Outcome of Neonatal Jaundice In ABO Incompatible Pregnancies

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ABSTRACT:

BACKGROUND:

Blood group mismatch between the mother and newborn carries substantial risk for neonatal jaundice

OBJECTIVE:

To study the outcome of neonatal jaundice due to ABO hemolytic disease of the newborn (ABO HDN) and study the relation of epidemiological risk factors and laboratory findings with it´s severity.

PATIENTS AND METHODS:

In this prospective study, 64 neonates with neonatal jaundice associated with ABO incompatibility were studies. Cases of ABO HDN were diagnosed as those with anemia, reticulocytosis and spherocytes or polychromasia on blood film with or without positive direct Coombs test. Severity of jaundice was regarded according to the type of treatment (phototherapy or exchange transfusion).

RESULTS:

Forty two patients (65.6%) were males, 46 patients (71.9%) were full term infants, 6 patients (9.4%) had family history of neonatal jaundice treated by exchange transfusion.

Only 9 patients (14.1%) presented with TSB level ≥ 20 mg/dl, 8 patients (12.2%) had PCV level < 45%, 8 patient (12.5%) had reticulocyte count ≥ 5%. Direct Coombs test was negative in all the patients. Twelve patients (18.8%) had abnormal blood film findings .

Eight cases (12.5%) had the features of ABO HDN and represented 2.9% from the total admitted cases of neonatal jaundice.

Full term babies, positive family history of exchange transfusion, abnormal blood film findings and reticulocyte count were found as significant risk factors for the severity of the jaundice, while gender, body weight, blood group, mode of delivery and parity of the mothers had no significant effect on the severity of the jaundice.

CONCLUSION:

Not all the cases of ABO incompatibility developed ABO HDN, so laboratory confirmation is required.

KEYWORDS: neonatal jaundice, ABO incompatibility, hemolytic disease of the newborn

INTRODUCTION:

ABO hemolytic disease of the newborn (ABO HDN) occur when maternal IgG antibodies with specificity for the ABO blood group system pass through the placenta to fetal circulation where they can cause hemolysis of fetal RBCs which can lead to anemia and jaundice[1].

In nearly all the cases, the mother blood group is O and the infants' blood group is A or B[2].

With declining incidence of Rhesus disease (Rh disease), ABO incompatibility is said to be the commonest cause of hemolytic jaundice in the newborn[1,3].

In contrast to Rh disease, about half of the cases of ABO HDN occur in a firstborn baby and ABO HDN does not become more severe after further pregnancies[4].

In about one-third of all ABO incompatible pregnancies maternal IgG anti-A or anti-B antibodies pass through the placenta to the fetal circulation leading to a weakly positive direct Coombs test for the neonate's blood[5].

Although ABO incompatibility occurs in 20-25% of pregnancies, hemolysis occur in 4% of cases, only 33% of such infants are Coombs positive [4].

Most cases are mild, with jaundice being the only clinical feature[1,6]. Jaundice usually appears during the first 24 to 72 hours of life[6], the infant is not generally affected at birth, pallor is not present[1].

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Clinically severe jaundice occur in 20% of cases. Features of hemolysis include pallor and rarely hydrops fetalis with ascitis, pleural and pericardial effusions with enlargement of the liver and spleen[7].

Diagnosis is based on the presence of ABO incompatability, hyperbilirubinemia is often the only laboratory abnormality. In 10-20% of affected infants, the unconjugated bilirubin level may reach 20 mg/dl or more.

The hemoglobin level is usually normal but may be as low as 10-12 g/dl with weakly to moderately positive direct Coombs test.

Reticulocytes may be increased to 10-15%, with spherocytes in the blood film, extensive polychromasia and increase numbers of nucleated RBCs[1].

Because not all ABO incompatibility pregnancies result in neonatal hemolysis, clinical and laboratory confirmation of a neonatal hemolytic disorder is necessary to confirm the diagnosis[2].

The goal of therapy is to prevent the concentration of unconjugated bilirubin in the blood from reaching levels at which neurotoxicity may occur. The types of treatment are phototherapy and exchange transfusion[8].

This study aimed to find the outcome of neonatal jaundice due to ABO hemolytic disease in relation to other types of neonatal jaundice, to study neonatal jaundice associated with ABO incompatible pregnancies; in relation to epidemiological factors and laboratory findings and to study the use of treatment modalities and the outcome of the ABO incompatibility jaundiced babies.

PATIENTS AND METHODS:

This prospective study was conducted in the pediatric ward in Al-Kadhymia Teaching Hospital for the period between 1st of January to 30th of June, 2010.

