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Original Research Article

Cord Blood Albumin as a Predictor of Significant Neonatal Hyperbilirubinemia in Healthy Term Neonates: A Prospective Observational Study

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Abstract

Background: Neonatal hyperbilirubinemia (NH) is one of the most common clinical conditions requiring medical attention in the first week of life. Early identification of newborns at risk of developing significant jaundice is critical, particularly with the trend toward early hospital discharge.

Objectives: To evaluate the role of cord blood albumin (CBA) as a predictor for significant neonatal hyperbilirubinemia in healthy term neonates.

Methods: This prospective observational study was conducted at Deen Dayal Upadhyay Hospital, New Delhi from January to August 2020. A total of 150 healthy term neonates meeting the inclusion criteria were enrolled. Cord blood samples were collected at birth to estimate serum albumin levels. Newborns were followed clinically for the first five days, and total serum bilirubin (TSB) was measured in those showing jaundice beyond Kramer's scale 3. CBA levels were correlated with TSB levels ≥17 mg/dl and the requirement for phototherapy.

Results: Among 150 neonates, 23% had CBA ≤2.8 g/dl, 30% had 2.9–3.3 g/dl, and 47% had >3.3 g/dl. Significant hyperbilirubinemia (TSB ≥17 mg/dl) was observed in 30 neonates (20%), 90% of whom had CBA ≤2.8 g/dl (p=0.003). Sensitivity, specificity, positive predictive value, and negative predictive value of CBA ≤2.8 g/dl were 90.00%, 58.33%, 84.38%, and 70.00% respectively.

Conclusion: Cord blood albumin level ≤2.8 g/dl is significantly associated with the risk of developing significant neonatal hyperbilirubinemia. CBA estimation at birth may serve as a useful screening tool to identify neonates requiring close monitoring and follow-up after early discharge.

Keywords: Neonatal Hyperbilirubinemia, Cord Blood Albumin, Phototherapy, Bilirubin, Jaundice, Term Newborns.

Introduction

Neonatal jaundice, or neonatal hyperbilirubinemia (NH), is the most common clinical condition observed during the first week of life, affecting nearly 60–70% of term and 80% of preterm newborns worldwide [1]. It is characterized by yellowish discoloration of the skin and sclera due to elevated serum bilirubin levels, which may be physiological or pathological depending on the underlying cause [2]

Physiological jaundice typically appears between the second and fourth days of life and resolves without treatment. However, significant or pathological hyperbilirubinemia may require interventions such as phototherapy or exchange transfusion to prevent bilirubin-induced neurologic dysfunction (BIND) and kernicterus [3,4]. Despite advances in neonatal care, bilirubin-induced brain damage remains a serious concern in many developing countries, especially in settings with limited postnatal follow-up [5]. Several guidelines, including those from the American Academy of Pediatrics (AAP), recommend early post-discharge surveillance of neonates for the detection of significant jaundice, particularly when discharged before 48 hours of life [6]. However, in resource-limited countries like India, early discharge, poor access to follow-up care, and low parental awareness contribute to delayed diagnosis and treatment of NH [7]

Albumin, a protein synthesized by the liver, plays a vital role in bilirubin transport and clearance. Unconjugated bilirubin in plasma binds to albumin,

preventing its neurotoxic effects by limiting its diffusion across the blood-brain barrier [8]. Low serum albumin levels in neonates have been postulated to reduce bilirubin clearance, increasing the risk of NH [9].

Recent studies have explored the predictive role of cord blood albumin (CBA) in identifying neonates at risk of developing significant hyperbilirubinemia. Research has shown that neonates with low CBA levels, particularly ≤2.8 g/dL, are more likely to develop clinically significant jaundice requiring treatment [10-13]. In contrast, CBA levels ≥3.4 g/dL are associated with a lower risk and may be considered safe for early discharge [14].

Given the high neonatal load and the increasing trend of early discharge in Indian hospitals, a simple, cost-effective predictive marker such as cord blood albumin could be valuable for early risk stratification. This study aims to evaluate the utility of cord blood albumin in predicting significant hyperbilirubinemia in healthy term neonates.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of Paediatrics at Deen Dayal Upadhyay Hospital, New Delhi, over a period of 8.5 months from January 1st to August 15th, 2020. The study was approved by the Institutional Scientific and Ethical Committee. Written informed consent was obtained from the parents or guardians of all participants.

Study Population and Sampling: A total of 150 healthy term neonates delivered in the hospital's labor room and operation theatre were included. Newborns were selected using purposive sampling based on the following criteria: Term neonates (gestational age 37–40 weeks) of both genders, with birth weight between 2.5 and 3.8 kg, delivered via normal vaginal delivery or cesarean section, and with APGAR scores ≥7 at 1 minute and 10 at 5 minutes.

Neonates with Rh or ABO incompatibility, instrumental delivery (vacuum/forceps), congenital anomalies, or maternal risk factors for neonatal sepsis (e.g., chorioamnionitis, premature rupture of membranes >18 hours, foul-smelling liquor) were excluded.

