Short Report

CORD SERUM BILIRUBIN AND ALBUMIN IN NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT

The cause of neonatal hyperbilirubinemia can be ABO/ Rh incompatibility or physiological jaundice. Attempts have been taken to protect neonates from developing kernicterus by estimating cord blood bilirubin. There is lack of data about Cord serum albumin levels in predicting hyperbilirubinemia. At our hospital, we investigated cord blood for CSTB, CSUB and CSA levels at birth and incidence of hyperbilirubinemia in first seven days of neonate’s life. Frequency of hyperbilirubinemia at our center is 33.88%, male genders are found at high risk. Cord serum unconjugated bilirubin level ≥2.0 mg/dl and total cord serum bilirubin level ≥2.5mg/dl appeared as high risk indicator towards predicting neonatal hyperbilirubinemia. Cord serum albumin level < 2.8 gm/dl was additional risk indicator in predicting neonatal hyperbilirubinemia.

KEY WORDS: Neonatal jaundice, Bilirubin, Albumin, Hyperbilirubinemia

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common problems in term and preterm babies. Though babies with ABO / Rh incompatibility are at high risk factor for developing subsequent hyperbilirubinemia, many times it is physiological. Physiological hyperbilirubinemia results from immature liver cell having very low uridine diphospho glucuronosyl transferase activity compared to mature hepatocyte, low concentration of Bilirubin binding ligand Albumin, and higher volume of short life erythrocytes in the circulation. Physiological jaundice arises as a "normal" response to the baby's limited ability to excrete bilirubin in the first days of life. Every newborn develops an unconjugated hyperbilirubinemia due to increased level of unconjugated Bilirubin above 1.0mg/dl. (1) Physiological Jaundice takes place in approximately 60% of newborns; though it is unimportant in most, a few (5-6%) will become deeply jaundiced requiring investigation and treatment. If inadequately managed, it may result in death survival with severe brain damage. (2) Development of hyperbilirubinemia in neonates is fretful for the parents and a concern for the pediatrician too.

Early discharge of healthy term newborns after normal vaginal delivery has become a common practice, because of medical reasons like prevention of nosocomial infections, social reasons like early naming ceremony and also due to economical constrains, but many have to be readmitted for the treatment of hyperbilirubinemia. (3) Requirement of phototherapy based on cord blood Bilirubin level has been predicted (4). So is it possible to predict hyperbilirubinemia on day one? There are a few references which predict postnatal hyperbilirubinemia by estimating cord blood bilirubin levels but vary in opinions. Robinson et al (5) reported cord bilirubin levels above 3mg/dl were suggestive of significant jaundice. Simpson et al(6) believed cord bilirubin greater than 2.5mg/dl was associated with development of significant jaundice, whereas Rosenfeld(7) in their study states cord blood bilirubin level more than 2.0mg/dl have more than 95% chances of developing hyperbilirubinemia. Thus
different authors have used different cutoff values for predicting significant jaundice. Early detection of risk factors is the first step towards prevention of hyperbilirubinemia and a step ahead in protecting newborns from complication at later age. Usually albumin binds with unconjugated Bilirubin and protects against Kernicterus (8) Blood albumin in neonates is mostly derived from maternal circulation till baby’s liver starts synthesis. There is paucity of reports on cord blood albumin level as predictor of hyperbilirubinemia.

We investigated cord serum total Bilirubin (CSTB), cord serum unconjugated Bilirubin (CSUB) levels at birth and incidence of hyperbilirubinemia in first seven days of their life. Cord serum albumin (CSA) levels were correlated with CSTB and CSUB to recognize the risk factor for hyperbilirubinemia in neonates.

METHOD
Present study was a follow up study, conducted on umbilical cord blood of babies born in our hospital during the period of June 2010 to May 2012. Sequentially born term babies (mean gestational age 38.85 weeks) of both genders were included in the study. A total of 605 healthy term babies were followed prospectively with daily clinical examination for the first 7 days of life.

