

## Original Research :

# Cord Serum Albumin As A Tool to Predict Neonatal Hyperbilirubinemia

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### Abstract:

**Objectives:** (1) To determine the critical value of cord serum albumin in predicting subsequent development of neonatal hyperbilirubinemia and need of photo therapy or exchange transfusion. (2) To predict proportion of newborn requiring intervention for hyperbilirubinemia, depending upon cord serum albumin.

**Design:** Prospective cohort study, **Setting:** Pediatrics department of a Medical College Hospital. **Study Population:** 174 neonates from delivery room, operation Theatre, maternity ward and paediatric intensive care unit from October 2013 to September 2015. **Methods:** Serum albumin was estimated from cord blood at birth. Followed-up for 5 days for development of Jaundice and estimation of bilirubin from blood. Data entered in Microsoft excel sheet, registered and analysed in registered version of Stata SE v 12.0 Results: Neonates were divided in three groups with cord Albumin <2.8 grp I) 2.9 – 33 gm/dl (grp II) and >3.4 gm/dl (grp3) with 77, 57 and 40 in three respective groups. 20 out of 174 developed hyperbilirubinemia requiring intervention. 19 in group I, 1 in group II and non in group III developed hyperbilirubinemia. Conclusion: Neonates with hyperbilirubinemia had significantly low levels (< 2.8 gm/dl) of cord albumin level and this group need to have meticulous follow up and early intervention.

**Keywords:** Neonatal Jaundice, Cord Serum Albumin, Serum Bilirubin, Phototherapy.

### Introduction:

Clinical jaundice is seen in 60-70% of term and about 80% of preterm newborns. Serum bilirubin over 15 mg% is found in 3% of normal term newborns.<sup>1</sup> Early discharge of healthy term newborns after normal vaginal delivery is a common practice because of concerns like prevention of nosocomial infections, social reasons like early naming ceremony and due to economical constraints. American Academic of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow-up visit after 48 to 72 hours for any significant jaundice and other problems.<sup>2</sup> This is not possible in India due to limited follow-up facilities. These babies may develop jaundice, which may be over-looked, or there may be delay in recognition unless closely monitored.

Concern to the early discharge is reports of bilirubin encephalopathy in healthy term infants even without hemolysis. The concept of prediction of jaundice offers an attractive option to pick up babies at risk of neonatal hyperbilirubinemia and early treatment of jaundice with phototherapy which is effective, simple and cheap.

Visual assessment of serum total bilirubin (STB) levels as suggested by Kramer<sup>3</sup> relies on the cephalocaudal progression of jaundice with a rising STB level (Head and neck 4 to 8 mg/dl [68 to 292 µmol/l); upper trunk 5 to 12 mg/dl (86 to 205 µmol/l); lower trunk and thighs 8 to 16 mg/dl (137 to 274 µmol/l); palms and soles, greater than 15 mg/dl (257 µmol/l) is now known not to be without error. There is also considerable inter-laboratory

variation in STB levels measured at different laboratories. Albumin helps in hepatic transportation of bilirubin and its clearance. Low serum albumin level will decrease bilirubin clearance and thus will increase significant hyperbilirubinemia. There is paucity of studies on cord blood albumin as a predictor of severity of neonatal jaundice.<sup>4,5</sup> In order to protect the newborn from the complication of neonatal hyperbilirubinemia, it is important to know the early risk factors. Cord serum albumin <3gm/dl is considered as a risk factor for neonatal jaundice.

The present study was conducted to determine the value of cord blood albumin in predicting subsequent development of neonatal jaundice that requires interventions like phototherapy or exchange transfusion.

#### **Material and Method:**

The study was conducted partly in the delivery room or Operation theatre of Obstetrics and Gynecology department and partly in the Neonatal Intensive Care Unit of Pediatric departments of Hi-tech medical college and hospital, Bhubaneswar. Approval of the institutional ethics committee was obtained.

