Research Article

SCISET
www.sciset.com

Research Chronicle in Health Sciences

2024
Vol. 10 No. 1: 101

Mental Health Integration in Primary Healthcare: Challenges and Opportunities

Hossain Sanghi[1]*, Sforza Maggi[2], Sryropoulou Dellis[3], Frank Jones[3,4], Gomberg Maitland[5], Jackson Leyrer[5]

[1]Division of Neonatal-Perinatal Medicine, Department of Pediatrics, Dalhousie University and IWK Health Center, Halifax, Nova Scotia, Canada
[2]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada
[3]Biostatistics Unit, Father Sean O'Sullivan Research Centre, St Joseph's Healthcare Hamilton, Hamilton, Ontario, Canada
[4]Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada
[5]Department of Pediatrics and Anesthesia, McMaster University, Hamilton, Ontario, Canada

Corresponding author:
Hossain Sanghi, Division of Neonatal-Perinatal Medicine, Department of Pediatrics, Dalhousie University and IWK Health Center, Halifax, Nova Scotia, Canada.
E-mail: sanghi.h2@gmail.com

Received: March 03, 2024; **Accepted:** March 20, 2024; **Published:** March 27, 2024

Citation: Sanghi H, et al. Mental Health Integration in Primary Healthcare: Challenges and Opportunities. Research Chronicle in Health Sciences, 2024, Vol. 10 No. 1: 101

Abstract

Background: Neonatal hyperbilirubinemia remains one of the most frequent metabolic conditions encountered in the early neonatal period, with potential progression to bilirubin encephalopathy if not identified and managed promptly. From a pharmacotherapeutic standpoint, serum albumin plays a critical role in modulating bilirubin toxicity through high-affinity binding of unconjugated bilirubin, thereby reducing the free bilirubin fraction available for neurotoxic interactions. Consequently, cord serum albumin concentration at birth has been proposed as a clinically relevant biomarker to stratify the risk of hyperbilirubinemia and guide early therapeutic interventions.

Aim: To evaluate the pharmacotherapeutic relevance of cord serum albumin as a predictive biomarker for neonatal hyperbilirubinemia and to analyze bilirubin kinetics using sequential transcutaneous bilirubin (TCB) monitoring.

Methods: A prospective observational study was conducted in the Department of Paediatrics, SDM College of Medical Sciences and Hospital, Dharwad, from June 2021 to June 2022. Fifty term neonates fulfilling inclusion criteria were enrolled. Cord serum albumin was quantified using the SIEMENS EXL-200 analyzer. Bilirubin progression was assessed using serial TCB measurements recorded at 12, 24, 36, 48, 72, and 96 hours with a Dräger JM-103 jaundice meter. Total serum bilirubin was estimated by the diazo method whenever clinically indicated. Statistical analysis was performed using SPSS version 22.0, with significance set at $p < 0.05$.

Results: Among the 50 neonates, 28 (56%) were male and 22 (44%) female. Cord serum albumin levels were <2.8 g/dL in 15 neonates (30%) and between 2.8–3.3 g/dL in 35 neonates (70%). Nineteen neonates (38%) required phototherapy during the study period. Although lower albumin levels displayed a trend toward higher bilirubin values, no statistically significant association was observed between cord albumin concentration, development of clinically significant jaundice, or phototherapy requirement ($p > 0.05$). Birth weight, however, demonstrated a significant correlation with phototherapy need ($p = 0.003$), highlighting its importance as a complementary risk determinant.

Conclusion: Cord serum albumin demonstrated limited predictive utility for guiding early pharmacological decision-making in neonatal hyperbilirubinemia. In contrast, serial bilirubin monitoring and birth-weight assessment remain robust, clinically meaningful tools for anticipating the need for phototherapy. Integrating biochemical biomarkers with dynamic bilirubin kinetics may enhance precision in neonatal pharmacotherapy and individualized care.

KEYWORDS: Serum albumin; Neonatal hyperbilirubinemia; Pharmacotherapy; Transcutaneous bilirubin; Biomarker; Phototherapy.

