

Incidence of early neonatal hyperbilirubinemia in ABO incompatibility and cord bilirubin as a predictor for phototherapy

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Abstract

Neonatal Hyperbilirubinemia is a common condition in neonates and the most common pathological cause leading to hyperbilirubinemia is Rh or ABO incompatibility. Although most newborns with jaundice are otherwise healthy, the greatest risk associated with indirect hyperbilirubinemia is the development of bilirubin induced neurologic dysfunction which typically occurs with higher indirect bilirubin levels. **Aim of the Study:** This study was done to (1) Find out the incidence of early hyperbilirubinemia and need for phototherapy in babies born to O+ve mother and (2) Cord Bilirubin as a marker for early phototherapy in ABO blood group incompatibility. **Method :** This was a prospective cohort study which included 50 consecutive term appropriate for gestational age babies with blood group either A or B born to O+ve mother as cases and another 50 consecutive term appropriate for gestational age babies with O+ve blood group born to O+ve mother served as control. **Result:** 88% of the babies in the case group required phototherapy for > 24 hours whereas in the control group only 55% required phototherapy for > 24 hrs. Based on statistical analysis, there was a probability that the newborns who needed early phototherapy had a cord bilirubin 2.05 or more. **Conclusion:** It may be concluded that babies with ABO incompatibility needed early and prolonged treatment compared to controls. A cord bilirubin above 2.05 can predict the need for treatment.

Keywords: Neonatal hyperbilirubinemia, Cord bilirubin, ABO incompatibility, Phototherapy, Neonatal Jaundice

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Introduction

Neonatal hyperbilirubinemia is one of the most common conditions that require medical attention in newborn. Jaundice is observed during the first week after birth in 60% term infants and 80% of preterm infants [1,2,3]. Although pathological jaundice was almost synonymous with Rh isoimmunisation, other causes like ABO incompatibility (most common being OAI) Red cell membrane defects (hereditary spherocytosis), Red cells enzyme defects (i.e. G6PD def), thalassemias etc. can contribute to significant number of neonates with pathological jaundice [4].

ABO hemolytic disease is the most common blood group incompatible hemolytic process of the newborn period and a major contributor of neonatal jaundice [5]. In general 15-25% of all maternal fetal pairs are ABO incompatible [4,5] but ABO hemolytic disease is confined to roughly 1% of such O group women who

have antenatal high titre antibodies. ABO isoagglutinins are present in the sera of all individuals whose red cells lack the corresponding antigen and are usually of the IgM class [4,6]. High titres of IgG antibodies are more likely to occur in group O individuals than Group A (or) Group B individuals and increased antibody production after antigenic stimulation can occur. Consequently group O mothers with potent IgG anti A, B or AB are at greatest risk of having affected infants. Among Group A or B infants born to group O mothers, 30-50% have detectable maternal IgG antibody bound to their red cells compared to 5% among all infants. Because ABO IgG antibodies can occur without prior red cell exposure they can result in hemolytic disease of newborn even in first pregnancy [6,7].

Early discharge of healthy term newborn after delivery has become a common practice because of medical, social and economical reasons. The most common cause for readmission during the early neonatal period is hyperbilirubinemia. Such readmissions besides

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involving extra expenses for both family and institution, also exposes a healthy newborn to the hospital environment in addition to causing emotional problems. Universal follow up within 1-2 days of early discharge, umbilical cord bilirubin concentration at birth, routine predischarge bilirubin [8], transcutaneous bilirubin measurement as well as universal clinical assessment of risk factors for developing Jaundice are various strategies to predict significant hyperbilirubinemia.

Early identification of high risk newborn is important to institute early treatment and prevention of bilirubin induced neurological dysfunction. Kernicterus although infrequent has at least 10% mortality and at least 70% [9] long term morbidity. Studies showed that phototherapy had an absolute risk reduction rate of 10% to 17% for prevention of serum bilirubin levels higher than 20mg/dl in healthy infants with jaundice. There is no evidence to suggest that phototherapy for neonatal hyperbilirubinemia has any long term adverse neurodevelopmental effects [9].

So it is desirable to be able to predict the risk of jaundice in order to implement early treatment and thereby minimize the risk of bilirubin dependent brain damage.

