Umbilical Cord Serum Albumin as a Predictor of Significant Neonatal Hyperbilirubinemia in Late Preterm and Term Neonates: A Cross-Sectional Study.

ABSTRACT

Background: Neonatal hyperbilirubinemia is one of the most common clinical conditions during the first week of life, affecting nearly 60% of term and 80% of preterm neonates. Late preterm neonates are at greater risk because of hepatic immaturity and reduced bilirubin-binding capacity. Early identification of newborns at risk allows timely monitoring and intervention. Umbilical cord serum albumin, a simple and inexpensive test available at birth, may serve as an early predictor of significant neonatal hyperbilirubinemia.

Methods: This hospital-based cross-sectional study included 95 late preterm and term neonates (gestational age ≥34 weeks). Umbilical cord blood was collected at birth for serum albumin estimation. Neonates were categorized into three groups based on cord serum albumin levels: ≤2.8 g/dL, 2.9–3.3 g/dL, and ≥3.4 g/dL. All neonates were followed for 72–96 hours, and serum bilirubin was measured. Phototherapy was initiated according to the 2022 American Academy of Pediatrics guidelines. The association between cord serum albumin and phototherapy requirement was analysed using the Chi-square test.

Results: Lower cord serum albumin levels were significantly associated with an increased requirement for phototherapy in both late preterm (p=0.0007) and term neonates (p=0.005). Among late preterm neonates, 79% of those with cord serum albumin ≤2.8 g/dL required phototherapy compared with 57% and 12% in the 2.9–3.3 g/dL and ≥3.4 g/dL groups, respectively. Among term neonates, the corresponding proportions were 64%, 46%, and 7%. Birth weight showed a significant association with phototherapy requirement only among term neonates (p=0.039), whereas gender and mode of delivery were not significantly associated.

Conclusions: Umbilical cord serum albumin is a simple, reliable, and cost-effective predictor of significant neonatal hyperbilirubinemia requiring phototherapy in both late preterm and term neonates. Routine estimation at birth may help identify newborns who require closer bilirubin surveillance and facilitate timely intervention, particularly in settings practicing early postnatal discharge.

Keywords: Umbilical cord serum albumin, neonatal hyperbilirubinemia, late preterm neonates, term neonates, phototherapy, predictor.

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common clinical conditions encountered during the first week of life, affecting nearly 60% of term and 80% of preterm newborns. Total bilirubin level peaks to 12.9 mg/dL in 6.1% of term newborns and to 15 mg/dL in 3% of normal term infants.[1]

Albumin is synthesized in the liver and serves as the principal carrier protein for unconjugated bilirubin. By binding bilirubin, it facilitates its transport to the liver for conjugation and reduces bilirubin toxicity by limiting the amount of free bilirubin available for tissue deposition. However, excessively strong albumin–bilirubin binding may delay hepatic uptake of unconjugated bilirubin, thereby reducing its clearance from the circulation.[2,3.] Reduced albumin synthesis decreases its bilirubin-binding and transport capacity, thereby increasing the risk of unconjugated hyperbilirubinemia, particularly in preterm neonates.[4]

Although the fetal liver is capable of producing albumin, preterm infants generally have lower serum albumin concentrations than term neonates because of hepatic immaturity.[5]Hyperbilirubinemia in preterm neonates is more common, severe, and prolonged than term neonates due to shorter RBC life span, liver, and gastrointestinal immaturity.[6]

Early discharge of the healthy term newborns is a common practice due to medical reasons like prevention of nosocomial infections, economic constraints and social reasons. There are many cases of bilirubin induced brain damage in healthy term infants even without hemolysis and its sequelae is dangerous as it results in cerebral-palsy, sensorineural hearing loss and mental retardation [7]. If the newborns at risk of developing hyperbilirubinemia are identified at the time of delivery, phototherapy can be initiated early more effectively, hence reducing bilirubin induced toxicity and its complications [8].

Present study aims at estimating cord albumin at birth to identify preterm and term infants at risk of developing neonatal hyperbilirubinemia and hence preventing associated complications

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Department of Paediatrics, Akash Institute of Medical Sciences and Research Centre, Bengaluru, over a period of 18 months from March 2024 to September 2025 after obtaining approval from the Institutional Ethics Committee. A total of 95 late preterm and term neonates (gestational age ≥34 weeks) fulfilling the inclusion criteria were enrolled after obtaining written informed consent from their parents.