##### **a. Inclusion Criteria:**

Term babies of both genders, Birth weight  $\geq 2.5$ kg, APGAR  $\geq 7/10$  at 1 min.

##### **b. Exclusion Criteria:**

Preterm, Rh incompatibility, Neonatal sepsis, Instrumental delivery, Birth asphyxia,

Respiratory distress, Meconium stained amniotic fluid, Neonatal jaundice within 24 Hours of life, Infant of diabetic mother.

##### **c. Sampling:**

Consecutive sampling was adopted for selecting the cases. All term neonates were counseled for including them in the cohort after obtaining informed consent of parents. Those who met the inclusion and criteria and gave consent for

drawing blood from the placental cord for albumin estimation were included in the study. The study period was 2 years and convenient sampling of approximately 200 newborns was considered.

#### **Method:**

Cord blood was collected from the placental side at the time of delivery. Gestational age was calculated using New Ballard Score 1 wherever the LMP was not available. The cases were assessed at the time of birth for inclusion and exclusion criteria. All those who had given consent and met inclusion criteria were included in the study and were followed up at least till day 5 of life for development of severe jaundice (involving palms and soles). Data with regards to clinical jaundice was assessed using Krammer criteria on days 3 to 5<sup>3</sup>. Serum bilirubin estimation (Total and direct) and blood group analysis was done using venous blood of children having jaundice involving palms and soles on any day of follow up. Those who developed desired criteria for phototherapy (Total serum bilirubin >17 mg/dl) on follow up days were given phototherapy and further followed up till discharge. Complications developed if any during phototherapy were noted. The data were collected using a pre-designed and pre-tested tool. Data was partly collected using interview with the mother and partly using case sheets of mother and laboratory investigation reports. Cord Serum Albumin was estimated using auto-analyzer while serum bilirubin estimation was done using Diazotized Sulfanilic test by spectrometry. Blood group estimation was done using anti-sera method. All the tests were done following standard laboratory procedure in the laboratory of Hi-tech Medical College and Hospital by a single laboratory technician. Interventions using phototherapy were well explained to arents.

#### **Data analysis:**

At the end of study period 174 newborns were enrolled for final analysis. Data was cleaned and entered in Microsoft excel sheet. It was then imported into registered version of Stata SE v 12.0. Data were analyzed using simple statistics like

mean and proportions for the general parameters. Bivariate correlation analysis was done for continuous variables like serum bilirubin and serum albumin. Chi-square test was done for finding association between two or more categorical variables. Receiver Operating Curve (ROC) analysis was done to find out the cut-off value which can best decide serum albumin levels at birth with high sensitivity for predicting onset of severe jaundice needing phototherapy.

### Results:

A total of 215 newborn cases were delivered over the period of 6 months. Out of which, 195 parents gave consent. Among these only 174 cases met inclusion and exclusion criteria. Thus study was conducted on a total of 174 newborns after obtaining a written consent from the parents. Samples collected for Cord serum albumin during delivery from the other cases who did not meet inclusion and exclusion criteria were discarded.

The histogram shows distribution of birth weight among the studied newborns. Low birth weight babies (< 2.5 kg) were excluded from the study. And among the study group 68.9% (n=120) newborns had birth weight between 2.5-3.0 kg.

The distribution of study cohort into three groups based on cord albumin level measured at birth is shown in Table-1. Group 1 consists of 77 newborns constituting to 44.25% of the study cohort. Whereas Group 2 consists of 57 newborns (32.75%) and Group 3 consists of 40 newborns (23%) of study cohort.

Table-2 shows the distribution of Total Serum Bilirubin level estimated at 48-120 hours of postnatal life in the study cohort. 20 out of 174 newborn developed Neonatal Hyperbilirubinemia.

