

Prediction of Significant Hyperbilirubinemia in Term Newborns Using Cord Blood Bilirubin

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Abstract

Background: Hyperbilirubinemia is a condition in which there is a buildup of bilirubin in the blood, causing yellow discoloration of the eyes and skin, called jaundice. Some conditions such as prematurity, infection, or certain blood disorders can lead to a rapid accumulation of bilirubin to a toxic level.

Aim: The present study was conducted to assess the usefulness of the cord blood bilirubin estimation as a predictor of subsequent neonatal hyperbilirubinemia in healthy term infants who require phototherapy.

Materials and Methods: This observational study was conducted at the tertiary care center. Fifty newborns were included in this study. Five ml of blood was collected from the umbilical cord during delivery and used for estimation of bilirubin. All enrolled babies were followed up for 5 days and clinically assessed for jaundice according to Kramer dermal scale. In these babies, bilirubin estimation was done on samples collected at birth (cord blood), 72 h, and the 5th day of life.

Results: In fifty babies included, 22% of babies had hyperbilirubinemia. In the present study, cord serum, bilirubin level of >2.15 mg/dl has a sensitivity of 63.64% and specificity of 64.10%, in the prediction of neonatal hyperbilirubinemia, at 72 h Cord bilirubin >9.45 mg/dl was present in 29 cases, and only ten developed hyperbilirubinemia.

Conclusion: It is recommended to have cord blood bilirubin estimation of all healthy term babies delivered in an institution to prevent the dangerous consequences of neonatal hyperbilirubinemia.

Key words: Bilirubin, Cord blood bilirubin, Jaundice, Neonatal hyperbilirubinemia, Newborn

INTRODUCTION

Neonatal hyperbilirubinemia is the most common problem encountered during the neonatal period among neonates, which prolongs hospital stay in most babies.^[1] Over 50% of all newborn infants become visibly jaundiced.^[2] Infants become clinically jaundiced when the bilirubin level reaches about 80 $\mu\text{mol/L}$.^[3] An association between the decreased length of stay and the risk of readmission due to neonatal hyperbilirubinemia to the hospital has been reported.^[4] Serum total bilirubin concentrations have been defined as non-physiologic. If the concentration exceeds 5 mg/dl on the 1st day of life is a term neonate, 10 mg/dl on the 2nd day, or 12–13 mg/dl after that.^[5]

The early diagnosis, follow-up, and early treatment of jaundice have been difficult due to early discharges. The concept of early prediction of jaundice would facilitate safe and cost-effective targeted intervention and follow-up. In addition, the timely detection of neonatal hyperbilirubinemia^[6-8] and optimal management is crucial to prevent brain damage and subsequent neuromotor retardation due to bilirubin encephalopathy.^[9] Examination of newborns, cord blood bilirubin levels is a non-invasive procedure and can increase early detection to prevent severe hyperbilirubinemia.

MATERIALS AND METHODS

This observational study was conducted in the Department of Paediatrics, Government Headquarters Hospital, Dindigul from January 2019 to 2019 June. Newborns with congenital malformation were excluded from the study. Other exclusion criteria include infant born to diabetic mother, neonatal sepsis, Rh incompatibility, and conjugated jaundice. After taking informed consent from the parents of the neonates, the cord blood bilirubin estimation was

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done at birth, and serum bilirubin level was done at 48 h of life. In addition, clinical data of those infants were collected, including sex, birth weight, gestational age, history of early neonatal infection, blood type, and Rh factor.

Maternal variables such as the history of jaundice, first trimester bleeding, gestational hypertension, mode of delivery, and drug use during pregnancy were collected. In addition, medication during labor, details of delivery, APGAR score, and maternal blood group were recorded.

Five ml of blood was collected from the umbilical cord during delivery. It was used for estimation for conjugated, unconjugated, total serum bilirubin levels, and blood group. All enrolled babies were followed up for 5 days and clinically assessed for jaundice according to Kramer dermal scale 2. In these babies, bilirubin estimation was done on samples collected at birth (cord blood), at 72 h of life (3rd day), at 120 h of life (5th day). In addition, all the babies were followed up daily for the first 5 postnatal days.

Serum bilirubin ≥ 12.9 mg/dl after 72 h of life was taken as hyperbilirubinemia needing phototherapy, and treatment is advised to all those full-term healthy babies as per the American Academy of the pediatrics practice parameter.

The critical cord bilirubin level with the highest sensitivity and specificity was determined by the receiver operating characteristics (ROC) curve analysis. Cord serum bilirubin concentration was used for developing a “prediction test.” The sensitivity and specificity were calculated for predicting hyperbilirubinemia.

