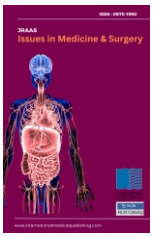
JRAAS
Special Issue in Medicine & Surgery
www.internationalmedicalpublishing.com



Research Article

Section: Paediatrics

Predictive Value of Cord Blood Albumin For Neonatal Hyperbilirubinemia in Term Newborns: A Prospective Study

Dr. Debabrata Debnath[1*], Dr. Manas Kumar Mahapatra[2] & Dr. Joydeep Das[3]

[1]3rd Year Post Graduate Resident, Department of Paediatrics, Jagannath Gupta Institute of Medical Sciences and Hospital

[2]Assistant Professor, Department of Paediatric, Jagannath Gupta Institute of Medical Sciences and Hospital

[3]Professor and Head, Department of Paediatrics, Jagannath Gupta Institute of Medical Sciences and Hospital

HIGHLIGHTS

- Depression is common in stroke survivors.
- Lesion site affects depression severity.
- Stroke duration influences depressive symptoms
- Early diagnosis improves mental health outcomes.
- Targeted therapy helps manage post-stroke depression.

ARTICLE INFO

Handling Editor: Dr. Sandeep Singh

Key Words:
Neonatal Hyperbilirubinemia
Cord blood Albumin
Phototherapy
Neonatal Jaundice
Bilirubin
Early Discharge
Risk Stratification

ABSTRACT

Aim: This study aimed to evaluate the predictive value of cord blood albumin (CBA) levels in assessing the risk of neonatal hyper-bilirubinemia (NNH) in term newborns and determine an optimal CBA threshold for phototherapy (PT) prediction. **Introduction:** Neonatal jaundice affects 60% of term and 80% of preterm infants. Severe cases need timely intervention to prevent kernicterus. Early discharge increases undiagnosed jaundice risk, especially in low-resource settings. CBA - Cord blood Albumin is a potential biomarker for identifying high-risk newborns, enabling early intervention and follow-up planning. **Methods:** This prospective observational study was conducted at Jagannath Gupta Institute of Medical Sciences and Hospital, Kolkata, over 18 months (July 2022 - December 2023). Eighty term newborns meeting inclusion criteria were enrolled. CBA levels were measured at birth, and total serum bilirubin (TSB) was assessed at 72 hours. The requirement for phototherapy was determined using AAP guidelines. Statistical analyses were conducted using SPSS version 26. **Results:** Of the 80 newborns, 13 (16.25%) developed significant jaundice, requiring phototherapy but not exchange transfusion. Newborns were categorized by CBA levels: ≤2.8 g/dL (81. 8% developed jaundice), 2.9–3.3 g/dL (9.3% developed jaundice), and ≥3.4 g/dL (0% developed jaundice). A significant negative correlation ($r = -0.41$, $p < 0.00001$) was found between CBA and TSB levels, confirming that lower CBA levels were associated with higher bilirubin levels. **Conclusion:** CBA ≤2.8 g/dL strongly predicts neonatal jaundice, while CBA ≥3.4 g/dL is protective. CBA measurement at birth serves as a low-cost screening tool for identifying newborns at risk, guiding early discharge and follow-up decisions. Larger studies are needed to establish standardized CBA thresholds for routine screening.

*** Corresponding Author:** Dr. Debabrata Debnath, 3rd Year Post Graduate Resident, Department of Paediatrics, Jagannath Gupta Institute of Medical Sciences and Hospital **E-mail:**debabratadebnath413@gmail.com

Article History: Received 11 January 2025; Received in Revised form 16 February 2025; Accepted 18 February 2025

How To Cite: Debabrata Debnath, Manas Kumar Mahapatra & Joydeep Das. Predictive Value Of Cord Blood Albumin For Neonatal Hyperbilirubinemia In Term Newborns: A Prospective Study. *JRAAS: Special Issue in Medicine & Surgery.*2025;40(1),18-23

INTRODUCTION

Neonatal jaundice, or neonatal hyperbilirubinemia (NNH), is one of the most common clinical conditions affecting newborns, particularly in the first week of life. It is characterized by elevated levels of serum bilirubin, leading to yellow discoloration of the skin, sclera, and mucous membranes. Although physiological jaundice is a normal transitional process due to immature hepatic function and increased red blood cell turnover, some neonates develop pathological jaundice, which requires timely intervention to prevent bilirubin-induced neurological dysfunction (BIND) and kernicterus [1].

