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EARLY PREDICTORS OF PATHOLOGICAL JAUNDICE DUE TO ABO HEMOLYTIC DISEASE

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ABSTRACT

ABO hemolytic disease is the most common blood group incompatible hemolytic processes of the newborn period and is the major cause of neonatal jaundice attributed to maternal infant blood incompatibility. This was a prospective cohort study which included 50 consecutive term appropriate for gestational age babies with blood group either A, B or AB, born to O +ve mothers as the study group and another 25 consecutive term appropriate for gestational age babies with O+ve blood group born to mothers with O +ve blood group served as controls. Cord blood was used for estimation of bilirubun levels. Mean cord bilirubin was increased in infants with group A and group B born to group O mothers. Significant jaundice was more often seen when mother-infant pair had O and A combinations respectively. When significant jaundice was going to develop serum bilirubin at 12 hours only was quite high and it kept on increasing and all the cases in the study group had developed significant jaundice by 24 hours, though we estimated serum bilirubin level upto 48 hours.

KEYWORDS : **cord bilirubin; ABO incompatibility; hyperbilirubinemia.**

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INTRODUCTION

ABO hemolytic disease is the most common blood group incompatible hemolytic processes of the newborn period and is the major cause of neonatal jaundice attributed to maternal and infant blood incompatibility.[1] Foeto maternal ABO incompatibility exist in about of 25% pregnancies, but hemolytic disease develops in only 1:10 of such offsprings. [2] ABO hemolytic disease can develop in any pregnancy including the first, but it is restricted to group A and group B infants born to group O mothers.[3] These babies are at potential risk of severe hyperbilirubinemia, when treatment is required, phototherapy has been shown to be beneficial in reducing the need for exchange transfusion.[4] ABO hemolytic disease results from the action of maternal anti A or anti B antibodies on fetal erythrocytes of the corresponding blood group. Hemolysis associated with ABO incompatibility is similar to Rh hemolytic disease in that maternal anti A or anti B antibodies enter the fetal circulation and react with A or B antigens on the erythrocyte surface. In type A and B individuals, naturally occurring anti B and anti A isoantibodies largely are IgM molecules that does not cross placenta. In contrast, the allo-antibodies present in type O individuals are predominantly IgG molecules. For this reason ABO incompatibility is largely restricted to type O mothers with type A or B fetus. The presence of IgG anti A or anti B antibodies in type O mothers also explains why hemolysis caused by ABO incompatibility frequently occurs during first pregnancy without prior sensitization.[5]

Jaundice is the visible manifestation of skin and sclera of elevated serum concentration of bilirubin. Neonatal jaundice may not appear until serum bilirubin exceeds 5 to 7 mg/dl. Any serum total bilirubin exceeding 17 mg/dl is considered pathologic and warrants investigations for a cause and possible therapeutic intervention.[6] Neonatal hyperbilirubinemia is a cause of concern for the parents and pediatricians as well. It occurs in 5-10% of healthy term infants.[7] Neonatal hyperbilirubinemia is the most common reason of readmission after early hospital discharge. Concerns regarding jaundice have increased after reports of bilirubin induced brain damage occurring in healthy term infants even without hemolysis.[8,9] Early discharge of healthy term newborns after delivery has become a common practice, because of medical and social reasons and economic constrains. Thus the recognition, follow up and early treatment of jaundice has become more difficult as a result of early discharge from the hospital. Severe jaundice and even kernicterus can occur in some full term healthy newborns discharged early with no apparent early findings of hemolysis.[10]

When the newborn stays at the hospital for a 72 hour post delivery period, it is possible to observe the peaking of the physiological jaundice, thus allowing medical intervention if necessary. However in cases of early discharge from the hospital, the newborn may be subject to readmission for phototherapy treatment, because of high levels of unconjugated bilirubin. Such readmission, besides involving extra expenses for both the family and the institution and also exposing a probably healthy newborn to the hospital environment.[11] The American Academy of Pediatrics recommends that newborns discharged within 48 hours should have a follow up visit after 2-3 days for any significant jaundice and other problems.[12] This recommendation is not appropriate for our country due to limited follow up facilities in the community. Therefore, it is difficult to predict which infants are at increased risk for significant and relatively late hyperbilirubinemia. The present study was conducted to find out the critical value of serum bilirubin in the cord blood in predicting the subsequent development of hyperbilirubinemia in healthy newborn.

