Original Article

Cord Blood Albumin as a Predictor of Neonatal Jaundice

AI Aasam, BM Hasan, RA Jalil[1], JM Hashim, AJ Nasrawi

Department of Pediatrics, University of Kufa, College of Medicine, [1]Al Najaf Health Directorate, Najaf, Iraq

ABSTRACT

Background and Aim: Bilirubin can have a toxic effect on the brain, so newborns must be carefully checked to identify those who may develop significant hyperbilirubinemia and bilirubin encephalopathy (kernicterus). The study aimed to determine if cord blood albumin could be utilized to predict the onset of significant newborn jaundice in healthy-term babies. **Patients and Methods:** A cohort study was carried out in AL-Zahraa teaching hospital in AL-Najaf city during the period from January 1 to November 1, 2020. A randomized 100 full-term healthy neonates were enrolled. A blood sample was drawn by milking the cord and sent for serum albumin estimation. Patients were then followed up on the third and fifth days of life for total serum bilirubin (TSB). **Results:** Out of 100 healthy-term neonates that were included in this study, 60 of them had low cord blood albumin (<2.8 g/dl), and 40 of them had normal cord blood albumin (≥2.8 g/dl) with an age range of 1–5 days. There is a statistically significant difference between low cord blood albumin and significant neonatal jaundice on the third day with a 5 times more risk of developing significant jaundice than neonates with normal cord blood albumin. **Conclusion:** Cord blood albumin levels are sensitive to predicting subsequent neonatal jaundice in the healthy term newborn.

KEYWORDS: *Albumin, cord blood, jaundice, neonate*

INTRODUCTION

Bilirubin in clinical practice

The outcome of hemoglobin breakdown is bilirubin. It is an endogenous molecule that can be harmful, especially to the developing brain. Unconjugated bilirubin (UCB) has some positive properties, including anti-oxidant action.[1] Bilirubin production can be boosted by excessively high peripheral hemoglobin breakdown, known as hemolysis, or dyserythropoiesis.[2]

Albumin aids bilirubin transit and elimination in the liver. Low levels of serum albumin reduce bilirubin elimination, resulting in severe hyperbilirubinemia. There is little research on cord blood albumin as a predictor of neonatal jaundice severity.[3] When serum UCB levels exceed 20 mg/dl, neurotoxicity can develop, but it can also happen at lower levels. UCB is tightly bound to albumin, which aids its preservation in the plasma. When the ratios of UCB to albumin increase, the amount of non-albumin bound or free UCB that enters the cells increases and causes toxicity.[4]

According to the American Academy of Pediatrics, each newborn who is discharged home should have a follow-up appointment within 48 to 72 h for a thorough examination.[5] These babies may develop jaundice, which may go unnoticed unless they are thoroughly checked and followed up. The indicators that may predict jaundice provide an appealing way to identify babies who are at risk of neonatal hyperbilirubinemia.[6] Hyperbilirubinemia is one of the most common reasons for newborn readmission.[7,8] The role of serum albumin had been recognized in the maintenance of good health, and the association of decreased its level with increased risk of morbidity and mortality.[9]

This research aims to explore if cord blood albumin can be utilized to predict the development of

Address for correspondence: Prof. AJ Nasrawi,
Faculty of Medicine, College of Medicine, University of Kufa, Iraq.
E-mail: alaaj.nasrawi@uokufa.edu.iq

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_170_22

significant neonatal hyperbilirubinemia that necessitates phototherapy or exchange transfusions.

PATIENTS AND METHODS

This cohort study was conducted in AL-Zahraa teaching hospital in AL-Najaf city from January 1 to November 1, 2020. The subjects consist of 100 full-term, healthy neonates. The follow-up was within the first 5 days of life. Exclusion criteria included neonatal sepsis, birth asphyxia, instrumental delivery (forceps or vacuum), respiratory distress, meconium-stained amniotic fluid, neonatal jaundice within 24 h of life, Rhesus (Rh) and (A, B & O blood group) incompatibility, and family history of jaundice. Data were collected using a pre-constructed data collection form formulated for this study's purpose. The data collected included name, gender, gestational age, body weight, Apgar score, laboratory results of cord blood albumin on the first day of life, and TSB (total serum bilirubin) on the third and fifth day of life. The gestational age was assessed by using the Ballard score.

