Original Research Article

Cord serum bilirubin as a predictor of neonatal hyperbilirubinemia in healthy term and late preterm neonates

Ramanathan R.*, Baby Praveena A.

Department of Pediatrics, Raja Muthiah Medical College and Hospital, Chidambram, Tamil Nadu, India

*Correspondence:
Dr. Ramanathan R.,
E-mail: drram78@gmail.com

ABSTRACT

Background: Icterus neonatorum is the most common neonatal illness occurring in the first 7 days of life. It is the most important cause for hospital readmissions during the early neonatal period and also the cause for neonatal morbidity. In this study our main objective is, to find out that whether detecting umbilical cord blood bilirubin levels soon after birth, will help to identify the development of significant jaundice in early neonatal period which requires immediate intervention

Methods: This was a prospective observational study carried out among 150 term and preterm babies. Their cord bilirubin level were estimated. Jaundice was determined by using yellowish appearance of eyes, skin and Kramer score. Statistics employed include Chi-square test and receiver operator characteristic curve

Results: Study participants enrolled into the study was 150. Cord serum bilirubin was significantly associated with Kramer score and yellowish discoloration of eyes and skin and not significantly associated with sex, mode of delivery, gestational age and birth weight. When cord serum bilirubin was compared against the occurrence of clinical jaundice, sensitivity was found to be 58.33%, specificity was 96.49% positive predictive value was 84% and negative predictive value was 88%. Receiver operator characteristics curve indicated that the area below the curve was 0.842.

Conclusions: Cord serum bilirubin can be used as a screening tool to identify the neonatal jaundice in both term and late preterm babies. Present study has shown increased specificity than sensitivity which warrants further exploration.

Keywords: Cord blood bilirubin, Neonatal hyperbilirubinemia, Predictive value, Sensitivity, Specificity

INTRODUCTION

Neonatal jaundice in newborn is common problem. Approximately 85% of all term newborns and most preterm infant develop clinical jaundice. A total serum bilirubin level >15 mg/dl is found in 3% on normal term infants.[1] Neonatal hyperbilirubinemia is most usual abnormal physical examination finding during the early post-natal life.[2] American academy of pediatrics recommends that newborn discharged within 48 hours should have a follow up visit after 48-72 hours for monitoring any significant jaundice and other problems.[3]

In babies born after 37 completed weeks physiological jaundice is seen to be appear between 36-72 hours of age, maximum rise of bilirubin is seen on 72-96 hours of life. Serum bilirubin doesn't exceed 15 mg/dl and jaundice disappear by 10th day of life.[2] This recommendation is not appropriate for our country due to limited follow up facilities in the community. These neonates may develop jaundice which may be overlooked or delay in recognition unless the baby is closely followed up. Concern of neonatologist regarding the earlier discharge are reports of many cases of bilirubin induced cerebral damage identified in healthy term and late preterm infants

even without any complications.[4] Prevention of serious complications depends on earlier identification effective early treatment of jaundice, but clinically significant jaundice may not develop until one or more days after delivery. Current practice, which usually promotes early discharge after delivery for social and medical reasons.[5] Estimation of cord blood bilirubin at delivery is a simple method which is practicable, cheap, non-invasive, no pain to the baby. Several previous studies have investigated the potential utility of umbilical cord bilirubin in predicting subsequent jaundice, which shows inconsistent results, the present study was undertaken to evaluate the critical cord bilirubin level and the predictive value of cord bilirubin in identifying term and late preterm infants at risk of hyperbilirubinemia.

METHODS

This prospective observational study was carried out at neonatal care unit Rajah Muthaih Medical College and Hospital Chidambaram, after getting permission from the Institute Human Ethical committee clearance. Study was done in 150 hospital born healthy term and late preterm babies over a period of six months.

Inclusion criteria

- Term and late preterm babies, birthweight >2.2 kg
- APGAR score of >7/10 at 5 minutes
- Delivered via both LSCS, labour natural.

Exclusion criteria

- Preterm babies <34 weeks,
- Rh and ABO incompatability,
- Neonates at risk of sepsis,
- Instrumental delivery,
- Perinatal asphyxia,
- Meconium stained liquor,
- Infant of diabetic mother,
- Neonatal jaundice within 24 hours.