INTRODUCTION

Neonatal hyperbilirubinemia (NH) is one of the most prevalent clinical conditions observed during the neonatal period, affecting approximately 60% of term and 80% of preterm infants within the first week of life [1]. The condition primarily results from the accumulation of unconjugated bilirubin in the bloodstream due to the immature hepatic conjugation system and increased red blood cell turnover typical in neonates [2]. When unbound bilirubin crosses the blood–brain barrier, it may exert neurotoxic effects, potentially progressing to acute bilirubin encephalopathy or kernicterus if not promptly identified and treated [3].

Bilirubin is predominantly transported in plasma bound to serum albumin, which serves as its principal carrier and detoxification agent [4]. Reduced albumin concentrations lower bilirubin-binding capacity, increasing the fraction of free bilirubin and thereby elevating the risk of bilirubin-induced neurotoxicity [5]. Thus, albumin levels in the immediate neonatal period play a crucial role in minimizing the risk of bilirubin-induced neurological dysfunction (BIND).

Several investigations have highlighted cord serum albumin as a valuable early biochemical marker for predicting neonatal hyperbilirubinemia [6]. Measuring cord blood albumin at birth offers a simple, non-invasive, and cost-effective strategy for identifying neonates who may be at increased risk for developing significant jaundice, particularly in low-resource settings [7]. Evidence suggests that neonates with cord serum albumin levels ≤2.8 g/dL demonstrate a notably higher likelihood of developing hyperbilirubinemia requiring phototherapy, whereas albumin values ≥3.4 g/dL are generally considered reassuring for early discharge [8].

Additionally, serial transcutaneous bilirubin (TCB) monitoring provides a convenient and reliable method for tracking bilirubin dynamics in neonates. TCB measurements correlate well with total serum bilirubin (TSB) and facilitate early detection of rising bilirubin levels, thereby supporting timely therapeutic decisions [9]. When used together, cord serum albumin assessment and serial bilirubin monitoring form a comprehensive approach for predicting, stratifying, and managing neonatal hyperbilirubinemia [10].

The present study aims to evaluate the correlation between cord serum albumin and neonatal hyperbilirubinemia, and to analyze bilirubin progression through sequential TCB measurements.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Paediatrics, Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Dharwad, from June 2021 to June 2022. Ethical approval was obtained from the Institutional Ethical Committee (Ref: SDMCMS&H/IEC:34:2021), and written informed consent was secured from the parents or legal guardians prior to enrolment [11].

A total of fifty term neonates who met the predefined inclusion and exclusion criteria were recruited. Eligible participants included healthy term newborns of either sex, delivered vaginally or by caesarean section, with an APGAR score greater than seven at one and five minutes. Neonates with Rh incompatibility, instrumental delivery, prematurity, intrauterine growth restriction, hemolytic anemia, congenital anomalies, meconium aspiration, birth asphyxia, or maternal risk factors such as chorioamnionitis, premature rupture of membranes, intrapartum fever, or foul-smelling liquor were excluded to avoid confounding variables.

Immediately after delivery, umbilical cord blood samples were collected under strict aseptic precautions for serum albumin estimation. Approximately 2 mL of cord blood was transported to the biochemistry laboratory, where serum albumin levels were analyzed using the SIEMENS EXL-200 autoanalyzer, with results expressed in grams per deciliter (g/dL). Based on the measured cord serum albumin concentrations, neonates were categorized into three predictive risk groups for developing hyperbilirubinemia: ≤2.8 g/dL (high risk), 2.9–3.3 g/dL (intermediate risk), and ≥3.4 g/dL (low risk) [12]. Total serum bilirubin (TSB) levels were quantified using the diazo method when clinically indicated or prior to initiating phototherapy, and values were expressed in milligrams per deciliter (mg/dL).

Serial transcutaneous bilirubin (TCB) measurements were performed at 12, 24, 36, 48, 72, and 96 hours of life using the Dräger JM-103 jaundice meter (REF Mu19526, No. 32040414). To maintain consistency, all readings were obtained from a single site on the sternum. Before phototherapy initiation, a 2.5 cm diameter photo-opaque patch was placed on a fixed sternal area to enable reliable protected-site measurements. All TCB assessments were conducted by the same trained observer to minimize inter-observer variability, and each final reading represented the mean of three consecutive measurements.

Newborns were monitored daily for the first five days of life for clinical signs of jaundice, feeding adequacy, activity, and hydration status. Infants developing significant hyperbilirubinemia—based on American Academy of Pediatrics (AAP) phototherapy guidelines—received appropriate management and were followed for therapeutic response.