Neonatal jaundice higher than 12 mg/dl was regarded as significant.

The data was analyzed by SPSS from IBM version 21; significant was defined as a *P* value of less than 0.05. Finally, all of the results were organized into tables, each with its explanation.

The study was approved by the ethical committee at the University of Kufa, Faculty of Medicine. Verbal consent was taken from each neonate parent before they were included in the study.
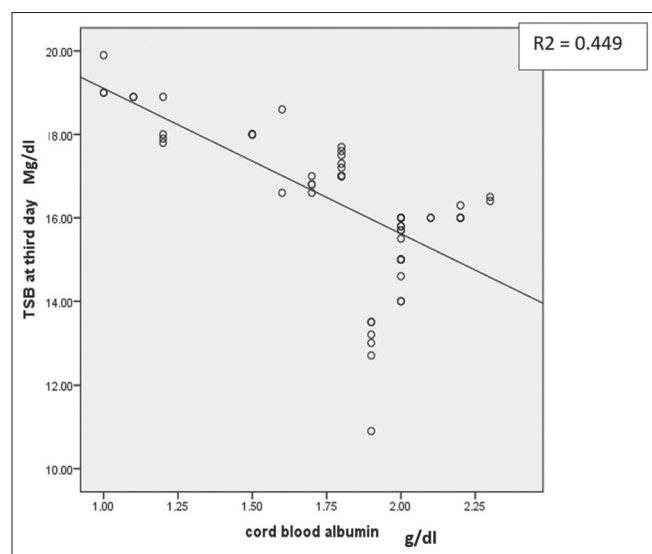
RESULTS

This study consists of 100 healthy term neonates, 60 of them had low cord blood albumin (<2.8 g/dl), and 40 of them had normal cord blood albumin (≥2.8 g/dl), with follow-up by serial estimation of the TSB starting from first to the fifth day of age their demographic charasterisctics (gender, mode of delivery, gestational age, birth weight and APGAR score) have been described in Tables 1 and 2. The percentage of neonates who developed significant jaundice that required treatment among those with low cord blood albumin was 66.6%,

Table 1: The relationship between gender, cord blood albumin, and mode of delivery

Serum albumin	Hypoalbuminemia *n* (%)	Normal *n* (%)	Total	*P*
Gender				
Male	30 (50%)	25 (62.5%)	55	0.2
Female	30 (50%)	15 (37.5%)	45	
Mode of delivery				
Normal	32 (53.3%)	25 (62.5%)	57	0.4
C/S	28 (46.7%)	15 (37.5%)	43	
Total	60	40	100	

Table 2: Association of birth weight, gestational age, APGAR score, and cord blood albumin (CBA)

Cord blood albumin	Mean	SD	*P*
Gestational age (weeks)			
Hypoalbuminemia	37.6	1.061	0.1
Normal albumin	73.93	0.944	
Birth weight (kg)			
Hypoalbuminemia	3.45	0.477	0.2
Normal albumin	3.34	0.437	
APGAR score (0-10)			
Hypoalbuminemia	8.87	0.769	0.4
Normal albumin	8.73	0.784	

Figure 1: Relationship between cord blood albumin and total serum bilirubin on the third day of life (which was a significant negative correlation)
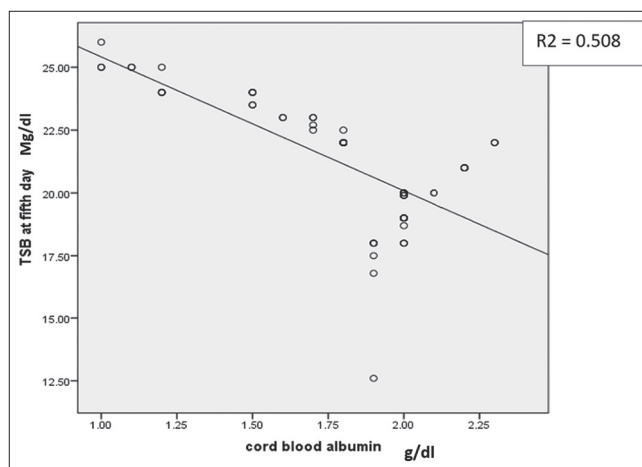