Our study was done to find out the incidence of hyperbilirubinemia in babies with blood group either A+ or B+ born to O+ve mothers and also the usefulness of cord bilirubin as a marker for early phototherapy in ABO blood group incompatibility.

Materials and Methods

This was a prospective cohort study which included 50 consecutive term appropriate for gestational age babies with blood group either A or B born to O+ve mothers which served as cases and another 50 consecutive term appropriate for gestational age babies with O+ve blood group born to O+ve mother served as controls. The study was carried out at the delivery room, postnatal ward and NICU of SUT Academy of Medical Sciences, Trivandrum during the 12 month period from January 2015 – December 2015.

Results

The study group consisted of 50 babies as controls with blood group O+ve born to O+ve mothers and another 50 babies as cases with blood group either A+ or B+ born to O+ve mothers. All babies enrolled as cases were AGA [Table 1]. Out of the cases 52% were male babies and 48% were female babies [Table 2].

Of the case group, 32 babies had A blood group and 18 had B blood group [Table 3]. 25 babies in the case group and 22 babies in the control group needed Phototherapy [Table 4].

Inclusion Criteria

1. Study group: 50 consecutive term AGA babies with blood group A or B born to O+ve mother during the period of study served as cases.
2. Control Group_: 50 consecutive term AGA babies with O+ve blood group born to mothers with O+ve blood group served as controls.
3. Apgar score of over 7 at 1' and 10 at 5' of life.
4. Absence of significant illness or major congenital malformation.

Exclusion Criteria

1. Preterm < 37 weeks
2. Rh incompatibility
3. Instrumental delivery (forceps and vacuum)

Institutional ethical committee approval and informed consent from parents were taken and babies which satisfied the inclusion criteria were enrolled for our study. Detailed history using a proforma (prenatal history, maternal complications and medications, type of delivery) and physical examination (birth weight, sex, Apgar score, general examination and gestational age by New Ballard's score) were done .

Cord blood was collected for estimating bilirubin, DCT and blood group for all the babies born to mother having O+ve blood group. The study and control group babies were followed up clinically and 3ml of venous blood samples were taken at 24, 48, 72hrs for estimating total serum bilirubin and conjugate bilirubin. Serum bilirubin was estimated using diazo method [10]. Guidelines by American Academy Of Pediatrics [11,12] were followed for deciding treatment.

Statistical analysis Control and case groups were compared for different parameters using Chi Square test. Receiver Operated Characteristic (ROC) curve was drawn for cord bilirubin to elucidate a cut off value for which the sensitivity and specificity was presented in its percentage along with its confidence interval (CI at 95%).

Table 1: Distribution of babies based on Birth weight.

Birth Weight	Group		Total
	Control	Cases	
2.5 - 4.0	49 98.00%	50 100.00%	99 99.00%
> 4.0 Kg	1 2.00%		1 1.00%
Total	50	50	100

Chi Square: 1.010; P > 0.05

Table 2: Distribution based on sex.

Gender of Baby	Group		Total
	Control	Cases	
Male	34 68.00%	26 52.00%	60 60.00%
Female	16 32.00%	24 48.00%	40 40.00%
Total	50	50	100

Chi Square: 2.667; P > 0.05

Table-3: Distribution of cases according to blood group.

Blood Group of Baby	Group		Total
	Control	Cases	
O	50 100.00%		50 50.00%
A		32 64.00%	32 32.00%
B		18 36.00%	18 18.00%
Total	50	50	100

Chi Square: 100.000; P < 0.001

Table 4: showing no: of babies in case and control group who needed phototherapy.

Treatment	Group		Total
	Control	Cases	
Nil	28 56.00%	25 50.00%	53 53.00%
Yes	22 44.00%	25 50.00%	47 47.00%
Total	50	50	100

Chi Square: 0.361; P > 0.05

Regarding the initiation of phototherapy fig.1 shows 16% of babies in the case group needed phototherapy within 24 hrs, 64% in 24 - 48 hrs and 20% needed phototherapy after 48 hours.

In the control group, majority of the babies (82%) received phototherapy after 48 hrs.

