



**TO STUDY CORD BLOOD BILIRUBIN, ALBUMIN AND BILIRUBIN ALBUMIN RATIO (BAR) IN PREDICTING HYPERBILIRUBINEMIA AMONG THE NEWBORNS IN TERTIARY CARE HOSPITAL**

**Madhulika C.<sup>1</sup> and M. Mathivanan<sup>2\*</sup>**

<sup>1</sup>Post Graduate, Department of Paediatrics, Aarupadai Veedu Medical College and Hospital, Puducherry.

<sup>2</sup>Professor, Head of the Department, Department of Paediatrics, Aarupadai Veedu Medical College and Hospital, Puducherry.

**\*Corresponding Author: Dr. M. Mathivanan**

Professor, Head of the Department, Department of Paediatrics, Aarupadai Veedu Medical College and Hospital, Puducherry.

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**ABSTRACT**

**Background:** Hyperbilirubinemia remains an important neonatal condition. Acute bilirubin encephalopathy, often known as kernicterus, is a serious bilirubin toxicity that causes severe morbidity and mortality. The aim of the study is to assess the value of cord blood bilirubin, albumin and bilirubin albumin ratio (BAR) in predicting hyperbilirubinemia. **Methodology:** This is a prospective cohort study conducted over a period of 18 months at Paediatric department of AVMC hospital among all the deliveries. All inborn born of  $\geq 35$  weeks of pregnancy were included in the study. Newborn with conditions like direct hyperbilirubinemia, and significant congenital anomalies were excluded from this study. The cord blood and blood samples were collected and analysed for bilirubin, albumin and bilirubin-albumin ratio among them and compared between the samples in predicting the hyperbilirubinemia. Continuous variables were represented as Mean and Standard Deviation, categorical variables as Frequency and percentage, statistical analysis using ROC curve was used to determine the best cut off value in predicting hyperbilirubinemia. **Result:** Total of 250 newborns were included in the study who met the inclusion criteria. The newborns were assessed for the hyperbilirubinemia in them requiring the phototherapy. There was significantly higher mean of cord blood bilirubin total among the patients required phototherapy ( $2.50 \pm 0.88$  mg/dl) compared to patients without hyperbilirubinemia ( $1.98 \pm 0.56$  mg/dl), similarly the BAR was found to be significantly higher in the patients with hyperbilirubinemia requiring the phototherapy ( $0.58 \pm 0.17$ ) compared to the newborn without requiring the phototherapy ( $0.56 \pm 0.23$ ). On statistical correlation of the serum BAR, it was found to be strongly correlated with the cord blood bilirubin, cord blood albumin and with serum total bilirubin. On ROC analysis, the best cut off values of cord blood bilirubin was 1.65 mg/dl with sensitivity of 91.43%, specificity of 60.56% cord blood albumin was 2.9 g/dl with sensitivity of 100%, specificity of 63.75% and cord blood bilirubin-albumin ratio (BAR) was 0.455 with sensitivity of 88.57%, specificity of 62.22%. **Conclusion:** Umbilical cord bilirubin, albumin and BAR are effective tools in predicting the hyperbilirubinemia among the infants requiring the phototherapy which might decide the total hospital stay.

**KEYWORD:** Cord blood bilirubin, Bilirubin-Albumin ratio, Hyperbilirubinemia, Newborn, Phototherapy.

**INTRODUCTION**

The word 'Jaundice' was derived from a Latin word 'Galbinus'. Neonatal jaundice also called Neonatal Hyperbilirubinemia (NNH) remains as one of the most common problem observed in the newborn babies in the first week of life.<sup>[1,2]</sup> 25 – 50 % of all term newborns and a higher percentage of premature infants develop clinical jaundice. 6.1% of well term newborns have a serum bilirubin level  $> 12.9$  mg/dl and only 3% of normal term babies have a serum bilirubin level of greater than 15 mg/dl.<sup>[3]</sup> As the intensity of jaundice increases, there is cephalo-caudal progression of yellow discoloration of skin. The potential toxicity of bilirubin is acute bilirubin encephalopathy or kernicterus, which is associated with

significant morbidity and mortality.<sup>[4,5]</sup> Unconjugated bilirubin has been noted to cross the blood-brain barrier, causing choreo-athetoid cerebral palsy, sensorineural deafness and mental retardation. So it is imperative that pathological hyperbilirubinemia is picked up early and vigorous treatment is initiated. When the newborn stays at the hospital for a 72-hour post-delivery period, the peaking of the physiological jaundice can be observed, thus allowing medical intervention, if necessary. However, in cases of early discharge from the hospital, the newborns may be subjected to re-admission for phototherapy treatment because of high levels of unconjugated bilirubin. According to the American Academy of Pediatrics newborns who are discharged

within 48 hours should have a follow-up visit after 2-3 days to detect significant jaundice and other problems. Through this study we may come to know whether bilirubin, albumin levels with the bilirubin/albumin ratio in cord blood could be a predictor of severity of neonatal hyperbilirubinemia. The present study was conducted to assess the correlation between bilirubin, albumin and bilirubin albumin ratio (BAR) in umbilical cord blood and in predicting hyperbilirubinemia among the newborns.

