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BILIRUBIN–ALBUMIN MOLAR RATIO AS A SCREENING TOOL FOR ELEVATED UNBOUND BILIRUBIN IN NEONATES

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ABSTRACT

Neonatal hyperbilirubinemia is a common condition and an important cause of neonatal morbidity. The bilirubin–albumin molar ratio (BAMR) is considered a better indicator of bilirubin toxicity than total serum bilirubin. This study aimed to evaluate the diagnostic performance of BAMR in predicting significant hyperbilirubinemia. A cross-sectional analytical study was conducted among 120 neonates evaluated for jaundice. Serum bilirubin and albumin were measured and BAMR calculated. Correlation was analysed using Pearson's coefficient and diagnostic utility by ROC curve. Mean bilirubin was 11.2 ± 3.1 mg/dL and BAMR 0.34 ± 0.09. A strong correlation was observed ($r = 0.948$, $p < 0.001$). ROC analysis showed excellent performance (AUC = 0.977). At cut-off 0.42, sensitivity was 100% and specificity 92.86%. BAMR is a reliable and sensitive screening tool for neonatal hyperbilirubinemia.

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common clinical conditions in the early neonatal period and remains a significant contributor to neonatal morbidity worldwide. Approximately 60% of term and 80% of preterm neonates develop jaundice during the first week of life, although only a subset progress to clinically significant hyperbilirubinemia requiring intervention.

The major concern associated with hyperbilirubinemia is its potential to cause bilirubin-induced neurological dysfunction (BIND), which may lead to irreversible complications such as kernicterus if not identified and treated promptly. Traditionally, total serum bilirubin has been used as the primary marker for assessing severity; however, emerging evidence suggests that the unbound fraction of bilirubin correlates more closely with neurotoxicity.

Bilirubin is normally bound to serum albumin, limiting its entry into the central nervous system. When binding capacity is exceeded, free bilirubin increases, leading to toxicity. Therefore, the bilirubin–albumin molar ratio (BAMR) has been proposed as a more reliable indicator of bilirubin toxicity.

Recent studies have demonstrated that BAMR correlates well with bilirubin levels and has strong diagnostic value in identifying neonates requiring treatment. Despite this, its use in clinical practice remains limited, particularly in resource-constrained settings. Hence, this study evaluates the diagnostic utility of BAMR in predicting significant hyperbilirubinemia.

Methodology

This cross-sectional analytical study was conducted in the Department of Pediatrics at a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from parents or legal guardians of all enrolled neonates.

The study included neonates admitted to the neonatal unit or evaluated for clinically suspected jaundice during the study period. Inclusion criteria were neonates with clinical jaundice undergoing serum bilirubin evaluation and whose parents provided consent. Neonates with major congenital anomalies, liver disorders, prior exchange transfusion, or conditions affecting serum albumin levels were excluded.

A total of 120 neonates were included based on feasibility. Demographic and clinical data, including gestational age and postnatal age, were recorded. Blood samples were collected aseptically, and total serum bilirubin and albumin levels were measured. The bilirubin–albumin molar ratio (BAMR) was calculated by dividing serum bilirubin by albumin concentration.

Data were analysed using statistical software. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency and percentage. Pearson's correlation coefficient assessed the relationship between BAMR and bilirubin. Receiver operating characteristic (ROC) curve analysis was performed to determine diagnostic accuracy, with $p < 0.05$ considered statistically significant.

RESULTS

Mean gestational age was 37.8 weeks and birth weight 2.82 kg. Mean bilirubin was 11.2 mg/dL and albumin 3.7 g/dL.

