Doi: 10.32677/IJCH.2017.v04.i04.025

Original Article

Cord bilirubin levels as a predictive marker for neonatal hyperbilirubinemia: A prospective study

Parul Sehgal, Sanober Wasim, Vipan Chandar, Alpa Gupta, Anil Rawat, Vinita Kalra, N K Bhat, Neerul Pandita

From Department of Pediatrics, Swami Rama Himalayan University, Doiwala, Dehradun, Uttarakhand, India

Correspondence to: Dr. Parul Sehgal, House No.187, C2C, Pocket 2, Janakpuri, New Delhi, India. E-mail: parulsehgal9@gmail.com

Received - 11 April 2017 Initial Review - 03 June 2017 Published Online - 02 September 2017

ABSTRACT

Background: Hyperbilirubinemia is the most common medical problem in newborn infants. Early discharge is recommended but hospital readmission is a cause of concern among clinicians. This in turn carries a risk of delayed recognition of significant hyperbilirubinemia. **Objective:** A cross-sectional analytical study was done to evaluate the predictive value of cord bilirubin level for identifying term and near-term neonates for subsequent hyperbilirubinemia. **Materials and Methods:** Cord bilirubin levels at birth and subsequently serum bilirubin levels at 72 h were assessed in 100 neonates. The cutoff value was estimated beyond which there was significant hyperbilirubinemia. **Results:** The cutoff value of cord bilirubin >2.02 mg/dl had sensitivity and specificity of 87.5-70.8%, respectively, with positive predictive value of 0.39 and negative predictive value of 0.965 for subsequent hyperbilirubinemia. **Conclusion:** The cutoff value of cord bilirubin level estimated is 2.02 mg/dl can be used to predict significant neonatal hyperbilirubinemia.

Key words: *Cord bilirubin, Hyperbilirubinemia, Neonate*

Jaundice is observed during the first week of life in approximately 60% term and 80% of preterm infants [1]. Due to social and family constraints; the pediatricians are practicing early discharge from hospitals [2]. This increases the risk of significant jaundice where subsequently intervention might be required. The problems encountered due to hyperbilirubinemia are neurological manifestations as seen in kernicterus leading brain damage. This is also seen in a full-term newborn with no apparent evidence of hemolysis [3]. Therefore, it is difficult to predict which infants are at increased risk for significant and relatively late hyperbilirubinemia. There is an obvious need to implement follow-up programs or to develop predictive guidelines that will enable the physicians to predict or to identify which of the early discharged newborn will develop significant hyperbilirubinemia [2].

Knowledge of infants at risk of developing jaundice allows simple bilirubin reducing methods to be implemented before jaundice becomes significant and could influence a decision regarding early discharge from Hospital. Predicting the high-risk neonates for subsequent hyperbilirubinemia will also help in detecting infants at low risk for postnatal hyperbilirubinemia and minimize an unnecessary prolongation of hospitalization or hospital readmission for hyperbilirubinemia [4]. We therefore, undertook this study to predict the value of cord bilirubin level beyond which a newborn might develop jaundice requiring intervention.

MATERIALS AND METHODS

The study was conducted in the Department of Paediatrics, Swami Rama Himalayan University, Dehradun, over a period of 12 months from 1st January 2015 to December 31st 2015. The study was approved by Institutional Ethics Committee. Written consent was obtained from the parents or legal guardians before recruitment. Only full-term and late preterm (gestational age >34 weeks and <42 weeks) neonates with Apgar score >7 in 1st min and 10 at 15th min were recruited to the study. Neonates of both gender delivered consecutively by any type of delivery in the Department of Obstetrics and Gynecology were prospectively enrolled in the study. Neonates with any significant illness (sepsis, respiratory distress syndrome, asphyxia, and infant of diabetic mother) that could aggravate hyperbilirubinemia, birth weight <2000 g and babies with Rh and ABO incompatibility were excluded from the study.

