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Original Research Article

A Study of Cord Blood Bilirubin as A Predictor of Neonatal Hyperbilirubinemia of All Term Newborns of O-Positive and All Rh-Negative Mothers at A Tertiary Care Hospital

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ABSTRACT

Background: Neonatal hyperbilirubinemia is one of the most common clinical conditions in the early neonatal period, affecting a large proportion of term newborns.Neonates born to **O-positive and Rh-negative mothers** are at increased risk due to immune-mediated hemolysis (ABO/Rh incompatibility).Therefore, this study was undertaken to evaluate the role of cord blood bilirubin as an early predictor of neonatal hyperbilirubinemia and to determine an optimal cut-off value for clinical use.

Methods: This study was a **prospective, hospital-based observational study** conducted in the Neonatal Intensive Care Unit and Department of Paediatrics of a tertiary care hospital over a period of **12 months**. 173 term neonates born to O positive or Rh-negative mothers were included.Data on demographic, clinical, maternal, and laboratory parameters were systematically collected.Correlation analysis between cord blood bilirubin and postnatal bilirubin,ROC curve used to determine optimal cut-off value,diagnostic accuracy assessed using sensitivity, specificity, PPV, and NPV .

Results: Among 173 term neonates, 46.2% developed significant hyperbilirubinemia requiring treatment. Mean cord blood bilirubin was 1.71 ± 0.44 mg/dL and was significantly higher in treated neonates ($p < 0.001$). A cut-off of 2.1 mg/dL showed 100% specificity and PPV, with low sensitivity (32.5%). Hyperbilirubinemia was more common in ABO/Rh incompatibility and DAT-positive cases. Cord bilirubin showed a moderate positive correlation with 48-hour serum bilirubin ($r = 0.354$, $p < 0.001$), indicating its utility as an early predictor.

Conclusion: Cord blood bilirubin is a simple and reliable early predictor of neonatal hyperbilirubinemia with high specificity. Although its sensitivity is limited, it is particularly useful in identifying high-risk neonates, especially in cases of ABO/Rh incompatibility. It should be used alongside clinical assessment and follow-up for optimal management.

Keywords*: Neonatal hyperbilirubinemia; Cord blood bilirubin; ABO incompatibility; Rh incompatibility; Phototherapy; Early prediction; Neonate.*

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common clinical conditions encountered in the early neonatal period, affecting a significant proportion of term newborns. Although most cases are physiological and self-limiting, a considerable number of neonates develop significant hyperbilirubinemia requiring interventions such as phototherapy or intravenous immunoglobulin. If not recognized and treated promptly, severe hyperbilirubinemia can lead to acute bilirubin encephalopathy and kernicterus, resulting in long-term neurological sequelae.

Early identification of neonates at risk has become increasingly important due to the trend toward early postnatal discharge and limited follow-up in many settings. Several risk factors, including ABO and Rh incompatibility,

prematurity, and hemolysis, are known to predispose neonates to higher bilirubin levels. However, reliable early predictors that can be assessed at birth are essential for timely intervention.

Cord blood bilirubin is a simple, non-invasive, and readily available biomarker that reflects bilirubin levels at birth and underlying hemolytic processes. It has been proposed as an early screening tool to predict the development of significant hyperbilirubinemia. This study aims to evaluate the predictive value of cord blood bilirubin and determine its utility in identifying high-risk neonates requiring closer monitoring and early management**.**

Table :1 Comparision of Screening Method

Method	Advantages	Limitations
Visual assessment (Kramer's scale)	Simple	Subjective
Serum bilirubin	Accurate	Invasive
TcB	Non-invasive	Costly
Cord blood bilirubin	Early, predictive	Needs validation

Study Design and Setting

This prospective observational study was conducted at a regional tertiary care referral center at a teaching hospital in South Gujarat, India. The study was conducted with patient enrollment taking place over a 12-month period from January 2024 to January 2025.

Sample Size and Calculation

The sample size was calculated based on the expected incidence of neonatal hyperbilirubinemia from previous studies, with appropriate precision and confidence interval. A minimum required sample was estimated, and a total of **173 term neonates** were included in the study.

Study Population

This prospective observational study included **173 term neonates (≥37 weeks gestation)** born to **O-positive or Rh-negative mothers** in a tertiary care hospital. Neonates with congenital anomalies, birth asphyxia, extramural births, same maternal–neonatal blood group, or inadequate samples were excluded.

