

Cord bilirubin as a Predictor of Neonatal Hyper bilirubinemia in healthy term babies

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Abstract

Objectives: To assess the value of cord blood bilirubin in identifying term healthy babies who develop significant hyperbilirubinemia. **Methodology:** This Prospective cohort study, conducted from May 2016 to September 2016 in a tertiary care hospital included 100 term healthy breastfed babies without Rh incompatibility or significant illness. Cord bilirubin was estimated in all babies. Neonates were followed up daily for 5 days for hyperbilirubinemia. Serum bilirubin levels were estimated on day 5 in all babies. Significant hyperbilirubinemia was defined as bilirubin > 15 mg/dl after 72 hours. **Results:** Mean cord bilirubin was 2.8 +2.4 mg /dl in those who developed hyperbilirubinemia and 2.5+2.91 mg/dl in those who did not. Clinically detectable jaundice was present in 72%. Twenty-two percent babies developed hyperbilirubinemia. Peak serum bilirubin of babies who developed significant hyperbilirubinemia was 23+ 2.8mg/dl at 120 hours. Cord bilirubin of > 2mg /dl was present in 64 babies and 19 (29%) developed hyper bilirubinemia. Cord bilirubin < 2mg was present in 36 and only 3(8%) developed hyper bilirubinemia (p=0.018). The sensitivity was 86% specificity was 40%, positive predictive value was 29% and negative predictive value was 91% at critical cord bilirubin value of >2mg/dl. ABO incompatibility was significantly associated with hyperbilirubinemia (p=0.0006) **Conclusion:** Cord bilirubin can be a good predictor of hyperbilirubinemia. Neonates with cord bilirubin < 2mg/dl are probably safe for early discharge and those with bilirubin levels >2 mg/dl need close follow up.

Keywords: Significant hyperbilirubinemia, Cordbilirubin, Healthy term babies, Predictor

Introduction

Clinical jaundice is seen in 60-70% of term and about 80% of preterm newborns [1]. Various methods have been suggested for prediction of neonatal jaundice such as physical examination, evaluation using risk factor table, routine predischarge transcutaneous bilirubin measurement and measuring expiratory carbon monoxide levels. Neonatal hyperbilirubinemia if not treated in time, may cause bilirubin induced neurological dysfunction, kernicterus [2].

American Academic of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow-up visit after 48 to 72 hours for any significant jaundice or other problems [3]. This is not possible in India due to limited follow-up facilities. Financial constraints, family and traditional beliefs have led to early discharge of healthy term neonates after delivery

[4,5]. The concept of prediction of jaundice using cord bilirubin has been studied by various investigators, but the results have been inconsistent [6,7,8,9]. There is a need for identifying healthy term babies at birth who may develop significant hyperbilirubinemia in order to implement early treatment and minimize the risk of bilirubin associated brain damage [7]. This study was aimed at evaluating the usefulness of cord bilirubin as a predictor of neonatal hyper bilirubinemia in healthy term babies.

Materials & Methods

Objective: To assess the value of cord blood bilirubin in identifying healthy term babies who developed subsequent hyperbilirubinemia.

Study design: Prospective study.

Stud area: The study was conducted in post-natal ward of a tertiary care teaching hospital in western Maharashtra.

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Study period: 1st may 2016 to September 2016 (6 months)

Study population: Healthy term babies (>37 weeks) delivered at our hospital.

Inclusion criteria: Healthy terms babies (Gestational age >37 weeks) and APGAR score of over 7 at first and fifth minute of life.

Exclusion criteria: The babies with significant morbidities that could aggravate hyperbilirubinemia, Rh incompatibility and APGAR score < 7 at one minute were excluded.

Methodology: Informed written consent was obtained from parents. Bilirubin estimations were done using DIAZO method in the biochemistry laboratory. Cord

bilirubin was done in all babies. Neonates were followed up daily for 5 days for hyperbilirubinemia. In neonates who developed significant jaundice, bilirubin estimation was done as required and treated with phototherapy as per Bhutani's nomogram [8]. Serum bilirubin levels were estimated in all babies on day 5. In the study, significant hyperbilirubinemia was defined as bilirubin > 15 mg/dl after 72 hours.

Statistical analysis: Data was entered in Microsoft excel sheet and analyzed using registered version of SPSS 20. Analysis was done using simple statistics like mean, median and proportions for general variables. Chi square test was done for finding the association between two or more categorical variables. The sensitivity, specificity positive predictive value and negative predictive value were calculated. The accuracy of the test was measured by using receiver operator curve.