Neonates with gestational age between 34 and 42 weeks, birth weight ≥2 kg, and an Apgar score ≥7 at one minute were included in the study. Neonates with gestational age <34 weeks, birth weight <2 kg, small for gestational age, Rh incompatibility, suspected neonatal sepsis, birth asphyxia, respiratory distress, meconium aspiration syndrome, instrumental delivery, neonatal jaundice within the first 24 hours of life, congenital malformations, infants born to diabetic mothers, and those with an Apgar score <7 at one minute were excluded.

Maternal and neonatal demographic details were collected using a structured proforma. Gestational age was assessed using the New Ballard Score and correlated with the last menstrual period. Umbilical cord blood (2 mL) was collected aseptically immediately after birth and analysed for cord serum albumin using an automated analyser. Based on cord serum albumin concentration, neonates were categorized into three groups: ≤2.8 g/dL, 2.9–3.3 g/dL, and ≥3.4 g/dL. All enrolled neonates were followed clinically for 72–96 hours. Venous blood samples were collected between the third and fourth day of life for estimation of total serum bilirubin, direct bilirubin, and blood grouping. Jaundice was assessed clinically using

Kramer's dermal scale[9,] and phototherapy was initiated according to the American Academy of Pediatrics guidelines[10]whenever indicated.

The primary outcome of the study was to assess the association between cord serum albumin and development of neonatal hyperbilirubinemia requiring interventions like phototherapy in late pre term and term neonates .

Data were entered into Microsoft Excel and analysed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were expressed as frequencies and percentages. Associations between categorical variables were analysed using the Chi-square test. A *p* value of <0.05 was considered statistically significant.

RESULTS

Table 1. Baseline characteristics of the study population (n=95)

VARIABLES	Late preterm (n=45)	Term (n=50)	Total (n=95)
Gender			
Male	23 (51.1)	22 (44.0)	45 (47.4)
Female	22 (48.9)	28 (56.0)	50 (52.6)
Mode of delivery			
Normal vaginal delivery	21 (46.7)	20 (40.0)	41 (43.2)
Caesarean section,	24 (53.3)	30 (60.0)	54 (56.8)
Birth weight (kg)			
2.0–2.5	21 (46.7)	0	21 (22.1)
2.5–3.0	21 (46.7)	33 (66.0)	54 (56.8)
3.0–3.5	3 (6.6)	17 (34.0)	20 (21.1)
>3.5	0	0	0
Cord serum albumin (g/dL)			
≤2.8	14 (31.1)	11 (22.0)	25 (26.3)
2.9–3.3	14 (31.1)	13 (26.0)	27 (28.4)
≥3.4	17 (37.8)	26 (52.0)	43 (45.3)

Table 2. Association of selected variables with phototherapy requirement among late preterm neonates (n = 45)

Variable	Phototherapy Yes n (%)	Phototherapy No n (%)	*p* value
Birth weight (kg)			
2.0–2.5	10 (47.6)	11 (52.4)	0.89
2.5–3.0	11 (45.8)	13 (54.2)	
>3.0	0	0	
Gender			

Variable	Phototherapy Yes n (%)	Phototherapy No n (%)	*p* value
Male	11 (47.8)	12 (52.2)	0.87
Female	10 (45.5)	12 (54.5)	
Mode of delivery			
LSCS	11(45.8)	13(54.2)	1.0
NVD	10(47.6)	11(52.4)	
Cord serum albumin(g/dL)			
≤2.8	11(79)	3(21)	0.0007
2.9–3.3	8(57)	6(43)	
≥3.4	2(12)	15(88)	

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107 **Table 3. Association of selected variables with phototherapy**
108 **requirement among term neonates (n = 50)**

Variable	Phototherapy Yes n (%)	Phototherapy No n (%)	*p* value
Birth weight (kg)			
2.0–2.5	0	0	
2.5–3.0	12 (35.3)	22 (64.7)	
3.0–3.5	3 (18.8)	13 (81.2)	**0.039**
>3.5	0	0	
Gender			
Male	6 (27.3)	16 (72.7)	
Female	9 (32.1)	19 (67.9)	0.71
Mode of delivery			
LSCS	7(23.3)	23(76.7)	0.345
NVD	8(40)	12(60)	
Cord serum albumin(g/dL)			
<≤2.8	7(64)	4(36)	0.005
2.9-3.3	6(46)	7(54)	
≥3.4	2(7)	24(93)	

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111 **DISCUSSION**

Neonatal hyperbilirubinemia remains one of the most common clinical conditions encountered during the neonatal period and is a leading cause of hospital readmission during the first week of life. Early identification of newborns at risk is essential for timely intervention and prevention of bilirubin-induced neurological complications. The present study was undertaken to evaluate the usefulness of umbilical cord serum albumin estimation at birth as an early predictor of neonatal hyperbilirubinemia requiring phototherapy among term and late preterm neonates. The findings demonstrated a significant association between lower cord serum albumin levels and the subsequent requirement for phototherapy in both term and late preterm neonates, suggesting that cord serum albumin may serve as a simple, inexpensive and reliable screening tool for early risk stratification.