Maternal and neonatal demographic details including age, gestational age, mode of delivery, birth weight, and APGAR scores were documented using a predesigned proforma. All clinical and biochemical data were entered into Microsoft Excel and subsequently analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0. Descriptive statistics were used to summarize baseline characteristics. The Chi-square test was applied to determine associations between categorical variables such as serum albumin levels and phototherapy requirement [13]. The independent t-test was used to compare continuous variables including birth weight, albumin levels, and bilirubin

concentrations. Pearson's correlation coefficient was employed to assess the relationship between cord serum albumin levels and both TSB and TCB values. A p-value <0.05 was considered statistically significant.

RESULTS

A total of fifty term neonates were enrolled in the study, comprising twenty-eight boys (56%) and twenty-two girls (44%), demonstrating a slight male predominance (Table 1). The mode of delivery analysis showed that the majority of infants were born through caesarean section. Among the deliveries, seven (14%) were elective LSCS and twenty-eight (56%) were emergency LSCS, whereas ten (20%) were full-term vaginal deliveries and five (10%) were vacuum-assisted births. Thus, caesarean deliveries accounted for 70% of the total births (Table 2).

Table 1: Gender Distribution of Newborns.

	Frequency(n=50)	Percent
BOY	28	56.0
GIRL	22	44.0
Total	50	100.0

Table 2: Albumin Groups.

	Frequency	Percent
<2.8	15	30.0
2.8 – 3.3	35	70.0
>3.3	0	0.0
Total	50	100.0

Cord serum albumin levels revealed that fifteen neonates (30%) had values below 2.8 g/dL and thirty-five neonates (70%) had concentrations between 2.8 and 3.3 g/dL. None of the newborns exhibited albumin levels ≥3.4 g/dL, indicating that all participants fell within the low to intermediate risk range for hyperbilirubinemia (Table 3).

Table 3: Gender and Phototherapy.

			PHOTOTHERAPY		Total
			YES	NO	
GENDER	BOY	Count	11	17	28
		%	57.9%	54.8%	56.0%
	GIRL	Count	8	14	22
		%	42.1%	45.2%	44.0%
Total		Count	19	31	50
		%	100.0%	100.0%	100.0%

CHI SQUARE = 0.045, P VALUE = 0.833 (NS)

Phototherapy was required in nineteen neonates (38%), while the remaining thirty-one (62%) did not require intervention (Table 4). When phototherapy requirement was assessed by gender, eleven boys (57.9%) and eight girls (42.1%) required treatment [14], but this difference was not statistically significant (χ^2 = 0.045, p = 0.833), suggesting no gender-based influence on phototherapy need (Table 5).

Comparison of phototherapy requirement across albumin groups showed that thirteen neonates (68.4%) in the 2.8–3.3 g/dL group and six (31.6%) in the <2.8 g/dL group required phototherapy. The association was statistically insignificant (χ^2 = 0.036, p = 0.849), indicating that albumin levels at birth did not significantly predict phototherapy requirement in this cohort (Tables 6 and 7).

Table 4: Albumin Group and Phototherapy.

			PHOTOTHERAPY		Total
			YES	NO	
ALBUMIN GROUP	<2.8	Count	6	9	15
		%	31.6%	29.0%	30.0%
	2.8 – 3.3	Count	13	22	35
		%	68.4%	71.0%	70.0%
Total		Count	19	31	50
		%	100.0%	100.0%	100.0%

CHI SQUARE = 0.036, P VALUE = 0.849 (NS)

Table 5: Albumin Group and Jaundice.

			JAUNDICE		Total
			YES	NO	
ALBUMIN GROUP	<2.8	Count	6	9	15
		%	40.0%	25.7%	30.0%
	2.8 – 3.3	Count	9	26	35
		%	60.0%	74.3%	70.0%
Total		Count	15	35	50
		%	100.0%	100.0%	100.0%

CHI SQUARE = 1.020, P VALUE = 0.312 (NS)

Assessment of jaundice occurrence between genders showed that ten boys (66.7%) and five girls (33.3%) developed jaundice, whereas eighteen boys (51.4%) and seventeen girls (48.6%) did not. This difference was not significant (χ^2 = 0.989, p = 0.320), indicating that jaundice incidence was similar across genders. Likewise, evaluation of jaundice incidence across albumin categories revealed that nine neonates (60%) in the 2.8–3.3 g/dL group and six (40%) in the <2.8 g/dL group developed jaundice, with no statistically significant association (χ^2 = 1.020, p = 0.312).