The global incidence of neonatal jaundice varies significantly based on genetic, ethnic, and environmental factors. Approximately 60% of term newborns and 80% of preterm infants experience some degree of jaundice within the first postnatal week [2]. In most cases, jaundice is benign and resolves without treatment. However, in about 10–15% of neonates, the serum bilirubin levels rise excessively, necessitating medical interventions such as phototherapy and, in severe cases, exchange transfusion [3]. Failure to detect and manage neonatal jaundice in a timely manner may result in severe complications such as acute bilirubin encephalopathy (ABE) or its chronic form, kernicterus, which leads to permanent neurological impairment, including cerebral palsy, sensorineural hearing loss, and cognitive disabilities [4].

Early hospital discharge practices have contributed to an increased risk of undetected neonatal jaundice, particularly in low-resource settings where routine post-discharge bilirubin monitoring is often inadequate [5]. The American Academy of Pediatrics (AAP) recommends that all newborns discharged within 48 hours of birth should undergo a follow-up evaluation within 48–72 hours to assess bilirubin levels and other risk factors for severe hyperbilirubinemia [6]. However, logistical and socioeconomic constraints often prevent timely follow-up, leading to delays in the diagnosis and management of significant jaundice [7].

Several risk factors have been associated with an increased likelihood of neonatal hyperbilirubinemia, including prematurity, exclusive breastfeeding with inadequate intake, hemolytic diseases such as ABO and Rh incompatibility, glucose-6-phosphate dehydrogenase (G6PD) deficiency, sepsis, cephalohematoma, and maternal diabetes[8]. Among these, the role of serum albumin has gained attention due to its ability to bind free bilirubin in circulation, preventing its toxic effects on the neonatal brain [9]. Albumin acts as a carrier protein for bilirubin, limiting its diffusion across the blood-brain barrier. Hence, low levels of albumin may increase the risk of bilirubin-induced neurotoxicity [10].

Cord blood albumin (CBA) has been proposed as a potential biomarker for predicting the risk of neonatal jaundice in term newborns [11]. The rationale behind this approach is that newborns with lower CBA levels may have a reduced capacity for bilirubin binding, making them more susceptible to develop significant hyperbilirubinemia [12]. Several studies have demonstrated a strong correlation between low CBA levels and increased serum bilirubin levels during the first 72–96 hours of life [13]. A CBA threshold of ≤2.8 g/dL has been associated with a higher risk of requiring phototherapy, while neonates with CBA ≥3.4 g/dL have a very low probability of developing clinically significant jaundice [14].

Despite accumulating evidence supporting the predictive value of CBA, its clinical utility in routine neonatal screening remains under investigation. Many studies have reported variable sensitivity and specificity values for different CBA cutoff levels [15] While some authors suggest that CBA estimation at birth can be used as a reliable screening tool for early risk stratification, others argue that it should be complemented with transcutaneous bilirubin (TcB) measurements or serial serum bilirubin assessments to improve diagnostic accuracy [16].

Given these considerations, this study aims to evaluate the utility of CBA as a predictor of neonatal hyperbilirubinemia in term newborns. By determining an optimal CBA threshold for predicting the need for phototherapy, we seek to establish a simple, cost-effective, and early risk assessment tool that can aid in neonatal jaundice screening. This could be particularly beneficial in resource limited settings, where bilirubin monitoring facilities are scarce, and early discharge is a common practice [17].

MATERIAL AND METHODS

This prospective observational study was conducted over 18 months (July 2022 – December 2023) at the Labour Room, Operation Theatre, and Nursery Ward of Jagannath Gupta Institute of Medical Sciences and Hospital, Kolkata, West Bengal, with ethical approval obtained.