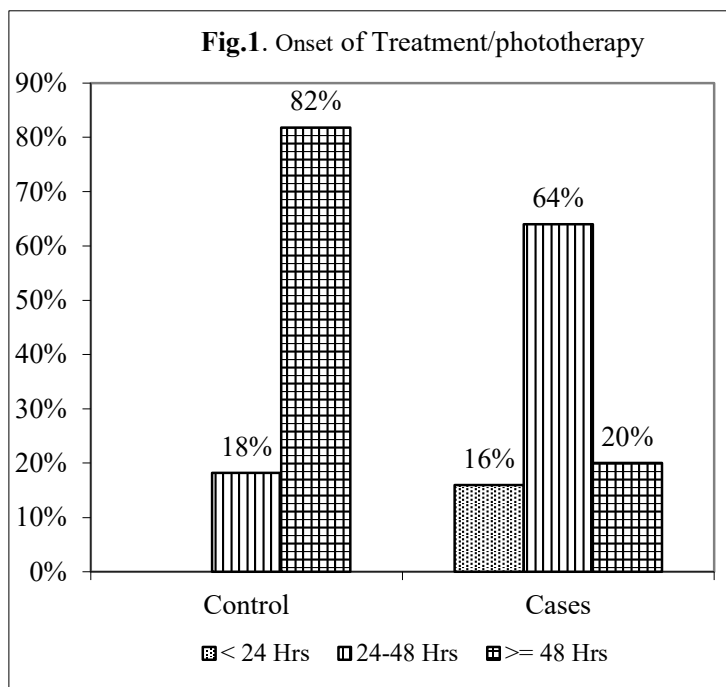


Fig. 2 Shows 88 % of babies in the case group needed phototherapy for more than 24 hours and 8% needed phototherapy for more than 72 hours. None of the babies in the control group required treatment for more than 72 hours.

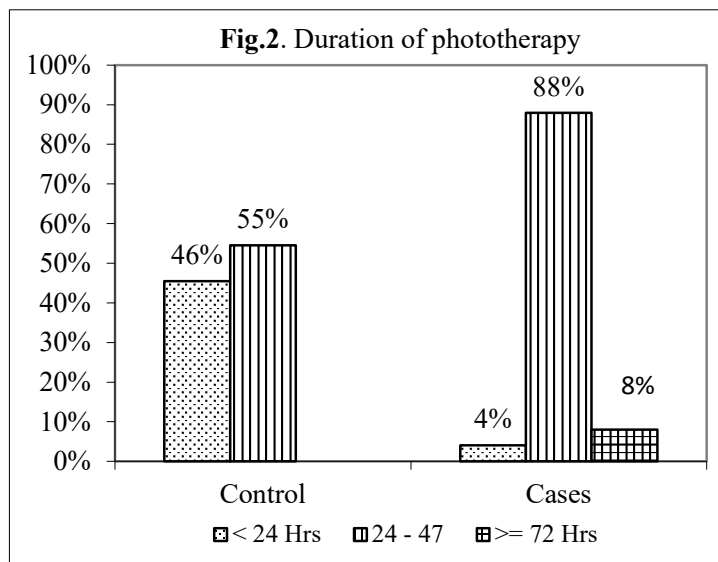
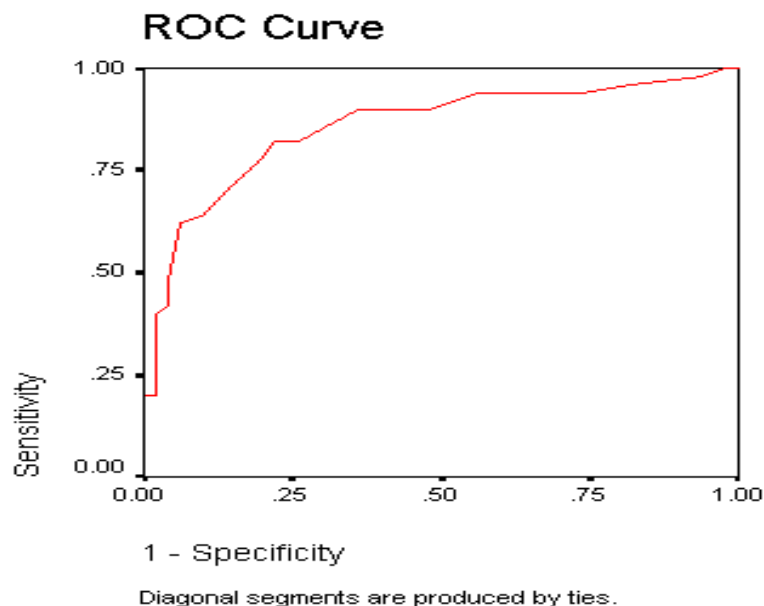