#### MATERIAL AND METHODS

A prospective cohort study was conducted in the paediatric department of Aarupadai Veedu Medical College and Hospital among the deliveries over a period of 18 months. A total of 250 All inborn – Term and Preterm ( $\geq 35$  weeks) were included in this study after obtaining written and informed consent/assent from parents/participants. Newborn with conditions like direct hyperbilirubinemia, and significant congenital anomalies were excluded from this study. After getting consent, a predesigned pro forma was explained to the mother or the caregiver. Informed consent regarding participation in the study was obtained in the regional language. All details were filled in the pro forma. A sample of 2 ml blood was collected during the delivery from placental end of the cord in a clean, plain vial and tested for bilirubin and albumin. Babies were clinically assessed for age, sex, gestational age, birth weight, day of onset of jaundice, pattern of feeding, fever and thorough clinical

examination of the baby was done to identify to pallor, temperature, icterus, hepatosplenomegaly and extravasation of blood. Newborns were visually assessed for the progression of icterus with the help of Kramer staging.<sup>[6]</sup> Venous blood sample sent for serum bilirubin, albumin at 48 hours. The levels of cord blood bilirubin, albumin and bilirubin albumin ratio, 48 hrs of serum bilirubin, albumin level and the development of neonatal hyperbilirubinemia were correlated. According to these parameters and also their gestational age, day of life, & presence of risk factors, babies were treated with phototherapy and if necessary with an exchange transfusion. All study variables were entered in Microsoft Excel and analyzed statistically. Continuous variables were represented as Mean and Standard Deviation, and categorical variables as Frequency percentage, and Statistical analysis using ROC curve. Mean difference between the variables was analysed using Student-T test. A p-value of  $<0.05$  was considered statistically significant and all the analysis was conducted using SPSS v21 operating on Windows 10.

#### RESULTS

A prospective cohort study was conducted in the paediatric department among all deliveries over a period of 18 months, a total of 250 newborns were included in this study. Among the included, 129 (51.6%) were boys and 121 (48.4%) were girls, with a mean birth weight of  $2.94 \pm 0.42$  kg. Other parameters which were observed are given in Table 1.

**Table 1: Demographic profile among the study population.**

		Frequency	Percent
Gender	Female	121	48.4
	Male	129	51.6
Mode	LSCS	175	70.0
	NVD	75	30.0
Cephalhematoma	No	243	97.2
	Yes	7	2.8
Phototherapy	Yes	70	28.0
	No	180	72.0
Exchange Transfusion	Yes	1	0.4
	No	249	99.6
Total		250	100.0

Out of 250 newborns, 70 (28%) developed hyperbilirubinemia and the newborns developing hyperbilirubinemia were treated with phototherapy as per

protocols and one baby required exchange transfusion. The comparison of cord blood parameters with phototherapy is given in Table 2.

**Table 2: Comparison of cord blood parameters with phototherapy.**

	Phototherapy				t-test (p-value)
	No		Yes		
	Mean	SD	Mean	SD	
Cord blood Bilirubin Total mg/dl	1.98	.56	2.50	.88	0.001**
Cord blood Albumin g/dL	3.	.39	3.63	.38	0.094
BA Ratio	0.56	0.23	0.68	0.17	0.001**
Serum Bilirubin Total mg/dl	9.5420	2.72	13.80	2.59	0.001**
Serum Albumin g/dL	3.77	.57	3.90	.57	0.100

