

# Cord blood albumin, a tool as predictor of neonatal hyperbilirubinemia requiring intervention

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## ABSTRACT

**Objective:** To find out the clinical significance of cord blood albumin level as predictor of neonatal hyperbilirubinemia (NBH) that requires intervention. **Methods:** Prospective observational study of 100 newborns of age 1-7 days delivered at Silchar Medical College, Assam, India from July 2018 to June 2019. Cord blood for albumin (CBA) and venous blood for total serum bilirubin (TSB) were collected and tested. Co-relation of CBA and TSB that required intervention was done. **Results:**  $CBA \leq 2.8$  g/dl is a high risk factor for significant NHB ( $p = 0.0005$ ) requiring early intervention. 58.3% and 16.7% of study population having  $CBA < 2.8$  g/dl required phototherapy and exchange blood transfusion respectively as the mode of intervention for NHB. A cut off level of CBA 3.05 g/dl has a sensitivity of 85.7%, specificity of 90.7%, PPV of 60%, NPV of 97.50% and accuracy of 88.21% in predicting NHB requiring intervention. **Conclusion:**  $CBA \leq 2.8$  g/dl is a significant risk factor developing NHB that requires early intervention and  $CBA > 3.3$  g/dl is probably safe for early discharge of newborns.

**Keywords:** Neonatal jaundice, cord blood albumin, serum bilirubin.

Neonatal jaundice or neonatal hyperbilirubinemia (NHB) has been observed since many centuries. About 84% of hospital admitted newborns are found to be with some degree of jaundiced and it is the most common cause for readmission during neonatal period<sup>1</sup>. Such readmission exposes a newborn to infections, metabolic complications, lactational failure, in addition to extra expenses for the family and medical institution. On the otherhand, considering the potential complications of NHB like apnea, seizure, sensorineural deafness, learning disabilities, cerebral palsy etc<sup>2</sup>, and early intervention of NHB can not be compromised. Therefore, there is a need for finding a reliable tool for early prediction of development of significant jaundice in newborns before they are discharged from the institutions where they are born. According to

American Academy of Pediatrics (AAP) recommendations, newborns discharged within 48 hours should have a follow up visit after 48-72 hours for any significant jaundice and other problems<sup>3</sup>. Many a times, this recommendation is not feasible in developing countries due to limited resources, socio-economic factors etc. There have been many studies by various worker to find a reliable, feasible and cost effective tool other than by measurement of total serum bilirubin (TSB) and follow up, for early prediction of development of significant NHB and to start early intervention to prevent complications. One of such tools is the estimation of cord blood albumin (CBA) level<sup>4</sup>.

Synthesis of albumin appears at approximately 7<sup>th</sup> – 8<sup>th</sup> week of human fetus. Albumin concentration is low in neonate (~2.5 g/dl), reaching adult level (~3.5 g/dl) after

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several months. Bilirubin and albumin binds in an equimolar ratio. Free bilirubin appears when the bilirubin to albumin (B : A) ratio is > 0.8. All albumin in the fetus is of fetal origin, because albumin does not cross the hemochorial placenta<sup>5</sup>. Albumin is a major binding protein in human neonate<sup>6</sup>. Albumin reduces toxicity of bilirubin by competing with tissue for bilirubin binding. Therefore, there are reasons to believe that cord blood level of albumin has definitive role in development of significant jaundice. Estimation of cord blood albumin (CBA) is a simple, feasible, cost effective test.

**Materials and methods**

This study was conducted at Silchar Medical College & Hospital, Assam, India, from July 2018 to June 2019. Prior Institutional Ethic committee approval of the protocol of study was obtained and informed consent was obtained from the parents before inclusion of newborns to the study.

Study design: Prospective observational study.

The study population was newborns of age day 1-7, born by normal delivery & lower segment caesarean section (LSCS). Study areas were CSOT, delivery room, SCNU & post natal ward. Both term and preterm babies of any birth weight, selected randomly after screening for exclusion criteria were included to the study. The exclusion criteria were Rh & ABO incompatibility, sepsis, birth asphyxia, respiratory distress, meconium aspiration syndrome, jaundice within 24 hours of life and congenital anomaly.

Sample size (n): 100 newborns.

Study tools: For estimation of CBA, 2ml of umbilical cord blood of all babies at birth were collected in a clot activated vial and sent to central clinical laboratory (CCL) immediately or stored in refrigerator. For estimation of total serum bilirubin (TSB), 1ml of venous blood was collected after 72 hours of life or earlier if clinical jaundice observed. Other relevant investigations were done wherever indicated. Interventions like phototherapy or exchange blood transfusion were done as per NHB management guidelines. Baseline demographic profiles such as mothers name, gender, birth weight, age, type of delivery were recorded in a predesigned proforma.

Data analysis: IBM SPSS statistics software 23.0 version was used for analysis of data. Percentage analysis was used for categorical variable. Mean and standard deviation (SD) were used for continuous variables. Receiver operator characteristic (ROC) curve analysis was used to find sensitivity, specificity, PPV & NPV. Chi-square tests were used to find significance in categorical data.