Appearance of clinical jaundice and progress from face to palms and soles as the days progressed is shown in Table 3. Most of the cases requiring phototherapy were found to present with jaundice on palms and soles on Day 5. All cases were sent for total bilirubin and direct bilirubin estimation so as to validate and confirm phototherapy requirement for

the severe jaundice cases.

The comparison between the newborns who developed significant Neonatal Hyperbilirubinemia requiring phototherapy in relation to cord albumin is shown in Table-4. It was seen that the means of the serum albumin levels were significantly different ( $p < 0.05$ ) for those requiring phototherapy and those who do not. Table-5 shows the need of Phototherapy in the three groups divided as per cord serum albumin. 19/20 required phototherapy with cord albumin < 2.8 gm/dl.

With Cord Serum Albumin < 2.8 gm those who developed Serum Bilirubin more than 17 mg% requiring phototherapy has a sensitivity of 95% and specificity of 62.34%. The positive predictive value is 24.68 and the Negative predictive value of 98.97. So the test can ideally predict 95% of Hyperbilirubinemia requiring intervention.

Adequacy of breast feeding was significantly associated with requirement of phototherapy in the child. Inadequate breast fed children have more risk of developing severe jaundice. Time of initiation of breast feeding was however not a risk factor. (Table 6).

### Discussion :

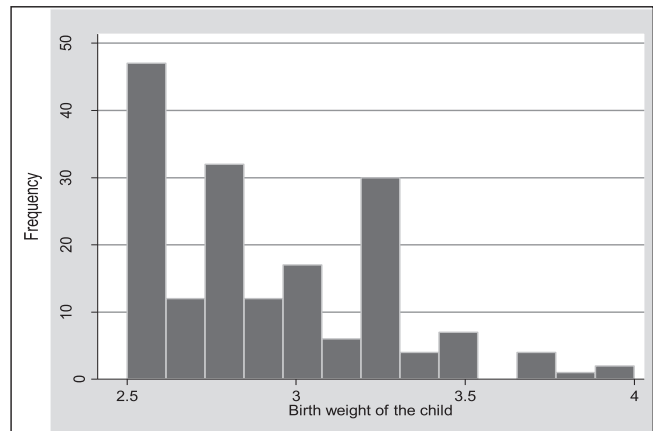
Neonatal hyperbilirubinemia is one of the most common causes for readmission of the newborns<sup>6</sup>. The need for early detection of hyperbilirubinemia in the early discharged newborns from the hospital is therefore important. Knowledge of the neonates at risk for developing jaundice allows simple bilirubin reducing methods to be implemented before bilirubin reaches critical levels.

Moreover, there is a concern regarding early discharge of healthy term newborns due to reports of bilirubin induced brain damage from kernicterus. Kernicterus is the chronic sequelae of acute bilirubin encephalopathy. Incidence of kernicterus is unknown. Hence defining a certain bilirubin level as physiological can be misleading and potentially dangerous. Neonatal hyperbilirubinemia is potentially correctable and kernicterus is preventable.

In this study Cord Serum Albumin level was obtained as a tool for screening for subsequent Neonatal Hyperbilirubinemia. It is interesting to note that lower levels of serum albumin at birth definitely correlated with higher levels of total and indirect bilirubin on the fifth day of life<sup>4,5,6</sup>. Thus it can be considered as a risk factor rather than a diagnostic tool, which can give a clue to the possibility of severe jaundice during neonatal period. It may help the treating physician and the parents stay alert to take action at the earliest. Thus it can be a useful tool in preventing Kernicterus or any other forms of toxicity due to hyperbilirubinemia. Incidence of hyperbilirubinemia varies from 8.3% to 12.8% 7–13. Hyperbilirubinemia in the present study of 11.5% correlates with most of other studies.

