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A PROGNOSTIC STUDY TO THE CORRELATION BETWEEN CORD BLOOD BILIRUBIN VALUES AND JAUNDICE IN APPARENTLY HEALTHY FULL-TERM NEONATES

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ABSTRACT

Background: Neonatal hyperbilirubinemia is a commonplace situation in newborns, with prevalence rates of about 60% in full-term and 80% in preterm infants. If left untreated, excessive unconjugated bilirubin can cross the blood-brain barrier, leading to Kernicterus. Predictive measures include cord blood bilirubin (CBB), transcutaneous bilirubin (TcB), and routine serum tests. CBB is a simple, inexpensive, and non-invasive method. **Aim:** To assess the relationship between CBB ranges and the development of hyperbilirubinemia in healthy full-term neonates. **Methods:** A prospective study involving 53 full-term healthy neonates was conducted from March 2024 to March 2025. CBB was measured at birth, and serum bilirubin was recorded on day three. **Results:** Among participants (66% male, 34% female), a significant correlation was found between birth weight and CBB levels with hyperbilirubinemia development on day three (P = 0.004 and P = 0.0001). Notably, CBB levels >2.05 mg/dL had been related toa higher risk of hyperbilirubinemia. **Conclusion:** A positive correlation exists among twine blood bilirubin degrees and neonatal hyperbilirubinemia. A cutoff of 2.05 mg/dL may predict its occurrence. Neonates with lower birth weight are at higher risk. Measuring CBB is a safe, cost-effective, and non-invasive screening tool that can help guide early discharge decisions and prevent complications.

KEYWORDS: Cord blood bilirubin; hyperbilirubinemia; neonates; physiological jaundice.

INTRODUCTION

Hyperbilirubinemia is one of the most common clinical situations requiring management during the neonatal period. it is usually a benign, self-limiting phenomenon that occurs during the first week of life.[1] Studies indicate that about 60% of full-term and 80% of preterm babies have hyperbilirubinemia.[2] Physiological jaundice in full-term neonates typically appears on the 2nd to 3rd day of life and resolves by 10 to 14 days of age.[3] It occurs due to the shortened lifespan of neonatal Red Blood Cells (RBCs) combined with immature liver and gastrointestinal function, leading to increased bilirubin production and reduced hepatic clearance, causing elevated total serum bilirubin (TSB) levels.[4] In contrast, neonatal hyperbilirubinemia can be an important clinical sign of underlying pathological conditions such as sepsis, liver dysfunction, hemolytic anemia, or inborn errors of metabolism.[5] Pathological jaundice typically presents within the first 24 hours after birth and may persist for more than two weeks.[6] If left untreated at the time, elevated levels of unconjugated bilirubin can pass the blood-brain barrier and deposit in the brain, especially affecting the basal ganglia, causing Kernicterus (chronic bilirubin encephalopathy).[7] Therefore, it is essential to monitor the neonates clinically and biochemically within 72–96 hours after birth in the hospital, but this is considered impossible, especially in developing countries.[8] Early discharge of apparently healthy full-term neonates has turn out to be in developing countries due to social, medical reasons, and economic constraints.[9] As practice, there are various measurements to predict the hyperbilirubinemia in neonates through follow-up within 1–2 days of early discharge, such as cord blood bilirubin (CBB) value at birth, transcutaneous bilirubin (TcB) monitoring, routine pre-discharge serum bilirubin tests, and clinical assessment of jaundice risk factors.[10] Despite these predictive factors for hyperbilirubinemia, it remains the most common cause of hospital readmission during the first 7 days of life.[11] Measurement of CBB value at birth is considered a simple, inexpensive, and non-invasive method for early prediction of neonatal hyperbilirubinemia.[12] Bhat et al.[13] reported a positive correlation between elevated CBB values and the development of neonatal jaundice. Similarly, Tahir A et al[14] found that the critical CBB value of greater than 2 mg\dL is a good predictor of hyperbilirubinemia. In the absence of anterior data in our region, we conducted this

prospective study to determine the correlation between CBB value and the development of jaundice in healthy full-term neonates, aiming to provide the appropriate management for severe cases before the onset of neurological complications.

METHODS AND PATIENTS

Study design: A prospective observational analytical study was conducted in the Department of Pediatrics and Neonatology, from March 20, 2024, to March 1, 2025.

Study population: The study comprised 53 healthy neonates, with a gestational age of 37 weeks or greater, of both sexes, delivered by either vaginal or cesarean section. Eligible neonates had a birth weight of 2500 grams or more and did not exhibit any congenital malformations. Exclusion criteria included significant illnesses requiring NICU admission, Rh or ABO incompatibility, or the presence of conjugated hyperbilirubinemia. Informed consent was obtained from the parents before participation.