Data Collection

Cord blood samples were collected at birth for bilirubin estimation. Neonates were followed up clinically, and serum bilirubin levels were measured at **48 hours, 72 hours, and day 5–7**. Maternal and neonatal details, blood group incompatibility, and DAT status were recorded. The need for phototherapy,phototherapy with IVIg and phototherapy with exchange transfusion was documented.

Statistical Analysis

Data were analyzed using appropriate statistical software. Continuous variables were expressed as mean ± SD, and categorical variables as proportions. Association between cord bilirubin and outcomes was assessed using appropriate tests. Correlation analysis was performed, and ROC curve analysis was used to determine the optimal cut-off value. Sensitivity, specificity, PPV, and NPV were calculated. A p-value <0.05 was considered statistically significant.

Ethical Consideration

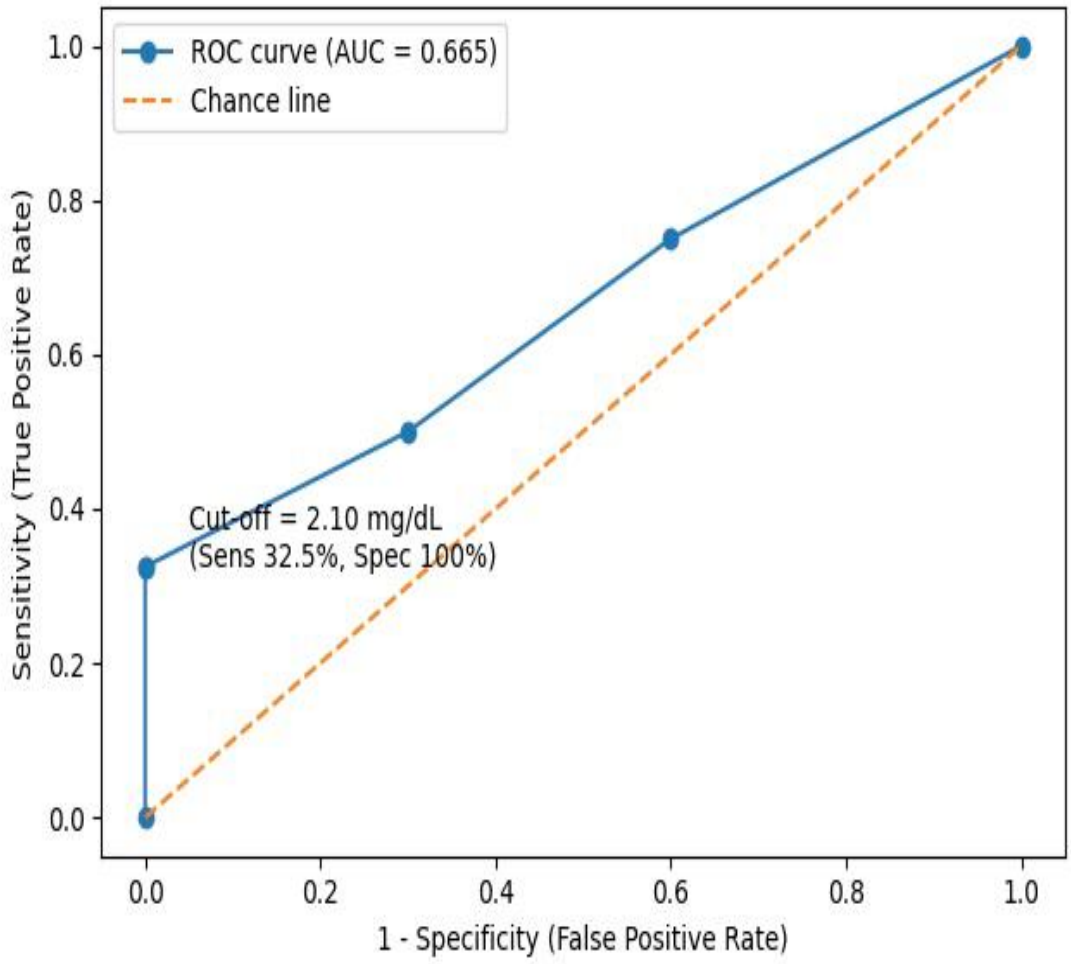
This study was approved by the Institutional Ethics Committee of SMIMER, Surat. Written informed consent was obtained from the parents or legal guardians of all enrolled neonates. The study adhered to ethical principles in accordance with the Declaration of Helsinki.

