

To Investigate the Relationship Between Cord Blood Albumin and Serum Bilirubin Levels in Term Healthy Babies At 48 Hours

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Abstract

Aim: To study the correlation between various levels of cord blood albumin & serum bilirubin at 48 hrs of age in term healthy newborns. **Methods:** A prospective study was conducted in the Department of Paediatrics, Patna Medical College and Hospital, Patna, Bihar India for 1 year. 100 terms healthy newborns with birth weight ≥ 2.5 kg was included in this study. Newborns with a congenital anomaly, birth asphyxia, traumatic birth, respiratory distress, sepsis, metabolic diseases, pathological hyperbilirubinemia before 24 hrs, infant of a diabetic mother, and haemolytic diseases requiring admission in NICU were excluded from the study. Cord blood was collected at birth and analysed by auto analyser method for Cord Serum Albumin level. Newborns were divided into 3 groups for data analysis according to their cord albumin levels (<2.8 , $2.8-3.4$, and >3.4 g/dl), and were analysed to find out association with 3 risk zone according to Bhutani nomogram. **Results:** Out of the 100 infants enrolled in our study, 60(60%) were males and 40(40%). 20% newborn had cord albumin <2.8 g/dl, 50% recorded values between 2.8 to 3.4 g/dl and 30(30%) recorded cord albumin >3.4 g/dl. Newborns with higher birth weight had a significantly lesser incidence of low cord albumin (<2.8 g/dl). Out of 100 newborns, 20(20%) serum bilirubin levels were at the low-risk zone, 57(57%) at the low intermediate risk zone, while 23 (23%) were at the high intermediate risk zone at 48 hrs of age. 60% of newborns with cord albumin level <2.8 g/dl recorded serum bilirubin at or above high intermediate risk zone, while 7 were at low intermediate risk zone and 1 new-born was at low-risk zone at 48 hrs of age. We found that a cut-off level of cord blood albumin of 2.8g/dl had 84.9% sensitivity, 82.7% specificity, and PPV 85.1% for prediction of hyperbilirubinemia at high intermediate cut-off level with a p-value of <0.05 in term newborns, with NPV of 76% indicating its usefulness. **Conclusion:** Neonates with cord blood albumin <2.8 gm/dl had a significant association of the development of hyperbilirubinemia at or above intermediate high-risk zone according to Bhutani nomogram at 48 hrs of life.

Keywords: Neonates, Cord Blood, Albumin, Bilirubin.

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Introduction

Jaundice in newborn is a very common problem. Neonatal Hyperbilirubinemia (NH) may lead to kernicterus in otherwise healthy newborns. This can be easily prevented if excessive hyperbilirubinemia for age is promptly identified and appropriately treated[1-3]. Newborns can be screened for severity of bilirubinemia before hospital discharge which may help in early detection of the newborns at risk for excessive hyperbilirubinemia during the first week of life[4]. It is difficult to predict which of these newborns are at risk for developing significant hyperbilirubinemia (Total Serum Bilirubin \geq 15mg/dl)[5]. Significant hyperbilirubinemia is usually found in 3% of normal term babies[6]. Depending on various methods of bilirubin estimation in different laboratories, the frequency of breast feeding, ethnic makeup of people and regional variations the incidence of hyperbilirubinemia changes[7-9]. The severe jaundice and kernicterus has been found in some healthy full term newborns discharged early with no apparent hemolysis[10].

The American Academy of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow-up visit after 2-3 days to detect significant jaundice and other problems[11]. In developing countries like India, this recommendation is not practical due to limited follow up facilities.

Early treatment of jaundice with phototherapy is effective, simple and cheap as compared to the treatment of severe neonatal jaundice with exchange transfusion, which is time consuming, costly, associated with complications and requires skilled personnel. Thus, the early prediction of jaundice offers an attractive option for picking up babies at risk of NH. Many investigators have tried to find a simple marker to predict hyperbilirubinemia and its subsequent course in newborns like cord bilirubin estimation, bilirubin estimation during 6 to

24 hours of age, predischage hour specific bilirubin estimation and transcutaneous bilirubin measurement[12,13].