The clinical and demographic factors were recorded: gender, birth weight, gestational age as determined by New Ballard score[15], mother and neonate blood group and Rh factor, CBB values at birth, and bilirubin on the 3rd day of life. Hyperbilirubinemia was described as a total serum bilirubin value above the phototherapy threshold based on age in hours.[16] Approximately 3 ml of CBB was collected using a sterile syringe after the placenta was separated. Total and direct bilirubin values (indirect bilirubin was calculated by subtracting direct from total bilirubin) were measured at birth and on the 3rd day of life. Additionally, blood grouping and typing were also performed on the CBB samples. Neonates were followed for 3–5 days after birth to monitor jaundice clinically and biochemically.

Statistical analysis: Descriptive statistics for quantitative variables were presented using measures of central tendency and dispersion. Categorical variables were described using frequencies and percentages. Inferential statistics included the Chi-square test to assess associations between categorical variables and the independent Student's t-test to compare means between two independent groups. The relationship between continuous variables was examined using Pearson's correlation coefficient. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated from Receiver Operating Characteristic (ROC) curves. A p-value of less than 0.05 was considered statistically significant. All data analyses were performed using IBM SPSS Statistics software (version 25).

The work has been reported in line with the STROCSS criteria.[24]

RESULTS

The study involved 53 healthy full-term neonates with a mean gestational age of 37.59 ± 0.6 weeks. Of these, 35 (66%) were male and 18 (34%) were female. The most common maternal blood group was A positive, present in 21 mothers (39.6%), while the most prevalent neonatal blood group was O positive, identified in 27 neonates (50.9%).

The average (± SD) cord blood bilirubin (CBB) level at birth was 2.15 ± 0.6 mg/dL, and the mean serum total bilirubin on the third day of life was 12.54 ± 4.9 mg/dL, as shown in Table 1.

Table 1: Mean cord and serum bilirubin values (n = 53).

Investigations	Min─Max	Mean± SD
Cord Blood Bilirubin (mg\dL) at birth	0.66─4.90	**2.15± 0.6**
Serum Total Bilirubin (mg\dL) at Day 3	6.20─20.50	**12.54± 4.9**
Direct Bilirubin (mg\dL) at Day 3	0.30─1.90	**1.01± 0.3**
Indirect Bilirubin (mg\dL) At Day 3	5.8─19.1	**11.53± 4.78**

SD: Standard deviation, Min: Minimum, Max: Maximum

Statistical analysis revealed a significant correlation between birth weight and cord blood bilirubin levels with the development of hyperbilirubinemia on the third day of life, with P-values of 0.004 and 0.0001, respectively. No significant association was observed between gender and hyperbilirubinemia (Table 2).

Table 2: Distribution of the neonates according to gender, birth weight, cord blood bilirubin, and the development of hyperbilirubinemia on the 3rd day of life.

Characteristics	N (%)	Hyperbilirubinemia		P-value
		Yes	No	
Gender				
Male	35 (66%)	8 (50%)	27 (73%)	0.1
Female	18 (34%)	8 (50%)	10 (27%)	
Birth weight (g)				
2500–3000	28 (52.8%)	14 (87.5%)	14(37.8%)	0.004
3000–3500	19 (35.8%)	2 (12.5%)	17 (45.9%)	

≥3500	6 (11.3%)	0	6 (16.2%)	
CBB (mg\dL)				
<2	18 (34%)	0	18 (48.6%)	0.0001
2–2.5	20 (37.7%)	2 (12.5%)	18 (48.6%)	
>2.5	15 (28.3%)	14 (87.5%)	1 (2.7%)	

g: Gram, CBB: Cord blood bilirubin

Additionally, there was no significant relationship between maternal or neonatal blood groups and the occurrence of hyperbilirubinemia on the third day, with P-values of 0.5 and 0.4, respectively.

The optimal cutoff value of CBB for predicting neonatal hyperbilirubinemia after 72 hours was 2.05 mg/dL. This threshold demonstrated a sensitivity of 77.8%, specificity of 64.7%, a positive predictive value (PPV) of 79.3%, and a negative predictive value (NPV) of 78.3%, as illustrated in Figure 1.