Preterm babies and babies with any complications arising during hospital stay were excluded. After obtaining informed consent from parent, 3 to 5 ml of cord blood was collected immediately after birth in the labor room. Blood was analyzed for blood group and Hemoglobin percentage. Serum obtained was used for estimation of Total, conjugated and unconjugated bilirubin and Albumin levels.

The neonates were followed up clinically for 7 postnatal days in neonatal ward to detect any development of jaundice. Blood group was detected by Blood group typing antisera from Ortho diagnostics. Hemoglobin estimation was performed by spectrophotometric method using Drabkin’s reagent from Nice Company. CST Bilirubin, CS conjugated and CSU Bilirubin, CSA estimation was performed on Hetachi902 Chemistry analyzer – Roche diagnostics, by commercially available kit.

Correlation between CSA and CSTB, CSA and CSUB levels and CSTB and day of development of hyperbilirubinemia were determined by linear regression analysis. Value of P<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Table 1: Distribution for 605 newborn’s hyperbilirubinemia pertaining to gender

<table>
<thead>
<tr>
<th></th>
<th>Female Babies</th>
<th>Male Babies</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exhibited hyperbilirubinemia</td>
<td>90</td>
<td>115</td>
<td>205</td>
</tr>
<tr>
<td>Did not exhibit hyperbilirubinemia</td>
<td>210</td>
<td>190</td>
<td>400</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>305</td>
<td>605</td>
</tr>
</tbody>
</table>

Table 1 shows, 605 babies (mean gestational age 38.85 weeks) included in study population; among them 305 (50.41%) were male and 300 (49.59%) were female babies. Out of total 605 babies included in the study population 205(33.88%) developed hyperbilirubinemia; whereas, 400 (60.11%) did not develop hyperbilirubinemia in first seven days of their life.

Splitting gender wise, amongst 300 female babies, 90 (30%) exhibited hyperbilirubinemia; whereas, 210 (70%) remained normal for seven days of observation. On the other hand, amongst 305 male babies 115 (37.70%) developed hyperbilirubinemia and 190 (62.29%) did not display jaundice. Overall 33.88% of babies from the study population developed hyperbilirubinemia within first seven days of life. Gender wise male babies have shown higher incidence of developing hyperbilirubinemia than female babies, this concurs once again male gender is at high risk for Hyperbilirubinemia (9).

Table 2: Bilirubin and Albumin levels in cord serum

<table>
<thead>
<tr>
<th></th>
<th>Hyperbilirubinemia</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=205)</td>
<td>No (n=400)</td>
</tr>
<tr>
<td>CST Bilirubin mg/dl Interval</td>
<td>3.83±1.72</td>
<td>2.11±0.58</td>
</tr>
<tr>
<td></td>
<td>2.23 – 7.10</td>
<td>0.82 – 3.29</td>
</tr>
<tr>
<td>CSU Bilirubin mg/dl Interval</td>
<td>3.76±1.28</td>
<td>1.91±0.59</td>
</tr>
<tr>
<td></td>
<td>1.27 – 5.91</td>
<td>0.64 – 2.89</td>
</tr>
<tr>
<td>CSC Bilirubin mg/dl Interval</td>
<td>0.27 ±0.14</td>
<td>0.30 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>0.18 – 0.28</td>
<td>0.141 – 0.141</td>
</tr>
<tr>
<td>CS Albumin gm/dl Interval</td>
<td>2.15 ± 0.81</td>
<td>3.64 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>1.8 – 2.7</td>
<td>3.1 – 3.9</td>
</tr>
<tr>
<td>CS Albumin/</td>
<td>3.13 ± 1.09</td>
<td>2.03 ± 0.14</td>
</tr>
</tbody>
</table>
Trivedi et al

| Table 2 | Shows the levels of CS bilirubin and CS Albumin levels observed in subjects under study. The cutoff point taken for unconjugated bilirubin in cord blood at our hospital was 2.0 mg/dl. Whenever

| Table 3 | Indicates the percentage distribution for development of jaundice during seven days of postnatal observations in the study group. Healthy term newborn have revealed typical pattern of physiological jaundice (10). Among 205 babies who exhibited hyperbilirubinemia, 41.32% (85) babies developed jaundice on 4th day. 83.80% (172) babies developed jaundice in the range of 3rd to 5th day. Relating their CSUB levels, 71.4% babies had cord serum unconjugated bilirubin level ≥2.0 mg/dl.