Materials and methods:

A prospective study was conducted in the Department of Paediatrics, Patna Medical College and Hospital, Patna, Bihar India for 1 year, after taking the approval of the protocol review committee and institutional ethics committee. 100 terms healthy newborns with birth weight \geq 2.5 kg were included in this study. Newborns with a congenital anomaly, birth asphyxia, traumatic birth, respiratory distress, sepsis, metabolic diseases, pathological hyperbilirubinemia before 24 hrs, infant of a diabetic mother, and haemolytic diseases requiring admission in NICU were excluded from the study.

Methodology:

Cord blood was collected at birth and analysed by auto analyser method for Cord Serum Albumin level. Venous blood samples were collected from the baby at 48 hours of life. Serum bilirubin estimation is done within 12 hours of collection of a sample by Diazotized sulfanilic test. Gestational age was assessed using Ballard score, SGA, AGA and LGA were defined using Fenton chart. Newborns were divided into 3 groups for data analysis according to their cord albumin levels (<2.8, 2.8-3.4, and >3.4 g/dl), and were analysed to find out association with 3 risk zone according to Bhutani nomogram. Bilirubin level at or above high intermediate risk zone (over 75th percentile cutoff value 11.3mg/dl) at 48 hrs of age was considered a cutoff value to find out the association with cord blood albumin level[14,15].

Statistical Analysis:

Data was entered on the computer using Microsoft Office Excel Software program for Windows, and then transferred to the Statistical Package of Social Science Software (SPSS) 21.0. Comparison

between groups was performed using the Mann-Whitney test for quantitative variables while comparison for qualitative variables was performed through Chi-square or Fisher's test. P values less than 0.05 were considered statistically significant.

Results:

Out of the 100 infants enrolled in our study, 60(60%) were males and 40(40%). 20% newborn had cord albumin <2.8 g/dl, 50% recorded values between 2.8 to 3.4 g/dl and 30(30%) recorded cord albumin >3.4 g/dl. Newborns with higher birth weight had a significantly lesser incidence of low cord albumin (<2.8). gestational age and gender of the study population did not have a significant association with low cord albumin. (Table 1)

Out of 100 newborns, 20(20%) serum bilirubin levels were at the low-risk zone, 57(57%) at the low intermediate risk zone, while 23 (23%) were at the high intermediate risk zone at 48 hrs of age. 60% of newborns with cord albumin level <2.8 g/dl recorded serum bilirubin at or above high intermediate risk zone, while 7 were at low intermediate risk zone and 1 new-born were at low-risk zone at 48 hrs of age. This correlation was statistically significant. [$\chi^2= 118.78$; Likelihood Ratio=113.11; $P<0.05^*$] (table 2) We found that a cut-off level of cord blood albumin of 2.8g/dl had 84.9% sensitivity, 82.7% specificity, and PPV 85.1% for prediction of hyperbilirubinemia at high intermediate cut-off level with a p-value of <0.05 in term newborns, with NPV of 76% indicating its usefulness.

Table 1: Demographic profile of study population according to cord blood albumin at birth

		Cord blood albumin(g/dl)			total	
		<2.8	2.8-3.4	>3.4		
Gender	Male	13	30	17	60(60%)	>0.05
	Female	7	20	13	40(40%)	
Birth Weight	2.5-3	10	17	3	30 (30%)	<0.05*
	3.1-3.5	5	30	7	42(42%)	
	>3.5	5	3	20	28 (28%)	
Gestational age	mean age	36.5	37.2	37.3	77(77%)	>0.05
	37-40 wk	13	45	19		
	>40 wk	7	5	11	23(23%)	

Table 2: Comparison of Cord blood albumin at birth and Total serum bilirubin at 48 hrs of age

Cord blood albumin(g/dl)	serum bilirubin at 48 hrs of age (mg/dl)				p-value
	Low-risk zone	Low intermediate-risk zone	High intermediate-risk zone	total	
<2.8	1(5%)	7 (35%)	12 (60%)	20	p <0.05*
2.8-3.4	1 (2%)	41 (82%)	8 (16%)	50	
>3.4	18 (60%)	9 (30%)	3 (10%)	30	
Total	20 (20%)	57(57%)	23 (23%)	100	

[P=<0.05*]

Discussion:

According to recent AAP guidelines, healthy term newborns should be discharged within 48 hours of birth[16].