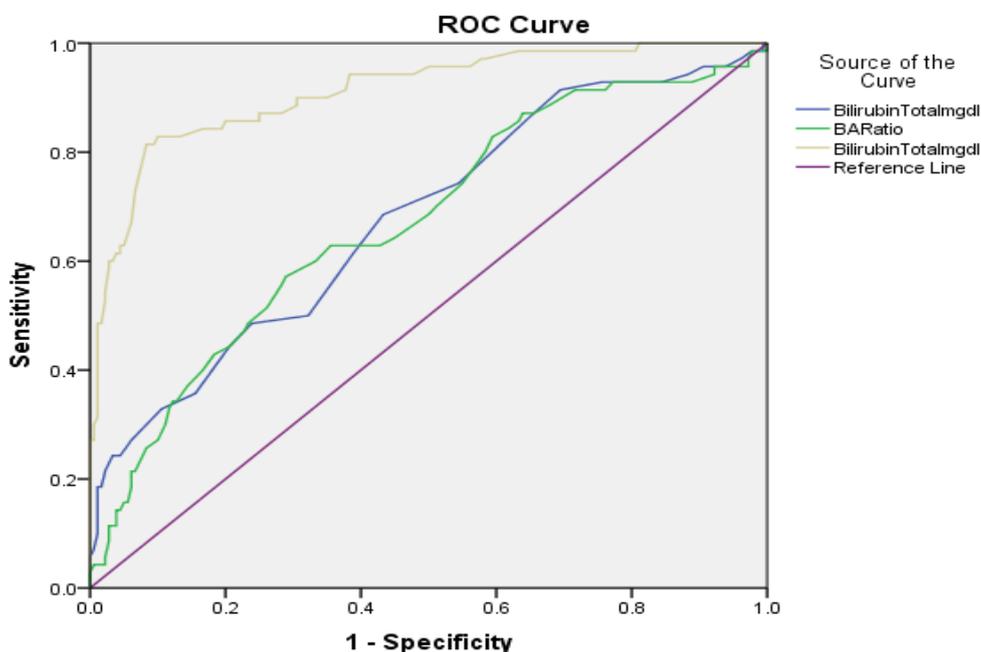
\*p<0.05 was considered statistically significant

Cord blood bilirubin, BAR and serum bilirubin showed a positive correlation with phototherapy and was statistically significant ( $P < 0.05$ ). The diagnostic

characteristics of cord blood parameters in predicting hyperbilirubinemia is shown in Table 3.

**Table 3: Diagnostic characteristics of cord blood parameters in predicting hyperbilirubinemia.**

Phototherapy	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Cord blood bilirubin	1.65mg/dl	91.43	60.56	33.86	90.16	47.60
Cord blood albumin	2.9gm/dl	100	63.75	36.89	100	38.40
Cord BAR	0.455	88.57	62.22	33.70	87.88	48.00



Diagonal segments are produced by ties.

The best cut off value for cord blood bilirubin was 1.65mg/dl as obtained by ROC curve in predicting hyperbilirubinemia, having a 91.43% sensitivity, 60.56% specificity, 33.86% PPV, 90.16% NPV and diagnostic accuracy of 47.60% respectively. The best cut off value for cord blood albumin was 2.9g/dl as obtained by ROC curve, determined to have the highest sensitivity of 100%, specificity of 63.75%, PPV of 36.89% and NPV of 100%. and diagnostic accuracy of 38.40% respectively. The best cut off value for cord blood bilirubin albumin ratio (BAR) was 0.45 as obtained by ROC curve, determined to have a sensitivity of 88.57%, specificity of 62.22%, PPV of 33.7% and NPV of 87.88% with high diagnostic accuracy of 88.0% respectively.

## DISCUSSION

Early detection of hyperbilirubinaemia will benefit in preventing re-hospitalization, and minimising the duration of hospital stay of newborns and mothers in resource-limited countries where the patient-to-bed proportion is significant. As a result, there is an ongoing need for a marker that can be utilised to anticipate the development of severe jaundice in a neonate.

To avoid the devastating repercussions of kernicterus and its adverse effects, public awareness educational campaigns, have significantly decreased over the previous decade. However, a small percentage of babies continue to succumb to the fatal side effects of neonatal hyperbilirubinemia, particularly in developing countries, owing to the lack of follow-up, scarcity of resources, and, most crucially, parental emotional connection. The purpose of this study was to assess and determine the best cut-off values for cord blood bilirubin, albumin, and bilirubin/albumin ratio, in the midst of trying that these values will help in predicting the development of subsequent neonatal jaundice.<sup>[7]</sup>

Total of 250 newborns were included in the study who fulfilled the inclusion criteria. In terms with the present study, studies by El- Mashad *et al.*, and Bhat *et al.*, showed majority of the newborn were males 41% and 56.3% followed by females 34% and 43.67% respectively with birth weight in the range of  $2.87 \pm 0.58$  and 2.6-3.5 kg respectively.<sup>[7,8]</sup>

The newborns were assessed for the hyperbilirubinemia requiring the phototherapy. In our study 28% of newborn required the phototherapy which was higher compared to

the studies done by Baht *et al.*, and Venkatamurthy *et al.*, documented the prevalence of neonatal hyperbilirubinemia requiring the phototherapy was 11% and 11.5% respectively.<sup>[7,9]</sup>

