulocyte percentage more than 5%. In Murat study , Hct was 55.386.47± and reticulocyte percentage was4.393.46±. Direct coomb>s test was negative in all the patients, while in Murat study ,(21%) were DAT positive and 79% were DAT negative .This result may be due to the fact that there is very little anti-A or anti-B antibody on the neonatal RBC in ABO hemolytic disease .(11,12). Seventy seven percentage of patients were treated with phototherapy and in (46%) the duration of phototherapy was 2448- hr, while (23%)treated with exchange transfusion and phototherapy(combined) and in (18%) the exchange transfusion was done just once and the total serum bilirubin was lowered immediately

after the exchange transfusion .These results indicate that phototherapy is effective in the treatment of hyperbilirubinemia and decrease the need for the exchange transfusion. This finding was similar to that reported by Yaseen H study.(13)

Eighty seven percentage of patients did well and were discharged from the hospital while (9%) of patients had kernicterus and (1%) died because of septicemia ,while (3%) were discharged on companion>s responsibility. So the prognosis in ABO- incompatibility is not good .

Conclusions: The severity of ABO incompatibility was related to neonatal age ,gestational age, birth weight and the parity of the mother ,while the sex has no relation. There was a delay in seeking medical advice. Negative direct coomb>s test will not exclude ABO incompatibility. Early Phototherapy is effective and important in decreasing the need for exchange transfusion. HDN-ABO is important cause of acute bilirubin encephalopathy. The outcome is not good, related to death or kernicterus.

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