Study Population:

The study enrolled 80 term newborns who met the inclusion criteria: inborn deliveries, gestational age ≥37 weeks, birth weight ≥2.5 kg, Apgar score ≥7 at 1 and 5 minutes, and parental consent. Exclusion criteria included forceps or vacuum-assisted deliveries, Rh/ABO incompatibility, birth asphyxia requiring resuscitation, major congenital anomalies, neonatal sepsis, hypothyroidism, infants of diabetic mothers (IDM), and G6PD deficiency. Data collection involved recording birth details, maternal blood group, and neonatal parameters. Cord blood albumin (CBA) levels were measured at birth using a semi-auto analyzer and newborns were clinically monitored for jaundice over 72–96 hours. Total

serum bilirubin (TSB) levels were measured at 72 hours with treatment decisions for phototherapy (PT) or exchange transfusion (ET) based on AAP guidelines.

Statistical Analyses:

Statistical analyses were performed using SPSS version 26. Categorical variables were expressed as frequencies and percentages, while Chi-square tests, t-tests, and ANOVA were used for comparisons. Receiver Operating Characteristic (ROC) curve analysis was conducted to determine the optimal CBA cutoff for predicting neonatal hyperbilirubinemia requiring intervention. Ethical approval was granted by the Institutional Ethics Committee of JIMS Hospital, and informed parental consent was obtained prior to enrollment.

RESULTS

This study included 80 term newborns, with a male predominance (54% males, 46% females). The mean gestational age of the newborns was 38.2 weeks, with the majority (48%) born at 38 weeks, followed by 31% at 39 weeks. The mean birth weight was 3.07 kg (SD 0.33), with most newborns (46%) weighing between 3-3.5 kg. Regarding the mode of delivery, 61% of newborns were delivered via LSCS, while 39% were delivered via normal vaginal delivery (NVD) (Figure 1).

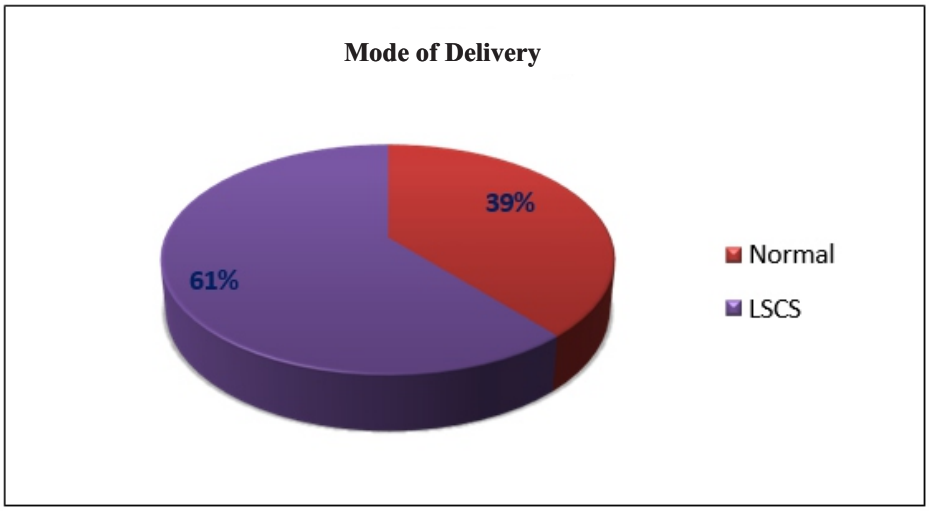


Figure 1: Pie diagram showing distribution of the new born based on mode of delivery.

Among the total newborns, 13 (16.25%) developed significant neonatal hyperbilirubinemia (NNH), defined as TSB levels reaching or exceeding the phototherapy threshold at 72 hours of life. All 13 newborns with Jaundice required phototherapy (PT), but none required exchange transfusion (ET). This suggests that while some infants developed significant jaundice, early identification and intervention prevented severe complications (Figure 2).