The sample size of 150 was determined based on a 60% estimated prevalence of neonatal jaundice among term neonates, using Cochrane's formula with a 95% confidence interval and an 8% margin of error.

Data Collection and Laboratory Analysis: At birth, 2 ml of cord blood was collected under aseptic conditions from the placental end of the umbilical cord to estimate serum albumin levels. Samples were transported immediately to the laboratory and analyzed using a Beckman Coulter AU-480 automated chemistry analyzer.

Based on cord blood albumin (CBA) levels, neonates were stratified into three groups: ≤2.8 g/dL, 2.9–3.3 g/dL, and >3.3 g/dL. All neonates were clinically assessed for jaundice using the modified Kramer's scale on day 1, day 3, and day 5 of life. If a neonate had a Kramer's score ≥3, a blood sample was taken to estimate total serum bilirubin (TSB).

Significant neonatal hyperbilirubinemia (NH) was defined as a TSB level ≥17 mg/dL and/or the requirement for phototherapy or exchange transfusion, as per standard clinical guidelines.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software (latest version). Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. The Chi-square test was used for comparison of categorical variables, and Student's t-test was used for continuous variables. Diagnostic validity (sensitivity, specificity, positive predictive value, and negative predictive value) of cord blood albumin was calculated. A p-value <0.05 was considered statistically significant.

Results

A total of 150 healthy term neonates were enrolled in the study. All participants met the inclusion and exclusion criteria and were followed for clinical signs of jaundice for up to five days postnatally. The mean gestational age was 37.94 ± 0.94 weeks, and the mean birth weight was 2.85 ± 0.19 kg. Male newborns constituted 55% of the study population.

Table 1: Baseline Characteristics of the Study Population (n = 150)

Variable	Value
Mean gestational age (weeks)	37.94 ± 0.94
Mean birth weight (kg)	2.85 ± 0.19
Male: female	82 (55%): 68 (45%)
Mode of delivery	Vaginal – 84 (56%), Caesarean – 66 (44%)
Most common blood group	B+ in both mothers (48%) and neonates (51%)

In present study, out of 150 enrolled babies majority 70 newborns (47%) had cord blood albumin (CBA) more than 3.3 gm/dl. 35 babies (23%) had CBA ≤2.8 gm/dl and other 45 (30%) had CBA levels 2.9-3.3 gm/dl. Of the 150 neonates, 115 (76%) developed clinical jaundice (Kramer's scale 1–5). Forty-two neonates had Kramer's scale ≥3 and were further evaluated for total serum bilirubin (TSB). Of these, 30 (20%) had significant hyperbilirubinemia (TSB ≥17 mg/dL).

Table 2: Correlation between Cord Blood Albumin and Significant Hyperbilirubinemia (TSB ≥17 mg/dL)

CBA Group (g/dL)	TSB ≥17 mg/dL (n)	TSB <17 mg/dL (n)	p-value
≤ 2.8	27	5	0.003*
2.9 – 3.3	2	4	0.081
> 3.3	1	3	0.114

***Statistically significant (p < 0.05)**

Cord blood albumin ≤2.8 g/dL was found to be a significant predictor of neonatal hyperbilirubinemia requiring phototherapy.

Table 3: Diagnostic Predictability of CBA ≤2.8 g/dL for Significant Hyperbilirubinemia

Diagnostic Parameter	Value (%)
Sensitivity	90.00%
Specificity	58.33%
Positive Predictive Value	84.38%
Negative Predictive Value	70.00%
Diagnostic Accuracy	80.95%

A significant inverse correlation was observed between CBA and TSB (Pearson's R = –0.573), suggesting that lower albumin levels were associated with higher bilirubin levels (figure 1).

