CORD BILIRUBIN AS A PREDICTOR OF SIGNIFICANT HYPERBILIRUBINEMIA IN ABO INCOMPATABILITY

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Abstract

Background and Objectives: ABO hemolytic disease results from the action of maternal anti A or anti B antibodies on fetal erythrocyte of corresponding blood group. Hyperbilirubinemia caused by hemolytic disease of ABO incompatibility can cause bilirubin encephalopathy and severe sequelae. The current study was undertaken to assess the estimation of cord bilirubin value and its correlation with significant hyperbilirubinemia to know if cord bilirubin can be used as a predictor to identify newborns at risk for developing hyperbilirubinemia.

Methods: Babies born in the hospital of O group mothers were included in the study (n=129). Blood samples were collected from umbilical cord incised at the time of birth for serum bilirubin, blood grouping and Rh typing. The neonates were followed up twice daily for clinical jaundice.

Results: Out of the 129 babies, 42% developed physiological hyperbilirubinemia and 13% developed pathological hyperbilirubinemia. The incidence of pathological hyperbilirubinemia for birth weight 2.5 – 3 kg was 70.6%, 3.1 – 3.5 kg was 23.5%, 3.6 – 4 kg was 5.9%. On conducting ANOVA, the above results gave significant F value of 74.84 (P <0.0001). Cut off value of 2.65 mg/dL had 73% specificity and 94.4% sensitivity in predicting pathological hyperbilirubinemia.

Conclusion: Cord bilirubin value is useful for predicting pathological hyperbilirubinemia in babies at risk for ABO incompatibility. Higher cord bilirubin values have good correlation with higher serum bilirubin values. Babies with a birth weight of <3 kg are at a higher risk of developing pathological hyperbilirubinemia.

Keywords: neonates; cord blood bilirubin; hyperbilirubinemia; predictor

Introduction

Hemolytic disease of newborn is one of the causes of hyperbilirubinemia. Since the introduction of Rh immunoglobulin as a treatment for Rh isoimmune hemolytic disease of newborn, ABO hemolytic disease has become the common blood group incompatible hemolytic process of newborn period. Feto-maternal ABO incompatibility exists in about 25% pregnancy, but hemolytic disease develops only in 1 per 10 of such offspring (3). 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.

ABO hemolytic disease results from the action of maternal anti A or anti B antibodies on fetal erythrocyte of corresponding blood group. Hemolysis associated with ABO incompatibility is similar to Rh hemolytic disease in that maternal anti A or anti B antibodies enter fetal circulation and react with A or B antigen on erythrocyte surface. In type A and B individuals, naturally occurring anti A and anti B isoantibodies, largely Ig M molecules, do not cross the placenta. In contrast, the alloantibodies present in type O individuals are predominantly Ig G molecules that cross the placenta. For this reason, ABO incompatibility is largely restricted to type O mothers with type A or type B fetus.
Thus, hyperbilirubinemia caused by hemolytic disease of ABO incompatibility can cause bilirubin encephalopathy and severe sequelae. So it is imperative that pathological hyperbilirubinemia is picked up early and vigorous treatment is started. Studies regarding early identification of newborns at risk of hyperbilirubinemia at birth are inadequate and more studies are needed in forth coming years. There are few ongoing studies on identifying newborns at risk by assessing their cord bilirubin, cord hemoglobin and cord blood reticulocyte count. These studies are yet to give any statistically proven guidelines. The current study was undertaken to assess the estimation of cord bilirubin value and its correlation with significant hyperbilirubinemia to know if cord bilirubin can be used as a predictor to identify newborns at risk for developing hyperbilirubinemia.

Materials and Methods

This prospective observational study was carried out from August 2010 to August 2011 in a tertiary care university hospital in Chennai. Babies born in the hospital of O group mothers were included in the study. Informed consent was obtained from the parents and the study was approved by Institutional Ethics Committee. In our study, pathological hyperbilirubinemia was defined as serum total bilirubin level > 15 mg/dl on 4th day of life or any total serum bilirubin more than 95th percentile for the age in hours.

Inclusion criteria:
- Newborn of gestational age ≥37 weeks
- Newborn of birth weight between 2.5 to 4 kg
- Apgar score > 7 at birth
- Babies born with A or B or AB blood group born to O positive mothers

Exclusion criteria:
- Neonatal problems causing hyperbilirubinemia such as prematurity, birth asphyxia, birth trauma such as cephalhemotoma, sepsis, hypothyroidism and congenital malformations
- Significant disease in mother which can cause hyperbilirubinemia in newborn like gestational diabetes mellitus

After initial stabilization, blood samples were collected from a 15 to 20 cm length of umbilical cord incised while severing it at the time of birth for serum bilirubin, blood grouping and Rh typing. Medical records of mother and baby were noted. Neonatal complications such as delayed passage of meconium, poor/delayed feeding etc. were noted. Weight, sex and Apgar score of babies were also noted. A detailed general examination was done to rule out congenital anomalies and the presence of concealed hemorrhage like cephalhematoma. Of the 129 babies screened, 111 were at risk of ABO incompatibility (A, B or AB blood groups) and the remaining was O group. The neonates were followed up twice daily for clinical jaundice. If they developed clinical jaundice, serum bilirubin was estimated and treatment was given. Bilirubin was estimated by Diaz method. Data was collected in a detailed predesigned proforma. Data was analyzed by SPSS 15.0.