Hence it is necessary to identify the newborns at risk of developing hyperbilirubinemia following an early discharge from the hospital to avoid

readmissions and complications as bilirubin encephalopathy and long-term complications[17]. Albumin has a role in the transport and clearance of bilirubin. Albumin acts as a carrier protein for the transport of bilirubin, which eventually helps in the transfer of bilirubin to the liver where conjugation occurs.

Bilirubin binds to albumin in an equimolar ratio. Around 8.5 mg of bilirubin will bind covalently to 1 g of albumin, this process is interrupted due to decreased albumin levels in newborns. It is documented in the literature that newborns have an immature liver function as compared to adults leading to decreased production and synthesis of all the major proteins including albumin which has a major role in the conjugation of bilirubin.

And the neonatal liver is also immature with less ability to excrete and handle excessive production of bilirubin than can be caused by various aetiologies in newborns. Low production of albumin in newborns will lower its transport and binding capacity and may increase bilirubin in these newborns[18]. In the present study we aimed to assess the correlation between cord blood albumin and serum bilirubin for early identification of hyperbilirubinemia and use of cord blood Albumin level as a tool for screening for the risk of subsequent Neonatal hyperbilirubinemia.

There are a few studies that predict Neonatal hyperbilirubinemia by estimating cord blood bilirubin levels but vary in opinion. In our study we found that a cut-off level of cord blood albumin of 2.8g/dl had 84.9% sensitivity, 82.7% specificity, and PPV 85.1% for prediction of hyperbilirubinemia for high intermediate cut-off level with a p-value of <0.05 in term newborns, with NPV of 76% indicating its usefulness. Reshad M, Ravichander B et al.[19] with the sample size of 175 terms and preterm newborn found that cord blood albumin level ≤ 2.8 g/dL is a sensitive limit, with good sensitivity and positive predictive value, in both term and preterm

neonates and Cord blood albumin level ≥ 3.4 g/dL was found to be relatively safe for neonates.

Similar observations were made by Gaurav Aiyappa et al.[20] [71.8%] with 71.8% sensitivity and 65.1% with a sample size of 165 newborns. In the present study, there is a statistically significant correlation between birth weight and cord blood albumin and between birth weight and serum bilirubin in term neonates with good sensitivity and specificity. As we did not take preterm neonates making our results more specific to term newborns. Sahu et al.[21] the study of 40 neonates also showed that 70% of newborns who developed significant neonatal hyperbilirubinemia had cord serum albumin level < 2.8 g/dl, 30% newborns had cord albumin level 2.9- 3.3 g/dl and none of the newborns with cord albumin >3.4g/dl developed neonatal hyperbilirubinemia, and 80% neonates with cord albumin less than 2.8 mg/dl required phototherapy.

Statistical significance was noted between cord albumin with development of significant hyperbilirubinemia (p-value <0.001). In a study by Trivedi et al.[22] 205 newborns out of 605 developed neonatal hyperbilirubinemia with 58.35% (120/205) of the neonates with cord albumin level <2.8 g/dl developing significant neonatal hyperbilirubinemia required intervention with statistical significance of P <0.05. A study by Meena KJ et al.[23] found that cord bilirubin level >2.5 mg/dl had a sensitivity of 77%, specificity of 98.6% with NPV of 96% which supports the results of the present study. Pahuja et al.[24] also observed that the predictive value of cord albumin to detect neonatal hyperbilirubinemia was 75% with 61.3% sensitivity, and 76.8% specificity following the Present study. Similar observations were also made by Asit Kumar et al.[25] Dr Pushpanjali et al.[26] Dhanjal SS et al.[27] and Pathak NN et al.[28].

Conclusion:

Neonates with cord blood albumin <2.8 gm/dl had a significant association of the development of hyperbilirubinemia at or above intermediate high-risk zone according to Bhutani nomogram at 48 hrs of life.

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