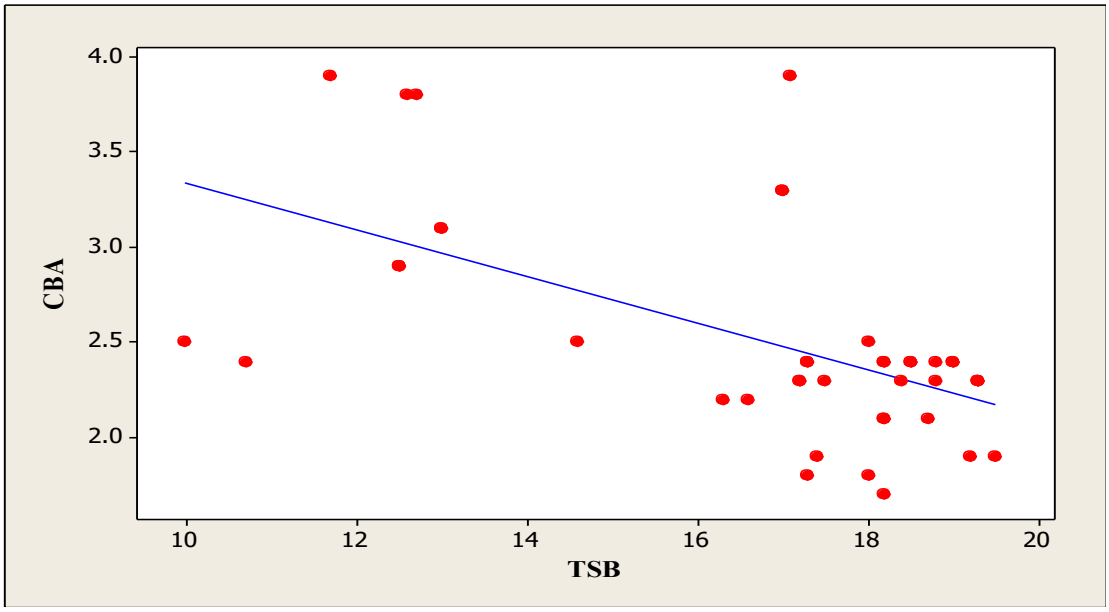

Figure 1: Scatter plot of cord blood albumin versus total serum bilirubin

Discussion

Neonatal hyperbilirubinemia (NH) remains one of the most commonly encountered conditions during the early neonatal period, especially among term infants [1]. Although often physiological, a subset of neonates develops significant hyperbilirubinemia that necessitates interventions such as phototherapy or, in rare cases, exchange transfusion [2,3]. Early discharge policies in hospitals have increased the risk of delayed recognition and management of NH, particularly in settings with limited postnatal follow-up [4,5]. In this study, we investigated whether cord blood albumin (CBA) levels at birth could serve as a predictor of significant neonatal hyperbilirubinemia (TSB ≥17 mg/dL) in healthy term neonates.

Our findings revealed that CBA ≤2.8 g/dL was significantly associated with higher rates of clinically significant jaundice requiring phototherapy, with a sensitivity of 90% and

positive predictive value of 84.38%. This result is consistent with previous studies by Meena et al., Reshad et al., and Raj et al., all of whom demonstrated that low cord albumin levels were predictive of significant hyperbilirubinemia [10-12]. In particular, Meena et al. reported that 95.5% of neonates with CBA <2.8 g/dL developed jaundice, of whom 81.8% required phototherapy [10]. Similarly, Raj et al. reported high sensitivity (95%) and negative predictive value (98.97%) at the same CBA threshold [12].

Our study population had a male-to-female ratio of 1.2:1, although no significant gender-based difference in phototherapy requirement was observed. This finding is in line with Rostami et al., who found no significant correlation between sex and NH [13]. In contrast, Maisels et al. noted a slightly higher risk in male neonates [14].

The majority (47%) of our neonates had CBA >3.3 g/dL, and none of these developed significant hyperbilirubinemia, corroborating findings by Sahu et al. and Bhat et al., who suggested that neonates with higher CBA levels are safe for early discharge [9,15]. This stratification could provide a useful screening tool in clinical settings, especially where follow-up systems are inadequate.

Importantly, our study also demonstrated a statistically significant inverse correlation (R = –0.573) between CBA and serum bilirubin levels. This reinforces the physiological role of albumin in binding and clearing unconjugated bilirubin, thereby reducing the risk of bilirubin neurotoxicity [6,8].

Compared to transcutaneous bilirubin screening or serial serum bilirubin estimation, cord blood albumin testing is cost-effective, simple, and feasible, especially in resource-limited neonatal units [7,16]. Furthermore, it can be integrated with routine blood sampling protocols at birth without added burden on the healthcare system.

However, the specificity in our study (58.33%) was relatively lower than that reported in some earlier works, such as Mishra et al. (62.4%) [17]. This may be due to sample size variation or the inclusion of neonates with borderline bilirubin levels in other studies. Nevertheless, the diagnostic accuracy of 80.95% in our cohort remains clinically useful.

Strengths and Limitations:

The prospective design, clear inclusion/exclusion criteria, and follow-up till day 5 strengthen the internal validity of our results. However, limitations include the single-center setting, relatively small sample size, and exclusion of preterm or at-risk neonates, which may limit generalizability.

Conclusion and Recommendations

This prospective observational study demonstrated that cord blood albumin (CBA) level ≤2.8 g/dL is a statistically significant predictor of neonatal hyperbilirubinemia requiring intervention. Neonates with low CBA were found to have a markedly higher risk of developing significant jaundice, with a sensitivity of 90%, positive predictive value of 84.38%, and a diagnostic accuracy of 80.95%. Furthermore, the negative correlation (R = –0.573) between CBA and serum bilirubin supports the pathophysiological role of albumin in bilirubin transport and clearance.

These findings support the clinical utility of measuring CBA at birth as a simple, inexpensive, and effective screening tool to predict the risk of significant hyperbilirubinemia in healthy term neonates. It may help identify high-risk neonates at the time of discharge and guide appropriate follow-up to prevent complications such as kernicterus.

Routine estimation of cord blood albumin in all term neonates can be considered as part of the newborn assessment, especially in resource-constrained settings where follow-up may be inconsistent.

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