Table 6: Comparison of Birth Weight, Albumin with Phototherapy by T-Test.

VARIABLE	PHOTOTHERAPY YES (N=19)		PHOTOTHERAPY NO (N=31)		P VALUE
	MEAN	SD	MEAN	SD	
BIRTH WEIGHT	2.7584	.39786	3.1490	.43882	.003
ALBUMIN	2.9074	.28724	2.8887	.22749	.800

Tabl 7: Correlation of Mean of Albumin Group and TCB.

VARIABLE	ALBUMIN <2.8 (N=15)		ALBUMIN 2.8-3.3 (N=35)		P VALUE
	MEAN	SD	MEAN	SD	
TCB 12 HRS	4.1033	1.75153	3.8986	1.27722	.645
TCB 24 HRS	7.2800	3.88352	6.1011	2.25371	.183
TCB 36 HRS	9.8480	3.17656	8.7771	3.12524	.275
TCB 48 HRS	12.1373	2.45649	10.7880	3.45923	.178
TCB 72 HRS	11.8407	2.18036	11.3834	2.78975	.575
TCB 96 HRS	9.5287	2.04164	9.5946	2.15069	.920

Mean birth weight analysis showed significant differences between neonates requiring and not requiring phototherapy. Those who required phototherapy had a lower mean birth weight (2.75 kg) compared to those who did not (3.15 kg), and this difference was statistically significant (p = 0.003). However, mean albumin levels did not differ significantly between these groups (p = 0.800), suggesting that birth weight, rather than albumin concentration, had a stronger association with phototherapy requirement.

Similarly, jaundiced neonates had a significantly lower mean birth weight (2.67 kg) compared to non-jaundiced neonates (3.13 kg) (p = 0.001). The difference in mean albumin levels between the two groups was not statistically significant (p = 0.347), indicating that reduced birth weight may predispose neonates to hyperbilirubinemia independent of albumin levels.

Correlation analysis showed a weak negative correlation between birth weight and total serum bilirubin (TSB) (r = –0.2), indicating that lower birth weight was associated with slightly higher

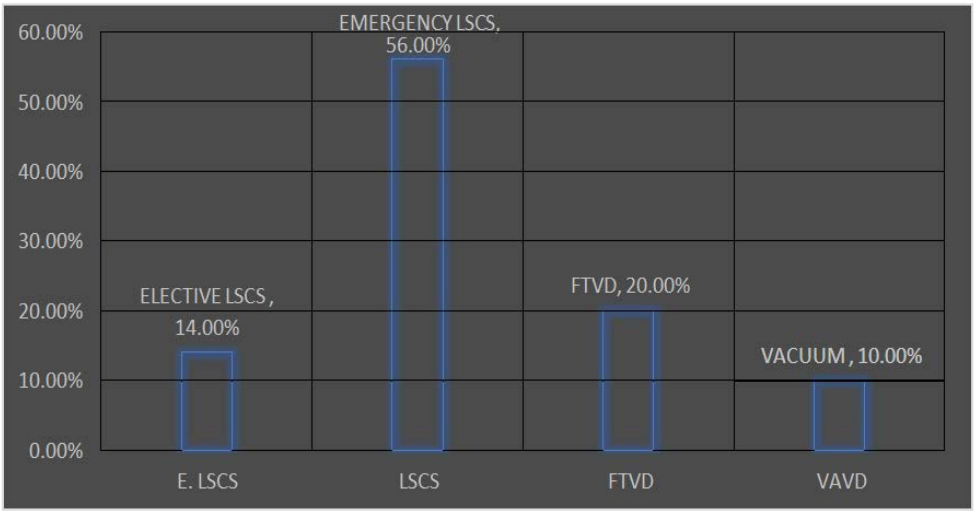


Figure 1: Mode of Delivery.