Sixty four patients with neonatal jaundice of ABO incompatibility were studied, all with blood group A or B whom mothers had blood group O with ages ranging from birth to one week.

Babies with respiratory distress, signs of sepsis and Rh^+ babies born to Rh^- mothers were excluded from the study.

Clinical information was taken by standardized questionnaires, including name, sex, date of birth, date of admission, onset of jaundice, gestational age, body weight, type of feeding, mode of delivery, mother parity and family history of neonatal jaundice among siblings and its treatment. Patients with gestational age ≥ 37 weeks regarded as terms, those with gestational age < 37 weeks regarded as preterms, patients with body weight < 2.5 kg regarded as low body weight and mothers with parity ≥ 5 considered as high parity, while those with parity < 5 considered as low parity mothers[6].

Thorough physical examination was done for all patients for exclusion of cases with abnormal findings like petechiae.

The following investigations were carried out to all the study sample:

1. TSB and PCV by a heel-prick, and a sample of blood was taken by a capillary tube, PCV was measured by a special ruler and TSB was measured by a standardized bilirubin analyzer (bilirubinmeter), PCV level of 45% was considered as the lower limit of normal[9,10].
2. Blood group and Rh.
3. Reticulocyte count (count between 0-5% regarded as normal)[9].
4. Direct Coombs test.
5. Blood film.
6. Blood group and Rh of the mothers.

Cases of ABO hemolytic disease of the newborn were diagnosed as those with anemia, reticulocytosis and spherocytes or polychromasia on blood film with or without positive direct Coombs test[1].

During hospitalization, all patients received treatment by either phototherapy alone or phototherapy and exchange transfusion.

Each case was followed by examination and frequent monitoring of TSB and PCV to assess the response to treatment until the discharge of the patient, TSB was measured immediately after exchange transfusion and until 24 hours after cessation of phototherapy.

Severity of jaundice was regarded according to the type of treatment (phototherapy or exchange transfusion) according to bilirubin nomogram[11].

The obtained results were analyzed using SPSS (Statistical Package for Social Sciences) version 16 and Microsoft Excel 2007. Chi square test was used to study the relation between two discrete variables, P value < 0.05 was considered to be significant.

RESULTS:

The total cases of neonatal jaundice admitted during the study period was 277 cases .

Forty two patients (65.6%) were males and twenty two (34.4%)were females with male to female ratio = 1.9:1. Forty six patients (71.9%) were term infants, and the remaining 18 patients (28.1%) were preterm. Forty nine patients

(76.6%) had body weight ≥ 2.5 kg, while the other 15patients (23.4%) had body weight < 2.5 kg. Thirty eight patients (59.4%) had blood group B, and 26 patients (40.6%) had blood group A.

Fifty patients (78.1%) had no family history of neonatal jaundice, 6 patients (9.4%) had family history of neonatal jaundice treated by exchange transfusion, 5 patients (7.8%) had family history of neonatal jaundice not required treatment and 3 patients (4.7%) had family history of neonatal jaundice required phototherapy. Forty six (71.9%) mothers had low parity. Thirty six patients (56.3%) were delivered by vaginal delivery, and 28 patients (43.7%) were delivered by cesarean section.

As shown in Table 1, the gestational age and presence of family history of neonatal jaundice were found to have statistically significant correlation with type of treatment and thus with severity of jaundice. While the distribution of patients according to gender, body weight, blood group, parity, mode of delivery was not statistically significant.

Laboratory findings as shown in table 2 revealed that only 9 patients (14.1%) presented with TSB level ≥20 mg/dl, while 32 patients (50%) had TSB level of 15-20 mg/dl, 21 patients (32.8%) had TSB values of 10-15 mg/dl, the remaining 2 patients (3.1%) had levels below 10 mg/dl .

The majority of the patients (87.5%) had PCV level ≥ 45%, while 8 (12.5%) had PCV level < 45%. Majority of the patients (87.5%) had reticulocyte count < 5%, while 7 patient (10.9%) had reticulocyte count between 5-10% and only 1 patient (1.6%) with reticulocyte count ≥ 10%. Direct Coombs test was negative in all the patients. Fifty two patients (81.2%) had normal blood film findings, while in 6 patients (9.4%) the blood film showed polychromasia, fragmented RBCs and spherocytes, and 6 patients (9.4%) had spherocytes only. Elusion test was not used because it is not available in our hospital.

Reticulocyte count and the blood film findings were significant in correlation with the severity of jaundice (P value < 0.001) as shown in table 3. From 64 patients with neonatal jaundice of ABO incompatibility, 8 cases (12.5%) had the features of ABO HDN and represented 2.9% from the total admitted cases of neonatal jaundice.