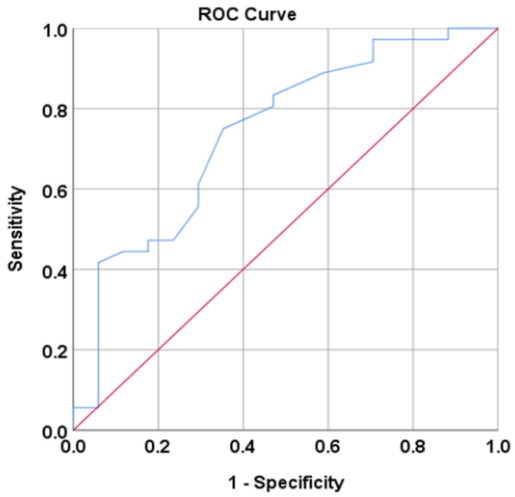

Figure 1: Receiver-operator curve analysis (ROC) showing predictability of cord total bilirubin.

These findings suggest that measuring cord blood bilirubin can serve as a valuable early predictor for hyperbilirubinemia in healthy term neonates.

DISCUSSION

Neonatal jaundice is a common condition that poses a significant clinical challenge in the neonatal period.[17] It is the leading reason for repeat hospital admissions among newborns, highlighting the importance of early identification of those at risk for hyperbilirubinemia. Prompt intervention is critical because delays can lead to serious long-term effects, such as kernicterus.[18] Research has shown a notable relationship between CBB (Cord Blood Bilirubin) levels and the onset of hyperbilirubinemia. A CBB cutoff value of 2.05 mg\dL was identified for predicting jaundice requiring treatment, with a sensitivity of 77.8% and a specificity of 64.7%. Furthermore, lower birth weights have been associated with a higher incidence of hyperbilirubinemia compared to infants with higher birth weights. Venkatraman L et al[19] reported a statistically significant association between CBB values and the development of neonatal hyperbilirubinemia. Ipek et al[12] established a CBB cutoff value of 1.7 mg\dL for predicting neonatal hyperbilirubinemia, with a sensitivity of 78.57% and a specificity of 54.76%. Similarly, Bhat JA et al[13] found that CBB value >3 mg\dL had a sensitivity of 97% and a specificity of 90% for predicting hyperbilirubinemia. Anjanappa S et al[20] found that the cutoff value of CBB requiring phototherapy after 48 hours was 2.6 mg\dL, with a sensitivity of 63.46% and a specificity of 90.5%. Tahir A et al[14] reported that 21.6% of neonates with a gestational age ≥35 weeks developed hyperbilirubinemia, and their CBB value at birth was approximately 2 mg\dl. Similarly, Rohini Y et al[21] identified a CBB cutoff value of >1.975 mg\dL for predicting hyperbilirubinemia, with a sensitivity of 76.54% and a specificity of 87.4%. The variability in cutoff values across studies may be attributed to the type of CBB sample, whether arterial, venous, or mixed. Jones K et al. found a strong correlation between venous and arterial CBB levels; however, venous levels were consistently lower than arterial levels.[22] Kardum D et al[9] found in their study that hyperbilirubinemia occurred in neonates who had a smaller birth weight of 3318.62 g (±503.31 g), with a P-value <0.01. Arisandi Y et al[23] observed a significant relationship between birth weight and the occurrence of hyperbilirubinemia, with a p-value of 0.019. In contrast, Bhat JA et al[13] found no statistically significant association between birth weight and the development of hyperbilirubinemia. This may be attributed to liver immaturity, as the liver is unable to conjugate bilirubin effectively, leading to elevated levels of unconjugated bilirubin and the development of hyperbilirubinemia, whether in neonates born at full-term or preterm.[23]

Several challenges were encountered in this study, including the inability to obtain CBB measurements for all neonates delivered at the hospital due to medical and economic constraints. Additionally, all data were collected from a single center, and no distinction was made between arterial and venous cord blood samples, which may limit the overall quality and generalizability of the findings. Despite these limitations, this study represents the first investigation of its kind conducted in this region.

It is recommended that future research place greater emphasis on distinguishing between venous and arterial CBB samples to improve the accuracy and reliability of the collected data.

CONCLUSION

There is a positive correlation between cord blood bilirubin values and the development of neonatal hyperbilirubinemia in apparently healthy full-term neonates. A cord blood bilirubin value of 2.05 mg\dL or greater may predict the occurrence of hyperbilirubinemia in this population. Neonates with smaller birth weight are at increased risk of developing hyperbilirubinemia. Screening neonates using cord blood bilirubin is a safe, cost-effective, and non-invasive method. This approach may assist in clinical decision-making regarding the safe discharge of neonates.

Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethics Committee Approval: This study received approval from the Ethics Committee of University (Approval No: 2676/18, dated 14/05/2024).

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Data availability statement

The datasets generated during and/or analyzed during the current study are available upon reasonable request.

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