Soon after the birth when a neonate was separated from placenta, 10 ml of blood was taken by passive let down in plain and ethylenediaminetetraacetic acid vials and were immediately sent for assessment and analysis. Hemolysed samples were discarded and the cord blood was not taken in mother with negative blood group considering the possibility of Rh incompatibility. Repeat serum bilirubin levels were assessed at 72 h of life by venous sampling of newborns, and it was sent immediately for bilirubin estimation by blinded observer technique.

A detailed maternal and perinatal history and clinical findings were recorded on a pre-structured format along with the laboratory investigations. Gestational age of the enrolled infants was determined on the basis of the date of the past menstrual period or first-trimester ultrasound (wherever available). It was confirmed by the expanded Ballard score done within 24 h of life [5]. All enrolled babies were followed up clinically for the development of jaundice using Kramer Dermal Scale* till discharge and further on follow-up till 1 month of age. Detailed physical examination was carried out daily by the investigator. Those babies who on visual inspection had Jaundice where the bilirubin level seemed to be above the 95th centile for age in hours of life as per Bhutani hour specific bilirubin nomogram were further investigated by estimation of serum total and direct bilirubin.

The newborns detected to have pathological hyperbilirubinemia were further investigated by doing Direct Coombs test, complete blood count, reticulocyte count, and peripheral smear and were managed according to standard protocols as per guidelines of American Academy of Pediatrics subcommittee on hyperbilirubinemia. The decision to start or stop phototherapy was based on AAP guidelines [6]. Bilirubin and its fractions were measured by spectrophotometric technique on an automated analyzer Unicel DXC 800 manufactured by Beckman Coulter. Neonates who were discharged before the third day of life were asked to return on day 3 for estimation of serum bilirubin at 72 h of life. Neonates who did not come for follow-up or in whom the 72 h serum bilirubin could not be collected were excluded from the study.

Result was analysed using statistical software statistical package for the social sciences 22. Qualitative data were expressed in frequency and percentage, while quantitative data were expressed in mean ± standard deviation. Paired t-test, receiver operating characteristic (ROC) curve, and logistic regression were used to analyze the pattern of bilirubin levels. The strength of association was found using Pearson's Correlation curve.

RESULTS

A total of 767 deliveries occurred during the study period of which 100 were enrolled in the study (Figure 1). Out of the total delivery sample, 350 were excluded as they were early preterms. From the remaining 417 neonates, 216 were assessed since the others had congenital anomalies or maternal risk factors or other risk factors which could lead to jaundice. The sample size of 100 (out of 216) was finalized once we observed saturation in the results, i.e., we started observing a significant pattern in estimating the cutoff value of cord bilirubin beyond which a neonate could have developed jaundice. Among the sample size of 100, 12 cases were excluded since their total bilirubin levels at 72 h of life were <2 mg/dl [7].

The baseline characteristic of the mothers and newborn enrolled in the study is given in Tables 1 and 2, respectively.

With ROC analysis, (Figure 2), the mean cord bilirubin level was 1.923±0.966 mg/dl. The area under curve was 0.791. The mean total bilirubin at 72 h was 10.56±3.18 mg/dl. There were 16 newborns who had serum bilirubin >14 mg/dl at 72 h (Table 3). The cord bilirubin of >2.02 had sensitivity and specificity of 87.5% and 70.8%, respectively, with positive predictive value of 0.39 and negative predictive value of 0.965. The strength of association of cord bilirubin >2.02 mg/dl and requirement of phototherapy at 72 h was found to be significant (p<0.001).

DISCUSSION

Serum bilirubin levels are usually 1-3 mg/dl at the time of birth and rise at the rate of <5 mg/dl/day, peaking at 2-3 days in term neonates [7]. Our aim was to quantify the relationship between cord blood bilirubin with peak serum bilirubin levels at 72-84 h of life. Cord blood estimation was chosen because it is a non-invasive method and the results are available within few hours after birth. Thus, the babies at risk for developing hyperbilirubinemia can be detected at birth in a non-invasive way if the neonate leaves the hospital within the first few postnatal days. In addition, the use of cord blood bilirubin values may help predict infants with low risk for hyperbilirubinemia and minimize an unnecessary prolongation of hospitalization [8-10]. In a study by Taksande et al., prevalence was 9.5% only because the cutoff for significant hyperbilirubinemia on 3rd day of life was taken as 17 mg% [11].