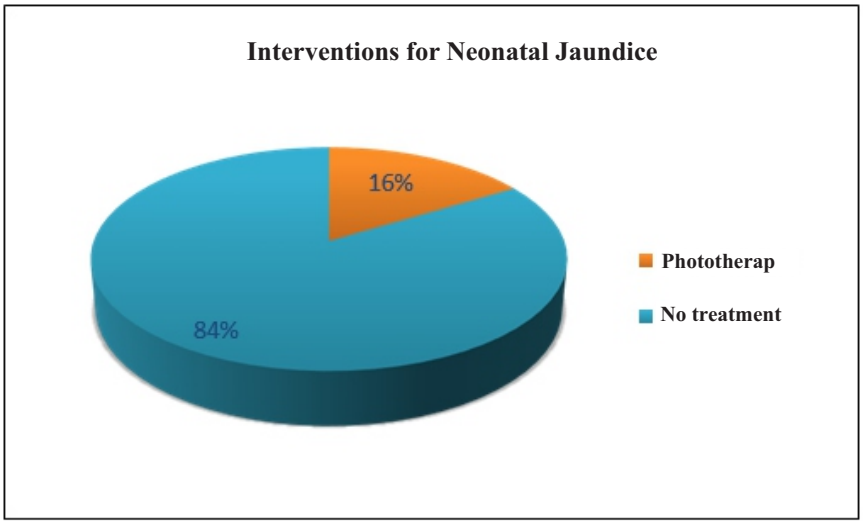


Figure 2: Pie diagram showing Intervention for Neonatal Jaundice

The mean cord blood albumin (CBA) level was 3.09 g/dL (SD 0.28), with a range of 2.3 to 3.6 g/dL. Based on CBA levels, newborns were categorized into three groups: ≤2.8 g/dL (14%), 2.9–3.3 g/dL (54%), and ≥3.4 g/dL (32%). Among the 11 newborns with CBA≤2.8 g/dL, 9 (81.8%) developedNNH, whereas only 4 (9.3%) of the 43 newborns with CBA between 2.9–3.3 g/dL developed NNH. Notably, none of the 26 newborns with CBA ≥3.4 g/dL developed NNH, suggesting a significantly lower risk of hyperbilirubinemia in this group(Figure 3).

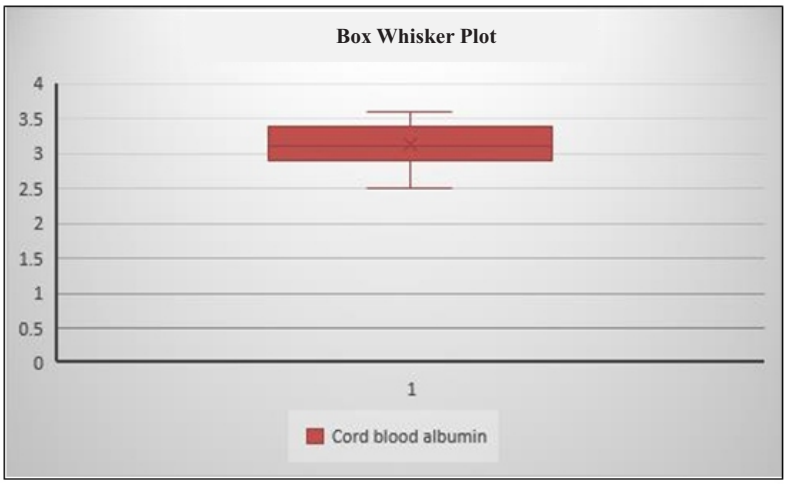


Figure 3: Box-whisker plot showing distribution of cord blood albumin in new born

A negative correlation was observed between CBA levels and TSB values at 72 hours of life, with lower CBA levels predicting higher bilirubin levels. The mean TSB levels were significantly different among CBA groups: newborns with CBA ≤2.8 g/dL had a mean TSB of 17.64 mg/dL (SD 1.44), while those with CBA 2.9–3.3 g/dL had a mean TSB of 12.33 mg/dL (SD 3.35), and those with CBA ≥3.4 g/dL had the lowest mean TSB of 12.16 mg/dL (SD 1.92). Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal CBA cutoff value for predicting NNH, showing that CBA ≤2.8 g/dL had a sensitivity of 69.2% and specificity of 97.02%, whereas CBA ≤2.9 g/dL had a higher sensitivity (84.6%) with an acceptable specificity (85.1%). Given the need for a high sensitivity screening tool to avoid missing high-risk cases, CBA ≤2.9 g/dL was identified as the best predictive cutoff value (Figure 4).