Results

The total number of deliveries in our hospital during the study period was 432. There were 129 neonates who satisfied the inclusion/exclusion criteria. Out of the 129 babies, 42% developed physiological hyperbilirubinemia and 13% developed pathological hyperbilirubinemia. The percentage of babies with physiological or pathological hyperbilirubinemia was not significantly different between mothers who underwent different modes of delivery (normal, instrumental and LSCS). The incidence of pathological hyperbilirubinemia was more among male children, but was not statistically different (8.52% vs. 4.65%, P=0.182).
The incidence of pathological hyperbilirubinemia for birth weight 2.5 – 3 kg was 70.6%, 3.1 – 3.5 kg was 23.5%, 3.6 – 4 kg was 5.9%. On conducting ANOVA, the above results gave significant F value of 74.84 (P <0.0001).

### Table 1: Blood group distribution of babies in different conditions

<table>
<thead>
<tr>
<th>Blood group</th>
<th>No jaundice hyperbilirubinemia</th>
<th>Physiological hyperbilirubinemia</th>
<th>Pathological hyperbilirubinemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>A+</td>
<td>13</td>
<td>26</td>
<td>9</td>
</tr>
<tr>
<td>A-</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B+</td>
<td>20</td>
<td>21</td>
<td>8</td>
</tr>
<tr>
<td>B-</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AB</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>O</td>
<td>16</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Incidence of physiological hyperbilirubinemia was higher in A group when compared to B group (P=0.006). No significant difference in incidence of pathological hyperbilirubinemia was noticed between A and B groups (P=0.523). None of the babies in the O group category developed pathological hyperbilirubinemia. On constructing Receiver Operation Curve, it was found that AUC was 0.969, which indicates that a randomly selected child with hyperbilirubinemia had score higher than a randomly selected child without hyperbilirubinemia 96% of the time. Cut off value of 2.65 mg/dL had 73% specificity and 94.4% sensitivity in predicting pathological hyperbilirubinemia. All 17 babies with hyperbilirubinemia recovered with phototherapy without complications.

### Discussion

Higher cord bilirubin levels were associated with a higher risk of the babies to develop pathological hyperbilirubinemia. In our study, we tried to determine the correlation between cord bilirubin with the development of pathological hyperbilirubinemia. Final outcome measurement is pathological hyperbilirubinemia which is defined in our study as a 4th day bilirubin value above 15 mg/dL or a serum bilirubin level of more than 95th percentile for age in hours. Incidence of pathological hyperbilirubinemia in various studies range from 3.7% to 32.95% (61.62). Earlier studies have shown that male gender is at risk factor for hyperbilirubinemia (64). However our study has showed only a positive association which is not statistically significant. Incidence of pathological hyperbilirubinemia was found to be higher among low birth weight neonates. Peak bilirubin is generally attained between 3rd and 4th day after birth, our study showed the same results (1). The cord bilirubin values which can predict hyperbilirubinemia range from 1.7 to 5 mg/dL in different studies (66,69). Our study also observed a range similar to the above studies – 1.6 – 4.2 mg/dL. The mean bilirubin values of babies with pathological, physiological and no hyperbilirubinemia were 3.7, 2.4 and 2.1 mg/dL respectively.

Earlier studies have shown a good correlation between cord blood bilirubin and pathological hyperbilirubinemia (62,64). In our study also, bilirubin had excellent correlation with the 4th day bilirubin levels, Pearson’s correlation r=0.71 (P value < 0.001). So cord bilirubin can effectively predict the risk of pathological hyperbilirubinemia. According to our study, cord bilirubin value of ≥ 2.65 mg/dl can be used as a cut-off for predicting pathological hyperbilirubinemia with a specificity of 73%, sensitivity of 94.4%, chi square value of 30.39 (P < 0.0001).
Conclusions

Cord bilirubin value is useful for predicting pathological hyperbilirubinemia in babies at risk for ABO incompatibility. Higher cord bilirubin values have good correlation with higher serum bilirubin values. Babies with a birth weight of <3 kg are at a higher risk of developing pathological hyperbilirubinemia. Neonates who received appropriate interventions recovered without any morbidity or mortality. However, larger population studies are required to achieve credible guidelines.

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References


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