Cord blood parameters were compared with the newborn requiring the phototherapy due to hyperbilirubinemia, there is significant higher mean of cord blood bilirubin and BAR among the patients with hyperbilirubinemia requiring phototherapy (2.50±0.88mg/dl) and (0.58±0.17) respectively which was similar to the study done by Ramteke *et al.*, documented significant correlation between the cord blood bilirubin, and cord BAR in predicting the hyperbilirubinemia requiring the phototherapy with high diagnostic accuracy.<sup>[10]</sup>

The best cut off value in predicting hyperbilirubinemia was cord blood bilirubin of 1.65mg/dl with a sensitivity of 91.43% and specificity of 60.56% was similar to the studies done by EI-Mashad *et al.*, and Taksanda *et al.*, who also documented higher sensitivity.<sup>[8,11]</sup>

The best cut off value in predicting hyperbilirubinemia was cord blood albumin of 2.9g/dl with highest sensitivity of 100%, specificity of 63.75% when compared to other studies by EI-Mashad *et al.*, Bhat *et al.*, and Thakur P *et al.*<sup>[7,8,12]</sup>

The best cut off value in predicting hyperbilirubinemia was cord blood bilirubin albumin ratio (BAR) of 0.45 was found to be 88.57% sensitive, 62.22% specific when compared to studies by Venkatamurthy *et al.*, Ramteke *et al.*, EI-Mashad *et al.* also documented similar sensitivity and specificity.<sup>[8,9,10]</sup>

#### LIMITATION OF THE STUDY

In my study, both Term and Preterm (≥35weeks) were included in the study. A cohort study with larger sample size including all newborn will be useful in giving significant picture about cord blood bilirubin, albumin and BAR in accurate prediction of NNH.

#### CONCLUSION

Umbilical cord bilirubin, albumin and BAR are useful tool in predicting the hyperbilirubinemia among the infants requiring the phototherapy which might decide the total hospital stay. It will also help to detect the infants at low risk of developing the hyperbilirubinemia not requiring the phototherapy for early discharge. This aids in minimizing the hospitalization and prevent the re-admissions of infants with hyperbilirubinemia.

#### REFERENCES

1. Ho NK. 6 - Neonatal jaundice in Asia. *Baillieres Clin Haematol.* 1992; 5(1): 131–42.
2. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. *Br J Hosp Med (Lond)*, 2017; 78(12): 699–704.
3. Camellia R, Cloherty. JP. Neonatal hyperbilirubinemia. In: Cloherty JP, C E,

Eichenwald, Stark AR, editors. *Manual of Neonatal care.* 6th ed. Lippincott Williams & Wilkins, 2008; 181–212.

4. Helal NF, Ghany EAGA, Abuelhamd WA, Alradem AYA. Characteristics and outcome of newborn admitted with acute bilirubin encephalopathy to a tertiary neonatal intensive care unit. *World J Pediatr*, 2019; 15(1): 42–8.
5. Usman F, Diala U, Shapiro S, Le Pichon J-B, Slusher T. Acute bilirubin encephalopathy and its progression to kernicterus: current perspectives. *Res Reports Neonatol*, 2018; 8: 33–44.
6. Neonatal Jaundice. 2012. *Queensl. Matern. Neonatal Clin. Guidel*, 1–35.
7. Bhat JA, Sheikh SA, Ara R. Cord blood bilirubin, albumin, and bilirubin /albumin ratio for predicting subsequent neonatal hyperbilirubinemia. *Paediatr Indones*, 2019; 59(5): 244–51.
8. El Mashad G, El Sayed H, El Shafie W. Cord blood albumin&#8211;bilirubin as a predictor for neonatal hyperbilirubinemia. *Menoufia Med J.*, 2019; 32(3): 1071–7.
9. Venkatamurthy M, Murali SM, Mamatha S. A comparison study: cord serum albumin is compared with cord serum bilirubin as a risk indicator in predicting neonatal jaundice. *J Evol Med Dent Sci.*, 2014; 3: 4017+.
10. Ramteke S, Shrivastava J, Agrawal A, Mishra NR, Saravanan A, Tikkas R. Comparison of cord bilirubin and bilirubin albumin ratio to predict significant hyperbilirubinemia in healthy full-term neonates. *Indian J Child Health*, 2018; 5(2): 108–12.
11. Taksande A, Vilhekar K, Jain M, Zade P, Atkari S, Verkey S. Prediction of development of neonatal hyperbilirubinemia by measuring umbilical cord bilirubin. *Curr Pediatr Res.*, 2005; 9: 5-9.
12. Thakur P, Mangashetty RB, Pawar SD. Cord blood albumin and cord blood bilirubin in early detection of neonatal hyperbilirubinemia. *Int J Sci Res (IJSR)*, 2017; 6: 1327-9.