RESULTS

This prospective hospital-based study included 173 term neonates born in a tertiary care center. Among them, 46.2% developed significant hyperbilirubinemia requiring treatment.The mean cord blood bilirubin was 1.71 ± 0.44 mg/dL, and was significantly higher in neonates requiring intervention ($p < 0.001$). A cut-off of 2.1 mg/dL showed 100% specificity

and PPV, with low sensitivity (32.5%).A moderate positive correlation was observed between cord bilirubin and 48-hour serum bilirubin ($r = 0.354$, $p < 0.001$). Higher incidence was noted in cases with ABO/Rh incompatibility and DAT positivity.

Graph 1.ROC ANALYSIS OF CORDBLOOD TOTAL BILIRUBIN FOR PREDICTING PHOTOTHERAPY REQUIREMENT



Neonatal Characteristics

A total of 173 term neonates were included in this study. Most neonates had a birth weight between 2.5–3.5 kg and were delivered either vaginally or by LSCS. A proportion of neonates had ABO and Rh incompatibility, with some showing DAT positivity, placing them at higher risk for developing significant hyperbilirubinemia**.**

Maternal and Obstetric Factors

The study included neonates born to O-positive and Rh-negative mothers, who are at higher risk for hemolytic disease of the newborn. A significant proportion of mothers had blood group incompatibility with their neonates (ABO and/or Rh incompatibility).Deliveries were conducted via both vaginal route and lower segment cesarean section (LSCS). These maternal and obstetric factors, particularly blood group incompatibility, were associated with an increased risk of neonatal hyperbilirubinemia and need for therapeutic intervention.Among 173 mothers, 66.5% were O-positive and 33.5% were Rh-negative, representing a population at higher risk for neonatal hyperbilirubinemia due to blood group incompatibility. Data on mode of delivery was not specified in the available dataset.

Table 2: Maternal blood group and Rh distribution (n = 173)

Parameter	Category	Number (n)	Percentage (%)
Maternal blood group and Maternal Rh type	**Rh positive**	**115**	66.5
	O+ve	115	66.5
	Rh Negative	**58**	33.5
	O-neg	17	9.8
	A-ve	16	9.2
	B-ve	15	8.7
	AB-ve	10	5.8

Clinical Features

Most neonates were asymptomatic at birth and developed visible jaundice within the first 48–72 hours of life. Higher-risk neonates, particularly those with ABO/Rh incompatibility and DAT positivity, showed earlier onset and more pronounced jaundice. No cases of acute bilirubin encephalopathy were reported.

Biochemical Profile

The mean cord blood bilirubin was 1.71 ± 0.44 mg/dL. Neonates who required treatment had significantly higher cord bilirubin levels compared to those who did not ($p < 0.001$). Cord bilirubin showed a moderate positive correlation with 48-hour serum bilirubin ($r = 0.354$, $p < 0.001$). Higher bilirubin levels were observed in neonates with ABO/Rh incompatibility and DAT positivity.

Outcome

Among 173 neonates, 53.8% required no treatment, while 46.2% developed significant hyperbilirubinemia requiring phototherapy with or without IVIg. A subset required intensive management (phototherapy + IVIg). No cases required exchange transfusion.

Table 3. Treatment outcomes (n = 173)

Treatment outcome	Number (n)	Percentage (%)
No treatment required	93	53.8
Phototherapy only	44	25.4
Phototherapy + IVIg	36	20.8
Phototherapy + exchange transfusion	0	0.0
Total	**173**	**100.0**

Maternal and Laboratory Predictors

Neonates born to O-positive and Rh-negative mothers showed a higher risk of developing significant hyperbilirubinemia due to underlying ABO and Rh incompatibility. DAT positivity further increased this risk, indicating immune-mediated hemolysis.

Among laboratory parameters, cord blood bilirubin was a significant predictor. Higher cord bilirubin levels were strongly associated with subsequent hyperbilirubinemia ($p < 0.001$), and values >2.1 mg/dL had high specificity for predicting need for treatment.