Results

In the study 100 babies were enrolled. Clinically detectable jaundice was seen in 72%. Twenty-two percent babies developed hyperbilirubinemia. Mean cord bilirubin was 2.8 +2.4 mg /dl in those who developed hyperbilirubinemia and 2.5+2.91 mg/dl in those who did not. However, this was not statistically significant (p=0.62). Peak serum bilirubin of babies who developed significant hyperbilirubinemia was 23+ 2.8mg/dl at 120 hours.

All the babies were exclusively breastfed. The baseline data is shown in table 1. There was no significant difference between the cases who did and who did not develop hyperbilirubinemia with respect to various factors such as gender, gestational age, birth weight, mode of delivery, use of oxytocin and pregnancy induced hypertension [Table 2]. However, ABO incompatibility was significantly associated with development of hyper bilirubinemia (p=0.0006)[Table 2].

Cord bilirubin level of > 2mg /dl was present in 64 babies and 19 (29%) developed hyperbilirubinemia. Cord bilirubin < 2mg was present in 36 and only 3(8%) developed hyperbilirubinemia. This difference was statistically significant (p=0.018) [Table 3]. Cord bilirubin >2mg/dl had sensitivity of 86%, specificity of 40%, positive predictive value of 29% and negative predictive value of 91%. Odds of developing hyperbilirubinemia in babies with cord bilirubin >2 mg/dl was 4.36 (95% confidence interval 2.40,3.17). The accuracy of the test was measured using receiver operator curve [Figure 1]. The area under the curve was 0.755 which is deemed to be fair test results.

Table-1: Baseline characteristics of study population (n=100).

Characteristics	Number
Female	56 (56%)
Mean Gestational age(weeks)	38.11 + 3.72*
Mean Birth weight(kg)	2.98+3.26*
Delivery by Cesarean section	64 (64%)
Normal vaginal delivery	36(36%)
Use of Oxytocin in mother	44 (44%)
PIH(pregnancy induced hypertension)	13 (13%)
History of Jaundice in previous sibling	2(2%)
ABO Incompatibility	23 (23%)

(* = mean + standard deviation)

Table-2: Characteristics of cases who did and who did not develop hyperbilirubinemia

Characteristics	No Hyperbilirubinemia	Hyperbilirubinemia (n=22)	P value
Male/Female	33/45	11/11	0.5
Mean Gestational age(weeks)	38.12 + 3.22*	38.11 + 4.22*	0.97
Mean Birth weight(kg)	3.15+3.01*	2.8 1+3.52*	0.41
Type of delivery: Cesarean section	48	16	0.10
Normal vaginal delivery	30	6	
Use of Oxytocin in mother	35	9	0.11
Pregnancy induced hypertension	10	3	0.51
History of Jaundice in previous sibling	-	2	-
ABO Incompatibility	12	11	0.0006

(p value <0.05 is significant, *=mean+ standard deviation)

Table- 3: Relationship of cord Bilirubin and Hyperbilirubinemia

Cord Bilirubin	Hyperbilirubinemia	No Hyperbilirubinemia	Total	P Value
> 2 mg/dl	19(29%)	45(71%)	64	0.018
< 2 mg/dl	3(8%)	33(92%)	36	
Total	22(22%)	78(78%)	100	Significant

(p value <0.05 is significant)

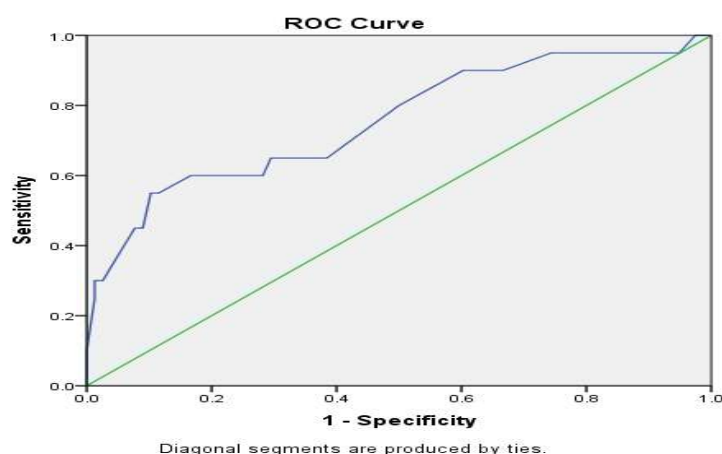


Figure-1: The receiver operating characteristics analysis of cord bilirubin level predicting the development of subsequent hyperbilirubinemia

Discussion

Neonatal jaundice is a benign condition observed during the first week of life. Hyperbilirubinemia in the newborn usually peaks between 3 and 7 days of age. This clinical condition is frequently asymptomatic and occurs after hospital discharge. It is worth noting that the most common cause for readmission during the early neonatal period is hyperbilirubinemia [10,11,12]. Higher

cord bilirubin levels among infants who develop significant hyperbilirubinemia as compared to non-hyperbilirubinemic infants indicate that mechanisms of subsequent jaundice are already active in fetal life. Nearly all fetal bilirubin is unconjugated and in plasma is totally bound to albumin. The unconjugated bilirubin is transferred to maternal circulation by

placenta for excretion [7]. The value of cord bilirubin for predicting significant hyperbilirubinemia is widely debated [6,7,8,9]. Many investigators have found cord bilirubin cut off values ranging 2-3.5mg/dl to have good predictive value. [7,8,13,14] However some others found cord serum bilirubin to have poor predictive value [6,15,16].