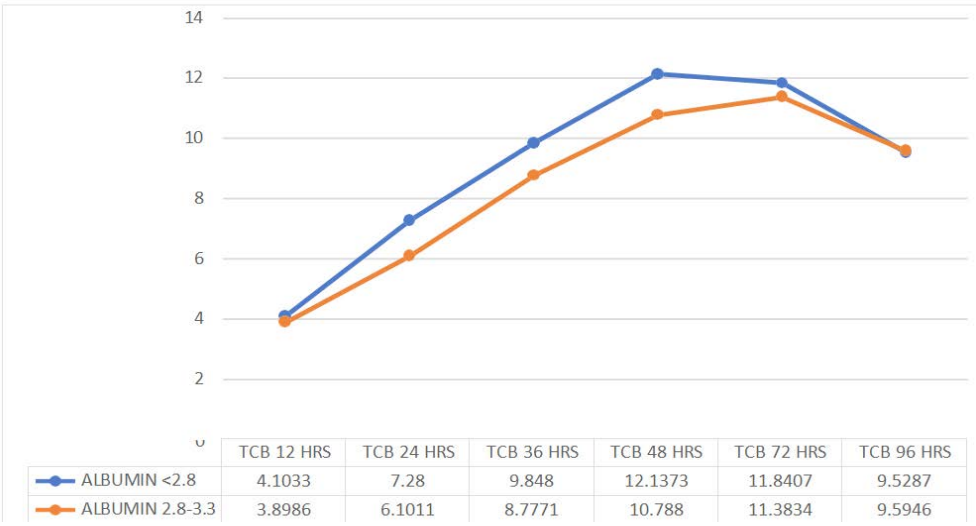


Figure 2: Comparison of Gender and Phototherapy.

bilirubin levels, although the relationship was not strong (Figure 1). The correlation between albumin and TSB was similarly weak (r = –0.1), demonstrating that lower albumin values were only marginally associated with higher bilirubin levels (Figure 2).

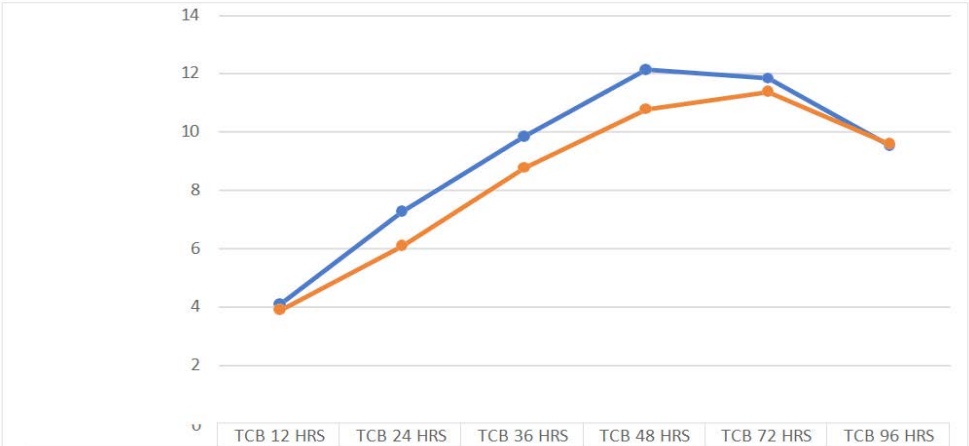
Serial transcutaneous bilirubin (TCB) measurements revealed a progressive rise in mean bilirubin levels up to 48 hours, followed by a steady decline through 96 hours of life. Comparison of mean TCB values between the two albumin groups (<2.8 g/dL and 2.8–3.3 g/dL) at each measurement interval showed no statistically significant differences ($p > 0.05$), indicating similar bilirubin kinetics across albumin strata. At 72 and 96 hours, mean TCB values remained nearly identical between the groups (11.5 mg/dL and 9.5 mg/dL, respectively), reinforcing the limited influence of albumin levels on bilirubin trends (Figure 3).

Receiver Operating Characteristic (ROC) curve analysis demonstrated an area under the curve (AUC) of 0.5, indicating limited diagnostic accuracy of cord serum albumin as a predictor of neonatal hyperbilirubinemia. The optimal predictive cut-off was identified as >2.89 g/dL, yielding a sensitivity of 57%, specificity of 61%, and a negative predictive value of 70.4%, reflecting modest predictive performance (Figure 4).