The relevant data were obtained from maternal case sheet and by asking history from the mother and 5 ml of cord blood was taken after obtained consent from the parents or guardians. The collected cord blood was sent to the laboratory for estimation of cord blood bilirubin levels by Diazotized sulfanilic method. According to the cord blood bilirubin levels babies were categorized into two groups. Group A cord bilirubin level <2 mg/dl, Group B includes bilirubin levels >2 mg/dl. These neonates were followed up daily for clinical appearance of jaundice till 5th day of life or hospital stay whichever was later as serum bilirubin reaches its peak between 3rd to 5th day in healthy neonates. Serum bilirubin levels were estimated between 72-96 hours of life for all neonates participated in the study or earlier if clinical examination shows rapid progression of jaundice. The main inference of the study was inferred in terms of cord serum bilirubin levels and

critical values of hyperbilirubinemia which required phototherapy or exchange transfusion. All data were entered in Excel sheet to prepare master chart. After preparing the master chart the variables were analyzed by using the software SPSS Version 21. Stastical data were analysed by using Pearson chi-square test. Sensitivity, specificity, positive predictive value, negative predictive value was calculated. Cord bilirubin levels having highest specificity and sensitivity was determined with the Receiver operating characteristics curve

RESULTS

Total study participants were 150. 60% of neonates participated in the study were male. 48.7% were born out of primi mothers. 48% born out of normal delivery. 33.3% of neonates participated in the study were preterm babies. 72.7% of the babies had birth weight lower than 3 kgs (Table 1).

Table 1: Baseline characteristics of the study participants.

Variable	Frequency (n)	Percentage
Sex		
Male	90	60
Female	60	40
Parity		
Primi	73	48.7
Multigravida	77	51.3
Normal delivery	72	48
LSCS	78	52
Gestational age		
Term	100	66.7
Preterm	50	33.3
Birth weight(kg)		
<3	109	72.7
3-3.5	35	23.3
>3.5	06	4

Table 2: Distribution of study participants according to skin discolouration, Kramers score and cord bilirubin level.

| Variables	Frequency (n)	Percentage
Yellowish discoloration		
Yes	50	33.3
No	100	66.7
Kramer score		
2	103	68.7
3	13	8.7
4	34	22.7
Cord bilirubin levels (mg/dl)		
<2	125	83.3
>2	25	16.7
Total	150	100

33.3% of the study participants had yellowish appearance of eyes and skin. 68.7% had Kramer's score of 2 and

22.7% had Kramer score of 4.83.3% had cord bilirubin <2 mg/dl, 16.7% had cord bilirubin >2 mg/dl (Table 2) on cross tabulation and applying chi-square test, strongly significant association were identified between cord bilirubin values and babies who underwent phototherapy with a P value of 0.01 (Table 3).

Table 3: Cross tabulation between cord bilirubin levels and phototherapy.

Cord bilirubin	Phototherapy	No phototherapy	Total	Chi value	P value
>2	21	4	25		
<2	15	110	125	149	<0.01
total	36	114	150		
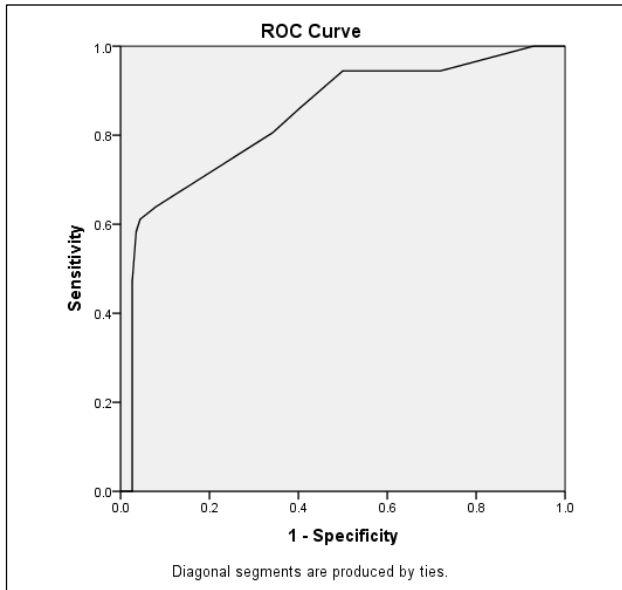
Area under the curve: 0.842; Sensitivity: 58.33; Specificity: 96.49; Positive predictive value: 84%; Negative predictive value: 88%

Figure 1: ROC curve.

When cord bilirubin was compared against the appearance of jaundice sensitivity 58.33, specificity 96.49, positive predictive value 84%, negative predictive value 88%. The receiver operator characteristic curve indicated that the curve was 0.842

DISCUSSION

This was a prospective observational study done among 150 term and late preterm babies born in a tertiary care hospital. The objective was to identify whether umbilical cord serum bilirubin values soon after birth could predict the risk of significant neonatal hyperbilirubinemia in early neonatal period.

High cord bilirubin levels among neonates who later become severely icteric is compared to cord bilirubin levels in non-jaundiced neonates. The above was based in the fact that the mechanisms of development of jaundice in early post-natal period had already occurred in late fetal life. Mostly all fetal bilirubin is unconjugated, due to a decreased ability of the fetal liver to conjugate bilirubin.