MATERIALS AND METHODS

This was a prospective cohort study carried out at department of Biochemistry in collaboration with Neonatal unit of department of Pediatrics and department of Obstretrics

and Gynaecology between Sept 2009 to Sept 2010.

Participants

50 consecutive term appropriate for gestational age babies with blood group either A, B or AB, born to O +ve mothers during the period formed the study group. Another 25 consecutive term appropriate for gestational age babies with O+ve blood group born to mothers with O +ve blood group served as controls. Babies with Rh incompatibility, respiratory distress syndrome, birth asphyxia, low birth weight and those born by instrumentation or born to diabetic mother were excluded from the study. A prospective cohort study model was adopted in which the group of newborns with the common characteristics previously mentioned was followed up clinically and by laboratory investigation during the period of their hospital stay. The inclusion of the newborns in the study was done after receiving written informed consent from their parents. The study was approved by Research Ethics Committee of J.J.M. Medical College, Davangere, Karnataka. 5-6ml of blood was collected from umbilical cord during delivery. It was immediately sent for estimation of conjugated, unconjugated and total serum bilirubin levels. The newborns were followed until discharge and unconjugated bilirubin that required phototherapy was compared with cord bilirubin assay.

Statistical Analysis

Descriptive data are presented as mean ± standard deviation. Student's t test was used for comparing the mean of the two groups. Relationship between measurements was assessed by Pearson's correlation co-efficient. For all the tests, a p value of 0.05 or less was considered for statistical significance.

RESULTS

In the present study, 50 consecutive babies born to O +ve mother and whose blood group was other than O +ve were studied.

Table 1
Mean cord bilirubin in study and control group

	Mean ± SD (cord bilirubin)
Study group n=50, Significant jaundice n=7	4.11 ± 0.28
Study group n=50, Insignificant jaundice n=43	2.05 ± 1.01
Control group n=25, Insignificant jaundice	1.66 ± 0.74

Table 1: In the study group (n=50), neonates who developed significant jaundice were 7, their mean cord bilirubin was 4.11 ± 0.28. Neonates who developed insignificant jaundice were 43, their mean cord bilirubin was 2.05 ± 1.01. In the control group (n=25), none of the neonates developed significant jaundice, their mean cord bilirubin was 1.66 ± 0.74

Table2
Correlation of cord bilirubin levels and significant jaundice.

Cord bilirubin	No of cases	Significant jaundice
≥ 4 mg/dl	6	6 (100%)
< 4 mg/dl	44	1 (2.2%)

Table 2: 6 of 50 cases had cord bilirubin > 4 mg/dl and all of them developed significant jaundice requiring phototherapy. In the remaining 44 cases, where cord bilirubin was <4 mg/dl only one baby developed significant jaundice and required phototherapy. In the control group, 25 babies with O +ve blood group born to O +ve mothes, none developed jaundice.

Table 3
Table showing frequency of blood group in study group And development of significant jaundice

Babies blood group	No of cases	Significant jaundice
A +ve	25	5
B +ve	23	2
AB +ve	2	Nil

Table 3 reveals that significant jaundice was more often seen when mother-infant pair had O and A combinations respectively.

Table 4
Mean serum bilirubin at different time interval in both study and control group

	Mean ± SD serum bilirubin		
	12 hours	24 hours	48 hours
Study group, Significant jaundice	9.71±0.76	15.37±0.60	17.11±1.45
Study group, Insignificant jaundice	2.26±1.58	4.42±2.08	6.65±2.96
Control group, Insignificant jaundice	2.09±1.55	3.90±2.22	4.81±2.29

Table 4: When significant jaundice was going to develop serum bilirubin at 12 hours only was quite high and it kept on increasing and all the cases in the study group had developed significant jaundice by 24 hours, though we estimated serum bilirubin level upto 48 hours.