Table 1: Baseline characteristics of mother enrolled

Maternal characteristics	Type	n (%)
Mode of delivery	LSCS	54 (61.3)
	Normal	34 (38.6)
Blood group	A+ve	21 (23.3)
	B+ve	21 (23.3)
	AB+ve	9 (10)
	O+ve	33 (37.3)
	AB-ve	1 (1.2)
	B-ve	3 (3.02)
MSL	-	14 (16)
Oxytocin therapy	-	2 (2.27)
Neonatal jaundice in previous sibling	-	1 (1.2)
PROM		2 (2.27)

MSL: Meconium stained liquor, PROM: Premature rupture of membrane, LSCS: Lower Segment Caesarean Section

Table 2: Baseline characteristics of newborn enrolled

Neonatal characteristics	Type	Mean±SD	n (%)
Gestational age (weeks)		37.82±1.09	
Sex	Female	-	31 (35.2)
	Male	-	57 (64.7)
Blood group	A+ve	-	8 (20)
	B+ve	-	11 (27.5)
	AB+ve	-	2 (5)
	O+ve	-	19 (47.5)
	B-ve	-	3 (3)
Birth trauma	-	-	0 (0)
Weight (kg)	-	2.77±0.39	-
Cord blood hemoglobin (g/dl)	-	14.86±1.626	-

SD: Standard deviation

Table 3: Relationship between cord bilirubin and serum bilirubin at 72 h

Serum bilirubin	Number of neonates n (%)		
	Cord bilirubin >2.02 mg/dl	Cord bilirubin <2.02 mg/dl	Total
2-13 mg/dl	21 (60)	51 (97)	72 (81.8)
>14 mg/dl	14 (40)	2 (3)	16 (18.2)
Total	35 (39.8)	53 (60.2)	88 (100)