**Results**

Total 100 number of newborn was taken in our study. The mean birth weight and gestational age was 3.48± 0.627

**Table 1: Base line demographic variables**

Variables	Number
Gender Male	57
Female	43
Birth weight in kg (mean)	3.48± 0.627
Gestational age (in weeks)	37.4±2.4

Kgs and 37.4±2.4 weeks respectively (Table 1). Gender distribution with CBA and neonatal hyperbilirubinemia requiring intervention was described in table 2 and 3. With

**Table 2: Gender distribution and CBA level**

CBA (g/dl)	Male N (%)	Female N (%)	Total	P value
≤2.8	5(41.7)	7(58.3)	12(100%)	0.520
2.9-3.3	19(59.4)	13(40.6)	32(100%)	
>3.3	33(58.9)	23(41.1)	56(100%)	

P value <0.05 is significant

cord blood albumin level ≤ 2.8 g/dl, 7 out of 12 neonates (58.3%) required phototherapy and 2 babies (16.7%) needed exchange blood transfusion in our study. In the other 2

**Table 3: Gender and NHB requiring intervention**

Gender	Intervention in NHB		P value
	Yes N (%)	No N (%)	
Male	8(57.1)	49(57)	0.991
Female	6(42.9)	37(43)	

groups; with CBA 2.8-3.3 g/dl, 5 numbers of neonate were required phototherapy (15.6%) and with CBA> 3.3 g/dl none developed significant jaundice requiring intervention (Table 4). Table 5 showed that CBA≤ 2.8 g/dl is a high risk factor

**Table 4: CBA and NHB requiring intervention**

CBA level (g/dl)	No. Of Babies (N)	Interventions	
		Phototherapy N (%)	Exchange blood transfusion N (%)
≤ 2.8	12	7(58.3)	2(16.7)
2.8-3.3	32	5(15.6)	0(0)
>3.3	56	0(0)	0(0)

for significant NHB (p = 0.0005) requiring early intervention. This study revealed that a cord blood albumin cut off level of <3.05g/dl has a sensitivity of 85.71%, specificity of 90.70%, positive predictive value of 60%, negative predictive value of 97.50% and accuracy of 88.21% in predicting NHB requiring intervention (Table 5).

**Table 5: Cut off value of CBA in predicting NHB requiring intervention**

CBA (g/dl)	Intervention		Total (N)	P Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
	Yes N (%)	No N (%)							
≤ 3.05	12(85.7)	8(9.3)	20	0.0005	85.7	90.70	60	97.5	88.21
>3.05	2(14.3)	78(90.7)	80						

**Discussion**

Because of increasing number of early discharged newborns, there is a corresponding danger of failing to diagnose severe hyperbilirubinemia in time, as kernicterus in full term healthy newborn also reported <sup>7</sup>. The reported

study, a cord blood albumin cut off level of <3.05g/dl has a sensitivity of 85.71%, specificity of 90.70%, positive predictive value of 60%, negative predictive value of 97.50% and accuracy of 88.21% in predicting NHB requiring intervention. This cut off value is very close to the cut off

**Table 6: Table showing cord blood albumin level as a risk indicator of NHB requiring intervention in some studies. (\* NHB requiring intervention)**

Authors	Total no. of case	NHB requiring intervention			P value
		CBA < 2.8 g/dl	CBA = 2.8-3.3 g/dl	CBA > 3.3 g/dl	
Sahu et al <sup>6</sup>	40	14	6	0	<0.001
Trivedi et al <sup>12</sup>	605	120	59	26	<0.05
Sandeep Kumar et al <sup>13</sup>	100	9*/36	1*/31	0*/33	0.0003
Surendra Kumar et al <sup>14</sup>	100	5*/13	7*/57	2*/30	0.02

**Table 7: Comparison of cut off value of CBA predicting NHB requiring intervention**

Author	Cut off value of CBA g/dl	Sensitivity %	Specificity %	PPV %	NPV %
Mahmoud Alalfy et al <sup>15</sup>	2.75	64.3	81.8	81.8	--
Venkatamurthy et al <sup>16</sup>	2.80	95	62	24.6	98.9
Our study	3.05	85.71	90.7	60	97.5

incidence of neonatal jaundice requiring intervention varies from 8.35% to 15.7% <sup>8-11</sup>. In the present study 14 babies required intervention which is comparatively higher. This may be due to small sample size and inclusion of all gestational ages. Trivedi et al reported the incidence of jaundice as 37.7% and 30% in male and female babies respectively in their study of 605 newborns <sup>12</sup>, though in the present study there was no significant variation ( p = 0.991) of incidence of jaundice on the basis of gender. This may be due to fact that male and female babies were not equally distributed. With cord blood albumin level ≤ 2.8 g/dl, 7 out of 12 neonates (58.3%) required phototherapy and 2 babies (16.7%) needed exchange blood transfusion in our study. In the other 2 groups; with CBA 2.8-3.3 g/dl, 5 numbers of neonate were required phototherapy (15.6%) and with CBA > 3.3 g/dl none developed significant jaundice requiring intervention. Therefore it can be presumed that CBA level ≤ 2.8 g/dl is a high risk factor for future development of neonatal hyperbilirubinemia requiring intervention and CBA level ≥ 3.3 g/dl is probably safe for early discharge of the newborn. Similar findings were reported by various authors in their studies as evident in the following table 6. In our

values of CBA in other studies by various authors (Table 7).

**Conclusion**

The incidence of neonatal hyperbilirubinemia requiring phototherapy is 12% and exchange blood transfusion is 2%. Thus the over all incidence of NHB requiring intervention is 14%. Cord blood albumin ≤ 2.8 g/dl is a significant risk factor that requires early intervention and CBA > 3.3 g/dl is probably safe for early discharge of newborn.

**Conflict of interest:** None. **Disclaimer:** Nil.

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