In the present study, incidence of hyperbilirubinemia was 22% and clinically detectable jaundice was 72%. Taksande et al [7] reported clinical jaundice in 56% and hyperbilirubinemia in 19% where as Hamdi et al [17] reported 85% and 26% respectively of clinical jaundice and hyperbilirubinemia. Our observations were similar to Hamdi et al [17]. Other investigators have reported much lower incidence of 9.5% and 12.5% [1,18].

The present study was uniformly distributed with male to female ratio of 56:44. There was no significant association of gender with development of hyperbilirubinemia (p 0.5). Other studies have also reported similar findings [1,7,8,17,19]. In contrast Rudy et al study observed that there was significant difference in cord bilirubin between both sexes and this difference may be due to increased incidence of G6PD enzyme deficiency among males as it is X linked recessive disorder [20].

In the present study, gestational age, birth weight, maternal hypertension and mode of delivery did not have any significant association with development of hyperbilirubinemia. Similar observations were reported by other studies [1,7,8,14,17,21,22].

We found significant association between ABO incompatibility and hyperbilirubinemia (p 0.0006). Earlier authors like Pradhan et al [1], Bernaldo et al [9] and Menon et al [23] also reported similar findings. Oxytocin use during labour was not associated with significant hyperbilirubinemia. This was similar to the study done by Taksande et al (7). In variance significant association between oxytocin use and hyperbilirubinemia was reported by Pradhan A, Nahar et al, Rajpurohit et al and Hamdi et al [1,8,14,17].

In the present study mean cord bilirubin value were 2.8 +2.4 mg /dl in those who developed hyperbilirubinemia and 2.5+2.91 mg/dl in those who did not. However, this was not statistically significant (p=0.62). The studies by Pradhan et al, Rajpurohit et al and Farahat et al found that mean cord bilirubin value was significantly higher than those who developed as compared to those who did not. [1,14,18]

We observed that cord bilirubin >2 mg/dl had the highest sensitivity (86%). At this critical level specificity was 40%, positive predictive value was 29 % and negative predictive value was 91%. ROC curve (figure 1) shows that area under curve (AUC) was 0.75 of the total area indicating the usefulness of test in predicting significant hyperbilirubinemia. Our findings are similar to Rajpurohit et al [14] study where the sensitivity was 90%, specificity was 53%, positive predictive value was 17.8% and negative predictive value 98% at critical bilirubin value > 2 mg/dl.

Taksande et al [7] reported high sensitivity (89%) as well as high specificity (85%), negative predictive value (98%) and positive predictive value (38%). Gatea et al also reported high negative predictive value of 98% but low positive predictive value 45.4% [24]. In contrast Rostami and Mehrabi found that cord bilirubin > 3 mg/dl is not a useful predictor and concluded that cord bilirubin cannot be used to predict subsequent hyperbilirubinemia [15].

Hemmati and Hashemi observed no significant relationship between cord bilirubin and development of hyperbilirubinemia but there was significant relation between predischarge bilirubin and development of hyperbilirubinemia.

Therefore, they concluded that best predictor for neonatal jaundice is assessment of clinical risk factors and predischarge bilirubin [25]

Our study had high negative predictive value which means that if cord bilirubin was < 2 mg/dl one could reasonably predict that the neonate would not develop hyperbilirubinemia. The ability of critical cord bilirubin value of >2 mg% to discriminate between those who developed and those who did not develop hyperbilirubinemia was fair as depicted by area under curve (0.75)

Conclusions

Mean cord bilirubin was higher in those who developed hyperbilirubinemia although this difference was not statistically significant. Cord serum bilirubin >2 mg/dl had high sensitivity and negative predictive value but low specificity and positive predictive value. Our findings suggest that cord bilirubin may be useful in identifying neonates who develop significant hyperbilirubinemia. Neonates with cord bilirubin < 2mg/dl are probably safe for early discharge but those with bilirubin levels >2 mg/dl will need close follow up.

What is already known?

The association between cord bilirubin levels and subsequent hyperbilirubinemia.

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What this study adds?: Cord bilirubin is a fairly good predictor for hyperbilirubinemia.

Contributors

GR: Data collection, statistical analysis, literature search and manuscript preparation. SD: Study concept and critical revision of manuscript

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