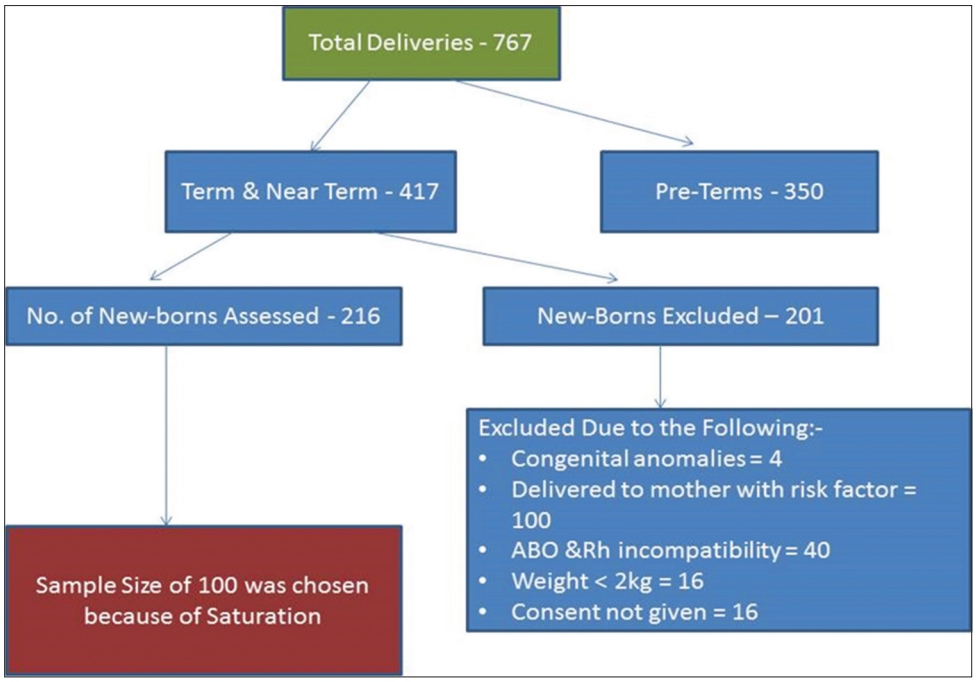

Figure 1: Flowchart showing neonates enrolled

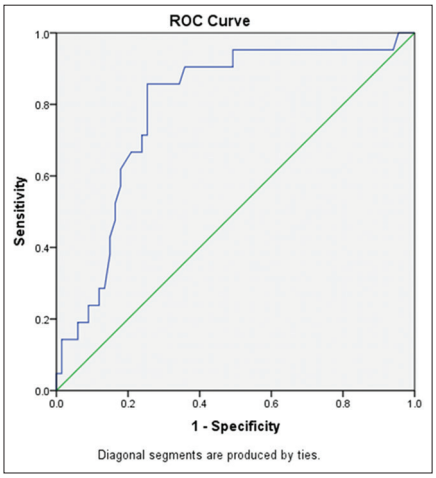

Figure 2: Receiver operating characteristic curve showing association of cord bilirubin levels and requirement of phototherapy at 72 h of life

Nagwa et al. observed that there was a positive correlation between umbilical cord serum bilirubin and subsequent development of hyperbilirubinemia and newborn with cord bilirubin >4 mg/dl were a group at risk of developing severe hyperbilirubinemia and were presented to have mean serum bilirubin levels higher than 16 mg/dl at 72 h with peak 17±4.3 mg/dl at 68±17.5 h of postnatal age [12]. Knudsen in his study demonstrated that jaundiced newborn presented with higher umbilical cord bilirubin levels than newborns without clinical jaundice. In addition, the number of jaundiced newborns undergoing phototherapy was significantly higher when these levels were >2.0 mg/dl, in comparison with the number of jaundiced newborns with no need for treatment and whose bilirubin levels were ≤2.0 mg/dl [10]. Ahire et al. predicted the serum bilirubin >3 mg/dl on the first day of life had 100% sensitivity of predicting subsequent jaundice at 48 h of life with bilirubin levels >10.58 mg/dl [13].

Knupfer et al. observed that serum bilirubin >1.74 mg/dl on the first day of life had 97% sensitivity of predicting a subsequent serum bilirubin levels >16 mg/dl at 72 h of life. At this critical serum bilirubin value, the negative predictive value was 99.8% [14]. Rataj et al. reported that if cord bilirubin was <1 mg/dl jaundice occurred in 2.4% newborns, whereas 89% of infants with cord bilirubin >2.5 mg/dl became jaundiced [15]. Taksande et al., in their study, predicted that cord bilirubin level >2 mg/dl had 89.5% sensitivity, and high (98.7%) negative predictive value, and fairly low (38.6%) of positive predictive value [11]. Dhanwadkar et al. found that 2.2% neonates developed significant jaundice with cord total bilirubin levels >3 mg/dl with high specificity (86%) and positive predictive value (92%) [16].

Pradhan et al. found significant association of high total cord bilirubin levels of >2.5 mg/dl and subsequent development

of jaundice within 24 h of life with sensitivity (84.1%) and specificity (88.5%) [17]. In our study, the cord bilirubin level >2.02 mg/dl had the highest sensitivity (87.5%), and this critical bilirubin levels had a very high negative findings, a critical cutoff level of cord bilirubin was 2.02 mg/dl predicted 88% of newborn who developed jaundice. However, the cord bilirubin <2.02 mg/dl did not completely exclude the development of significant hyperbilirubinemia. Only 3% of newborn with cord bilirubin levels of <2.02 mg/dl developed jaundice. A 96% of negative predictive value suggests that the measurement of cord serum bilirubin can help in identifying those newborn who are unlikely to require further evaluation and intervention.

Just like all studies, our case study also has some limitations. The sample size was small which causes difficulty in creating significant relationships between the two values of bilirubin levels. The volume of cord blood collected was inadequate in few of the cases. In addition, some of the blood collected got hemolyzed which could not be considered for analysis. Some of the neonates did not turn up in outpatient department for follow-up and the access to sample collection at 72 h of life was denied by some of the parents which made it difficult to consider them as cases.