RESULTS

A total of fifty newborn infants were recruited for the study. Out of those fifty neonatal babies, 29 (58%) were male, and 21 (42%) were female, as depicted in Figure 1. Umbilical cord bilirubin levels were measured in all infants from mothers. The gestational age of more than 37 weeks was seen in 42 cases (84%), whereas in eight cases (16%), it was observed between 35 and 37 weeks, as depicted in Figure 2.

Out of those, 38 (76%) were vaginal delivery whereas 12 (24%) were cesarean mode of delivery as depicted in Figure 3.

The average birth weight of neonatal < 2.5 kg were 12 (24%), and the average birth of neonatal between 2.6 kg and 3.5 kg was in 31 (61%) cases whereas, the cases with > 3.5 kg were identified as 7 (14%), respectively, as shown in Figure 4.

The present study infers that cord serum bilirubin levels of babies with neonatal hyperbilirubinemia (> 12.9 mg/dl) were seen in 11 cases (22%), and 39 (78%) were reported with no such conditions, as depicted in Figure 5.

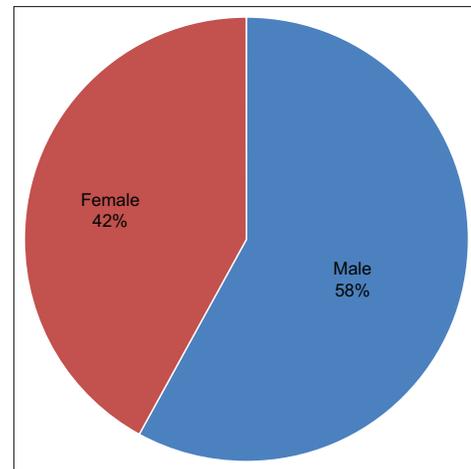


Figure 1: Gender distribution

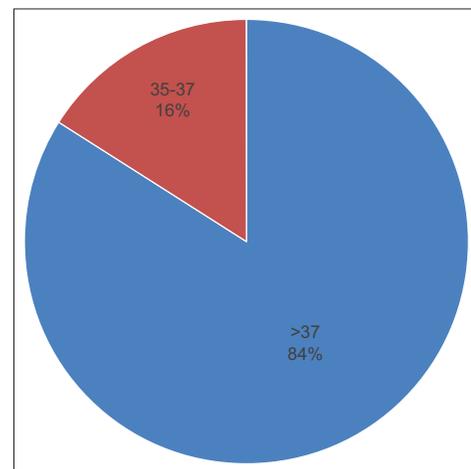


Figure 2: Gestational age distribution

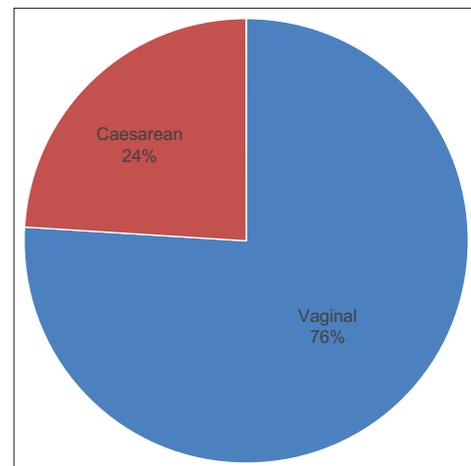


Figure 3: Mode of delivery distribution

Bilirubin profile of first 5 days of postnatal life infers that babies with neonatal hyperbilirubinemia have significantly higher bilirubin levels than babies without hyperbilirubinemia, as depicted in Table 1.

Cord bilirubin level of >2.15 mg/dl cut-off value is chosen based on the ROC analysis. In the present study, cord serum, bilirubin level of >2.15 mg/dl [Table 2] has a sensitivity of 63.64% and specificity of 64.10% in the prediction of neonatal hyperbilirubinemia. Hence, the cord serum bilirubin level of >2.15 mg/dl can be an early predictor of neonatal hyperbilirubinemia in newborn infants.