Table 4. Factors associated with phototherapy requirement

Variable	No phototherapy (n = 93)	Phototherapy required (n = 80)	p-value
Maternal/baseline Factors			
Maternal age (years), mean ± SD	25.44 ± 2.30	25.64 ± 2.41	0.629
Primi, n (%)	47 (50.5)	39 (48.8)	0.879
Rh-negative mother, n (%)	31 (33.3)	27 (33.8)	1.000
LSCS, n (%)	31 (33.3)	27 (33.8)	1.000
Oxytocin-induced labour, n (%)	31 (33.3)	30 (37.5)	0.633
Gestational age (weeks), mean ± SD	38.84 ± 0.95	38.81 ± 0.95	0.888
Birth weight (g), mean ± SD	2771.94 ± 199.25	2891.50 ± 251.08	0.001
Male sex, n (%)	62 (66.7)	52 (65.0)	0.873
APGAR at 1 minute, mean ± SD	8.51 ± 0.50	8.45 ± 0.50	0.523
APGAR at 5 minutes, mean ± SD	9.51 ± 0.50	9.46 ± 0.50	0.576
Rh-positive baby,n(%)	137(79.1)	63(45.9)	0.89
Haemolytic/ Incompatibility factors			
DAT positive, n (%)	21 (22.6)	36 (45.0)	0.002
ABO incompatibility present, n (%)	85 (49.1)	41(48.2)	
Rh incompatibility present, n (%)	45 (26.0)	31 (68.8)	
ABO+Rh incompatibility	6(3.4)	4(66.6)	
Birth hemoglobin (g/dL), mean ± SD	16.07 ± 0.56	15.22 ± 1.39	<0.001
Neurotoxicity risk factors			
Risk factor category (overall)	—	—	0.011
None, n (%)	57 (61.3)	38 (47.5)	—
DAT positive alone, n (%)	17 (18.3)	26 (32.5)	—
Low albumin alone, n (%)	15 (16.1)	6 (7.5)	—
DAT positive + low albumin, n (%)	4 (4.3)	10 (12.5)	—
Cord blood biochemical factors			

Cord blood total bilirubin (mg/dL), mean ± SD	1.55 ± 0.19	1.90 ± 0.55	<0.001
Albumin at birth (g/dL), mean ± SD	3.23 ± 0.26	3.23 ± 0.26	0.962
Albumin at 48 hours (g/dL), mean ± SD	3.07 ± 0.27	3.07 ± 0.27	0.972
Postnatal bilirubin profile			
Bilirubin at 48 hours (mg/dL), mean ± SD	7.98 ± 0.58	13.44 ± 1.10	<0.001
Bilirubin at 72 hours (mg/dL), mean ± SD	10.83 ± 0.74	14.53 ± 3.38	<0.001
Bilirubin at day 5–7 (mg/dL), mean ± SD	5.52 ± 0.48	10.44 ± 1.67	<0.001

Outcome Analysis

Out of 173 neonates, 46.2% developed significant hyperbilirubinemia requiring intervention. Most were managed with phototherapy, while a subset required phototherapy with IVIg. No cases required exchange transfusion, and no mortality was observed.

Higher rates of intervention were seen in neonates with ABO/Rh incompatibility, DAT positivity, and elevated cord bilirubin levels.

Biochemical and Outcome Association

Higher cord blood bilirubin levels were significantly associated with the development of hyperbilirubinemia and need for treatment ($p < 0.001$). Neonates requiring phototherapy and IVIg had higher mean cord bilirubin compared to those not requiring treatment. Cord bilirubin also showed a moderate positive correlation with 48-hour serum bilirubin ($r = 0.354$, $p < 0.001$), indicating its value as an early biochemical predictor.

Table 5. Diagnostic accuracy of optimal cord blood bilirubin cut-off for predicting phototherapy requirement

Diagnostic parameter	Value
Cut-off used (cord blood total bilirubin)	2.10 mg/dL
True positives (TP)	26
False positives (FP)	0
True negatives (TN)	93
False negatives (FN)	54
Sensitivity	32.5%
Specificity	100.0%
Positive predictive value (PPV)	100.0%
Negative predictive value (NPV)	63.3%
Overall accuracy	68.8%