In the present study, birth weight showed a statistically significant association with phototherapy requirement among term neonates (p=0.039), whereas no significant association was observed among late preterm neonates (p=0.89). The influence of birth weight on neonatal jaundice has been inconsistently reported in previous studies. Aiyappa et al. demonstrated a significant relationship between lower birth weight and low cord serum albumin levels, suggesting that infants with lower birth weight are more likely to develop hyperbilirubinemia requiring treatment.[11]In contrast, Mishra et al. and Chandan et al. did not observe birth weight as an independent predictor of neonatal hyperbilirubinemia after excluding high-risk neonates.[5],[6] The difference may be explained by variations in study population, inclusion criteria and gestational age distribution.

In the present study, gender was not significantly associated with the requirement for phototherapy in either late preterm (p=0.87) or term neonates (p=0.71). Similarly, mode of delivery did not demonstrate a statistically significant association with the development of neonatal hyperbilirubinemia in either group. These findings are consistent with those reported by **Reshad et al.**[12]and **Trivedi et al.**[3] who also observed that neonatal sex and mode of delivery had no significant influence on the occurrence of significant neonatal jaundice. These variables therefore appear to have limited predictive value for identifying newborns at risk of hyperbilirubinemia.

In the present study, the incidence of phototherapy progressively decreased with increasing cord serum albumin levels in both term and late preterm neonates. Among term neonates, **64%** of newborns with cord serum albumin ≤2.8 g/dL required phototherapy, compared to **46%** with cord serum albumin 2.9–3.3 g/dL and only **7%** with cord serum albumin ≥3.4 g/dL. Similarly, among late preterm neonates, 79**%** of newborns with cord serum albumin ≤2.8 g/dL required phototherapy, compared to 57**%** in the 2.9–3.3 g/dL group and **12%** in those with cord serum albumin ≥3.4 g/dL. This association was statistically significant in both groups, indicating that lower cord serum albumin levels are associated with a greater risk of developing significant neonatal hyperbilirubinemia requiring phototherapy.

These findings are consistent with those reported by Mishra et al., who observed that 95% of neonates with cord serum albumin ≤2.8 g/dL developed significant neonatal hyperbilirubinemia, whereas none of the neonates with cord serum albumin ≥3.4 g/dL required treatment.[8] Trivedi et al. reported that 58.5% of neonates who developed hyperbilirubinemia had cord serum albumin levels <2.8 g/dL, while only 28.8% had albumin

levels between 2.8 and 3.5 g/dL, concluding that cord serum albumin <2.8 g/dL is an important risk indicator for neonatal hyperbilirubinemia.[3] Similarly, Reshad et al. studied 150 term and preterm neonates and demonstrated that 61.2% of term and 80.5% of preterm neonates requiring phototherapy had cord serum albumin ≤2.8 g/dL, while none of the preterm neonates with cord serum albumin ≥3.4 g/dL developed significant hyperbilirubinemia, confirming that lower cord serum albumin is a reliable predictor of neonatal hyperbilirubinemia.[12] Similar observations have also been reported by Aiyappa et al. and Chandan et al., further supporting the role of cord serum albumin as an effective early screening marker for neonatal hyperbilirubinemia.[11,13]

Thus, the CSA level appears to have a predictive value in NH. Thisstudy indicates that a CSAlevel of 2.8 g/dl can be considered as afactor for the subsequent development of significant jaundice and alevel of _3.4 g/dl is safe for early discharge in the absence of otherrisk factors.

CONCLUSION

Umbilical cord serum albumin is a simple, reliable, and cost-effective predictor of neonatal hyperbilirubinemia requiring phototherapy in both term and late preterm neonates. Newborns with lower cord serum albumin concentrations are at significantly higher risk of developing clinically significant jaundice and therefore warrant closer bilirubin monitoring. Routine estimation of cord serum albumin at birth may aid in early risk stratification, facilitate timely intervention, and reduce bilirubin-related morbidity, especially in centres practicing early postnatal discharge.

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