Cord blood albumin as predictor of neonatal hyperbilirubinemia

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ABSTRACT

Background: Measuring the Cord blood Albumin level and predicting neonatal hyperbilirubinemia.

Methods: Prospective study was performed on 160 healthy term neonates. Relevant maternal history was collected. Cord blood was collected from the healthy term neonates at birth and cord serum albumin measured. Neonate was assessed for jaundice every day using transcutaneous bilirubinometer. Total Serum Bilirubin (TSB) was assessed if the Transcutaneous Bilirubin (TCB) values were found high and treated according to NICU protocol.

Results: Study cohort was grouped as Group A, Group B and Group C based on Cord Serum Albumin (CSA) level ≤3.3 g/dl, 3.3-3.8 g/dl and ≥3.8 g/dl respectively. Statistical analysis was done for correlation of CSA with Neonatal Hyperbilirubinemia (NH). It showed that cord serum albumin level ≤3.8 g/dl is critical, as it was seen in 9.1% of neonates who developed neonatal hyperbilirubinemia (p value 0.032).

Conclusions: There is a correlation between cord serum albumin level and neonatal hyperbilirubinemia. Cord serum albumin level of ≤3.8 g/dl is a risk indicator in predicting the development of neonatal hyperbilirubinemia.

Keywords: Albumin, Cord blood, Neonatal hyperbilirubinemia, Transcutaneous bilirubin

INTRODUCTION

Neonatal jaundice is a common problem. Approximately 85% of all term newborns and most preterm infants develop clinical jaundice. A total serum bilirubin level >15 mg/dl is found in 3% of normal term infants.1 Uridine Diphosphoglucuronyl Transferase (UDPGT) is an important liver enzyme for conjugation and excretion of bilirubin which is detectable at 18-20 weeks of gestation. Adult value of this enzyme activity is demonstrable by 6-14 weeks of postnatal life.2

Neonatal hyperbilirubinemia is most common abnormal physical examination finding during the first week of life.

In term babies, physiological jaundice is seen to appear between 36-72 hours of age and maximum intensity of jaundice is seen between 72-96 hours of life. Serum bilirubin doesn’t exceed 15 mg/dl and jaundice disappears by 10th day of life.3 Albumin is the major binding protein in a neonate. Synthesis of albumin appears at approximately the 7th-8th week in the human fetus. Albumin concentrations are low in a neonate (~2.5 g/dl), reaching adult levels (~3.5 g/dl) after several months. Albumin binds to potentially toxic products like bilirubin. Bilirubin binds to albumin in an equimolar ratio. One gram of albumin binds around 8.5 mg of bilirubin.4 Low production of albumin will lower the transport of bilirubin. Free bilirubin is anticipated when the molar bilirubin- to- albumin (B: A) ratio is >0.8. It is the free bilirubin which can cross the blood brain barrier.

American academy of pediatrics recommends that newborn discharged within 48 hours should have a follow up visit.
after 48-72 hours to check any significant jaundice and other problems. This recommendation is difficult to follow-up in India due to limited follow up facilities in the community. These neonates may develop jaundice which may be overlooked or may have delay in recognition unless the baby is closely followed up.

Concern of a neonatologist regarding earlier discharge are reports of many cases of bilirubin induced cerebral damage identified in healthy term and late preterm infants even without any risk factors. Synthesis of albumin occurs in liver and it binds to bilirubin and helps in its transport. Decreased synthesis of albumin will decrease its binding capacity and transport. Hence, identification of at-risk neonates or neonates with low cord blood albumin levels early will help to avoid the complication and sequelae associated with neonatal jaundice. Objective of the study was measuring the Cord Serum Albumin level (CSA) and predicting neonatal hyperbilirubinemia based on cord serum albumin levels.

**METHODS**

This prospective study was conducted in the department of Pediatrics at Father Muller Medical College Hospital and Research Centre, Mangaluru, India. The study group consisted of 160 selected eligible term neonates delivered at our hospital from 1st January 2019 to 30th April 2019. Ethical clearance was obtained from the research board of hospital. 

**Inclusion criteria**

- Term inborn babies of both genders with a birth weight ≥2500 grams and APGAR ≥7/10 at 1 min.

**Exclusion criteria**

- Preterm babies, Rh and ABO incompatibility and babies discharged within 48 hours of delivery. 

Demographic profile and relevant maternal information were collected from maternal case record. Cord blood of 2 ml was collected using plain vacutainer after the delivery from placental end and sent for analysis. Cord blood albumin was estimated by bromo cresol dye binding method.

According to the cord blood albumin levels, babies were categorized into three groups. Group A comprised of babies with cord albumin level <3.3 gm/dl. Group B with cord albumin level 3.3-3.8 gm/dl and Group C with cord albumin >3.8 gm/dl. All the babies were followed up daily for at least 48 hours and babies were daily assessed for jaundice using Transcutaneous Bilirubinometer (TCB) (Drager JM 103 device).

Total Serum Bilirubin (TSB) estimation was done if the TCB values were found high during the hospital stay and treated as per NICU protocol.