As shown in Table 4, 34 patients (53.1%) had the onset of jaundice in the second day of life, 13 patients (20.3%) in the first day of life, 11 patients (17.2%) on the third day of life, while 6 patients (9.4%) had the onset after the third day of life.

Phototherapy alone was used in the treatment of 43 patients (67.2%), while phototherapy and exchange transfusion were used in the treatment of 21 patients (32.8%).

Regarding the duration of phototherapy, the majority of patients (83.7%) need 24 – 48 hours as duration of phototherapy, 5 patients (11.7%) need 72 hours , 1 patient (2.3%) need 96 hours and only 1 patient (2.3%) needs 120 hours . In exchange transfusion group, 13 patients (61.9%) had immediate TSB decline of 25-50% after the procedure, while 6 patients (28.6%) had < 25% decline and 2 patients (9.5%) had > 50% decline. All the patients were discharged well.

DISCUSSION:

The percentage of cases of neonatal jaundice due to ABO-HDN represents 2.9% from the total cases of neonatal jaundice admitted to the hospital during the study period. In other studies, ABO-HDN represents 6% of the cases in a study from Baghdad[12], 19% in a study from Canada[13] and 15.95% from a Croatian study [14] . Although ABO incompatibility occurs in 20-25% of pregnancies, hemolysis occurs only in 4% of cases[4], this may explain these variable percentages in addition to geographical regions and sample size of the study group.

Similar to Hameed N .N et al study from Baghdad [15] , Male patients were more affected than female patients in this study, this is understood as male gender is a risk factor for neonatal jaundice[1, 4, 6] . The severity of jaundice among our patients was not affected statistically by gender, the same finding were found by Bucher et al. and by Dufour D. R. et al. in their studies [16, 17] .

We found that full term neonates had significant statistical correlation with the severity of jaundice. This is related to that RBC surface antigens are not fully developed in the fetus and preterm neonates[18].

The body weight had no significant relationship with the severity of the jaundice in this study; the same was found by Dufour D. R. et al.[17] and by Isam S.[19].

Most of the patients were found to have blood group B. This is in contrast to other studies which reported that most infants with ABO incompatibility jaundice had blood group A[16,19]. Blood group was not statistically significant for the severity of jaundice; similar finding was reported by Bucher et al.[16] , Dufour D. R. et al.[17], M. W. Quinn et al.[20],

Also family history of neonatal jaundice treated by exchange transfusion was found to be a significant risk factor for the severity of jaundice. Similar findings were found in Saric S. V. et al study [21] It was found that some mothers are sensitized by feto-maternal transfusion and produce immune IgG antibodies against the antigen they do not have and their babies do have. This can explain the occurrence of neonatal jaundice with ABO incompatibility in more than one family member. In addition, severity was found to be constant among different family members[4,9].

The parity of the mother does not affect the severity of the jaundice in this study. Similar finding were reported by Dufour D. R. et al[17] and Isam S.[19]. It was reported that ABO incompatibility jaundice was seen in the first born baby[1, 9], and it may affect subsequent pregnancies with no increase in the severity of jaundice[4, 9, 22]

The mode of delivery was not significant for the severity of the jaundice in this study; the same findings were reported by M. W. Quinn et al.[20]

A previous study reported that 10-20% of ABO incompatibility patients have TSB level ≥20 mg/dl[3] , and this finding was highlighted among our patients .

PCV was normal in the majority of our patients.This is similar to Hameed N .N et al study[15] This is because ABO incompatibility rarely present with severe anemia[1,2,4,6,9] as found by N. McIntosh[22] and hemolysis occurs in only 4% of cases[4].

In Hameed N .N et al study, 81% of patients had retics count < 5% [15] , this is nearly similar to results of this study . Abnormal findings on blood film and reticulocytosis were found to be significant for the severity of the disease. Similarly Saric S. V. et al. found that reticulocytosis is a good predictor for the severity of ABO hemolytic disease[21].

Regarding direct Coombs test, all our patients had negative result. Same finding was obtained by Hameed N .N et al study [15] . There are conflicting data regarding the significance of positive Coombs test as a predictor for the severity of jaundice in ABO incompatibility. Dufour D. R. et al. and Saric S. V. et al concluded that positive direct Coombs test is a good screening test for ABO-HDN[17, 21], while M. W. Quinn et al. in their study reported that Coombs positive cases may be useful in predicting the occurrence of jaundice but not of its severity[20]. R. S. Procianoy et al. found that positive predictive accuracy of the direct Coombs test was just 42%[23].