CONCLUSION

Cord bilirubin level >2.02 mg/dl had sensitivity and specificity of 89.5% and 87.5% and can be taken as a cutoff value above which, a neonate would develop hyperbilirubinemia and would require phototherapy.

REFERENCES

1. Stoll BJ, Kleigman RM. In: Behrman RE, Kleigman RM, Jenson HB. Jaundice and hyperbilirubinemia in new-born: In Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: WB Saunders Company; 2015. p. 871-3.
2. Carty EM, Bradley CF. A randomized, controlled evaluation of early postpartum hospital discharge. Birth. 1990;17(4):199-204.
3. Rosenfeld J. Umbilical cord bilirubin levels as a predictor of subsequent hyperbilirubinemia. J Fam Pract. 1986;23(6):556-8.
4. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. Pediatrics. 1995;96:730-3.
5. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New ballard score, expanded to include extremely premature infants. J Pediatr. 1991;119(5):417-23.
6. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114(1):297-316.
7. Gregory ML, Martin CR, Cloherty JP. Neonatal hyperbilirubinemia. In: Cloherty JP, Eichenwald EC, Hansen AR, Stark AR, editors. Manual of Neonatal Care. 7th ed. New Delhi (India): Wolter Kluwer; 2011. p. 304.
8. Watchko JF. Neonatal Indirect hyperbilirubinemia and kernicterus. In: Gleason CA, Devaskar SU, editors. Avery's Diseases of the Newborn. 9th ed. Philadelphia (USA): Elsevier; 2012. p. 1123-42.
9. Suchonska B, Wielgos M, Bobrowska K, Marianowski L. Concentration of bilirubin in the umbilical blood as an indicator of hyperbilirubinemia in newborns. Ginekol Pol. 2004;75(10):749-53.
10. Knudsen A. Prediction and non-invasive assessment of neonatal jaundice in the term healthy newborn infant. Acta Paediatr. 1996;85(4):393-7.
11. Taksande A, Vilhekar K, Jain M, Zade P, Atkari S, Verkey S. Prediction of the development of neonatal hyperbilirubinemia by increased umbilical cord blood bilirubin. Curr Pediatr Res. 2005:9(1-2):59.
12. Nagwa H, Elgayae A, Salah MH. Cord blood bilirubin as a predictor of neonatal hyper-bilirubinemia. Med J Cairo Univ. 2012;80(2):31-6.
13. Ahire N, Sonawane R, Gaikwad R, Patil S, Sonawane T. Study of correlation of cord blood bilirubin with neonatal hyper bilirubinaemia. MVP J Med Sci. 2016;3(1):60-6.
14. Knüpfer M, Pulzer F, Gebauer C, Robel-Tillig E, Vogtmann C. Predictive value of umbilical cord blood bilirubin for postnatal hyperbilirubinaemia. Acta Paediatr. 2005;94(5):581-7.
15. Rataj J, Kornacka M, Korman E. Usefulness of measuring bilirubin levels in cord blood for predicting hyperbilirubinemia in newborns. Ginekol Pol. 1994;65(6):276-80.
16. Dhanwadkar SS, Rasalam CS, Masood Z. Effectiveness of early clinical assessment and bilirubin estimation for prediction of neonatal hyper bilirubinaemia. Int J Contemp Pediatr 2016;3(2):477-84.
17. Pradhan A, Lamichaney R, Sharma V. Cord Blood Bilirubin level as a predictor of development of pathological hyperbilirubinemia in new-borns. Int J Contemp Pediatr. 2017;4(4):1519-24.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Sehgal P, Wasim S, Chandar V, Gupta A, Rawat A, Kalra V, Bhat NK, Pandita N. Cord bilirubin levels as a predictive marker for neonatal hyperbilirubinemia: A prospective study. Indian J Child Health. 2017; 4(4):571-574.