Figure 2: Relationship between cord blood albumin and total serum bilirubin on the fifth day of life

Table 3: Comparison between our study and four other studies about the percentage of significant jaundice in normal and low cord blood albumin

Study	Percentage of significant jaundice	
	Cord blood albumin <2.8 g/dl	Cord blood albumin >2.8 g/dl
Sahu *et al.* (2011)	82.35%	40%
Sharawat IK, *et al.* (2016)	95.5%	79.4%
Trivedi *et al.* (2013)	86.66%	20%
Bangladesh Zakia Nahar *et al.* (2009)	86%	20%
Our study	66.6%	12%

and 12% among those with normal cord blood albumin [Table 3]. There is a statistically significant association between low cord blood albumin and significant neonatal jaundice on the third day, with a 5 times more risk of developing significant jaundice than neonates with normal cord blood albumin [Figures 1 and 2].

DISCUSSION

According to the present study, we grouped our subjects according to their serum cord blood albumin levels less than 2.8 g/dl and 2.8 g/dl or more; 66.6% of babies with cord blood albumin <2.8 g/dl developed significant hyperbilirubinemia, all of them required phototherapy and 10% required exchange transfusion. In the group with cord blood albumin >2.8 g/dl, a lesser percentage (12.5%) of babies developed significant hyperbilirubinemia and they were all treated with phototherapy. In a study in India (Suchanda Sahu, *et al.*), 2011,[10] 82.35% of babies with cord blood albumin <2.8 g/dl developed significant hyperbilirubinemia, all of them required exchange transfusion, and 40% of the group with cord blood albumin between 2.8 and 3.3 g/dl developed significant hyperbilirubinemia and they were all treated with phototherapy. In another study in India (Sharawat IK, *et al.*), 2016,[11] 95.5% of neonates with low blood albumin <2.8 g/dl developed jaundice; of them, 81.8% required phototherapy, and 9.1% needed exchange transfusion. A 79.4% of the neonate with cord blood albumin >2.8 g/dl developed jaundice that required phototherapy.

In a study done by Trivedi *et al.* 2013,[12] 86.66% of neonates with cord blood albumin <2.8 g/dl developed jaundice, and 20% of neonates with cord blood albumin >2.8 g/dl developed jaundice similar to an above study in Bangladesh (Zakia Nahar MD, *et al.*, 2009)[13]; 86% of the neonate with cord blood albumin <2.8 g/dl developed jaundice and 20% of neonates with cord blood >2.8 g/dl developed jaundice.

When we compare our study with the other studies above, we found that the percentage of significant neonatal jaundice in the low cord blood albumin group was less than that found in these comparative studies.

The difference in the percentage may be related to the characteristics of collected samples including sample size and method of collection.

According to Aiyappa *et al.*,[14] the sensitivity of cord albumin in detecting hyperbilirubinemia in newborns was examined and found to be 71.8%, while specificity was found to be 65.1%. The positive predictive value was found to be 38.9% and the negative predictive value was found to be 88.2%. The accuracy rate was 67.3%.

Several assays were investigated to see if they could predict hyperbilirubinemia in healthy full-term babies. The cord blood bilirubin level was utilized by Buam *et al.*[15] to predict later neonatal hyperbilirubinemia in healthy-term infants who needed phototherapy. According to this study, the probability that a neonate with cord bilirubin higher than 3 mg/dl would later develop hyperbilirubinemia (positive predictive values) was 66%. The negative predictive value of the cord bilirubin lower or equal to 3 mg/dl was 100%. The bilirubin/albumin ratio (B/A) may provide a better estimate of free bilirubin (Bf), according to Khairy *et al.*,[16] because it contains two of the three components that determine Bf (TSB, albumin, and the albumin binding affinity).