In a study conducted by Mishra S, Chawla D, Agarwal R, Deorari AK, Paul VK, it was observed that Transcutaneous Bilirubin levels (TCB) estimation by TCB had high negative predictive value (99.8%) and acceptable positive predictive value (16.4%) for prediction of hyperbilirubinemia.5

In a study conducted by Mahajan G, Kaushal RK, Sankhyan N, Sharma RL and Nakra M using Bilicheck TM, they found good sensitivity and specificity of the meter to pick up bilirubin >13 mg/dl.6

**RESULTS**

The study comprised of 160 neonates. Eighty-three (83) were male, seventy-seven (77) were female. Authors grouped their subjects according to their cord blood albumin levels (Table 1).

Two babies had cord blood albumin <3.3 gm/dl and one of them developed hyperbilirubinemia requiring phototherapy. Nine babies with cord blood albumin between 3.3-3.8 gm/dl developed hyperbilirubinemia and all were treated with phototherapy whereas only 2 babies with cord blood albumin >3.8 gm/dl developed hyperbilirubinemia and required phototherapy. On cross tabulation and applying chi square test, no significant association was found between hyperbilirubinemia and variables like sex, mode of delivery and birth weight (Table 2). However significant correlation was found between babies with cord blood albumin 3.3-3.8 gm/dl and neonatal hyperbilirubinemia (p value 0.032).

**Table 1: Group based on cord serum albumin level.**

<table>
<thead>
<tr>
<th>Cord serum albumin</th>
<th>Numbers (n=160)</th>
<th>%</th>
<th>N=percentage developed hyperbilirubinemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.3 gm/dl (group A)</td>
<td>2</td>
<td>1.25%</td>
<td>1(50%)</td>
</tr>
<tr>
<td>3.3-3.8 gm/dl (group B)</td>
<td>100</td>
<td>62.5%</td>
<td>9(9%)</td>
</tr>
<tr>
<td>&gt;3.8 gm/dl (group C)</td>
<td>58</td>
<td>36.25%</td>
<td>2(3.4%)</td>
</tr>
</tbody>
</table>

**Table 2: Correlation of clinical variables with neonatal hyperbilirubinemia (NNH).**

<table>
<thead>
<tr>
<th>Variables</th>
<th>NNH No</th>
<th>NNH Yes</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male (77)</td>
<td>72</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Female (83)</td>
<td>77</td>
<td>6</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>LSCS</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>NVD</td>
<td>147</td>
<td>11</td>
</tr>
<tr>
<td>Cord albumin (gm/dl)</td>
<td>&lt;3.3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3.3-3.8</td>
<td>91</td>
<td>9(9%)</td>
</tr>
<tr>
<td></td>
<td>&gt;3.8</td>
<td>56</td>
<td>2(3.4%)</td>
</tr>
</tbody>
</table>
DISCUSSION

This prospective study was done with the objective to find out the critical value of cord blood albumin in detecting the subsequent development of significant neonatal jaundice. The basic hypothesis behind is that lower the albumin levels in cord blood; more is the chance for the baby to develop neonatal jaundice.

About 50% of term and 80% of preterm babies develop jaundice which usually appears 2 to 4 days after birth and resolves spontaneously after 1 to 2 weeks. Incidence of hyperbilirubinemia in this study was 6.87%. The study cohort consisted of 160 term babies out of which 83 were male and 77 were female babies.

In this study no significant relationship was found between cord blood albumin levels and variables like sex, mode of delivery, gestational age and birth weight. In a study done by Hardik C, Alpa P, Jayendra G no correlation was observed between the gender, gestational age, birth weight, mode of delivery of the neonate and the neonatal hyperbilirubinemia. Similar results were reported by Reshad M, Ravichander B, Raghuraman T S.

Sahu S, Abraham R, John J, Mathew A, George AS found that 82% of neonates who had albumin levels less than 2.8 gm/dl developed hyperbilirubinemia requiring phototherapy and about 12% needed exchange transfusion. At higher levels of albumin i.e., 2.8-3.3 gm/dl, 40% needed phototherapy and neonates with cord blood albumin >3.3 gm/dl did not need any intervention for hyperbilirubinemia.

In this study, out of 160 neonates, 11 neonates developed hyperbilirubinemia. In group A (CSA level <3.3 g/dl) 1 baby, Group B (CSA level 3.3-3.8 g/dl) 9% (9/100) and in Group C (CSA level ≥3.8 g/dl) 2% (2/58) developed hyperbilirubinemia and were treated with phototherapy. It was noted that majority of these babies were from group B (p<0.032).

In this study, infants with neonatal hyperbilirubinemia had significantly lower levels of cord serum albumin (<3.8 g/dl). Therefore, it is possible to define a group of neonates at risk of developing jaundice at birth based on cord serum albumin.

Cord serum albumin level ≥3.8 g/dl can be considered safe. Limitations of the study was that only full term healthy neonates were taken for the study.

CONCLUSION

Cord serum albumin level of ≤3.8 g/dl can be used as a risk indicator in predicting the development of neonatal hyperbilirubinemia at birth. Cord serum albumin level ≥3.8 g/dl can be considered safe for early discharge. Hence routine estimation of cord serum albumin can be implemented to keep track of at-risk neonates.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Research Board of Hospital

REFERENCES