DISCUSSION

The present investigation assessed whether cord blood serum albumin could serve as a reliable early predictor of neonatal hyperbilirubinemia. Among the 50 neonates enrolled, 38% required phototherapy during the early neonatal period. Although a trend toward higher jaundice incidence was observed among neonates with lower albumin levels (<2.8 g/dL), the association did not reach statistical significance ($p > 0.05$). Furthermore, ROC analysis yielded an AUC of 0.5, suggesting that cord albumin, when used in isolation, has minimal discriminatory value in identifying neonates at risk [15].

These findings show partial agreement with the results of Pathak et al. (2022), who reported that albumin concentrations below 2.8 g/dL increased the likelihood of hyperbilirubinemia and proposed



	TCB 12 HRS	TCB 24 HRS	TCB 36 HRS	TCB 48 HRS	TCB 72 HRS	TCB 96 HRS
ALBUMIN <2.8	4.1033	7.28	9.848	12.1373	11.8407	9.5287
ALBUMIN 2.8-3.3	3.8986	6.1011	8.7771	10.788	11.3834	9.5946

Figure 3: Correlation of Mean of Albumin Group and TCB.

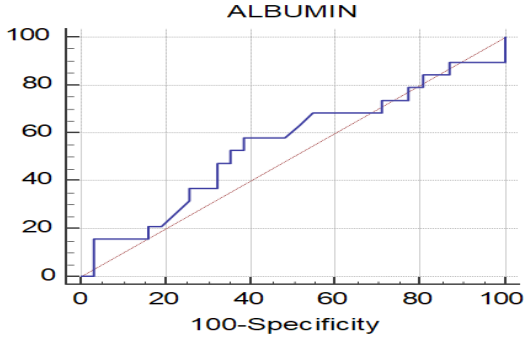


Figure 4: Roc Curve.

≥3.4 g/dL as a safe threshold for early discharge. Mishra and Naidu (2018) similarly documented a strong correlation between low cord albumin (≤2.8 g/dL) and jaundice, with 95% of affected neonates falling within this albumin range. However, the lack of significance in our study may reflect the relatively small sample size and the limited variability in albumin values (2.8–3.3 g/dL), which could restrict the ability to detect meaningful differences [16].

Conversely, our observations align more closely with those of Chandel and Chittal (2020), who reported that although more than half of the neonates with albumin <2.8 g/dL developed jaundice, the strength of association was insufficient to recommend albumin as a standalone predictor. Praveena (2017), however, demonstrated far greater diagnostic accuracy (AUC 0.876; sensitivity 69.4%; specificity 98.2%), indicating that significant inter-study variability exists. Differences in population characteristics, cutoff selection, laboratory methods, and sample size may explain these inconsistencies.

Moderate predictive performance has also been described by Manu Shekhar et al. (2020), who reported a sensitivity of 83% and specificity of 48%, suggesting that albumin may be more valuable as a supportive screening parameter. Bhat et al. (2020) similarly noted that albumin ≤3.3 g/dL was associated with higher risk, while levels above this threshold indicated relative safety.

Notably, our study identified birth weight as a more robust predictor of hyperbilirubinemia than albumin. Neonates who ultimately required phototherapy had significantly lower mean birth weights ($p < 0.05$). This finding corresponds with results from Khairy et al. (2019), who emphasized that both low birth weight and albumin ≤3.0 g/dL increased vulnerability to bilirubin elevation.

Correlation analysis demonstrated weak negative relationships between albumin and bilirubin ($r = –0.1$) as well as between birth weight and bilirubin ($r = –0.2$). This pattern is consistent with Pak et al. (2024), who reported a negative correlation ($r = –0.389$) between albumin concentration and total bilirubin levels, suggesting a physiological but modest association.

Overall, while several previous studies highlight cord serum albumin as a potentially valuable early marker, the present study indicates that its predictive ability is limited when used independently. Perinatal variables such as birth weight, gestational age, and clinical risk factors appear to play complementary and potentially more influential roles. Future research may consider combining cord albumin with parameters such as cord bilirubin or albumin-to-bilirubin ratio to enhance predictive performance.