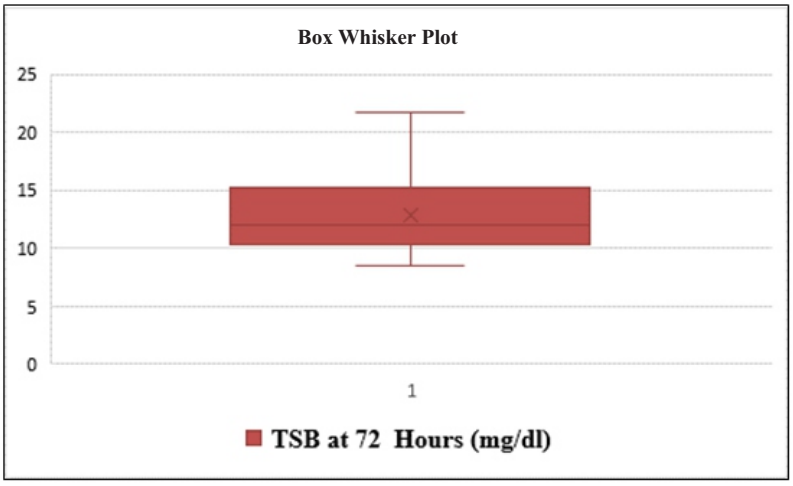


Figure 4: Box-whisker plot showing distribution of TSB (mg/dl) at 72 hours of age innewborns.

DISCUSSION

Neonatal jaundice is a common condition in newborns and a leading cause of hospital readmission during the early neonatal period. Early detection and timely management of neonatal hyperbilirubinemia (NNH) are crucial for preventing bilirubin-induced neurological dysfunction (BIND), which can lead to kernicterus, prolonged hospital stays, increased morbidity, and even mortality. The challenge lies in the fact that many newborns are discharged early, and parents may not bring them back for follow-up, increasing the risk of undetected severe jaundice. Identifying at-risk newborns based on cord blood albumin (CBA) levels can help guide clinical decisions regarding early discharge and follow-up visits.

In this study, the incidence of neonatal jaundice was 16.25%, which aligns with findings from Khairy et al. (16%), Daraz et al. (15.7%), and Shah et al. (15.5%)[5,18,19]. However, Dhanjal et al. (12.66%) and Kumar et al. (11.49%) reported a lower incidence [4]. The observed differences in neonatal jaundice prevalence across studies may be attributed to racial, genetic, and ethnic variations, as well as differences in hospital discharge policies and breastfeeding practices.

Several clinical variables were analyzed in relation to neonatal jaundice. Gender differences have been suggested as a contributing factor to NNH in various studies. In our study, although male newborns had a slightly higher incidence of NNH, this association was not statistically significant ($p = 0.22$). However, studies by Dhanjal et al., Satrya et al., and Maisels et al. found that male newborns are at a higher risk of developing neonatal jaundice [4,20,21].

The mode of delivery did not show a significant association with the development of jaundice in this study ($p = 0.73$), which is consistent with findings from Parikh et al. and Meshram et al.[22,23] The mean birth weight in our study was 3.07 kg (SD 0.33), and no significant correlation was found between birth weight and NNH ($p = 0.12$), which aligns with the results of Sapkota et al[24].

The findings of this study indicate that CBA levels are significantly associated with neonatal jaundice. Newborns were categorized into three groups based on CBA levels:

- Group A (≤2.8 g/dL): 81.8% (9/11) developed NNH
- Group B (2.9–3.3 g/dL): 9.3% (4/43) developed NNH
- Group C (≥3.4 g/dL): 0% (0/26) developed NNH

Statistical analysis revealed a significant difference in total serum bilirubin (TSB) levels between Group A and Group B, as well as between Group A and Group C. However, there was no significant difference in TSB levels between Group B and Group C, suggesting that CBA ≥3.4 g/dL may act as a protective factor against NNH. These findings are consistent with previous studies conducted by Trivedi et al., Kumar et al., Meshram et al., and Shah et al., which also reported that newborns with CBA levels ≥3.4 g/dL did not develop NNH [26,21,19,23].