DISCUSSION

ABO incompatibility is the most common materno-fetal blood group incompatibility which is usually a problem of the neonate rather than the fetus. Anaemia in the neonatal period is usually slight in degree. The main clinical problem is jaundice in the first 24 hours of life (i.e icterus praecox). Approximately 50% of the cases occur in first born infant. There is no predictable pattern of recurrence in subsequent infants. Hydrops fetalis in association with ABO incompatibility is extremely rare, and has been reported in two cases.[13] The diagnosis of ABO hemolytic disease depends on the clinical, serological and biochemical findings in the newborn. Micro-spherocytosis is the most prominent feature of ABO hemolytic disease. Coombs test may be negative or only weakly positive. A positive coombs test in ABO incompatible infants does not necessarily indicate disease. It has been observed that one third of A or B blood group babies born to O group mother have a positive direct Coombs test. In recent years, lot of efforts have gone in to predict babies likely to develop neonatal hyperbilirubinemia. Reliable predictors can reduce hospital stay for normal babies resulting in discharge and identifying at risk or high risk neonates likely to develop pathological jaundice. These neonates would need close monitoring so that potential risk for bilirubin induced brain damage can be reduced amongst term healthy newborn discharged early from hospital. Several factors are recognized as early predictors of significant jaundice in ABO incompatibility. These factors include: presence of Ig G anti A or anti B hemolysis in maternal serum in high titre, Coomb's test, Serum bilirubin, Cord bilirubin. The present study is an attempt to find out the role of cord bilirubin in predicting significant jaundice in ABO incompatibility.

In the present study we observed 6 neonates with cord bilirubin >4mg/dl developed significant jaundice (serum bilirubin >15mg/dl at 24-48 hours of age) where as only 1 neonate with cord bilirubin <4mg/dl developed jaundice. In a previous study by Robinson et al [14], it was observed that cord bilirubin levels above 3mg/dl were suggestive of significant jaundice. In another study by Simpson et al [15], it was noted cord bilirubin >2.5mg/dl was associated with development of significant jaundice. Thus it can be seen that different authors have used different cutoff value for predicting significant jaundice. This variability is mainly because of technical error in estimating bilirubin levels. Bilirubin estimation varies from laboratory to laboratory. Hence the cutoff value taken in different studies are different. Therefore it is important that local laboratory should define what is the cutoff value that should be used as a predictor for development of significant jaundice. In the present study significant jaundice was more often seen when mother-infant pair had O and A combination. In a previous study by Kumari K C Usha et al[16], similar observation was made in their study. In White population. A group neonates are more affected and in black, the B blood group.[17] Thus it can be seen that mother infant pair with O-A combination had a higher incidence of significant jaundice and hence need more careful evaluation.

Further we analysed the relationship between serum bilirubin and development of jaundice. We found that serum bilirubin levels

measured at 12 and 24 hours of life, also correlated with subsequent hyperbilirubinemia. The results of this study are in accordance with that of Awasthi et al [18] which concluded that serum bilirubin levels of the first postnatal day is a good predictor of its own peak achieved later in first week. The results of the present study together with previously published data clearly indicate that serum bilirubin at 12 hour is an equally important predictor for pathological jaundice in ABO incompatibility. Those babies whose bilirubin at 12 hours is high need very close observation and appropriate treatment. As speculation, one may consider the umbilical cord blood to be a kind of 'file' for the newborn. As such, it could be collected, stored and used for further analysis of unconjugated bilirubin levels, should a slightly or moderately jaundiced child be considered for early discharge from hospital. Such a proposal may therefore constitute an additional predictive method that is available for evaluating the occurrence of severe hyperbilirubinemia by the third day of life. In association with other resources that were already available [19] this proposal may help in assuring safer early discharge for these newborns.

CONCLUSION

The highlight of our study is that, the cord bilirubin more than 4mg/dl and higher serum bilirubin level at 12 hours of life are good predictors of pathological jaundice in babies with A and B blood group born to O group mothers. The babies with A group are at increased risk of developing jaundice. Hence the policy of early discharge of babies from hospital should be based on prior knowledge of value of cord bilirubin and serum bilirubin at 12 hours to avoid serious consequences of hyperbilirubinemia at a later date at home.

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