Table 1. Baseline Characteristics of the Study Population

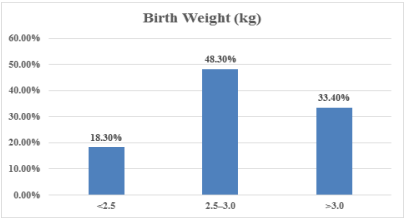
Variable	Mean ± SD	Median (IQR)	Range
Gestational Age (weeks)	37.8 ± 1.6	38 (36–39)	33–40
Birth Weight (kg)	2.82 ± 0.42	2.78 (2.52–3.16)	1.66–4.04
Postnatal Age (days)	3.9 ± 1.8	3 (3–5)	2–11
Total Serum Bilirubin (mg/dL)	11.2 ± 3.1	10.7 (9.0–12.8)	4.2–18.2
Albumin (g/dL)	3.7 ± 0.3	3.7 (3.5–3.9)	2.8–4.5
BAMR (mmol/mol)	0.34 ± 0.09	0.33 (0.27–0.39)	0.11–0.52

Table 2. Distribution of Demographic and Clinical Characteristics

Variable	Category	n (%)
Gestational Age (weeks)	Preterm (<37)	18 (15.0%)
	Term (37–40)	102 (85.0%)
Postnatal Age (days)	≤3 days	68 (56.7%)
	4–6 days	40 (33.3%)
	>6 days	12 (10.0%)
Phototherapy	Yes	35 (29.2%)
	No	85 (70.8%)
Lipid Infusion	Yes	0 (0%)
	No	120 (100%)
Hemolytic Disease	Yes	0 (0%)
	No	120 (100%)

Surgical History	Yes	0 (0%)
	No	120 (100%)

Graph 1. Birth Weight (Kg) Distribution.



BAMR showed strong correlation with bilirubin (r = 0.948). ROC analysis showed AUC of 0.977 indicating excellent diagnostic accuracy.

Table 3. Correlation Between BAMR and Total Serum Bilirubin

Variables Compared	Correlation Coefficient (r)	p-value
BAMR vs Total Serum Bilirubin	0.948	<0.001

Table 4. ROC Curve Analysis of BAMR for Predicting Significant Hyperbilirubinemia (TB ≥ 15 mg/dL)

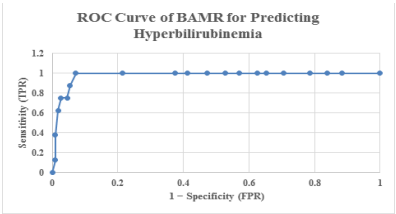
Parameter	Value	p-value
Area Under Curve (AUC)	0.977	<0.001

Optimal cut-off: 0.42
Sensitivity: 100%
Specificity: 92.86%
Diagnostic accuracy: 93.33%.

Table 5. Diagnostic Performance of BAMR at Optimal Cut-off

Parameter	Value
Optimal Cut-off (BAMR)	0.42
Sensitivity (%)	100%
Specificity (%)	92.86%
Positive Predictive Value (PPV) (%)	50.00%
Negative Predictive Value (NPV) (%)	100%
Diagnostic Accuracy (%)	93.33%

Graph 2. ROC Curve Analysis of BAMR



DISCUSSION

The present study demonstrated a strong positive correlation between the bilirubin–albumin molar ratio (BAMR) and total serum bilirubin, suggesting that BAMR reliably reflects the bilirubin burden in neonates. This observation is consistent with earlier studies by Sharma et al. (2020) and Chandel et al. (2020), reinforcing the validity of BAMR as a surrogate marker of bilirubin toxicity. Notably, the receiver operating characteristic (ROC) analysis in the present study revealed excellent diagnostic performance (AUC = 0.977), indicating a near-perfect ability of BAMR to discriminate significant hyperbilirubinemia. Comparable findings have been reported by Kosigi et al. (2024), who demonstrated high sensitivity and specificity of BAMR in identifying neonates requiring intervention.

A key strength of this study is the high sensitivity and negative predictive value of BAMR, underscoring its potential as an effective screening tool for early detection and risk stratification. This is particularly relevant in resource-limited settings, where rapid and reliable markers are essential. Mantry et al. (2024) similarly highlighted the clinical utility of BAMR in early screening of neonatal jaundice. From a pathophysiological perspective, bilirubin neurotoxicity is primarily mediated by the unbound fraction, as described by Ahlfors et al. (2009). Therefore, BAMR, which reflects the balance between bilirubin load and albumin binding capacity, offers a more clinically meaningful assessment than total bilirubin alone.