Majority of our cases treated by phototherapy need 24 – 48 hours as duration; similarly ,a percentage of 46% and 56.2% was reported by two previous Iraqi studies respectively [15, 19] . Phototherapy is an effective measure in the treatment of jaundice due to ABO incompatibility and reduce the need for repeated exchange transfusion [1,6,8].

Isam et al in his study found that TSB values were lowered by 25-50% of the pre-exchange level in most of the patients treated by exchange transfusion [19] , this indicates that exchange transfusion was an effective measure in the treatment, however phototherapy should not be used as a substitute for exchange transfusion[24] .

Table 1: Correlation of treatment type with epidemiological factors.

epidemiological factors	Exchange Transfusion (ET)	Phototherapy (P)	Total
Gender Male Female	 16 (25%) 5 (7.8%)	 26 (40.6%) 17 (26.6%)	 42 (65.6%) 22 (34.4%)
P= 0.168 (not significant)			
Gestational age Preterm Term	 2 (3.1%) 19 (29.7%)	 16 (25%) 27 (42.2%)	 18 (28.1%) 46 (71.9%)
P= 0.021 (significant)			
Body weight < 2.5 kg ≥ 2.5 kg	 3 (4.7%) 18 (28.1%)	 12 (18.7%) 31 (48.5%)	 15 (23.4%) 49 (76.6%)
P= 0.187 (not significant)			
Blood group A B	 8 (12.5%) 13 (20.3%)	 18 (28.1%) 25 (39.1%)	 26 (40.6%) 38 (59.4%)
P= 0.773 (not significant)			
Family History of Neonatal Jaundice			
H of ET H of P H of J, no treatment No H of J	5 (7.8%) 2 (3.1%) 3 (4.7%) 11 (17.2%)	1 (1.6%) 1 (1.6%) 2 (3.1%) 39 (60.9%)	6 (9.4%) 3 (4.7%) 5 (7.8%) 50 (78.1%)
P = 0.005 (significant)			
Parity < 5 ≥ 5	 16 (25%) 5 (7.8%)	 30 (46.9%) 13 (20.3%)	 46 (71.9%) 18 (28.1%)
P= 0.592 (not significant)			
Mode of delivery Vaginal Cesarean	 11 (17.2%) 10 (15.6%)	 25 (39.1%) 18 (28.1%)	 36 (56.3%) 28 (43.7%)
P = 0.663 (not significant)			

Table 2: Laboratory findings in 65 jaundiced patients.

Laboratory Features		No. of cases (%)
TSB level (mg/dl)		
	< 10	2 (3.1%)
	10-15	21 (32.8%)
	15-20	32 (50%)
	≥20	9 (14.1%)
PCV level		
	≥ 45%	56 (87.5%)
	< 45%	8 (12.5%)
Reticulocyte count		
	0-5%	56 (87.5%)
	5-10%	7 (10.9%)
	> 10%	1 (1.6%)
Direct Coombs test		
	Negative	64 (100%)
	Positive	0 (0%)
Blood film		
Normal		52 (81.2%)
Spherocytes only		6 (9.4%)
Hemolytic picture (polychromasia, fragmented RBC, spherocytes)		6 (9.4%)

Table 3: Correlation between Laboratory findings and treatment type.

Laboratory findings	Exchange Transfusion	Phototherapy	Total
reticulocyte count			
0 – 5%	13 (20.3%)	43 (67.2%)	56 (87.5%)
5 – 10%	7 (10.9%)	0	7 (10.9%)
>10%	1 (1.6%)	0	1 (1.6%)
P = 0.001 (significant)			
blood film findings			
Normal	11 (17.1%)	41 (64.1%)	52 (81.2%)
spherocytes	4 (6.3%)	2 (3.1%)	6 (9.4%)
*Hemolytic	6 (9.4%)	0	6 (9.4%)
P = < 0.001 (significant)			

*Hemolytic picture : polychromasia, fragmented RBC, spherocytes

Table 4: Criteria of jaundice and it´s treatment.

Onset of jaundice	No. (%)
1 day	13 (20.3%)
2 day	34 (53.1%)
3 day	11 (17.2%)
>3 day	6 (9.4%)
Type of treatment	
Phototherapy alone	43 (67.2%)
phototherapy and exchange transfusion	21 (32.8%)
Duration of phototherapy	
24 – 48 hours	36 (83.7%)
72 hours	5 (11.7%)
96 hours	1 (2.3%)
> 96 hours	1 (2.3%)
TSB decline immediately after exchange transfusion	
Percentage of decline	
< 25%	6 (28.6%)
25-50%	13 (61.9%)
> 50%	2 (9.5%)

CONCLUSION:

Not all the cases of ABO incompatibility developed ABO HDN, so laboratory confirmation is required.

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