CONCLUSION

The findings of the present study indicate that cord serum albumin, when considered independently, has limited utility in predicting neonatal hyperbilirubinemia, as no statistically significant association was observed with either the development of jaundice or the need for phototherapy. In contrast, birth weight demonstrated a more meaningful relationship with bilirubin levels, highlighting the multifactorial nature of neonatal jaundice. Although existing literature reports varying degrees of diagnostic accuracy for cord albumin, the inconsistency across studies suggests that it should not be used as a solitary marker. A combined approach incorporating cord albumin with complementary parameters—such as cord bilirubin levels, albumin–bilirubin ratio, and relevant perinatal factors—may provide more reliable early risk stratification. Integrating such multimodal assessments into routine neonatal evaluation could support timely identification of at-risk infants and facilitate prompt clinical intervention to improve neonatal outcomes.

REFERENCES

1. Ullah, S., Rahman, K., & Hedayati, M. (2016). Hyperbilirubinemia in neonates: types, causes, clinical examinations, preventive measures, and treatments. Iranian Journal of Public Health, 45(5), 558–566.
2. Bhutani, V. K., Wong, R. J., & Stevenson, D. K. (2016). Hyperbilirubinemia in preterm neonates. Clinics in Perinatology, 43(2), 215–232.
3. Olusanya, B. O., Kaplan, M., & Hansen, T. W. (2018). Neonatal hyperbilirubinaemia: a global perspective. The Lancet Child & Adolescent Health, 2(8), 610–620.
4. Hegyi, T., & Kleinfeld, A. (2022). Neonatal hyperbilirubinemia and the role of unbound bilirubin. Journal of Maternal-Fetal & Neonatal Medicine, 35(25), 9201–9207.
5. Cayabyab, R., & Ramanathan, R. (2019). High unbound bilirubin for age: a neurotoxin affecting the developing brain. Pediatric Research, 85(2), 183–190.
6. Khairy, M. A., Abuelhamd, W. A., Elhawary, I. M., & Nabayel, A. S. (2019). Early predictors of neonatal hyperbilirubinemia in full-term newborns. Pediatrics & Neonatology, 60(3), 285–290.
7. Bhardwaj, K., Locke, T., Biringer, A., Booth, A., Darling, E. K., Dougan, S., et al. (2017). Newborn bilirubin screening for preventing severe hyperbilirubinemia and encephalopathy: a rapid review. Current Pediatric Reviews, 13(1), 67–90.
8. Mishra, A. K., & Naidu, C. S. (2018). Association of cord serum albumin with neonatal hyperbilirubinemia among term appropriate-for-gestational-age neonates. International Journal of Pediatrics and Adolescent Medicine, 5(4), 142–144.
9. Hulzebos, C. V., Vitek, L., Coda Zabetta, C. D., Dvořák, A., Schenk, P., van der Hagen, E. A., et al. (2021). Diagnostic methods for neonatal hyperbilirubinemia: benefits, limitations, and novel developments. Pediatric Research, 90(2), 277–283.
10. Nagar, G., Vandermeer, B., Campbell, S., & Kumar, M. (2013). Reliability of transcutaneous bilirubin devices in preterm infants: a systematic review. Pediatrics, 132(5), 871–881.

11. Pathak, A., Siddalingesha, R., Prasad, K., Kamal, N., Sinha, A., Ghosh, A., et al. (2022). Association between cord serum albumin levels and significant hyperbilirubinemia requiring intervention. Journal of Family Medicine and Primary Care, 11(7), 2483–2487.

12. Chandel, A. S., & Chittal, R. Y. (2020). Cord blood albumin as a predictor of significant hyperbilirubinemia in term and preterm neonates. Asian Journal of Clinical Pediatrics and Neonatology, 8(1), 1–6.

13. Praveena, A. (2017). Cord blood albumin as a predictor of neonatal hyperbilirubinemia. Journal of Medical Science and Clinical Research, 5(11), 186–190.

14. Shekhar, M., Kumar, V., Bhalke, S., & Goel, A. (2020). Umbilical cord albumin and serum bilirubin as predictors of hyperbilirubinemia in term neonates. International Journal of Contemporary Pediatrics, 7(1), 128–133.

15. Bhat, P., Agarkhedkar, S., & Salunke, S. (2020). Predictive value of umbilical cord blood albumin levels as an indicator of neonatal jaundice in healthy term newborns. Indian Journal of Child Health, 7(2), 65–69.

16. Pak, A., Noreen, A., Malik, F. A., & Razzaq, A. (2024). Cord blood albumin as a predictor of neonatal jaundice. Annals of PIMS–Shaheed Zulfiqar Ali Bhutto Medical University, 19(4), 1028–1033.