| Table 4 | Distribution for 205 newborn’s jaundice relating to day of development

<table>
<thead>
<tr>
<th>Day of Development of HB</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>05</td>
<td>19</td>
<td>49</td>
<td>85</td>
<td>38</td>
<td>7</td>
<td>2</td>
<td>205</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>2.48%</td>
<td>09.26%</td>
<td>24.13%</td>
<td>41.32%</td>
<td>18.35%</td>
<td>3.31%</td>
<td>1.16%</td>
<td>100%</td>
</tr>
</tbody>
</table>

This study shows a significant correlation between Cord serum total bilirubin, unconjugated bilirubin levels and occurrence of neonatal jaundice. When CSTB were correlated with the day of development of jaundice it exhibited significant negative correlation (r= -0.348, P<0.001) indicating level of total bilirubin in cord blood is inversely proportional to the day of development of neonatal jaundice. Similarly, Cord Serum unconjugated and total bilirubin levels have shown positive correlation with Baby’s serum unconjugated and Total Bilirubin levels on 4th day of life. This suggests, cord serum unconjugated bilirubin level ≥2.0 mg/dl and total cord serum bilirubin level ≥2.5mg/dl as high risk indicator towards predicting neonatal hyperbilirubinemia in the first week of life, and our finding parallels with the findings of Sun G et al(11), Bernaldo AJ et al(12).

Though Bilirubin estimation varies from laboratory to laboratory, it is important for local laboratory to use reference level to define cutoff values at one’s own hospital which can predict development of significant jaundice.

Lower normal limit for cord serum albumin in term babies is 2.8gm/dl(13). In the present study we estimated albumin levels from the cord blood after delivery and found statistically significant difference (P<0.05) between mean cord serum albumin levels in babies who did not develop hyperbilirubinemia (3.64 ± 0.30gm/dl) and in the babies who developed hyperbilirubinemia (2.15 ± 0.81 gm/dl). Similar results were reported by S. Sahu et al(14).

Among 205 babies who developed hyperbilirubinemia, 58.53% babies (120) had cord serum albumin level < 2.8gm/dl. 28.78% babies (59) having cord serum albumin level in the range of 2.8 – 3.5gm/dl, also developed hyperbilirubinemia. Whereas 12.68% (26) babies developed hyperbilirubinemia even though cord serum albumin level was more than 3.5gm/dl.

Cord serum albumin level and cord serum conjugated bilirubin shows positive correlation (r=0.2, <0.05) whereas, Cord serum albumin levels correlated with unconjugated bilirubin shows negative correlation (r =- 0.1917). Thus cord serum albumin level appears risk indicator in predicting neonatal hyperbilirubinemia. Source of cord serum albumin is the mother’s circulation, as cord serum albumin levels were estimated on delivery it indirectly suggests the nutritional status of mother during gestational period. Thus higher albumin levels from mothers maintaining good nutritional status resulted in lower incidences of neonatal jaundice.
CONCLUSION
We conclude in short CS bilirubin level is useful in predicting the subsequent jaundice in healthy term infants. The use of CS bilirubin values may help detect infants at low or high risk for hyperbilirubinemia. CS albumin gives additional clue in visualizing future hyperbilirubinemia to protect them from latter age complications.

This study however had a few limitations like, being a single center cohort study it includes subjects admitted to our hospital only. Complete follow up of neonates was possible only with prolonged hospital stay due to neonatal illness or some maternal cause. More than half the newborns that were healthy got discharged early and were dropouts from follow up. Thus we believe a further carefully planned population study which may throw light on predicting neonatal jaundice and help the pediatrician.

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