Despite these strengths, the study has certain limitations, including its single-centre design and relatively small sample size, which may limit generalizability. Additionally, long-term neurodevelopmental outcomes were not assessed. Future large-scale, multicentric studies incorporating longitudinal follow-up are warranted to establish standardized BAMR cut-off values and strengthen its role in clinical practice.

CONCLUSION

BAMR is a simple, reliable, and effective screening tool for neonatal hyperbilirubinemia and should be used in clinical practice.

REFERENCES

1. Watchko JF. Bilirubin-Induced Neurotoxicity in the Preterm Neonate. Clin Perinatol. 2016 Jun;43(2):297-311. doi: 10.1016/j.clp.2016.01.007. Epub 2016 Mar 2. PMID: 27235209.
2. Maisels MJ, McDonagh AF. Phototherapy for neonatal jaundice. N Engl J Med. 2008 Feb 28;358(9):920-8. doi: 10.1056/NEJMct0708376. PMID: 18305267.
3. Ahlfors CE, Amin SB, Parker AE. Unbound bilirubin predicts abnormal automated auditory brainstem response in a diverse newborn population. J Perinatol. 2009 Apr;29(4):305-9. doi: 10.1038/jp.2008.199. Epub 2009 Feb 26. PMID: 19242487; PMCID: PMC4285409.
4. Sgro M, Campbell D, Barozzino T, Shah V. Acute neurological findings in a national cohort of neonates with severe neonatal hyperbilirubinemia. J Perinatol. 2011 Jun;31(6):392-6. doi: 10.1038/jp.2010.137. Epub 2010 Dec 9. PMID: 21151009.
5. Sharma IK, Kumar D, Singh A, Mahmood T. Ratio of cord blood bilirubin and albumin as predictors of neonatal hyperbilirubinaemia. Clin Exp Hepatol. 2020 Dec;6(4):384-388. doi: 10.5114/ceh.2020.102170. Epub 2020 Dec 30. PMID: 33511288; PMCID: PMC7816632.
6. Ganguly A, Bhadesia PJ, Phatak AG, Nimbalkar AS, Nimbalkar SM. Pain profile of premature infants during routine procedures in neonatal intensive care: An observational study. J Family Med Prim Care. 2020 Mar 26;9(3):1517-1521. doi: 10.4103/jfmpc.jfmpc_1033_19. PMID: 32509642; PMCID: PMC7266194.
7. Kosigi A, R. GK. Prediction of Neonatal Hyperbilirubinemia from Cord Blood Bilirubin and Cord Blood Albumin Ratio in Healthy Term Indian Neonates. Journal of Neonatology. 2024;38(1):111-117. doi:10.1177/09732179231193897
8. Weng Y, Zhang J, Chen Z. Effect of non-pharmacological interventions on pain in preterm infants in the neonatal intensive care unit: a network meta-analysis of randomized controlled trials. BMC Pediatr. 2024 Jan 3;24(1):9. doi: 10.1186/s12887-023-04488-y. PMID: 38172771; PMCID: PMC10765718.
9. Chandel, Anuragsingh & Chittal, Ravindra. (2020). Cord Blood Albumin as a Predictor of Significant Hyperbilirubinemia in Term and Preterm Neonates. Asian Journal of Clinical Pediatrics and Neonatology. 8. 01-04. 10.47009/ajcpn.2020.8.1.1.
10. Mantry R, Ghosh S, Agrawal A. Comparison of cord blood bilirubin and bilirubin–albumin ratio in early prediction of neonatal jaundice. Int J Life Sci Biotechnol Pharma Res. 2024;13(4):518–522.
11. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. British Journal of Hospital Medicine. 2017 Dec 2;78(12):699-704.