In plasma, indirect bilirubin is tightly bound to albumin, which is an important bilirubin binding protein in blood. In these circumstances no indirect bilirubin deposition in fetal tissue takes place. Indirect bilirubin is rapidly transferred to the maternal circulation by the placenta, whereas only minimal amount of conjugated bilirubin crosses the placenta. Thus, bilirubin synthesized by the fetus is excreted by the mother, due to a larger capacity for bilirubin excretion, and only minor differences in maternal bilirubin concentrations can be expected. A clear correlation between umbilical cord serum bilirubin (UCB) and subsequent development of hyperbilirubinemia was shown among all the two study groups by the observation is that out of the 150 babies 36 babies had increased bilirubin values in post-natal period and underwent phototherapy. Out of 36 babies 21 babies had phototherapy (84%) and cord bilirubin values of >2 mg/dl, as against only 15 babies with bilirubin value of <2 mg/dl.

In the present study, ROC curve analysis with cord bilirubin levels >2 mg/dl had area under the curve of 84%. Sensitivity was found to be 58.33% while specificity was found to be 96.49%. The above indicated that at the bilirubin value of >2 mg/dl, the test would predict more false positives than false negatives.

Several studies also reported the importance of cord bilirubin levels at birth in prediction of hyperbilirubinemia. Taksande et al found that the cord serum bilirubin values >2 mg/dl has a sensitivity 89.5%, specificity 85%, negative predictive value of 98.7% and positive predictive value of 38.8% which is similar to that of the present study.[6]

Bernaldo and Segre found that the critical level for indirect bilirubin in cord serum was ≥2.0 mg/dl the probability that the neonate needed intervention was 53%.[7] When cord blood bilirubin was 2.5 mg/dl the probability needing phototherapy was 72%, when the level was 3.0 mg/dl, the probability of needing treatment was 86%, and if it was 3.5 mg/dl, the probability went up to 93%. This could be explained because the newborns with higher cord bilirubin level have more rapid increase in serum bilirubin and have high chances of neonatal hyperbilirubinemia and more chances of requiring phototherapy.

Satrya et al and Sun et al studies were in association with the present study.[8] Rostami and Mehrabi on their study found out that the well neonates had risk to be jaundiced by identify bilirubin values in cord blood in 643 full. The total bilirubin ≥239 μmol/L (14 mg/dl) was defined as significant hyperbilirubinemia. They find out that cord serum bilirubin level cannot be used as a marker for identifying subsequent significant hyperbilirubinemia.[9] Present study observes that cord blood bilirubin >2 mg/dl can be used as an early predictor of neonatal jaundice. This difference could be because of geographical difference in the study population.

The main limitation of the present study was taking the cord serum bilirubin values as qualitative variable with a cut off at 2 mg/dl rather than taking it as quantitative variable. The above limited our ability to explore the effect of cut off values other than 2 mg/dl. This variation in cut off value can be attributed to the genetic variation present in indigenous population which warrants further exploration.

CONCLUSION

Cord blood bilirubin values can be used as a predictor of neonatal jaundice. The present study shows more specificity than sensitivity. Most of the neonates with cord bilirubin value of more than 2 mg/dl developed hyperbilirubinemia but still it was also developed by considerable proportion of neonates with cord bilirubin value of less than 2 mg/dl.

REFERENCES

1. Cloherty JP, Eichenwald EC, Stark AR. Neonatal Hyperbilirubinemia. Manual of neonatal. care 8th edition. New Delhi: Lippincot Williams and Wilkins, a Wolters Kluwer Business; 2016;26:336-339.
2. Bhutani V, Johnson L, Sivieri E. Predictive ability of pre-discharge hour specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near term newborns. Paediatr. 1999:103(1):6-14.
3. American Academy of Pediatrics, Subcommitee on Hyperbilirubinemia. Management of hyperbilirubinemia in the new born infant 35 or more weeks of gestation. Pediatr. 2004;114(1):297-316.
4. Venkatamurthy M, Murali S, Mamatha S. A comparison study: cord serum albumin is compared with cord serum bilirubin as an indicator in neonatal jaundice. J Evol Med Dent Sci. 2014:3(15):4017-22.
5. Maisels MJ, Kring E. Length of stay, Jaundice and hospital readmission. Pediatr. 1998;101:995-8.
6. Taksande A, Vilhekar K, Jain M, Zade P, Atkari S. Prediction of the developmentof neonatal hyperbilirubinemia by increased umbilical cord blood bilirubin. Ind Medica. 2005;9(1):5-9.
7. Bernaldo AJ, Segre CA. Bilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia. Sao Paulo Med J. 2004;122(3):99-103.
8. Satrya R, Effendi SH, Gurnida DA. Correlation between cord blood bilirubin level and incidence of hyperbilirubinemia in term newborns. Paediatrica Indonesiana. 2009;49(6):349-54.
9. Rostami N, Mehrabi Y. Identifying the newborns at risk for developing significant hyperbilirubinemia by measuring cord bilirubin levels. J Arab Neonatal Forum. 2005;2:81-5.