Table 5: Cut off points for total cord bilirubin for Predicting phototherapy.

Cord Bilirubin Positive if	Sensitivity (%)	Specificity (%)	95% CI
2.05	78	80	
2.15	70	86	
2.25	64	90	78.1 - 93.3
2.35	62	94	

The positive likelihood ratio is computed for each cut off point as sensitivity / 1-Specificity. A high positive likelihood ratio is more important for a diagnostic test than for a screening test. Receiver operating characteristic (ROC) curve in fig:3 shows that area under the curve was 0.857 of total area; $P < 0.001$ indicating the usefulness of test in predicting the need for phototherapy. Thus a cord bilirubin level above 2.05 can predict the need for treatment and is statistically significant.

Fig: 3



Discussion

ABO hemolytic disease is the most common blood group incompatible hemolytic process of the newborn period and is the major cause of neonatal jaundice. To rely on clinical observation [13] to notice the jaundiced infants may not be reliable in infants whose skin pigmentation makes the diagnosis of jaundice difficult. So measuring serum bilirubin at different hours of life may be a reasonable compromise. In this study we investigated the incidence of early hyperbilirubinemia and need for phototherapy in babies born to O+ve mothers and relation between cord bilirubin level and development of hyperbilirubinemia. Our study population had 50 babies with blood group either A or B as cases and 50 O+ve babies as controls born to O+ve mother. The babies enrolled in the case group have equal number of males and females and it was noted that incidence of hyperbilirubinemia is almost the same in both sexes. This shows that neonatal hyperbilirubinemia is independent of the sex of the neonate. This is in correlation with Amar Taksande et al [14,15] study on 200 neonates who found no correlation between the sex of the neonate and neonatal hyperbilirubinemia. Among the 50 babies in the case

group 32 had A+ve blood group and 18 had B+ve blood group.

The incidence of neonatal hyperbilirubinemia was almost the same in the case and control group in our study. This did not agree with the study by Kalakheti et al [1] which showed 2.6 times higher chance of hyperbilirubinemia in babies with ABO incompatibility. Eventhough in our study the incidence of hyperbilirubinemia was almost equal in cases and controls, none of the control group babies required phototherapy in the first 24 hours and majority needed only few hours of phototherapy when compared to cases. According to Wood et al [16] few other factors like inadequate breastfeeds, previous sibling with jaundice, oxytocin induction can also affect neonatal jaundice. These factors may have contributed to the jaundice in these babies.

In our study babies in the case group required early and prolonged phototherapy compared to controls and this is in accordance with the study done by Murray et al [4] which showed that babies with ABO incompatibility

needed early phototherapy. Bhutani et al [11,12] recommends phototherapy to prevent severe neonatal hyperbilirubinemia.

In our study, by ROC analysis the cut off point for total cord bilirubin is 2.05. A critical cut off level of cord bilirubin was predicted in 85% of newborn. Amar et al [15] found that cord bilirubin >2mg/dl had the highest sensitivity and this critical bilirubin level had a very high negative predictive value. Suresh and Clark [17] found the cord bilirubin could predict the development of jaundice in healthy newborns. Their study showed that bilirubin critical level of >2mg/dl had positive predictive value for detection of developing significant hyperbilirubinemia. The study by Zeiuton et al [2] also showed cord bilirubin as a strong predictor of phototherapy.

Conclusion

ABO hemolytic disease is one of the important cause of early neonatal hyperbilirubinemia requiring treatment. In our study the cases needed early and prolonged treatment compared to controls. A cord bilirubin level above 2.05 can predict the need for treatment.

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