**Conclusion:**

Neonatal hyperbilirubinemia occurs in 5-10% of healthy term neonates. Up to 4% of term neonates who were readmitted to the hospital during their first week of life, approximately 85% were for jaundice. In the present study neonates with hyperbilirubinemia ( $\geq 17\text{mg/dl}$ ) had significantly lower levels of cord serum albumin ( $\leq 2.8\text{g/dl}$ ). So it is possible to define a group of neonates at risk of developing jaundice needing intervention. Knowledge of risk factors of Neonatal Hyperbilirubinemia in neonates could influence decision of early discharge Vs. prolonged observation. From the present study, cord serum albumin level of  $\leq 2.8\text{g/dl}$  has a correlation with incidence of significant hyperbilirubinemia in term newborns. So this  $\leq 2.8\text{g/dl}$  of cord serum albumin level can be used as risk indicator to predict the development of significant hyperbilirubinemia. Whereas cord serum albumin level  $\geq 3.4\text{g/dl}$  is considered safe, as none of developed in this group had significant hyperbilirubinemia. It was noted that cord serum albumin level of  $< 2.8\text{g/dl}$  had sensitivity of 95% and specificity of 62.34%, positive predictive value of 98.97% in predicting the risk of neonatal hyperbilirubinemia. Variables that were found to be associated with neonatal hyperbilirubinemia were inadequate breast feeding and low serum albumin levels.



**Fig. 1:** Histogram of weight distribution of newborns under the study.

**Table - 1** Grouped based on Cord Serum Albumin (g/dl) level.

Cord Serum Albumin (g/dl)	No. of patients	%
$\leq 2.8$ (Gr 1)	77	44.25
2.9-3.3 (Group 2)	57	32.75
$\geq 3.4$ (Group 3)	40	23.0
Total	174	100.0

**Table-2.** Distribution of total Serum Bilirubin.

Total Serum Bilirubin (mg/dl)	No. of patients	%
$\leq 10$	7	4.0
10-14	133	76.4
15-17	14	8.0
$\geq 17$	20	11.5
Total	174	100.0

**Table-3** Appearance of clinical jaundice in new-borns during follow up in the post-natal period

Sl	Region as per Kramer rule	Day 3 No. (%)	Day 4 No. (%)	Day 5 No (%)
1	Face	68 (39.1)	1 (0.6)	0 (0.0)
2	Upper trunk	24 (13.8)	82 (47.1)	1 (0.6)
3	Lower trunk	82 (47.1)	67 (38.5)	68 (39.1)
4	Hands and Legs	0 (0.0)	24 (13.8)	80 (46.0)
5	Palms and soles	0 (0.0)	0 (0.0)	25 (14.4)

**Table – 4.** Comparison of mean Serum albumin levels in cases requiring phototherapy Vs. those not requiring phototherapy

Sl	Phototherapy need	Mean Serum Albumin (SE)	95% Confidence Interval
1	No	3.025 (0.040)	2.95 - 3.11
2	Yes	2.016 (0.090)	1.83 - 2.20
	Difference of mean	1.010 (0.120)	0.78 - 1.24

df = 172; p < 0.05

**Table :5.** Comparison of Need for Phototherapy with Cord Serum Albumin level as per groups

Phototherapy	Cord Albumin levels			Total
	≤ 2.8	2.9-3.3	≥ 3.4	
No	58(75.3%)	56(98.2%)	40(100%)	154(88.5%)
Yes	19(24.7%)	1(1.8%)	0(0%)	20(11.5%)
Total	77(100%)	57(100%)	40(100%)	174(100%)

**Table – 6.** Association of breast feeding adequacy with phototherapy requirement

Breast feeding	Phototherapy		Total
	No	Yes	
Adequate	152 (94.4%)	9 (5.6%)	161 (100%)
Inadequate	2 (15.38%)	11 (84.6%)	13 (100%)
Total	154 (88.5%)	20 (11.5%)	174 (100%)

Chi-square - 73.84; p value - 0.000

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**Competing Interest:-** None stated.

**RR-carried out technical and clinical work, did analysis and statistics, SGD-conceptualized and did review of literature, guidance**

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