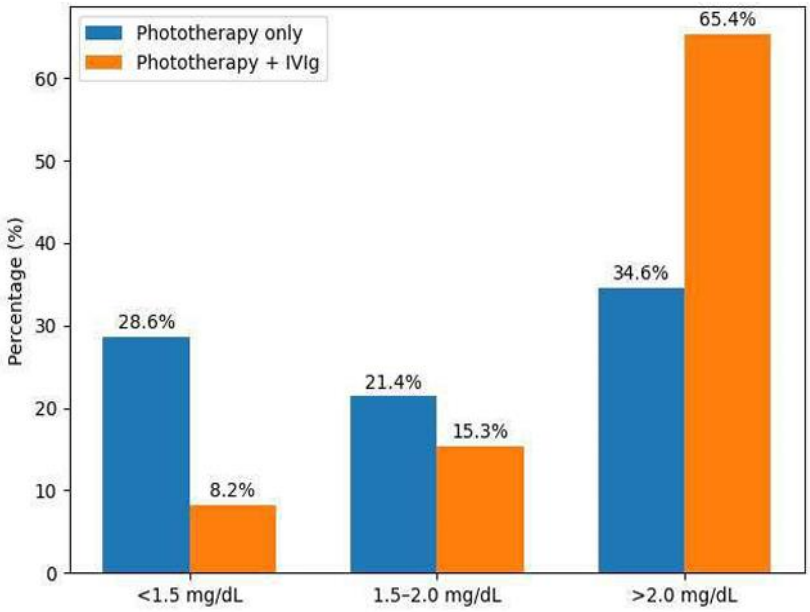
DISCUSSION

This study demonstrates that cord blood bilirubin is a useful early predictor of neonatal hyperbilirubinemia, with high specificity at a cut-off of 2.1 mg/dL. The findings are consistent with previous studies highlighting the role of hemolytic risk factors such as ABO/Rh incompatibility and DAT positivity. Although sensitivity is limited, cord bilirubin can effectively identify high-risk neonates who require close monitoring. Incorporating cord bilirubin assessment at birth may help in early risk stratification and timely management, especially in settings with early discharge.

Table 6. Distribution of treatment modalities according to cord blood bilirubin level

Cord blood bilirubin level (mg/dL)	Total (n)	Phototherapy only, n (%)	Phototherapy + IVIg, n (%)	Phototherapy + exchange transfusion, n (%)
<1.5	49	14 (28.6)	4 (8.2)	0 (0.0)
1.5–2.0	98	21 (21.4)	15 (15.3)	0 (0.0)
>2.0	26	9 (34.6)	17 (65.4)	0 (0.0)

Graph 2 Comparison of mean cordblood bilirubin fraction according to treatment required



Neonatal Characteristics and Outcome

All included neonates were term. A higher incidence of significant hyperbilirubinemia was observed among neonates with ABO/Rh incompatibility and DAT positivity. Nearly half (46.2%) required treatment, with a subset needing intensive therapy (phototherapy + IVIg), indicating that high-risk neonatal profiles are associated with worse outcomes.

Maternal and Obstetric Influences

Maternal factors, particularly O-positive and Rh-negative blood groups, played a key role in predisposing neonates to hemolysis and hyperbilirubinemia. Blood group incompatibility between mother and neonate was strongly associated with increased need for intervention. Mode of delivery had no clearly established impact based on available data.

ABO/Rh Incompatibility – Treatment & Outcomes In our study, hemolytic incompatibility was observed in a significant proportion of neonates, with ABO incompatibility (57.1%) being more common than Rh incompatibility (37.8%), while combined incompatibility was rare (5%). Among affected neonates, 46.2% required treatment, predominantly phototherapy alone (25.4%) or phototherapy with IVIg (20.8%), and no cases required exchange transfusion, indicating effective early management.

Table 7. Type of incompatibility and treatment requirement (n = 173)

Type of incompatibility	Total n(%)	Phototherapy ± IVIg yes, n (%)	Phototherapy no, n (%)
No incompatibility	37 (21.3)	20(54.0)	17(45.9)
ABO incompatibility alone	85 (49.1)	41(49.1)	44(50.1)
Rh incompatibility alone	45 (26.0)	16(35.5)	29(64.4)
Both ABO and Rh incompatibility	6 (3.4)	4(66.6)	2(33.3)

CONCLUSION

ABO incompatibility is the leading cause of hemolytic neonatal hyperbilirubinemia, while Rh incompatibility, though less frequent, is associated with relatively more severe disease. Early identification using cord blood bilirubin and timely initiation of phototherapy significantly reduces disease severity and prevents the need for exchange transfusion.

Comparison with Global Morbidity

Globally, 5–15% of neonates require treatment for hyperbilirubinemia, whereas in our cohort, 46.2% required intervention, reflecting a higher burden likely due to inclusion of high-risk groups (O-positive and Rh-negative mothers). However, the absence of exchange transfusion and severe complications in our study suggests outcomes comparable or better than many low- and middle-income settings, where delayed diagnosis often leads to higher morbidity.

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