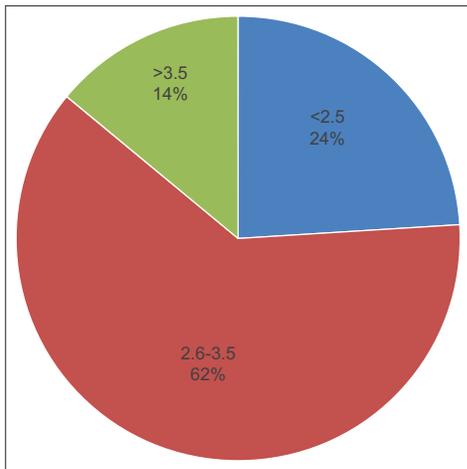


Figure 4: Birth weight distribution

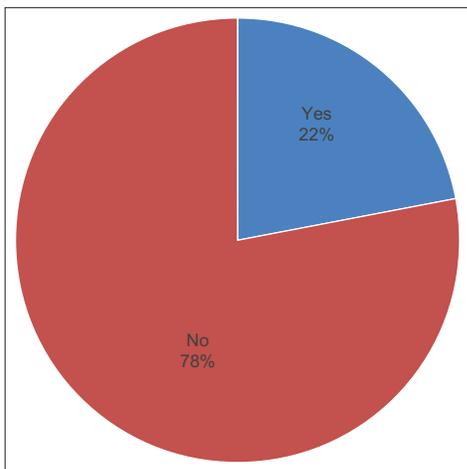


Figure 5: Hyperbilirubinemia distribution

Table 1: Levels of bilirubin on day 1, day 3, day 5 consecutively

Neonatal hyperbilirubinemia	Cord blood bilirubin	3 rd day	5 th day
Yes	3.11±0.62	11.12±2.36	14.92±3.61
No	1.82±0.87	7.98±2.65	8.45±2.13

Similarly, on the 3rd-day bilirubin level of >9.45 mg/dl cut-off value is chosen based on the ROC analysis with high sensitivity and specificity both at 90.91% 76.92%, respectively. In the present study, 3rd-day serum bilirubin [Table 3] level >9.45 mg/dl was analyzed. Cord bilirubin >9.45 mg/dl was present in 29 cases, and only ten developed hyperbilirubinemia, whereas cord bilirubin <9.45 mg/dl was present in 31 cases and only one developed hyperbilirubinemia.

DISCUSSION

Neonatal jaundice is a benign condition observed during the 1st week of life. Hyperbilirubinemia in the newborn usually peaks between 3 and 7 days of age. It is worth noting that the most common cause for readmission during the early neonatal period is hyperbilirubinemia.^[10] Nearly all fetal bilirubin is unconjugated and, in plasma, is bound to albumin. The unconjugated bilirubin is transferred to maternal circulation by the placenta for excretion.^[11] The value of cord bilirubin for predicting significant hyperbilirubinemia is widely debated. Many investigators have found cord bilirubin cut-off values ranging 2–3.5 mg/dl to have good predictive value.^[12,13] However, some others found cord serum bilirubin to have poor predictive value.^[11] Practices on cord bilirubin evaluation vary across different institutions. Risemberg *et al.*^[14] suggest that cord blood should be sent for bilirubin estimation in all infants of mothers.

In the present study, gestational age, birth weight, and mode of delivery did not have any significant association with the development of hyperbilirubinemia. Similar observations were reported by other studies.^[15,16]

Table 2: Cord bilirubin with hyperbilirubinemia on 5th day

Cord blood bilirubin	Neonatal hyperbilirubinemia 5 th day		Total	P-value
	Yes	No		
>2.15	7	14	21	0.031
<2.15	4	25	29	
Total	11	39	50	

Table 3: 3rd-day bilirubin with hyperbilirubinemia on 5th day

3 rd -day bilirubin	Neonatal hyperbilirubinemia 5 th day		Total	P-value
	Yes	No		
>9.45	10	9	29	0.002
<9.45	1	30	31	
Total	11	39	50	

The studies by Pradhan *et al.*, Rajpurohit *et al.*, and Farhat *et al.* found that mean cord bilirubin value was significantly higher than those who developed hyperbilirubinemia those who did not.^[17-19]

In our study, we investigated whether cord bilirubin levels could be used to predict early neonatal infection. On ROC curve analysis, critical cord bilirubin level (≥ 2.15 mg/dl) with high sensitivity and high specificity is selected at 65%. If a child becomes hyperbilirubinemia, the cord bilirubin's probability was ≥ 2.15 mg/dl was 65% (sensitivity). Similarly, in this study, on ROC curve analysis, critical 3rd-day bilirubin level with high sensitivity and high specificity ≥ 9.45 mg/dl was selected. The probability of non-hyperbilirubinemia given 3rd-day bilirubin was lower than ≥ 9.45 mg/dl was 76%. If a child becomes hyperbilirubinemia, the probability that the 3rd-day bilirubin was ≥ 10.15 mg/dl was 91% (sensitivity).

CONCLUSION

The study finds that there is a substantial relationship between cord blood serum bilirubin and neonatal jaundice development. As a result, a group of newborns at risk of developing jaundice and requiring phototherapy at birth can be identified.

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