Of the 13 newborns who developed significant jaun-dice, all required phototherapy, but none required exchange transfusion. CBA levels were significantly lower in newborns requiring phototherapy ($p < 0.01$). The strong association between CBA and the need for phototherapy supports the potential role of CBA as an early risk stratification tool for neonatal jaundice [25].

A negative correlation (correlation coefficient -0.41) was observed between CBA and TSB values at 72–96 hours, indicating that lower CBA levels were associated with higher bilirubin levels. The association between CBA and neonatal jaundice was highly significant ($p < 0.00001$), further confirming the utility of CBA as an early biomarker for predicting hyperbilirubinemia.

A comparison of different studies examining the relationship between CBA levels and neonatal jaundice is presented below:

Study	Year	Sample Size	NNH Cases	Group A (≤2.8 g/dL)	Group B (2.9–3.3 g/dL)	Group C (≥3.4 g/dL)	p-value
Trivedi et al.[26]	2013	605	205	120 (≤2.8)	59 (2.8–3.5)	26 (>3.5)	<0.05
Kumar et al.[20]	2016	100	10	9 (≤2.8)	1 (2.9–3.3)	0 (≥3.4)	0.003
Meshram et al. [24]	2018	1040	120	105 (≤2.8)	15 (>2.8)	-	<0.001
Harisha et al. [27]	2019	100	19	10 (≤2.8)	9 (2.8–3.3)	0 (>3.3)	<0.001
Shah et al.[19]	2020	142	22	17 (≤2.8)	5 (2.9–3.3)	0 (≥3.4)	<0.001
Current Study	2024	80	13	9 (≤2.8)	4 (2.9–3.3)	0 (≥3.4)	<0.001

The findings of the current study align closely with previous research, further validating the predictive role of CBA in neonatal jaundice.

CONCLUSION

Neonatal hyperbilirubinemia is a common condition requiring early identification to prevent bilirubin-induced neurological dysfunction. This study confirms that cord blood albumin (CBA) levels at birth can predict neonatal jaundice risk. Newborns with CBA ≤2.8 g/dL had a significantly higherrisk, while those with CBA ≥3.4 g/dL did not develop reinforces its predictive value. CBA screening at birth could guide early discharge decisions and targeted follow-ups. Integrating CBA-based risk stratification into neonatal care can optimize management, though larger studies are needed to establish standardized thresholds.

REFERENCES

1. Gale R, Seidman DS, Stevenson DK. Hyperbili-rubinemia and early discharge. J Perinatol. 2001; 21(1):40–3.
2. Ansong-Assoku B, Shah SD, Adnan M, Ankola PA. Neonatal
3. Mitra S, Rennie J. Neonatal jaundice: aetiology , diagnosis

and treatment. Br J Hosp Med (Lond). 2017 Dec 2;78(12):699–704.