CONCLUSION

According to the findings of the current study, serum cord blood albumin is an excellent predictor of hyperbilirubinemia and early jaundice evaluation, particularly in underdeveloped countries where regular follow-up is difficult.

Recommendation

To avoid the hazardous implications of neonatal hyperbilirubinemia, such as kernicterus, cord blood bilirubin and cord blood albumin estimates should be conducted for all healthy term neonates who are delivered in an institution.

Another large study is indicated to investigate the sensitivity of the bilirubin/albumin ratio (B/A) as a predictor of significant hyperbilirubinemia.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Tiribelli C, Ostrow JD. The molecular basis of bilirubin encephalopathy and toxicity: Report of an EASL single topic conference, Trieste, Italy, 1–2 October 2004. J Hepatol 2015;43:156-66.
2. Wickramasinghe SN, Wood WG. Advances in the understanding of congenital dyserythropoietic anemias. Br J Haematol 2005;131:431-46.
3. Bhutani VK, Johnson-Hamerman L. The clinical syndrome of bilirubin-induced neurologic dysfunction. Semin Fetal Neonatal Med 2015;20:6-13.
4. Singh A, Koritala T, Jialal I. Unconjugated Hyperbilirubinemia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549796/. [Updated 2022 Apr 02].
5. Gazzin, S, Strazielle N, Tiribelli C, Ghersi-Egea JF. Transport and metabolism at blood-brain interfaces and in neural cells: Relevance to bilirubin-induced encephalopathy. Front Pharmacol 2012;3:89.
6. Shapiro SM, Bhutani VK, Johnson L. Hyperbilirubinemia and kernicterus. Clin Perinatol 2006;33:387-410.
7. Hulzebos CV, van Imhoff DE, Bos AF, Ahlfors CE, Verkade HJ, Dijk PH. The usefulness of the bilirubin/albumin ratio for predicting bilirubin-induced neurotoxicity in premature infants. Arch Dis Child Fetal Neonatal Ed 2008;93:F384-8.
8. Mhaske S, Bulsara L, Akolkar N, Kothari R. Cord blood albumin as a predictor of neonatal jaundice. Indian J Matern Fetal Neonatal Med 2016;3:69-71.
9. Doumas BT, Peters T. Serum and urine albumin: A progress report on their measurement and clinical significance. Clin Chim Acta 1997;258:3-20.
10. Sahu S, Rebecca A, John J, Mathew AA, George AS. Cord blood albumin as a predictor of neonatal jaundice. Int J Biol Med Res 2011;2:436-8.
11. Sharawat IK, Singh J, Dawman L, Singh A. Evaluation of risk factors associated with neonatal jaundice. J Clin Diagn Res 2016;10:SC10-3.
12. Trivedi DJ, Markande DM, Vidya BU, Bhat M, Hegde PR. Cord serum bilirubin and albumin in neonatal hyperbilirubinemia. Int J Int Sci Inn Tech Sec. 2013;2:39-42.
13. Nahar Z, Shahidullah M, Mannan A, Dey SK, Mitra U, Selimuzzaman S. The value of umbilical cord blood bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy newborn. Bangladesh J Child Health 1970;33:50-4.
14. Aiyappa GKC, Shriyan A, Raj B. Cord blood albumin as a predictor of neonatal hyperbilirubinemia in healthy neonates. Int J Contemp Pediatr2017;4:503-6.
15. Buam HB. Evaluation of critical cord blood bilirubin level as a predictor of significant hyperbilirubinemia in term newborns. J Med Sci Clin Res 2019;7:601-7.
16. Khairy MA, Abuelhamd WA, Elhawary IM, Mahmoud Nabayel AS. Early predictors of neonatal hyperbilirubinemia in the full-term newborn. Pediatr Neonatol 2019;60:285-90.