4. Dhanjal DGS, Rathi DRK, Agrawal DS, Savita D. Cord serum albumin as a predictor of neonatal hyper bilirubinemia in healthy full-term neonates. Pediatric Review: International Journal of Pediatric Research. 2018 Apr 30;5(4):203–8.
5. Khairy MA, Abuelhamd WA, Elhawary IM, Nabayel ASM. Early predictors of neonatal hyperbilirubinemia in full term newborn.Pediatrics& Neonatology. 2019 Jun 1;60(3):285–90.
6. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation | Pediatrics | American Academy of Pediatrics [Internet].[cited 2024 Jan 2]. Available from: https://publications.aap.org/pediatrics/article/150/3/e2022058859/188726/ Clinical Practice Guideline Revision-Management-of ? autolog in check redirected
7. Wusthoff CJ, Loe IM. Impact of bilirubin-induced neurologic dysfunction on neurodevelopmental out comes. Semin Fetal Neonatal Med. 2015 Feb;20(1):52–7.
8. Hamza A. Kernicterus. Autops Case Rep. 2019 Jan 14;9(1):e2018057.
9. Ovid - Cloherty and Stark's Manual of Neonatal Care | Wolters Kluwer [Internet]. [cited 2023 Dec 16]. Availablefrom https:// www.wolterskluwer. com/ en/ solu -tions /ovid / cloherty and dstarks-manual-of-neonatal-care-4934
10. Rathore S, Kumar VK C, R S. A critical review on neonatal hyperbilirubinemia-an Ayurvedic perspective. J Ayurveda Integr Med. 2020;11(2):190–6.
11. Herta T, Beuers U. A historical review of jaundice: May the golden oriole live forever. Clin Liver Dis (Hoboken). 2022 Dec 11;20(Suppl 1):45–56.
12. Roberts GF. Comparative Aspects of Haemolytic Disease of the Newborn. Butterworth- Heinemann; 2013. 201 p.
13. Hansen TWR. Pioneers in the Scientific Study of Neonatal Jaundice and Kernicterus. Pediatrics. 2000 Aug 1;106(2):e15.
14. Scott RB, Jenkins ME, Kessler AD. Erythroblastosis fetalis in the Negro infant: Report of five cases, including four cases due to A-B-O incompatibilities. The Journal of Pediatrics. 1951 Dec 1;39(6):680–6.
15. Crigler JF, Najjar VA. Congenital familial nonhemolytic jaundice with kernicterus. Pediatrics. 1952 Aug; 10(2) : 169–80.
16. Cremer RJ, Perryman PW, Richards DH. Influence of light on the hyperbilirubinaemia of infants. Lancet. 1958 May 24;1(7030):1094–7.
17. Hart AP. Familial Icterus Gravis of the New-Born and its Treatment. Can Med Assoc J. 1925 Oct;15(10):1008–11.
18. Bhardwaj U, Kohli V, Thukral A. Management of Hyperbilirubinemia in Newborn Infants 35 or More Weeks of Gestation: American Academy of Pediatrics, 2022. Indian Pediatr. 2023 Jan;60(1):63–6. Daraz DZH, Shabir DB, Afshan Dr. Performance of Cord Blood Albumin At Birth For Prediction of Significant Neonatal Hyperbilirubinemia.
19. Shah SK, Jha AK, Sharma S, Gupta S. Association of neonatal hyperbilirubinemia with cord albumin among term appropriate for gestational age neonates. International Journal of Contemporary Pediatrics. 2023 Nov 27;10(12) : 1771–7.
20. Kumar V, Shrangi G, Jangid S, Yadav M, Verma MK. Association of cord serum albumin with neonatal hyper-bilirubinemia among term-neonates. International Journal of Research in Medical Sciences. 2020 May 26;8(6):2099–104.
21. Satrya R, Effendi SH, Gumida DA. Correlation between cord blood bilirubin level and incidence of hyperbiliru-binemia in term newborns. Paediatrica Indonesiana. 2009 Dec 31;49(6):349–54.
22. Maisels MJ, Gifford K. Neonatal Jaundice in Full-term Infants: Role of Breast-feeding and Other Causes. American Journal of Diseases of Children. 1983 Jun 1;137(6):561–2.
23. Parikh YN, Ghetia JC, Makawana AM. Utility of cord blood albumin as a predictor of significant neonatal jaundice in healthy term newborns. International Journal of Contemporary Pediatrics. 2019;6(1):102–5.
24. Meshram R, Merchant S, Bhongade S, Pathan S. Utility of cord blood bilirubin as a predictors of significant neonatal Hyperbilirubinemia in healthy term neonate. International Journal of Contemporary Pediatrics. 2019 Aug 23;6:2058.
25. Sapkota P, Gami F. Study of cord blood albumin as a predictor of neonatal jaundice. Asian Journal of Medical Sciences. 2020 Jul 1;11:58–63.
26. Trivedi D. Cord Serum Bilirubin And Albumin In Neonatal Hyperbilirubinemia. IJIIT. 2013 Apr 1;2:39–42
27. Harisha C, Vr SR, Kn S. A Study of Cord Blood Albumin as a Predictor of Significant Neonatal Jaundice. JCBS. 2019 Nov 11;9(1):19–22.